Supporting Information for

**Fast and Highly Chemoselective Alkynylation of Thiols with Hypervalent Iodine Reagents Enabled Through a Low Energy Barrier Concerted Mechanism**

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1. Computational Details

**Figure S1.** Electronic energies along the intrinsic reaction coordinate for the a pathway. Computations at the M06-2X/def2-SVP level.
Figure S2. Selected geometries along the IRC for the a pathway. Structures correspond to labels from figure S1.

TS-5  TS-4  TS-3

TS-2  TS-1  TS+1

TS+2  TS+3  TS+4

TS+5  TS+6  TS+7
Table S1. Electronic energies, free energy corrections, and solvation corrections for relevant compounds using the TIPS-EBX reagent. PBE0-dDsC/TZ2P and M06-2X/def2-TZVP electronic energies obtained from single point computations on M06-2X/def2-SVP geometries.

| Compound | M06-2X/def2-SVP Electronic Energy (hartree) | M06-2X/def2-SVP Free Energy Correction (hartree) | M06-2X/def2-TZVP Electronic Energy (hartree) | PBE0-dDsC/TZ2P Electronic Energy (hartree) | COSMO-RS Solvation Energy (kcal/mol) |
|----------|--------------------------------------------|-----------------------------------------------|--------------------------------------------|--------------------------------------------|----------------------------------------|
| a₀       | -2106.082266                               | 0.440280                                      | -2107.606383                               | -16.332255                                 | -52.866                                 |
| b₀       | -2106.074669                               | 0.441889                                      | -2107.598451                               | -16.315327                                 | -48.750                                 |
| a₁TS₁    | -2106.066858                               | 0.438536                                      | -2107.587790                               | -16.318528                                 | -49.640                                 |
| b₁TS₁    | -2106.064275                               | 0.443031                                      | -2107.584800                               | -16.306042                                 | -48.055                                 |
| b₁       | -2106.090006                               | 0.441073                                      | -2107.608545                               | -16.327049                                 | -51.620                                 |
| b₁TS₂    | -2106.089913                               | 0.442080                                      | -2107.608026                               | -16.328147                                 | -52.324                                 |
| a₂TS₂    | -2106.187915                               | 0.442548                                      | -2107.702682                               | -16.413023                                 | -50.590                                 |
| b₂TS₂    | -2106.177060                               | 0.438296                                      | -2107.694266                               | -16.408391                                 | -53.279                                 |

Table S2. Reaction free energies (in kcal/mol) for the a and b pathways using the TIPS-EBX reagent. PBE0-dDsC/TZ2P and M06-2X/def2-TZVP free energies include free energy corrections obtained from M06-2X/def2-SVP computations and solvation corrections (in THF) from COSMO-RS (at the PBE0-dDsC/TZ2P theoretical level).

| Reaction     | PBE0-dDsC Free Energy | M06-2X Free Energy |
|--------------|-----------------------|--------------------|
| a₀ → a₁TS₁  | 10.75                 | 13.80              |
| a₁TS₁ → a₂TS₂| -57.73                | -70.53             |
| b₀ → b₁TS₁  | 7.24                  | 9.98               |
| b₁TS₁ → b₁  | -17.98                | -19.69             |
| b₁ → b₁TS₂  | -0.76                 | 0.25               |
| b₁TS₂ → b₂TS₂| -53.68                | -57.45             |
| a₀ → b₀     | 15.75                 | 10.10              |
| a₁TS₁ → b₁TS₁| 11.04                 | 6.28               |

Table S3. Electronic energies, free energy corrections, and solvation corrections for relevant compounds using the Methyl-EBX reagent.

| Compound | M06-2X/def2-SVP Electronic Energy (hartree) | M06-2X/def2-SVP Free Energy Correction (hartree) | M06-2X/def2-TZVP Electronic Energy (hartree) | PBE0-dDsC/TZ2P Electronic Energy (hartree) | COSMO-RS Solvation Energy (kcal/mol) |
|----------|--------------------------------------------|-----------------------------------------------|--------------------------------------------|--------------------------------------------|----------------------------------------|
| a₀       | -1501.355114                               | 0.209054                                      | -1502.419519                               | -9.927595                                 | -51.671                                 |
| b₀       | -1501.348373                               | 0.210347                                      | -1502.413181                               | -9.916856                                 | -48.546                                 |
| a₁TS₁    | -1501.330293                               | 0.208068                                      | -1502.393028                               | -9.905776                                 | -48.827                                 |
| b₁TS₁    | -1501.332390                               | 0.211039                                      | -1502.395983                               | -9.904429                                 | -46.844                                 |
| b₁       | -1501.364149                               | 0.212440                                      | -1502.424548                               | -9.930714                                 | -49.940                                 |
| b₁TS₂    | -1501.351776                               | 0.208410                                      | -1502.411644                               | -9.909202                                 | -55.178                                 |

ADF computes energies relative to basic atom fragments, rather than to separated particles (e.g., nuclei and electrons), as is done in Gaussian. This gives rise to the magnitude difference in the reported M06-2X (computed in Gaussian) and PBE0-dDsC (computed in ADF) electronic energies. Note that absolute electronic energies computed using different density functionals cannot be directly compared with one another.
| S4. Reaction free energies (in kcal/mol) for the a and b pathways using the Methyl-EBX reagent. PBE0-dDsC/TZ2P and M06-2X/def2-TZVP free energies include free energy corrections obtained from M06-2X/def2-SVP computations and solvation corrections (in THF) from COSMO-RS (at the PBE0-dDsC/TZ2P theoretical level). |
|-----------------|-----------------|-----------------|-----------------|-----------------|-----------------|
| Reaction        | PBE0-dDsC Free Energy | M06-2X Free Energy |
| aₐ → aₜS₁       | 15.92            | 18.85            |
| aₜS₁ → a₃₅      | -64.40           | -74.57           |
| b₀ → bₜS₁       | 9.94             | 12.93            |
| bₜS₁ → b₃₅      | -18.71           | -20.14           |
| b₁ → bₜS₂       | 5.73             | 0.33             |
| bₜS₂ → b₃₅      | -55.32           | -54.70           |
| a₀ → b₀         | 10.67            | 7.91             |
| aₜS₁ → bₜSₖα²   | 4.69             | 1.99             |

α In addition calculation at the B3LYP-dDsC and B3LYP-D3 level gave energies of 4.33 and 3.28 kcal/mol respectively.

| S5. Reaction free energies (in kcal/mol) for the a pathways using the TIPS-EBX reagent and different nucleophiles. PBE0-dDsC/TZ2P free energies include free energy corrections obtained from M06-2X/def2-SVP computations and solvation corrections (in THF) from COSMO-RS (at the PBE0-dDsC/TZ2P theoretical level). |
|-----------------|-----------------|-----------------|
| Reaction        | Nucleophile     | PBE0-dDsC Free Energy |
| a₀ → aₜS₁       | MeOH            | Not located      |
| a₀ → aₜS₁       | MeNH₂           | +30.8            |
| a₀ → aₜS₁       | Acetate         | +18.1            |
| a₀ → aₜS₁       | HP(O)(OMe)₂     | Not located      |
| a₀ → aₜS₁       | P(O)(OMe)₂      | +12.2            |

| S1. Alternative mechanistic pathways involving participation of the base. |
|-----------------|-----------------|
| b) Lewis base activation | |
| c) H-bond activation | |
| d) Protonation   | |

Further reactions on this intermediate
Table S6. Highest energy points on potential energy surface leading to formation of thioalkynes with TMS-EBX.

| Mechanistic Pathway          | Highest Energy Value on PES (kcal/mol) |
|------------------------------|----------------------------------------|
| Direct Attack (discussed in manuscript) | 9.4                                    |
| Lewis Base Activation         | 14.9                                   |
| H-bond Activation             | 13.1                                   |
| Protonation                   | 47.2                                   |
### Cartesian Coordinates of Relevant Compounds

| Compound | Coordinates         |
|----------|---------------------|
| A0 - TIPS |                     |
| C        | 0.00761, -0.50119, -0.12839 |
| S        | -1.54444, 2.11166, 0.81379  |
| C        | -1.58265, 2.36457, -0.98721 |
| I        | 1.11052, 0.91818, 0.91545  |
| Cl       | 4.03583, 0.16549, 1.28576  |
| C        | 5.22483, -0.56318, 1.18742  |
| S        | 2.87919, -0.36166, 0.70101  |
| C        | 6.11038, -0.11520, 1.64231  |
| C        | 2.88171, -1.59918, 0.06270  |
| C        | 4.07735, -2.31724, -0.00823  |
| H        | 6.17801, -2.37086, 0.49123  |
| C        | 1.96761, -2.00409, -0.37454  |
| H        | 4.08989, -3.28884, -0.50676  |
| C        | 4.01459, 1.52706, 1.96834  |
| O        | 5.05014, 1.95513, 2.44925  |
| Si       | -0.65855, -1.30664, -0.76087  |
| C        | -1.80244, -2.45433, -1.64628  |
| C        | -1.40363, -2.30970, -3.0183  |
| C        | -1.39408, -0.84972, -3.96938  |
| H        | -2.19784, -2.85271, -4.04723  |
| C        | -0.05426, -2.96912, -3.81116  |
| C        | -3.5906, -2.02718, -1.7690  |
| C        | -3.65991, -1.33812, 0.19409  |
| H        | -4.09876, -3.01177, -1.0709  |
| C        | -4.35237, -1.20329, -2.22500  |
| C        | -1.40573, -4.22089, -1.05749  |
| H        | -0.32442, -4.35803, -1.23633  |
| C        | -2.17146, -5.26800, -1.87223  |
| C        | -1.66478, -4.39045, 0.44178  |
| C        | -2.95046, 2.31355, -1.64282  |
| H        | -1.13245, 3.33982, -1.24238  |
| H        | -0.96221, 1.60070, -1.49048  |
| C        | -4.14115, 2.27659, -0.91056  |
| C        | -5.37773, 2.23690, -1.55810  |
| C        | -5.44945, 2.23046, -2.94986  |
| C        | -3.03696, 2.31732, -3.04361  |
| C        | -4.26830, 2.27215, -3.69381  |
| C        | -4.07733, 2.26647, 0.17870  |
| C        | -6.29489, 2.20308, -0.96576  |
| H        | -6.41702, 2.19014, -3.45403  |
| H        | -2.11368, 2.34631, -3.62966  |
| H        | -4.30731, 2.26508, -4.78536  |
| H        | -5.41149, -1.09391, -1.93925  |
| H        | -3.94052, -0.18537, -2.29802  |
| H        | -4.31940, -1.66031, -2.32695  |
| H        | -4.70798, -1.14493, 0.47823  |
| H        | -3.20166, -1.94898, 0.98680  |
| H        | -3.12510, -0.37319, 0.19027  |
| H        | -1.15272, -0.78431, -5.04356  |
| H        | -2.35746, -0.34757, -3.80744  |
| H        | -0.63015, -0.27729, -3.41859  |
| H        | 0.20743, -2.84981, -4.87543  |
| H        | 0.74942, -2.49773, -3.22124  |
| H        | -0.04773, -4.04547, -3.58038  |
| H        | -1.92205, -6.29052, -1.54333  |
| H        | -3.26015, -5.14499, -1.74942  |
| H        | -1.95247, -5.20080, -2.94916  |
| H        | -1.35946, -5.39190, 0.78772  |
| H        | -1.11737, -3.64248, 1.03458  |
| H        | -2.73716, -4.27754, 0.87013  |
| Atom | X     | Y     | Z     |
|------|-------|-------|-------|
| C    | 0.12497 | -0.37979 | -0.59944 |
| S    | -0.78602 | -2.35245 | -1.29791 |
| C    | -1.45144 | -2.74401 | 0.34942 |
| I    | 2.00638 | -1.38546 | -0.47819 |
| C    | 4.56173 | -0.03758 | 0.40668 |
| C    | 5.40473 | 0.99182 | 0.83065 |
| C    | 3.22651 | -1.45144 | 0.34942 |
| H    | 6.44819 | 0.72764 | 1.01255 |
| C    | 2.00638 | 1.53978 | 0.11766 |
| C    | 4.56173 | -0.03758 | 0.40668 |
| C    | 5.40473 | 0.99182 | 0.83065 |
| C    | 4.91103 | 2.28216 | 1.00284 |
| C    | 6.44819 | 0.72764 | 1.01255 |
| C    | 1.53978 | 0.11766 | |
| C    | 4.56173 | -0.03758 | 0.40668 |
| C    | 5.40473 | 0.99182 | 0.83065 |
| C    | 4.91103 | 2.28216 | 1.00284 |
| C    | 6.44819 | 0.72764 | 1.01255 |
| C    | 1.53978 | 0.11766 | |
| C    | 4.56173 | -0.03758 | 0.40668 |
| C    | 5.40473 | 0.99182 | 0.83065 |
| C    | 4.91103 | 2.28216 | 1.00284 |
| C    | 6.44819 | 0.72764 | 1.01255 |
| C    | 1.53978 | 0.11766 | |
| C    | 4.56173 | -0.03758 | 0.40668 |
| C    | 5.40473 | 0.99182 | 0.83065 |
| C    | 4.91103 | 2.28216 | 1.00284 |
| C    | 6.44819 | 0.72764 | 1.01255 |
| C    | 1.53978 | 0.11766 | |
| C    | 4.56173 | -0.03758 | 0.40668 |
| C    | 5.40473 | 0.99182 | 0.83065 |
| C    | 4.91103 | 2.28216 | 1.00284 |
| C    | 6.44819 | 0.72764 | 1.01255 |
| C    | 1.53978 | 0.11766 | |
| C    | 4.56173 | -0.03758 | 0.40668 |
| C    | 5.40473 | 0.99182 | 0.83065 |
| C    | 4.91103 | 2.28216 | 1.00284 |
| C    | 6.44819 | 0.72764 | 1.01255 |
| C    | 1.53978 | 0.11766 | |
| C    | 4.56173 | -0.03758 | 0.40668 |
| C    | 5.40473 | 0.99182 | 0.83065 |
| C    | 4.91103 | 2.28216 | 1.00284 |
| C    | 6.44819 | 0.72764 | 1.01255 |
| C    | 1.53978 | 0.11766 | |
| C    | 4.56173 | -0.03758 | 0.40668 |
| C    | 5.40473 | 0.99182 | 0.83065 |
| C    | 4.91103 | 2.28216 | 1.00284 |
| C    | 6.44819 | 0.72764 | 1.01255 |
| C    | 1.53978 | 0.11766 | |
| C     | S     | I     | Si    |
|-------|-------|-------|-------|
| -1.95407 | -0.33338 | -1.12674 |
| -2.15209 | -1.63564 | -2.18561 |
| -1.24705 | -2.96589 | -1.28118 |
| 1.57604 | -0.62852 | 1.57417 |
| 2.32633 | 0.58242 | 2.32633 |
| 3.04163 | 1.47393 | 0.52519 |
| 4.07090 | 2.26444 | 1.47393 |
| 2.74384 | 1.52883 | 1.47393 |
| 3.68593 | 1.33374 | 1.24705 |
| 4.39671 | 2.19251 | 1.24705 |
| 5.19526 | 2.81104 | 1.24705 |
| 1.22731 | -0.26745 | 2.15209 |
| 0.60799 | 0.31570 | 2.15209 |
| 1.10768 | -1.43176 | 2.15209 |
| 1.23718 | 0.62675 | 2.15209 |
| -1.72633 | 2.16098 | 2.15209 |
| -1.88399 | 1.82821 | 2.15209 |
| -2.23563 | 0.36323 | 2.15209 |
| -2.73272 | 2.46449 | 2.15209 |
| -0.65284 | 2.23899 | 2.15209 |
| -3.11118 | 3.12140 | 2.15209 |
| -3.33374 | 3.50651 | 2.15209 |
| -3.91344 | 1.28874 | 2.15209 |
| -4.61327 | 2.94288 | 2.15209 |
| -5.19526 | 2.81104 | 2.15209 |
| -1.21957 | -3.78912 | 2.15209 |
| -0.23427 | -2.58790 | 2.15209 |
| -3.02051 | -4.60027 | 2.15209 |
| -3.67827 | -4.60027 | 2.15209 |
| -3.33374 | 3.50651 | 2.15209 |
| -3.91344 | 1.28874 | 2.15209 |
| -4.61327 | 2.94288 | 2.15209 |
| 1.22731 | -0.26745 | 2.15209 |
| 0.60799 | 0.31570 | 2.15209 |
| 1.10768 | -1.43176 | 2.15209 |
| 1.23718 | 0.62675 | 2.15209 |
| Atom | X  | Y  | Z  |
|------|----|----|----|
| S    | 1.7329  | -0.0764 | 2.0927 |
| C    | 0.2790  | -0.0527 | -0.4686 |
| O    | -0.0847 | -1.0854 | 0.4451 |
| C    | 0.0124  | -0.5211 | 2.0311 |
| N    | 1.7365  | 0.0552  | 2.0655 |
| S    | 3.0643  | 0.0518  | -0.7182 |
| C    | 3.0350  | 0.0537  | 3.1067 |
| C    | 4.3764  | 1.6350  | -0.9273 |
| H    | 3.8737  | 2.6954  | 3.2606 |
| H    | 4.5096  | 1.3397  | 2.7779 |
| C    | 2.3894  | -0.2822 | 2.7454 |
| H    | 2.7776  | -1.1328 | 3.6984 |
| H    | 3.1746  | -0.0842 | 2.6835 |
| H    | 4.8985  | 0.3736  | 3.0935 |
| H    | 5.1175  | -0.9903 | 2.8083 |
| H    | 6.2914  | -1.2303 | 3.3078 |
| H    | 6.4692  | -0.0754 | 2.8045 |
| H    | 4.7659  | 0.3862  | 2.6681 |

S13
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B_35 - TIPS
I 0.82404  -3.12097  -2.07083
C 1.23190  1.31448   0.75103
C 0.46955  -2.81227   -0.00279
O -1.06323  -0.59719  -1.39694
C -1.54508  -1.17118  -0.40529
O -2.70454  -1.13160   0.03833
C -0.56003  -1.99349   0.46065
C -0.72690  -1.89751  1.85060
H -1.55539  -1.27590  2.19535
C 0.11001  -2.56275  2.73964
H 0.03443  -2.45062  3.81620
C 1.12478  -3.38629  2.29400
C 1.78489  -3.92599  2.93167
C 1.29568  -3.52276  0.87421
H 2.07538  -4.17463  0.47769
C 0.04905  1.50251  1.00187
S -1.57138  1.76574  1.39027
C -2.28033  2.07704  1.95355
C -2.81490  3.92599  2.93167
C -1.29568  3.52276  0.87421
H -2.07419  1.80424  0.89456
C -3.74916  2.34601  1.64632
H -4.64643  2.71377  1.39027
C  0.25730  -0.12832
C -6.00837  1.51798  0.11490
H  0.67777  0.1428
C  6.48730  2.82495  0.22036
C  -7.55669  3.01004  0.35066
C  -5.95337  3.89544  1.6047
C  -5.96152  4.92075  0.24456
C  -4.23229  3.65391  0.00663
H  -3.52855  4.48925  0.05009
Si  2.99246  1.08256  0.27262
C  3.91296  0.11602  1.64632
C  3.13385  0.13957  2.96670
H  4.86712  0.65673  1.79213
C  4.23735  -1.32655  1.24910
C  3.07980  0.18517  -1.39455
H  2.97358  -0.88579  -1.14445
C  4.44644  0.38876  -2.05999
C  1.92169  0.53883  -2.33441
C  3.77329  2.82208  0.17918
C  3.73664  3.50104  1.55185
C  3.10147  3.70481  -0.87534
H  4.83088  2.66841  -0.10718
H  3.52638  4.72318  -0.87247
H  3.21638  3.29542  -1.88941
H  2.02115  3.79100  -0.67503
H  4.18944  4.50631  1.51238
H  2.69557  3.61620  1.89508
H  4.27683  2.92089  2.31565
H  3.70729  -0.35142  3.77134
H  2.89356  1.16328  3.29166
H  2.17796  -0.39638  2.85387
H  4.77430  -1.84476  2.06192
H  3.31380  -1.89196  1.05316
H  4.86102  -1.38312  0.34420
H  4.53978  -0.23669  -2.96195
H  4.58174  1.43733  -2.37238
H  5.28688  0.13672  -1.39076
H  2.04191  0.01091  -3.29593
H  0.94906  0.23656  -1.91263
H  1.88729  1.61893  -2.55299

S15
$a_0 - R=Methyl$

| Atom | $x$ | $y$ | $z$ |
|------|-----|-----|-----|
| I    | 0.88458 | -0.73501 | -0.08159 |
| C    | -0.49172 | 0.79511 | -0.31004 |
| S    | -1.57801 | -2.26922 | -0.14014 |
| C    | -2.49773 | -1.33418 | 1.11799 |
| C    | 3.77113 | 0.22788 | 0.11812 |
| C    | 4.86901 | 1.09082 | 0.15239 |
| C    | 2.49517 | 0.75910 | -0.04543 |
| C    | 4.68784 | 2.46506 | 0.02391 |
| H    | 5.85177 | 0.63348 | 0.28240 |
| C    | 2.29493 | 2.13093 | -0.17565 |
| C    | 3.40085 | 2.98275 | -0.13980 |
| H    | 5.54715 | 3.13837 | 0.05056 |
| H    | 1.28929 | 2.53407 | -0.30299 |
| H    | 3.52542 | 4.06016 | -0.24128 |
| C    | 3.98291 | -1.28484 | 0.26030 |
| O    | 5.12141 | -1.70276 | 0.40240 |
| C    | -1.34784 | 1.65275 | -0.38041 |
| C    | -3.64429 | -0.46402 | 0.63053 |
| H    | -2.92226 | -2.04352 | 1.84993 |
| H    | -1.81642 | -0.68464 | 1.69599 |
| C    | 4.14749 | -0.54713 | -0.67139 |
| C    | -5.23694 | 0.23149 | -1.06790 |
| C    | -5.84176 | 1.11518 | -0.17375 |
| C    | -4.25479 | 0.43570 | 1.51732 |
| C    | -5.33991 | 1.21749 | 1.12544 |
| H    | -3.64571 | -1.23287 | -1.35730 |
| H    | -5.61551 | 0.14807 | -2.08936 |
| H    | -6.69276 | 1.72394 | -0.48628 |
| H    | -3.86483 | 0.51936 | 2.53605 |
| H    | -5.79615 | 1.91112 | 1.83552 |
| C    | -2.40219 | 2.65881 | -0.47774 |
| H    | -3.35361 | 2.17637 | -0.74799 |
| H    | -2.54688 | 3.17077 | 0.48321 |
| H    | -2.15972 | 3.41255 | -1.24090 |
b0 = R=Methyl

-1.49657  1.73626  0.57577
+0.56754  1.69702  0.60080
-1.61749  0.20840 -0.91549
-3.73307  1.50235  0.25784
-4.09855  0.63955 -0.62694
-5.23441  0.37174 -0.96247
-2.92384 -0.08082 -1.27563
-3.11028 -1.07027 -2.24149
-4.13858 -1.29958 -2.52661
-2.00902 -1.72800 -2.78998
-2.16162 -2.51029 -3.53598
-0.71540 -1.40886 -2.37488
+0.17190 -1.93485 -2.73729
-0.49367 -0.41270 -1.41662
+0.54100 -0.22289 -1.10186
+1.78005  1.60575  0.57150
+2.76305  1.60426 -1.05641
+2.34458 -1.99174  0.68550
+2.92421 -2.87109  1.01981
+2.63081 -1.16154  1.35859
+0.87844 -2.27768  0.90063
+0.09635 -1.52340  1.78250
+0.57190 -0.72155  2.35433
+1.27607 -1.75787  1.91523
+1.87143 -1.14222  2.59444
+1.89113 -2.75997  1.16927
+2.96632 -2.92943  1.25286
+1.11588 -3.53724  0.30248
+1.59007 -4.32110 -0.29302
+0.24722 -3.29600  0.17056
+0.85256 -3.85075 -0.55064
+3.22392  1.44128  0.49324
+3.40912  0.51454 -0.10417
+3.69217  2.29903 -0.00984
+3.66239  1.32991  1.49501
$\alpha_{TS1} - R=\text{Methyl}$

\[
\begin{align*}
\text{I} & : 1.02859 -0.90253 -0.50778 \\
\text{C} & : -0.64767 0.20721 -1.10224 \\
\text{S} & : -1.82399 -1.77012 -1.32441 \\
\text{C} & : -2.47434 -1.58012 0.37167 \\
\text{C} & : 3.59260 0.35460 0.47549 \\
\text{C} & : 4.48455 1.36603 0.83721 \\
\text{H} & : 5.46746 1.04995 1.19170 \\
\text{C} & : 1.92441 2.04528 -0.08921 \\
\text{C} & : 2.83440 3.03849 0.27864 \\
\text{H} & : 4.81055 3.49111 1.02397 \\
\text{H} & : 0.92264 2.28364 -0.45515 \\
\text{H} & : 2.53686 4.08622 0.20079 \\
\text{C} & : 4.00198 -1.12073 0.58452 \\
\text{O} & : 5.12430 -1.38151 0.99047 \\
\text{O} & : 3.08117 -1.91801 0.22367 \\
\text{C} & : -1.12348 1.35223 -1.30130 \\
\text{C} & : -3.45707 -0.44759 0.53003 \\
\text{H} & : -2.96744 -2.52706 0.64539 \\
\text{H} & : -1.64308 -1.43701 1.08154 \\
\text{C} & : -4.61721 -0.39647 -0.25421 \\
\text{C} & : -5.53782 0.63646 -0.10388 \\
\text{C} & : -5.31086 1.65117 0.82916 \\
\text{C} & : -3.23510 0.57939 1.45234 \\
\text{C} & : -4.15258 1.62075 1.60339 \\
\text{H} & : -4.76527 -1.17184 -1.00974 \\
\text{H} & : -6.43504 0.65894 -0.72619 \\
\text{H} & : -6.02801 2.46659 0.94178 \\
\text{H} & : -2.31803 0.56864 2.04601 \\
\text{H} & : -3.95382 2.41730 2.32340 \\
\text{C} & : -2.39221 1.95555 -1.75759 \\
\text{H} & : -3.03560 1.19232 -2.23526 \\
\text{H} & : -2.94694 2.36318 -0.89642 \\
\text{H} & : -2.23427 2.78551 -2.46381
\end{align*}
\]
\( \text{TS1} \rightarrow R=\text{Methyl} \)

\[
\begin{array}{ccc}
I & -1.15410 & 1.69526 & 0.37074 \\
C & 0.85083 & 1.53231 & 0.38078 \\
C & -1.64179 & 0.13152 & -1.01683 \\
O & -3.53047 & 1.64621 & 0.25820 \\
C & -4.04485 & 0.77388 & -0.51685 \\
O & -5.22512 & 0.55936 & -0.73413 \\
C & -2.99267 & -0.07323 & -1.23909 \\
C & -3.34762 & -1.08032 & -2.13533 \\
H & -4.41424 & -1.23969 & -2.30848 \\
C & -2.35945 & -1.83241 & -2.77296 \\
H & -2.64209 & -2.62175 & -3.47267 \\
C & -1.09111 & -1.58604 & -2.51148 \\
H & -0.22702 & -2.18688 & -2.98334 \\
C & -0.62327 & -0.58687 & -1.61655 \\
H & 0.43650 & -0.42483 & -1.38277 \\
C & 2.04719 & 1.17761 & 0.31718 \\
S & 2.76752 & -0.97687 & -0.69177 \\
C & 2.35131 & -1.85082 & 0.86360 \\
H & 2.97012 & -2.76061 & 0.92886 \\
H & 2.61191 & -1.21964 & 1.73085 \\
C & 0.89686 & -2.23177 & 0.95043 \\
C & -0.00432 & -1.50956 & 1.74001 \\
H & 0.37020 & -0.67213 & -2.23471 \\
C & -1.36638 & -1.81820 & 1.74352 \\
H & -2.05900 & -1.21885 & -2.33944 \\
C & -1.85009 & -2.86721 & 0.96450 \\
H & -2.91771 & -3.09285 & 0.94736 \\
C & -0.95635 & -3.61170 & 0.19114 \\
H & -1.32712 & -4.42981 & -0.43062 \\
C & 0.39825 & -3.29363 & 0.18326 \\
H & 1.09203 & -3.84400 & -0.45772 \\
C & 3.43585 & 1.54644 & 0.68516 \\
H & 3.90210 & 0.75376 & 1.28586 \\
H & 4.05229 & 1.66130 & -0.21562 \\
H & 3.42364 & 2.49111 & 1.25264 \\
\end{array}
\]
b₂ – R=Methyl

I  -0.09943  1.36403  -1.08330
C  1.51888  2.49163  -0.18443
C  -0.16703  -0.79712  -1.26989
O  -2.74067  0.46544  -1.15609
C  -2.75898  -0.76984  -0.99241
O  -3.69181  -1.51874  -0.67607
C  -1.38517  -1.46812  -1.20184
C  -1.36045  -2.86342  -1.32014
H  -2.32723  -3.36431  -1.23874
C  -0.16936  -3.55639  -1.50729
H  -0.17537  -4.64515  -1.59831
C  1.03672  -2.85578  -1.57884
H  1.98000  -3.38609  -1.72639
C  1.04107  -1.46710  -1.46062
H  1.97934  -0.91481  -1.50015
C  2.52182  1.98737  0.54637
S  3.00833  0.28111  0.82313
C  2.20665  -0.05892  2.44625
H  2.83639  -0.82406  2.92231
H  2.27691  0.86112  3.04393
C  0.78706  -0.53677  2.32607
C  -0.27534  0.37029  2.27055
H  -0.06527  1.44120  2.34123
C  -1.58047  -0.07568  2.05695
H  -2.39185  0.64397  1.93764
C  -1.84576  -1.43865  1.93334
H  -2.85483  -1.77441  1.69088
C  -0.79295  -2.35193  2.01252
H  -0.98818  -3.41847  1.88567
C  0.51202  -1.90414  2.19754
H  1.33806  -2.62045  2.21812
C  3.44624  2.99041  1.21106
H  3.47021  2.83469  2.30302
H  4.47756  2.87114  0.84360
H  3.10746  4.01558  1.01125
\begin{verbatim}
35  
\textbf{b122 - R=Methyl}  
I  -0.31561 1.23805 -1.65068  
C  1.87787 2.95373 0.07141  
C  -0.37692 -0.87855 -1.48647  
O  -3.07752 0.19961 -0.94477  
C  -2.96139 -1.03031 -0.88686  
O  -3.78614 -1.89406 -0.54128  
C  -1.53803 -1.60897 -1.22630  
C  -1.40954 -3.00669 -1.18624  
H  -2.33147 -3.55029 -0.97609  
C  -0.19272 -3.65041 -1.37842  
H  -0.13481 -4.74091 -1.33849  
C  0.95702 -2.89305 -1.60876  
H  1.92715 -3.37550 -1.74866  
C  0.86316 -1.50604 -1.66644  
H  1.75149 -0.90010 -1.84879  
C  2.79355 2.35814 0.80163  
S  2.92583 0.59587 0.57967  
C  2.21358 -0.01138 2.17066  
H  2.87572 -0.83111 2.48334  
H  2.32830 0.80638 2.89649  
C  0.79092 -0.48713 2.08547  
C  -0.26166 0.41776 1.90449  
H  -0.04251 1.48345 1.79777  
H  -1.57451 -0.03600 1.80006  
C  -2.38085 0.65985 1.56657  
C  -1.85521 -1.39981 1.90089  
H  -2.87536 -1.75398 1.75584  
C  -0.81197 -2.30512 2.09334  
H  -1.02131 -3.37557 2.13637  
C  0.50435 -1.85293 2.16925  
H  1.32298 -2.56880 2.28383  
C  3.74091 3.10280 1.70436  
H  3.63964 2.73975 2.73840  
H  4.77547 2.92706 1.37726  
H  3.53416 4.18192 1.69403  
\end{verbatim}
| Atoms | X   | Y   | Z   |
|-------|-----|-----|-----|
| I     | -1.73195 | 0.11662 | -2.13224 |
| C     | 1.97592 | 0.19127 | -1.42058 |
| S     | 1.85021 | 1.81727 | -1.86988 |
| C     | 1.21000 | 2.53548 | -0.28668 |
| C     | -1.02942 | -1.89475 | 0.13844 |
| C     | -1.00678 | -3.19013 | 0.67847 |
| C     | -1.62261 | -1.73867 | -1.11709 |
| C     | -1.55274 | -4.28239 | 0.01430 |
| H     | -0.51605 | -3.29254 | 1.64783 |
| C     | -2.15577 | -2.83144 | -1.81114 |
| C     | -2.12805 | -4.10222 | -1.24421 |
| H     | -1.52250 | -5.27453 | 0.46982 |
| C     | -2.53247 | -2.67988 | -2.79575 |
| H     | -2.55289 | -4.94705 | -1.79057 |
| C     | -0.37716 | -0.77347 | 0.99927 |
| O     | 0.48788 | -1.18317 | 1.79893 |
| O     | -0.78128 | 0.38104 | 0.80810 |
| C     | 2.08110 | -0.97501 | -1.97922 |
| C     | 2.26109 | 2.55423 | 0.78456 |
| H     | 0.90457 | 3.55291 | -0.57222 |
| C     | 0.33497 | 1.94209 | 0.02267 |
| C     | 3.24518 | 3.55106 | 0.80933 |
| O     | 4.23330 | 3.55425 | 1.79017 |
| C     | 4.25195 | 2.54673 | 2.75919 |
| C     | 2.28170 | 1.54650 | 1.75726 |
| C     | 3.27878 | 1.55104 | 2.73525 |
| H     | 3.23526 | 4.32899 | 0.04051 |
| H     | 4.99153 | 4.34048 | 1.79930 |
| H     | 5.02616 | 2.54560 | 3.52974 |
| H     | 1.52075 | 0.75707 | 1.75523 |
| H     | 3.28436 | 0.75787 | 3.48540 |
| C     | 2.16494 | -2.36131 | -0.64862 |
| H     | 3.19249 | -2.74915 | -0.71435 |
| H     | 1.82412 | -2.38359 | 0.39946 |
| H     | 1.49708 | -3.00987 | -1.23615 |
35

b_{35} - R=Methyl

I  -2.89563  -2.25129  0.90395
C   3.32814  -0.37016  1.21630
C  -2.66233   -0.29794  1.70312
O   -1.30214  -0.33225  -0.94034
C   -1.74567   0.76027  -0.54082
O   -1.80085  1.85008  -1.12763
C   -2.22311   0.78920   0.94414
C  -2.15096   2.03077   1.59303
H   -1.83274   2.87008   0.97291
C   -2.46572  2.18358   2.93875
H   -2.38071  3.16276   3.41467
C   -2.89499   1.07894   3.67510
H   -3.15117   1.17726   4.73208
C   -3.00480  -0.16164   3.05249
H   -3.35473  -1.02947   3.61299
C   2.16443   -0.66736   1.40408
S   4.90057   0.13551   0.84144
C   4.73238   0.40636  -0.98745
H   5.67017   0.91465  -1.25438
C   4.71302  -0.58109  -1.46703
C   3.52276   1.21170  -1.34912
C   2.33476   0.55900  -1.69473
H   2.32036  -0.53224  -1.75524
C   1.15843   1.27452  -1.91003
H   0.21969   0.75224  -2.10811
C   1.16496   2.66366  -1.78530
H   0.21889   3.19315  -1.90747
C   2.35134   3.32845  -1.46708
H   2.36065   4.41641  -1.36913
C   3.52304   2.60687  -1.24343
H   4.44285   3.12385  -0.95560
C   0.75251  -0.98338   1.59586
H   0.19449  -0.83147   0.65216
H   0.60793  -2.02652   1.91202
H   0.29981  -0.32225   2.35040
2. General Methods

Technical grade solvents were used for quantitative flash chromatography. HPLC grade solvents purchased from Sigma-Aldrich or freshly distilled solvents were used for flash chromatography for compounds undergoing full characterization. Reaction solvents were dried by passage over activated alumina under nitrogen atmosphere (H₂O content < 30 ppm, Karl-Fischer titration). We note; however, that the thiol-alkynylation reaction gives identical results when using HPLC grade THF purchased from Sigma-Aldrich or dried THF from the solvent system. Commercially available reagents were purchased from Acros, Aldrich, Fluka, VWR, Aplichem or Merck and used without any further purification. Chromatographic purification was performed as flash chromatography using Macherey-Nagel silica 40-63, 60 Å, using the solvents indicated as eluent with 0.1-0.5 bar pressure. TLC was performed on Merck silica gel 60 F254 TLC plates and visualized with UV light and permanganate stain. Melting points were measured on a calibrated Büchi B-540 melting point apparatus using open glass capillaries. ¹H NMR spectra were measured on a Brucker DPX-400 400 MHz spectrometer, all signals are reported in ppm with the corresponding internal solvent peak or TMS as standard. The data is being reported as (s = singlet, d = doublet, t = triplet, q = quadruplet, qi = quintet, m = multiplet or unresolved, br = broad signal, coupling constant(s) in Hz, integration; interpretation). ¹³C NMR spectra were carried out with ¹H-decoupling on a Brucker DPX-400 100 MHz. All signals are reported in ppm with the corresponding internal solvent signal or TMS as standard. Infrared spectra were obtained on a JASCO FT-IR B4100 spectrophotometer with an ATR PRO410-S and a ZnSe prisma and are reported as cm⁻¹ (w = weak, m = medium, s = strong, sh = shoulder). High resolution mass spectrometric measurements were performed by the mass spectrometry service of ISIC at the EPFL on a MICROMASS (ESI) Q-TOF Ultima API.
3. Preparation of Reagents

1-[(Triisopropylsilyl)ethynyl]-1,2-benziodoxol-3(1H)-one (1a)

Following a reported procedure,² NaIO₄ (77.2 g, 0.361 mol, 1.0 equiv) and 2-iodobenzoic acid (7) (89.5 g, 0.361 mmol, 1.0 equiv) were suspended in 30% (v:v) aq. AcOH (700 mL) under air in a 4-neck sulfonation flask equipped with a mechanic stirrer, a thermometer and a condenser. The mixture was vigorously stirred and refluxed for 4 h. The reaction mixture was then diluted with cold water (500 mL) and allowed to cool to room temperature, protecting it from light. After 45 min, the suspension was added to water (1.5 L) and the crude product was collected by filtration, washed on the filter with ice water (3 x 300 mL) and cold acetone (3 x 300 mL), and air-dried in the dark overnight to give 2-iodosylbenzoic acid (77.3 g, 0.292 mol, 81% yield) as a colorless solid.¹H NMR (400 MHz, (CD₃)₂SO) δ 8.02 (dd, J = 7.7, 1.4 Hz, 1 H, ArH), 7.97 (m, 1 H, ArH), 7.85 (dd, J = 8.2, 0.7 Hz, 1 H, ArH), 7.71 (td, J = 7.6, 1.2 Hz, 1 H, ArH).¹³C NMR (100 MHz, (CD₃)₂SO) δ 167.7, 134.5, 131.5, 131.1, 130.4, 126.3, 120.4. IR ν 3083 (w), 3060 (w), 2867 (w), 2402 (w), 1601 (m), 1585 (m), 1564 (m), 1440 (w), 1338 (s), 1302 (m), 1148 (m), 1018 (w), 834 (m), 798 (w), 740 (s), 694 (s), 674 (m), 649 (m). The values of the NMR spectra are in accordance with reported literature data.²

Following a modified reported procedure,³ trimethylsilylacetylene (30.3 ml, 213 mmol, 1 equiv) was charged in a 4-neck 500 mL flask equipped with a thermometer, an agitator magnetic and a nitrogen arrival. THF (330 mL) was added via a dropping funnel and the reaction was cooled to -78 °C. nBuLi (86 mL, 0.21 mmol, 0.98 equiv) was added and the reaction was stirred for 5 minutes at -78 °C, then warmed to 0 °C and stirred for 5 minutes. The reaction was then cooled back to -78 °C and tPr₃SiCl (29) (45.5 mL, 213 mmol, 1 equiv) was added dropwise via a dropping funnel. The mixture was then allowed to warm to r.t. and stirred overnight. A saturated solution of NH₄Cl (300 mL) was added and the

² Kraszkiewicz, L.; Skulski, L. Arkivoc 2003, 6, 120.
³ Helal, C. J.; Magriotis, P. A.; Corey, E. J. J. Am. Chem. Soc. 1996, 118, 10938.
reaction was extracted with Et₂O (2x300 mL). The organic layer was dried over MgSO₄, filtered and concentrated. Distillation of the crude product (1.4 mbar, 55°C) afforded trimethylsilyl (triisopropylsilyl) acetylene (30) (51.4 g, 203 mmol, 95%) as a colorless liquid. ¹H NMR (400 MHz, CDCl₃) δ 1.08 (m, 21 H, TIPS), 0.18 (s, 9 H, TMS). The values of the NMR spectra are in accordance with reported literature data.³

Caution: reaction carried out behind a safety shield! Following a modified reported procedure,⁴ 2-iodosylbenzoic acid (26.4 g, 100 mmol, 1.0 equiv) was charged in a four-neck flat-bottom flask equipped with a thermometer, a dropping funnel, a mechanic stirrer and a nitrogen arrival. The system was flushed with N₂ by three vacuum/N₂ cycles. Anhydrous acetonitrile (350 mL) was then canulated. The reaction mixture (white suspension) was cooled to 4 °C and then trimethylsilyltriflate (20.0 mL, 110 mol, 1.1 equiv) was added dropwise for 15 min via a dropping funnel. The dropping funnel was rinsed with anhydrous acetonitrile (10 mL). No increase of temperature was observed. The ice bath was removed and the reaction stirred for 15 min. Trimethylsilyl(triisopropylsilyl)acetylene (30) (28.0 g, 110 mmol, 1.1 equiv) was added dropwise via dropping funnel over 15 min (the colorless suspension was converted to a yellow solution). The dropping funnel was rinsed with anhydrous acetonitrile (10 mL) and the reaction was stirred for 30 min. Then pyridine (9.9 mL, 25 mmol, 1.1 equiv) was added dropwise via a dropping funnel over 5 min. After 15 min, the reaction mixture was transferred in a one-neck 1L flask and reduced under reduced pressure until a solid was obtained. The solid was dissolved in CH₂Cl₂ (250 mL) and transferred in a 2L separatory funnel. The organic layer was added and washed with 1 M HCl (150 mL) and the aqueous layer was extracted with CH₂Cl₂ (250 mL). The organic layers were combined, washed with a saturated solution of NaHCO₃ (2x250 mL), dried over MgSO₄, filtered and the solvent was evaporated under reduced pressure. The resulting solid (44.8 g) was then recrystallized in CH₃CN (110 mL). The colorless solid obtained over cooling down was then filtered over Büchner, washed with hexanes (2x40 mL) and dried for 1 h at 40 °C at 5 mbar. TIPS-EBX (1a) (36.2 g, 84.5 mmol, 85%) was obtained as white crystals. Mp 173-177 °C (decomposition). ¹H NMR (400 MHz, CDCl₃) δ 8.37 (m, 1 H, ArH), 8.28 (m, 1 H, ArH), 7.72 (m, 2 H, ArH), 1.13 (m, 21 H, TIPS). ¹³C NMR (101 MHz, CDCl₃) δ 166.4, 134.5, 132.3, 131.4, 131.4, 126.1, 115.6, 113.9, 64.7, 18.4, 11.1. The values of the NMR spectra are in accordance with reported literature data.⁴

⁴ Brand, J. P.; Waser, J. Synthesis 2012, 44, 1155.
Propynyl-1,2-benziodoxol-3(1H)-one (1b)

Following a slightly modified procedure, 5 2-iodobenzoic acid (7) (1.07 g, 4.30 mmol, 1.00 eq.), *para*-toluenesulfonic acid monohydrate (TsOH · H2O, 818 mg, 4.30 mmol, 1.00 eq.) and *meta*-chloroperoxybenzoic acid (*mCPBA-70%, 1.17 g, 4.73 mmol, 1.10 eq.) were dissolved in dichloromethane (7 mL) and 2,2,2-trifluoroethanol (7 mL). The mixture was stirred at room temperature under nitrogen for 1 hour, after which propynyl-1-boronic acid pinacol ester (4.85 g, 21.2 mmol, 1.40 eq.) was added in one portion. The reaction mixture was stirred for 2.5 hours at room temperature, filtered and concentrated *in vacuo*. The resulting oil was dissolved in dichloromethane (30 mL) and under vigorous stirring, saturated aq. NaHCO3 (30 mL) was added. The mixture was stirred for 15 minutes, the two layers were separated and the aqueous phase was extracted with additional portions of dichloromethane (3 x 25 mL). The combined organic layers were washed with brine (25 mL), dried over MgSO4, filtered and concentrated *in vacuo*. The crude product was purified by flash column chromatography (ethyl acetate) to afford **1b** (1.03 g, 3.60 mmol, 84%) as a white solid. Rp (EtOAc) = 0.10. Mp 124-150 °C (decomposition). 1H NMR (CDCl3, 400 MHz) δ 8.41-8.35 (m, 1 H, ArH), 8.22-8.14 (m, 1 H, ArH), 7.79-7.68 (m, 2 H, ArH), 2.27 (s, 3 H, CH3). 13C NMR (CDCl3, 100 MHz): δ 166.7, 134.8, 132.5, 131.6, 126.4, 115.6, 105.1, 39.0, 5.7. IR ν 2183 (w), 1607 (s), 1559 (m), 1350 (m), 746 (m), 730 (m). HRMS (ESI) C10H8IO2 [M+H]+ calc. = 286.9564; [M+H]+ obs. = 286.9561.

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5 Bouma, M. J.; Olofsson, B. *Chem. Eur. J.* 2012, 18, 14242.
6 One aromatic carbon signal was not resolved.
Octynyl-1,2-benziodoxol-3(1H)-one (1d)

Following a slightly modified procedure,\(^7\) a solution of 1-octyne (31) (747 mg, 6.78 mmol, 1.00 eq.) and dry diethyl ether (7.0 mL) was cooled to -78 °C, at which temperature 1.6 M nBuLi in hexanes (4.24 mL, 6.78 mmol, 1.00 eq.) was added dropwise. The mixture was stirred at -78 °C for 90 minutes and then cannulated into a to -78 °C pre-cooled solution consisting of triisopropyl borate (1.56 mL, 6.78 mmol, 1.00 eq.) and dry diethyl ether (7.0 mL). The reaction mixture was stirred at -78 °C for 2 hours, after which 2.0 M HCl in diethyl ether (3.73 mL, 7.46 mmol, 1.10 eq.) was added. The cooling bath was removed and the mixture was stirred for an additional 60 minutes. After filtration and solvent removal, Kugelrohr distillation (75 °C at 0.6 mbar) furnished pure diisopropyloct-1-ynylboronate (32, 940 mg, 3.95 mmol, 58% yield) as a colorless liquid. \(^1\)H NMR (CDCl\(_3\), 400 MHz): δ 4.55 (sept, 2 H, J = 6.2 Hz, iPr-CH), 2.27 (t, 2 H, J = 7.0 Hz, propargyl CH\(_2\)), 1.60-1.48 (m, 2 H, CH\(_2\)), 1.45-1.24 (m, 6 H, CH\(_2\)), 1.19 (d, 12 H, J = 6.2 Hz, iPr-CH\(_3\)), 0.89 (t, 3 H, J = 6.9 Hz, alkyl CH\(_3\)). The values of the \(^1\)H NMR spectrum are in accordance with reported literature data.\(^8\)

Following a slightly modified procedure,\(^5\) 2-iodobenzoic acid (7) (692 mg, 2.79 mmol, 1.00 eq.), para-toluenesulfonic acid monohydrate (TsOH\(\cdot\)H\(_2\)O, 531 mg, 2.79 mmol, 1.00 eq.) and meta-chloroperoxybenzoic acid (mCPBA-70%, 756 mg, 3.07 mmol, 1.10 eq.) were dissolved in dichloromethane (4.5 mL) and 2,2,2-trifluoroethanol (4.5 mL). The mixture was stirred at room temperature under nitrogen for 1 hour, after which diisopropyloct-1-ynylboronate (32, 930 mg, 3.90 mmol, 1.40 eq.) was added in one portion. The reaction mixture was stirred for 2 hours at room temperature, filtered and concentrated in vacuo. The resulting oil was dissolved in dichloromethane (30 mL) and under vigorous stirring, saturated aq. NaHCO\(_3\) (30 mL) was added. The mixture was stirred for 15 minutes, the two layers were separated and the

\(^7\) Brown, H. C.; Bhat, N. G.; Srebnik, M. Tetrahedron Lett. 1988, 29, 2631.

\(^8\) Morita, R.; Shirakawa, E.; Tsuchimoto, T.; Kawakami, Y. Org. Biomol. Chem. 2005, 3, 1263.
aqueous layer was extracted with additional portions of dichloromethane (3 x 10 mL). The combined organic layers were dried over MgSO₄, filtered and concentrated in vacuo. The crude product was purified by flash column chromatography (ethyl acetate) to afford 1d (940 mg, 2.64 mmol, 95%) as a white solid. Rf (EtOAc) = 0.25. Mp 50-63 °C. ¹H NMR (CDCl₃, 400 MHz): δ 8.42-8.35 (m, 1 H, ArH), 8.20-8.13 (m, 1 H, ArH), 7.78-7.69 (m, 2 H, ArH), 2.59 (t, 2 H, J = 7.1 Hz, CCCH₂), 1.70-1.58 (m, 2 H), 1.51-1.39 (m, 2 H), 1.38-1.26 (m, 4 H), 0.94-0.86 (m, 3 H, CH₂CH₃). ¹³C NMR (CDCl₃, 100 MHz): δ 166.7, 134.7, 132.5, 131.7, 131.6, 126.3, 115.7, 109.9, 39.4, 31.3, 28.7, 28.3, 22.6, 20.6, 14.1. IR ν 2930 (w), 2858 (w), 2166 (w), 1619 (s), 1561 (w), 1439 (w), 1331 (m), 1297 (m), 832 (w), 748 (m). HRMS (ESI) C₁₅H₁₈IO₂⁺ [M+H]⁺ calc. = 357.0346; [M+H]⁺ obs. = 357.0339.

**Hexadecynyl-1,2-benziodoxol-3(1H)-one (1e)**

To a mixture of trimethylsilylacetylene (8.33 g, 85.0 mmol, 1.20 eq.) and dry THF (46 mL) was added at -78 °C under nitrogen 2.5 M nBuLi in hexanes (33.9 mL, 85.0 mmol, 1.20 eq.) over a 10 minute time period. The resulting light yellow solution was stirred at -78 °C for 60 minutes, after which a mixture consisting of 1-bromotetradecane 33 (19.6 g, 70.7 mmol, 1.00 eq.), hexamethylphosphoramide (HMPA, 14.2 mL, 78.0 mmol, 1.10 eq.) and dry THF (23 mL) was slowly added via cannula over a 20 minute time period. The reaction mixture was stirred for 60 minutes at -78 °C, followed by 24 hours of stirring at room temperature. The reaction was quenched at 0 °C with saturated aq. NH₄Cl (50 mL) and diluted with water (10 mL) and EtOAc (50 mL). The two layers were separated and the aq. layer was extracted with additional portions of EtOAc (3 x 50 mL). The combined organic layers were washed with water (2 x 100 mL), brine (100 mL), dried over MgSO₄, filtered and concentrated in vacuo. The light brown crude liquid was finally pushed through a small plug of silica gel with pentane as eluent to afford pure hexadec-1-yn-1-yltrimethylsilane (34, 19.3 g, 65.5 mmol, 92.7% yield) as a colorless liquid. Rf (pentane) = 0.78. ¹H NMR (CDCl₃, 400 MHz): δ 2.19 (t,
2 H, J = 7.1 Hz, CCH$_2$), 1.54-1.44 (m, 2 H, CH$_2$), 1.42-1.18 (m, 22 H, CH$_2$), 0.87 (t, 3 H, J = 6.7 Hz, CH$_2$CH$_3$), 0.13 (s, 9 H, TMS). $^1$H NMR (CDCl$_3$, 100 MHz): $^9$ δ 107.7, 84.3, 32.2, 29.9, 29.8, 29.7, 29.6, 29.3, 29.0, 28.9, 22.9, 20.0, 14.3, 0.3. IR ν 2924 (m), 2854 (m), 2175 (w), 1461 (w), 1249 (w), 841 (s), 761 (w), 736 (m). HRMS (ESI) C$_{19}$H$_{38}$AgSi$^+$ [M+Ag$^+$] calc. = 401.1794; [M+Ag$^+$] obs. = 401.1798.

Following a slightly modified procedure, $^5$ 2-iodobenzoic acid (7) (8.00 g, 32.2 mmol, 1.00 eq.), para-toluensulfonic acid monohydrate (TsOH · H$_2$O, 6.13 g, 32.2 mmol, 1.00 eq.) and meta-chloroperoxybenzoic acid (mCPBA·70%, 8.74 g, 35.5 mmol, 1.10 eq.) were dissolved in dichloromethane (60 mL) and 2,2,2-trifluoroethanol (60 mL). The mixture was stirred at room temperature under nitrogen for 1 hour, after which hexadec-1-yn-1-yltrimethylsilane (34, 13.3 g, 45.1 mmol, 1.40 eq.) was added in one portion. The reaction mixture was stirred for 14 hours at room temperature, filtered and concentrated $\textit{in vacuo}$. The resulting oil was dissolved in dichloromethane (400 mL) and under vigorous stirring, saturated aq. NaHCO$_3$ (400 mL) was added. The mixture was stirred for 60 minutes, the two layers were separated and the aqueous layer was extracted with additional portions of dichloromethane (3 x 100 mL). The combined organic layers were dried over MgSO$_4$, filtered and concentrated $\textit{in vacuo}$. The crude product was purified by flash column chromatography (ethyl acetate) to afford 1e (6.02 g, 12.9 mmol, 40%) as a white solid. $R_f$(EtOAc) = 0.36. Mp 102.6-105.3 °C. $^1$H NMR (CDCl$_3$, 400 MHz): δ 8.44-8.37 (m, 1 H, ArH), 8.21-8.14 (m, 1 H, ArH), 7.80-7.70 (m, 2 H, ArH), 2.59 (t, 2 H, J = 7.1 Hz, CCCH$_2$), 1.65 (p, 2 H, J = 7.1 Hz, CCCH$_2$CH$_2$), 1.52-1.40 (m, 2 H), 1.39-1.19 (m, 20 H, CH$_2$), 0.86 (t, 3 H, J = 6.7 Hz, CH$_2$CH$_3$). $^1$H NMR (CDCl$_3$, 100 MHz): $^9$ δ 166.6, 134.7, 132.5, 131.7, 131.6, 126.2, 115.7, 109.9, 39.5, 32.1, 29.8, 29.7, 29.6, 29.5, 29.2, 29.1, 28.3, 22.8, 20.6, 14.3. IR ν 2924 (s), 2853 (m), 2166 (w), 1649 (m), 1623 (m), 1439 (w), 908 (m), 736 (s). HRMS (ESI) C$_{23}$H$_{34}$IO$_2$$^+$ [M+H$^+$]$^+$ calc. = 469.1598; [M+H$^+$]$^+$ obs. = 469.1614.

$^9$ Some signals were not resolved at 100 MHz.
3,3-Dimethylbutynyl-1,2-benziodoxol-3(1H)-one (1f)

Following a slightly modified procedure, 2-iodobenzoic acid (7) (1.64 g, 6.59 mmol, 1.00 eq.), \( \text{para-toluenesulfonic acid monohydrate} \) (TsOH\( \cdot \)H\( \text{H}_2 \text{O} \), 1.25 g, 6.59 mmol, 1.00 eq.) and \( \text{meta-chloroperoxybenzoic acid} \) (mCPBA-70\%, 1.79 g, 7.25 mmol, 1.10 eq.) were dissolved in dichloromethane (12 mL) and 2,2,2-trifluoroethanol (12 mL). The mixture was stirred at room temperature under nitrogen for 1 hour, after which diisopropyl (3,3-dimethylbut-1-yn-1-yl)boronate (35, 1.94 g, 9.23 mmol, 1.40 eq.) was added in one portion. The reaction mixture was stirred for 1 hour at room temperature, filtered and concentrated \( \text{in vacuo} \). The resulting oil was dissolved in dichloromethane (120 mL) and under vigorous stirring, saturated aq. NaHCO\(_3\) (120 mL) was added. The mixture was stirred for 60 minutes, the two layers were separated and the aqueous layer was extracted with additional portions of dichloromethane (3 x 50 mL). The combined organic layers were dried over MgSO\(_4\), filtered and concentrated \( \text{in vacuo} \). The crude product was purified by flash column chromatography (ethyl acetate) to afford 1f (2.06 g, 6.28 mmol, 95\%) as a white solid. R\(_f\) (EtOAc) = 0.36. Mp 189-192 °C. \(^1\)H NMR (CDCl\(_3\), 400 MHz): \( \delta \) 8.39-8.33 (m, 1 H, Ar\( \text{H} \)), 8.13-8.07 (m, 1 H, Ar\( \text{H} \)), 7.78-7.66 (m, 2 H, Ar\( \text{H} \)), 1.34 (s, 9 H, tBu). \(^{13}\)C NMR (CDCl\(_3\), 100 MHz): \( \delta \) 166.7, 134.7, 132.4, 131.6, 131.5, 126.0, 117.5, 115.7, 38.2, 30.6, 29.7. IR \( \nu \) 3463 (w), 2971 (w), 2171 (w), 1646 (s), 1622 (s), 1440 (w), 1332 (m), 1248 (m), 913 (w), 832 (m), 745 (s). HRMS (ESI) \( \text{C}_{13}\text{H}_{14}\text{IO}_2^+ \) \([\text{M+H}]^+ \) calc. = 329.0033; \([\text{M+H}]^+ \) obs. = 329.0023.

\( \text{(Oct-6-en-1-ynyl)-1,2-benziodoxol-3(1H)-one} \) (1g)

\( \text{Br} \quad \text{36} \)
To a mixture of trimethylsilylacetylene (7.23 g, 73.6 mmol, 1.20 eq.) and dry THF (40 mL) was added at -78 °C under nitrogen 2.5 M nBuLi in hexanes (31.9 mL, 80.0 mmol, 1.30 eq.) over a 10 minute time period. The resulting light yellow solution was stirred at -78 °C for 60 minutes, after which a mixture consisting of 6-bromohexene (36) (10.0 g, 61.3 mmol, 1.00 eq.), hexamethylphosphoramide (HMPA, 12.0 mL, 67.5 mmol, 1.10 eq.) and dry THF (20 mL) was slowly added via cannula over a 20 minute time period. The reaction mixture was stirred for 60 minutes at -78 °C, followed by 24 hours of stirring at room temperature. The reaction was quenched at 0 °C with saturated aq. NH₄Cl (50 mL) and diluted with water (5 mL) and EtOAc (50 mL). The two layers were separated and the aq. layer was extracted with additional portions of EtOAc (3 x 50 mL). The combined organic layers were washed with water (2 x 100 mL), brine (100 mL), dried over MgSO₄, filtered and concentrated in vacuo. The light brown crude liquid was finally pushed through a small plug of silica gel with pentane as eluent to afford pure trimethyl(oct-7-en-1-yn-1-yl)silane (37, 10.6 g, 58.8 mmol, 95.9% yield) as a colorless liquid. ¹H NMR (CDCl₃, 400 MHz): δ 5.79 (ddt, 1 H, J = 16.9, 10.2, 6.7 Hz, CH₂CH₂), 5.04-4.91 (m, 2 H, CH₂CHCH₂), 2.22 (t, 2 H, J = 6.9 Hz, CH₂), 2.11-2.01 (m, 2 H, CH₂), 1.58-1.43 (m, 4 H, CH₂), 0.14 (s, 9 H, TMS). ¹³C NMR (CDCl₃, 100 MHz): δ 138.8, 114.7, 107.6, 84.5, 33.3, 28.2, 28.1, 19.9, 0.3. The values of the NMR spectra are in accordance with reported literature data.¹⁰

Following a slightly modified procedure, 2-iodobenzoic acid (7) (9.82 g, 39.6 mmol, 1.00 eq.), para-toluenesulfonyl acid monohydrate (TsOH·H₂O, 7.53 g, 39.6 mmol, 1.00 eq.) and meta-chloroperoxybenzoic acid (mCPBA-70%, 10.7 g, 43.6 mmol, 1.10 eq.) were dissolved in dichloromethane (73 mL) and 2,2,2-trifluoroethanol (73 mL). The mixture was stirred at room temperature under nitrogen for 1 hour, after which trimethyl(oct-7-en-1-yn-1-yl)silane (37, 10.0 g, 55.4 mmol, 1.40 eq.) was added in one portion. The reaction mixture was stirred for 14 hours at room temperature, filtered and concentrated in vacuo. The resulting oil was dissolved in dichloromethane (700 mL) and under vigorous stirring, saturated aq. NaHCO₃ (700 mL) was added. The mixture was stirred for 1 hour, the two layers were separated and the aqueous layer was extracted with additional portions of dichloromethane (3 x 200 mL). The combined organic layers were dried over MgSO₄, filtered and concentrated in vacuo. The crude product was purified by flash column chromatography (ethyl acetate) to afford 1g (2.60

¹⁰ Urabe, H.; Sato, F. J. Am. Chem. Soc. 1999, 121, 1245.
g, 7.34 mmol, 19%) as a white solid. In addition, starting trimethyl(oct-7-en-1-yn-1-yl)silane (35, 3.20 g, 17.7 mmol) was recovered and re-submitted to the above described conditions to afford additional 1g (1.18 g, 3.33 mmol, 28%) as a white solid, giving an overall yield of 27% brsm. Rf (EtOAc) = 0.34. Mp 48-58 °C. 1H NMR (CDCl3, 400 MHz): δ 8.43-8.36 (m, 1 H, ArH), 8.21-8.13 (m, 1 H, ArH), 7.80-7.69 (m, 2 H, ArH), 5.81 (ddt, 1 H, J = 17.0, 10.2, 6.7 Hz, CH2CHCH3), 5.10-4.95 (m, 2 H, CH2CHCH3), 2.61 (t, 2 H, J = 7.0 Hz), 2.17-2.07 (m, 2 H), 1.73-1.51 (m, 4 H). 13C NMR (CDCl3, 100 MHz): δ 166.7, 138.1, 134.8, 132.5, 131.6, 131.6, 126.2, 115.7, 115.2, 109.5, 39.7, 33.2, 28.1, 27.7, 20.4. IR ν 3294 (w), 2912 (w), 2869 (w), 1731 (w), 1650 (w), 1625 (w), 1447 (m), 1265 (w), 1101 (s), 1018 (m), 747 (s). HRMS (ESI) C15H16O2+[M+H]+ calc. = 355.0189; [M+H]+ obs. = 355.0182.

4-(Prop-2-yn-1-yloxy- but-1-yn-1-yl)-1,2-benziodoxol-3(1H)-one (1h)

A 50-mL flame-dried two-necked round-bottomed flask equipped with a magnetic stirring bar, a rubber septum and a nitrogen inlet adapter was charged with silane 38 (2.00 g, 14.1 mol, 1.00 eq.) and dry DCM (30 mL). The clear colorless solution was cooled to 0 °C and tetrabutylammonium hydrogensulfate (0.239 g, 0.703 mmol, 0.05 eq.) and NaOH (1.12 g, 28.1 mmol, 2.00 eq.) were added to the mixture. After stirring at 0 °C for 5 minutes, propargyl bromide (2.09 g, 14.1 mmol, 1.00 eq.) was added. The resulting yellow reaction mixture was continuously stirred at 0 °C under nitrogen and monitored by TLC (EtOAc:Pentane 30:1, KMnO4 staining). After 2 h, 30 mL of water was added to the reaction mixture at 0 °C and the aqueous layer was extracted with 30 mL of DCM. The combined organic layers were dried over MgSO4, filtered and concentrated in vacuo. The crude yellow oil was purified by flash chromatography columns using EtOAc:Pentane 1:299 as mobile phase to afford pure trimethyl(4-(prop-2-yn-1-yloxy)but-1-yn-1-yl)silane (39, 0.245 g, 1.36 mmol, 10% yield) as a colorless liquid. 1H NMR (CDCl3, 400 MHz): δ 4.17 (d, 2 H, J = 2.3
Hz, CCCH$_2$O), 3.64 (t, 2 H, $J = 7.2$ Hz, OCH$_2$), 2.53 (t, 2 H, $J = 7.2$ Hz, OCH$_2$CH$_2$), 2.43 (t, 1 H, $J = 2.4$ Hz, CCH), 0.14 (s, 9 H, TMS). $^{13}$C NMR (CDCl$_3$, 100 MHz): $\delta$ 103.3, 86.0, 79.6, 74.7, 68.2, 58.3, 21.2, 0.19. IR $\nu$ 3291 (w), 2932 (w), 2859 (w), 2179 (w), 1612 (w), 1511 (m), 1250 (s), 1104 (m), 1036 (w), 843 (s), 761 (w).

Following a slightly modified procedure,$^5$ 2-iodobenzoic acid (7) (0.211 g, 0.832 mmol, 1.00 eq.), para-toluenesulfonic acid monohydrate (TsOH$\cdot$H$_2$O, 0.160 g, 0.832 mmol, 1.00 eq.) and meta-chloroperoxybenzoic acid (mCPBA-70%, 0.226 g, 0.915 mmol, 1.10 eq.) were dissolved in dichloromethane (1.5 mL) and 2,2,2-trifluoroethanol (1.5 mL). The mixture was stirred at room temperature under nitrogen for 1 hour, after which trimethyl(4-(prop-2-yn-1-yloxy)but-1-yn-1-yl)silane (39, 0.210 g, 1.17 mmol, 1.40 eq.) was added in one portion. The reaction mixture was stirred for 14 h at room temperature, filtered and concentrated in vacuo. The resulting oil was dissolved in dichloromethane (15 mL) and under vigorous stirring, saturated aq. NaHCO$_3$ (15 mL) was added. The mixture was stirred for 1 h, the two layers were separated and the aqueous layer was extracted with additional portions of dichloromethane (3 x 15 mL). The combined organic layers were dried over MgSO$_4$, filtered and concentrated in vacuo. The crude product was purified by flash column chromatography (ethyl acetate) to afford 1h (0.177 g, 0.500 mmol, 60%) as a colorless oil. $R_f$ (EtOAc) = 0.1. $^1$H NMR (CDCl$_3$, 400 MHz): $\delta$ 8.30 (dd, 1 H, $J = 7.3$, 1.8 Hz, ArH), 8.23 (dd, 1 H, $J = 8.3$, 1.1 Hz, ArH), 7.76-7.69 (m, 1 H, ArH), 7.66 (td, 1 H, $J = 7.3$, 1.1 Hz, ArH), 4.19 (d, 2 H, $J = 2.4$ Hz, OCH$_2$CCH), 3.72 (t, 2 H, $J = 6.2$ Hz, OCH$_2$CH$_2$), 2.85 (t, 2 H, $J = 6.3$ Hz, OCH$_2$CH$_2$), 2.47 (t, 1 H, $J = 2.4$ Hz, CCH). $^{13}$C NMR (CDCl$_3$, 100 MHz): $\delta$ 167.1, 134.8, 132.1, 131.5, 131.3, 126.8, 115.8, 105.6, 79.1, 75.2, 67.3, 58.3, 40.8, 21.8. IR $\nu$ 3465 (w), 3253 (w), 2920 (w), 2870 (w), 2175 (w), 1611 (s), 1330 (m), 1298 (m), 1100 (s), 832 (m), 748 (s). HRMS (ESI) C$_{14}$H$_{12}$IO$_3$ + [M+H]$^+$ calc. = 354.9826; [M+H]$^+$ obs. = 354.9824.

(5-Chloropent-1-ynyl)-1,2-benziodoxol-3(1H)-one (1i)
meta-chloroperoxybenzoic acid (mCPBA-70%, 4.11 g, 16.7 mmol, 1.10 eq.) were dissolved in dichloromethane (30 mL) and 2,2,2-trifluoroethanol (30 mL). The mixture was stirred at room temperature under nitrogen for 1 hour, after which 5-chloro-1-pentynyl-1-boronic acid pinacol ester (4.85 g, 21.2 mmol, 1.40 eq.) was added in one portion. The reaction mixture was stirred for 90 minutes at room temperature, filtered and concentrated in vacuo. The resulting oil was dissolved in dichloromethane (15 mL) and under vigorous stirring, saturated aq. NaHCO$_3$ (15 mL) was added. The mixture was stirred for 10 minutes, the two layers were separated and the aqueous layer was extracted with additional portions of dichloromethane (3 x 15 mL). The combined organic layers were dried over MgSO$_4$, filtered and concentrated in vacuo. The crude product was purified by flash column chromatography (ethyl acetate) to afford 1i (3.76 g, 10.8 mmol, 71%) as a white solid. R$_f$ (EtOAc) = 0.15. Mp 138.5-141.7 °C.

1H NMR (CDCl$_3$, 400 MHz): δ 8.41-8.34 (m, 1 H, ArH), 8.22-8.13 (m, 1 H, ArH), 7.82-7.68 (m, 2 H, ArH), 3.71 (t, 2 H, J = 6.1 Hz, ClCH$_2$CH$_2$), 2.82 (t, 2 H, J = 6.9 Hz, CCCH$_2$CH$_2$), 2.18-2.05 (m, 2 H, ClCH$_2$C$_2$H$_5$). 13C NMR (CDCl$_3$, 100 MHz): δ 166.8, 134.9, 132.5, 131.6, 131.6, 126.4, 115.8, 107.1, 43.4, 41.2, 30.7, 18.0. IR ν 2942 (w), 2866 (w), 2171 (w), 2091 (w), 1727 (w), 1617 (s), 1556 (w), 1441 (w), 1339 (m), 1023 (w), 846 (w), 742 (s).

HRMS (ESI) C$_{12}$H$_{11}$ClIO$_2$ $^{+}$ [M+H]$^+$ calc. = 348.9487; [M+H]$^+$ obs. = 348.9484.

(4-Azidobut-1-ynyl)-1,2-benziodoxol-3(1H)-one (1j)

Following a slightly modified procedure,$^{11}$ triphenylphospine (27.7 g, 105 mmol, 1.00 eq.) was added at 0 °C to a colorless solution of 4-(trimethylsilyl)but-3-yn-1-ol 40 (15.0 g, 105 mmol, 1.00 eq.) in THF (400 mL). After dissolution, imidazole (7.18 g, 105 mmol, 1.00 eq.) and iodine (26.8 g, 105 mmol, 1.00 eq.) were added to the mixture. The cooling bath was removed after 5 minutes and the reaction mixture was stirred at room temperature for 2 hours. Next, the mixture was diluted with diethyl ether (300 mL) and extracted with 10% aq.

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$^{11}$ Rodier, F.; Rajzmann, M.; Parrain, J. L.; Chouraqui, G.; Commeiras, L. Chem. Eur. J. 2013, 19, 2467.

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Na$_2$S$_2$O$_3$ (300 mL). The aq. layer was washed with additional portions of diethyl ether (2 x 100 mL) and the combined organic layers were washed with brine (300 mL), dried over MgSO$_4$, filtered and concentrated in vacuo. The resulting white suspension was filtered and the filtrate was purified by Kugelrohr distillation (95 °C at 0.5 mbar) to furnish pure (4-iodobut-1-yn-1-yl)trimethylsilane (25.3 g, 100 mmol, 95.2% yield) as a colorless liquid. $^1$H NMR (CDCl$_3$, 400 MHz): δ 3.19 (t, 2 H, $J = 7.5$ Hz, CH$_2$CH$_2$I), 2.76 (t, 2 H, $J = 7.5$ Hz, CH$_2$CH$_2$I), 0.13 (s, 9 H, TMS). $^{13}$C NMR (CDCl$_3$, 100 MHz): δ 105.1, 86.8, 25.2, 1.1, 0.1. The values of the NMR spectra are in accordance with reported literature data.$^{12}$

0.5 M sodium azide in DMSO (220 mL, 110 mmol, 1.10 eq.) was added to (4-iodobut-1-yn-1-yl)trimethylsilane (25.2 g, 99.9 mmol, 1.00 eq.) and the reaction mixture was stirred for 24 hours at room temperature. The mixture was next slowly added to ice water (500 mL) and extracted with diethyl ether (3 x 200 mL). The combined organic layers were washed with water (2 x 100 mL), brine (100 mL), dried over MgSO$_4$, filtered and concentrated in vacuo. The light yellow crude liquid was finally pushed through a small plug of silica gel with pentane as eluent to afford pure (4-azidobut-1-yn-1-yl)trimethylsilane (41, 15.0 g, 90.0 mmol, 94.6% yield) as a colorless liquid. $^1$H NMR (CDCl$_3$, 400 MHz): δ 3.36 (t, 2 H, $J = 6.8$ Hz, CH$_2$CH$_2$N$_3$), 2.50 (t, 2 H, $J = 6.9$ Hz, CH$_2$CH$_2$N$_3$), 0.14 (s, 9 H, TMS). $^{13}$C NMR (CDCl$_3$, 100 MHz): δ 102.7, 87.3, 49.8, 21.1, -0.1. The values of the $^1$H NMR spectrum are in accordance with reported literature data.$^{13}$

Following a slightly modified procedure,$^5$ 2-iodobenzoic acid (7, 15.9 g, 64.0 mmol, 1.00 eq.), para-toluenesulfonic acid monohydrate (TsOH•H$_2$O, 12.2 g, 64.0 mmol, 1.00 eq.) and meta-chloroperoxybenzoic acid (mCPBA-70%, 17.4 g, 70.5 mmol, 1.10 eq.) were dissolved in dichloromethane (120 mL) and 2,2,2-trifluoroethanol (120 mL). The mixture was stirred at room temperature under nitrogen for 1 hour, after which (4-azidobut-1-yn-1-yl)trimethylsilane (41, 15.0 g, 90.0 mmol, 1.40 eq.) was added in one portion. The reaction mixture was stirred for 14 hours at room temperature, filtered and concentrated in vacuo. The resulting oil was dissolved in dichloromethane (750 mL) and under vigorous stirring, saturated aq. NaHCO$_3$ (750 mL) was added. The mixture was stirred for 1 hour, the two layers were separated and the aqueous layer was extracted with additional portions of dichloromethane (3 x 250 mL). The combined organic layers were dried over MgSO$_4$, filtered

$^{12}$ Berkessel, A.; Kramer, J.; Mummy, F.; Neudorfl, J. M.; Haag, R. Angew. Chem. Int. Ed. 2013, 52, 739.

$^{13}$ Diaz, L.; Bujons, J.; Casas, J.; Llebaria, A.; Delgado, A. J. Med. Chem. 2010, 53, 5248.
and concentrated in vacuo. The crude product was purified by flash column chromatography (ethyl acetate) to afford \textbf{1j} (9.20 g, 27.0 mmol, 42%) as a light beige solid. In addition, starting (4-azidobut-1-yn-1-yl)trimethylsilane (41, 1.81 g, 10.8 mmol) was recovered and re-submitted to the above described conditions to afford additional \textbf{1j} (953 mg, 2.79 mmol, 36%) as a light beige solid, giving an overall yield of 47% brsm. \(R_f\) (EtOAc:MeOH 9:1) = 0.47. Mp 114-125 °C (explosive decomposition). \(^1\)H NMR (CDCl\(_3\), 400 MHz): \(\delta\) 8.32 (dd, 1 H, \(J = 7.0, 2.1 \text{ Hz, } \text{Ar}H\)), 8.21 (d, 1 H, \(J = 7.9 \text{ Hz, } \text{Ar}H\)), 7.79-7.63 (m, 2 H, \(\text{Ar}H\)), 3.54 (t, 2 H, \(J = 6.5 \text{ Hz, } \text{CH}_2\text{C}_2\text{H}_2\text{N}_3\)), 2.85 (t, 2 H, \(J = 6.5 \text{ Hz, } \text{CH}_2\text{C}_2\text{H}_2\text{N}_3\)). \(^{13}\)C NMR (CDCl\(_3\), 100 MHz): \(\delta\) 167.2, 134.9, 132.3, 131.5, 131.4, 126.8, 115.8, 104.5, 49.4, 42.7, 21.5. IR \(\nu\) 3452 (w), 2170 (w), 2112 (s), 1647 (s), 1624 (s), 1439 (w), 1331 (m), 1297 (m), 835 (w), 749 (m). HRMS (ESI) \(\text{C}_{11}\text{H}_{29}\text{N}_3\text{O}_2^+\) [M+H]\(^+\) calc. = 341.9734; [M+H]\(^+\) obs. = 341.9734.

5-Pentanoylethynyl-1,2-benziodoxol-3(1H)-one (1k)

\[
\begin{align*}
\text{OH} & \quad 1. \text{mCPBA, TsOH-H}_2\text{O} \\
& 2. \text{TMS} \\
& \text{then NaHCO}_3
\end{align*}
\]

\[
\begin{align*}
\text{then NaHCO}_3 & \Rightarrow \text{OH} \\
& \text{nBuLi, DMAP} \\
& \text{TMS-Cl, then HCl}
\end{align*}
\]

Following a slightly modified procedure,\(^{14}\) 2.5 M \(n\text{BuLi}\) in hexanes (39.2 mL, 98.0 mmol, 2.20 eq.) was added at -78 °C under nitrogen to a mixture of hept-6-yn-1-ol (42) (5.00 g, 44.6 mmol, 1.00 eq.) and dry THF (150 mL), followed by 4-dimethylaminopyridine (DMAP, 1.36 g, 11.1 mmol, 0.25 eq.). The mixture was stirred at -78 °C for 60 minutes, after which trimethylsilyl chloride (TMS-Cl, 20.4 mL, 156 mmol, 3.50 eq.) was added dropwise. The cooling bath was removed and the reaction stirred for 2 hours. Next, 1.0 N aq. HCl (50 mL) was added and the solution was stirred vigorously for 30 minutes at room temperature. The mixture was diluted with EtOAc (200 mL) and extracted. The aqueous layer was extracted with additional portions of EtOAc (3 x 50 mL). The combined organic layers were washed with sat. aq. NaHCO\(_3\) (100 mL), brine (50 mL), dried over MgSO\(_4\), filtered and concentrated in vacuo. The crude product was purified by flash column chromatography (pentane:EtOAc 4:1) to afford 7-(trimethylsilyl)hept-6-yn-1-ol (43, 8.22 g, 43.5 mmol, 97%) as a colorless oil.

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\(^{14}\) Peixoto, P. A.; Richard, J. A.; Severin, R.; Chen, D. Y. \textit{Org. Lett.} \textbf{2011}, \textit{13}, 5724.
\(^1\)H NMR (CDCl\(_3\), 400 MHz): \(\delta\) 3.61 (t, 2 H, \(J = 6.5\) Hz, CH\(_2\)OH), 2.21 (t, 2 H, \(J = 7.0\) Hz, C\(\text{CH}_2\)), 1.73 (bs, 1 H, CH\(_2\)OH), 1.61-1.48 (m, 4 H), 1.48-1.38 (m, 2 H), 0.11 (s, 9 H, TMS).

\(^{13}\)C NMR (CDCl\(_3\), 100 MHz): \(\delta\) 107.4, 84.6, 62.8, 32.3, 28.5, 25.1, 19.9, 0.3. The values of the \(^1\)H NMR spectrum are in accordance with reported literature data.\(^{15}\)

Following a slightly modified procedure,\(^5\) 2-iodobenzoic acid (7) (7.69 g, 31.0 mmol, 1.00 eq.), para-toluenesulfonic acid monohydrate (TsOH.H\(_2\)O, 5.90 g, 31.0 mmol, 1.00 eq.) and meta-chloroperoxybenzoic acid (mCPBA-70\%, 8.41 g, 34.1 mmol, 1.10 eq.) were dissolved in dichloromethane (57 mL) and 2,2,2-trifluoroethanol (57 mL). The mixture was stirred at room temperature under nitrogen for 1 hour, after which 7-(trimethylsilyl)hept-6-yn-1-ol (43, 8.00 g, 43.4 mmol, 1.40 eq.) was added in one portion. The reaction mixture was stirred for 18 hours at room temperature, filtered and concentrated in vacuo. The resulting oil was dissolved in dichloromethane (500 mL) and under vigorous stirring, saturated aq. NaHCO\(_3\) (500 mL) was added. The mixture was stirred for 60 minutes, the two layers were separated and the aqueous layer was extracted with additional portions of dichloromethane (3 x 150 mL). The combined organic layers were dried over MgSO\(_4\), filtered and concentrated in vacuo. The crude product was purified by flash column chromatography (EtOAc:MeOH 95:5) to afford 1k (3.56 g, 9.94 mmol, 32\%) as a white solid. R\(_f\) (EtOAc:MeOH 9:1) = 0.24. Mp 115-120 °C. \(^1\)H NMR (CDCl\(_3\), 400 MHz): \(\delta\) 8.33 (dd, 1 H, \(J = 7.2, 2.0\) Hz, Ar\(H\)), 8.15 (d, 1 H, \(J = 8.0\) Hz, Ar\(H\)), 7.79-7.64 (m, 2 H, Ar\(H\)), 3.66 (t, 2 H, \(J = 5.9\) Hz, CH\(_2\)OH), 2.59 (t, 2 H, \(J = 6.9\) Hz, C\(\text{CH}_2\)), 1.73-1.49 (m, 7 H, CH\(_2\) and OH). \(^{13}\)C NMR (CDCl\(_3\), 100 MHz): \(\delta\) 167.0, 134.8, 132.3, 131.6, 126.5, 115.7, 109.7, 62.3, 39.2, 32.1, 28.0, 25.3, 20.6. IR \(\nu\) 3351 (w), 2934 (w), 2170 (w), 1623 (s), 1585 (m), 1561 (w), 1439 (w), 1333 (m), 1300 (w), 1058 (w), 911 (m), 832 (w), 732 (s), 689 (m). HRMS (ESI) C\(_{14}\)H\(_{16}\)IO\(_3\)\(^+\) [M+H]\(^+\) calc. = 359.0139; [M+H]\(^+\) obs. = 359.0136.

\(^{15}\) Rodier, F.; Rajzmann, M.; Parrain, J. L.; Chouraqui, G.; Commeiras, L. Chem. Eur. J. 2013, 19, 2467.
1-[2,4,6-Trimethylphenylethynyl]-1,2-benziodoxol-3(1H)-one (11)

Following a reported procedure,\textsuperscript{2} NaIO\textsubscript{4} (77.2 g, 0.361 mol, 1.0 equiv) and 2-iodobenzoic acid (7) (89.5 g, 0.361 mmol, 1.0 equiv) were suspended in 30% (v:v) aq. AcOH (700 mL) under air in a 4-neck sulfonation flask equipped with a mechanic stirrer, a thermometer and a condenser. The mixture was vigorously stirred and refluxed for 4 h. The reaction mixture was then diluted with cold water (500 mL) and allowed to cool to room temperature, protecting it from light. After 45 min, the suspension was added to water (1.5 L) and the crude product was collected by filtration, washed on the filter with ice water (3 x 300 mL) and cold acetone (3 x 300 mL), and air-dried in the dark overnight to give 2-iodosylbenzoic acid (77.3 g, 0.292 mol, 81% yield) as a colorless solid.\textsuperscript{1}H NMR (400 MHz, (CD\textsubscript{3})\textsubscript{2}SO) \( \delta \) 8.02 (dd, \( J = 7.7, 1.4 \) Hz, 1 H, Ar\textsubscript{H}), 7.97 (m, 1 H, Ar\textsubscript{H}), 7.85 (dd, \( J = 8.2, 0.7 \) Hz, 1 H, Ar\textsubscript{H}), 7.71 (td, \( J = 7.6, 1.2 \) Hz, 1 H, Ar\textsubscript{H}).\textsuperscript{13}C NMR (100 MHz, (CD\textsubscript{3})\textsubscript{2}SO) \( \delta \) 167.7, 134.5, 131.5, 131.1, 130.4, 126.3, 120.4, 158, 155. IR \( \nu \) 3083 (w), 3060 (w), 2867 (w), 2402 (w), 1601 (m), 1585 (m), 1564 (m), 1440 (m), 1338 (s), 1302 (m), 1148 (m), 1018 (w), 834 (m), 798 (w), 740 (s), 694 (s), 674 (m), 649 (m). The values of the NMR spectra are in accordance with reported literature data.\textsuperscript{2}

Following a reported procedure,\textsuperscript{16} mesityl iodide (44) (1.05 g, 4.27 mmol, 1 equiv) was dissolved in Et\textsubscript{3}N (10 mL) (without prior drying). After three freeze-thaw-pump cycle, PdCl\textsubscript{2}(PPh\textsubscript{3})\textsubscript{2} (30 mg, 0.42 mmol, 0.1 equiv) and CuI (16 mg, 0.84 mmol, 0.2 equiv) were added under N\textsubscript{2}. After the addition of trimethylsilylacetylene (1.2 mL, 8.5 mmol, 2 equiv), the green suspension was stirred at RT for 1 h. The reaction mixture was reduced under vacuum, dissolved in CH\textsubscript{2}Cl\textsubscript{2} (30 mL), washed with 5% EDTA solution (30 mL) and water (30 mL). The organic layers were them dried over MgSO\textsubscript{4}, filtered and reduced under vacuum.

\textsuperscript{16} Brand, J. P.; Chevalley, C.; Scopelliti, R.; Waser, J. Chem. Eur. J. 2012, 18, 5655.
resulting oil was purified by column chromatography (PET) to afford 45 (526 mg, 2.43 mmol, 66%) along with 15% of starting material. \( R_f \) 0.5 (PET). \(^1\)H NMR (400 MHz, CDCl\(_3\)) \( \delta 6.87 \) (s, 2 H, ArH), 2.41 (s, 6 H, CH\(_3\)), 2.29 (s, 3 H, CH\(_3\)), 0.28 (s, 9 H, TMS). Used without further purification.

Following a reported procedure,\(^{16}\) trimethylsilyl triflate (212 \( \mu \)L, 1.15 mmol, 1.1 equiv) was added to a suspension of 2-iodosylbenzoic acid (1.00 g, 1.05 mmol, 1 equiv) in CH\(_2\)Cl\(_2\) (4 mL) at RT. The resulting yellow mixture was stirred for 1 h, followed by the dropwise addition of (mesitylethynyl)trimethylsilane (45) (250 mg, 1.15 mmol, 1.1 equiv) dissolved in CH\(_2\)Cl\(_2\) (1 mL). The resulting suspension was stirred for 6 h at RT. A saturated solution of NaHCO\(_3\) (5 mL) was then added and the mixture was stirred vigorously. The layers were separated and the organic layer was washed with sat. NaHCO\(_3\) (10 mL), dried over MgSO\(_4\), filtered and evaporated under reduced pressure. The resulting solid was recrystallized in CH\(_3\)CN (ca 20 ml). The mother liquors were concentrated and and the obtained solid recrystallized in CH\(_3\)CN (4 mL). Both solids were combined, washed with pentane and dried under high vacuum to afford 1l (120 mg, 0.307 mmol, 30%) as a tan solid. Mp 171-175 °C (decomposition). \(^1\)H NMR (400 MHz, CDCl\(_3\)) (ca 0.01 mmol/ml) \( \delta 8.38 \) (m, 1 H, ArH), 8.28 (m, 1 H, ArH), 7.72 (m, 2 H, ArH), 6.92 (s, 2 H, MesH), 2.45 (s, 6 H, CH\(_3\)), 2.31 (s, 3 H, CH\(_3\)). \(^{13}\)C NMR (101 MHz, CDCl\(_3\)) \( \delta 166.7, 142.1, 140.5, 134.5, 132.2, 131.5, 131.3, 128.0, 126.2, 117.5, 116.5, 105.1, 55.6, 21.4, 21.0. IR 2979 (w), 2916 (w), 2247 (w), 2131 (w), 1650 (m), 1623 (m), 1562 (w), 1439 (w), 1333 (w), 1292 (w), 1212 (w), 1146 (w), 1008 (w), 906 (s), 855 (w), 833 (w), 729 (s), 647 (m). The data are in accordance with reported literature.\(^{16}\)

(4-Hydroxybut-1-yn-1-yl)-1,2-benziodoxol-3(1H)-one (1m)

\[
\begin{align*}
\text{O} & \quad \text{H} \\
\text{7} & \quad \text{O} \\
\begin{array}{c}
1. mCPBA, \text{TsOH-H}_2\text{O} \\
2. \text{TMS}, \text{then NaHCO}_3
\end{array} & \rightarrow \\
\text{O} & \quad \text{I} & \quad \text{O} \\
\text{1m} & \quad \text{O} & \quad \text{H}
\end{align*}
\]

Following a slightly modified procedure,\(^5\) 2-iodobenoic acid (7) (10.2 g, 40.2 mmol, 1.00 eq.), para-toluene sulfonic acid monohydrate (TsOH, 7.64 g, 40.2 mmol, 1.00 eq.) and meta-chloroperoxybenzoic acid (mCPBA-70%, 10.9 g, 44.2 mmol, 1.10 eq.) were dissolved in dry dichloromethane (70 mL) and 2,2,2-trifluoroethanol (70 mL). The mixture was stirred at room temperature under nitrogen for 1 h, after which 4-(trimethylsilyl)but-3-yn-1-ol (46) (8.00 g,
56.2 mmol, 1.40 eq.) was added in one portion. The reaction mixture was stirred for 17 hours at room temperature, filtered and concentrated in vacuo. The resulting oil was dissolved in dichloromethane (150 mL) and under vigorous stirring, saturated aq. NaHCO₃ (150 mL) was added. The mixture was stirred for 15 minutes, the two layers were separated and the aqueous layer was extracted with additional portions of dichloromethane (3 x 100 mL). The combined organic layers were dried over MgSO₄, filtered and concentrated in vacuo. The crude product was purified by flash column chromatography (ethyl acetate then flushed with acetone) to afford a white solid, which was further purified by trituration in pentane, filtered, washed twice with pentane and then dried under air to afford 1m (4.24 g, 40.2 mmol, 33 %) as a white solid. Analytically pure sample was obtained by recrystallization in EtOH/AcOEt (6/4). Mp 165-174 °C (decomposition). ¹H NMR (400 MHz, DMSO-d₆): δ 8.33 (dd, J = 8.2, 1.0 Hz, 1H), 8.10 (dd, J = 7.4, 1.8 Hz, 1H), 7.85 (ddd, J = 8.2, 7.2, 1.8 Hz, 1H), 7.78 (td, J = 7.2, 1.0 Hz, 1H), 5.07 (t, J = 5.4 Hz, 1H), 3.65 (t, J = 6.4, 5.5 Hz, 2H), 2.80 (t, J = 6.4 Hz, 2H). ¹³C NMR (100 MHz, DMSO-d₆): δ 166.1, 134.7, 132.2, 131.1, 127.5, 115.7, 106.2, 59.3, 40.7, 24.2. IR ν 3143 (w), 2983 (w), 2363 (m), 2337 (w), 2166 (w), 1605 (s), 1557 (m), 1436 (w), 1347 (s), 1044 (s), 988 (w), 831 (m), 738 (s). HRMS (ESI) C₁₁H₁₀IO₃⁺ [M+H]⁺ calc. = 316.9669; obs. = 316.9679.

3-(Benzyloxy)-3-methyl-but-1-yn-1-yl)-1,2-benziodoxol-3(1H)-one (1n)

47 (850 mg, 4.90 mmol, 1.00 eq.) was dissolved in 10 mL of dry THF. Next, ⁷BuLi (2.5 M in hexane, 5.1 mL, 13 mmol, 2.6 eq.) was added through syringe dropwise over 10 minutes and the reaction mixture was stirred for another 10 minutes to get a brownish-red solution. Next, TMSCl (0.70 mL, 5.5 mmol, 1.1 eq.) was added dropwise to get a clear solution and the reaction mixture was stirred for 1.5 h at 0 °C. The resulting reaction mixture was continuously stirred at room temperature for 2.5 h until a white solid precipitated. It was then diluted with
hexane (30 mL), washed with water (3 x 20 mL), brine (20 mL), dried over MgSO₄, filtered and concentrated in vacuo. The crude product was purified by flash chromatography using EtOAc:Pentane 1:20 as mobile phase to afford (3-(benzyloxy)-3-methylbut-1-yn-1-yl)trimethylsilane (362 mg, 1.47 mmol, 33%), which was used directly in the next step.

Trimethylsilyltriflate (1.60 mL, 8.56 mmol, 1.1 eq.) was added dropwise to a stirred solution of 2-iodosylbenzoic acid (48) (2.12 g, 7.99 mmol, 1.0 eq.) in acetonitrile (40 mL) at 0 °C. After 15 minutes, (3-(benzyloxy)-3-methylbut-1-yn-1-yl)trimethylsilane (2.07 g, 8.89 mmol, 1.05 eq.) was added dropwise, followed, after 30 min, by the addition of pyridine (6 mL). The mixture was stirred for 20 minutes. The solvent was then removed under reduced pressure and the crude oil was dissolved in dichloromethane (100 mL). The organic layer was washed with 0.5 M HCl (100 mL) and the aqueous layer was extracted with CH₂Cl₂ (100 mL). The organic layers were combined, washed with a saturated solution of NaHCO₃, brine (100 mL), dried over MgSO₄, filtered and the solvent was evaporated under reduced pressure. Recrystallization from hot EtOAc afforded 1n (770 mg, 0.183 mmol, 23%) as a light yellow solid. Mp 146.6-148.0 °C. ¹H NMR (CDCl₃, 400 MHz): δ 8.39 (dd, 1 H, J = 7.3, 1.8 Hz, ArH), 8.11 (dd, 1 H, J = 8.2, 1.1 Hz, ArH), 7.78-7.62 (m, 2 H, ArH), 7.39-7.31 (m, 4 H, ArH), 7.31-7.27 (m, 1H, ArH), 4.70 (s, 2 H, ArC₂H₅), 1.69 (s, 6 H, 2 x CH₃). ¹³C NMR (CDCl₃, 100 MHz): δ 166.6, 138.3, 135.0, 132.6, 131.7, 131.4, 128.6, 127.9, 127.6, 126.1, 115.8, 110.0, 71.9, 67.2, 45.5, 28.8. IR ν 2986 (w), 2868 (w), 2159 (w), 1618 (s), 1561 (m), 1446 (w), 1330 (m), 1299 (m), 1224 (m), 1159 (m), 1054 (m), 888 (w), 834 (m), 742 (s). HRMS (ESI) C₁₉H₁₈IO₃⁺ [M+H]⁺ calc. = 421.0295; [M+H]⁺ obs. = 421.0305.

1-[Phenylethynyl]-1,2-benziodoxol-3(1H)-one (Ph-EBX, 1o)

Following a reported procedure,¹⁶ trimethylsilyltriflate (1.60 mL, 8.56 mmol, 1.1 eq.) was added dropwise to a stirred solution of 2-iodosylbenzoic acid (48) (10.0 g, 37.7 mmol, 1 equiv) in CH₂Cl₂ (100 mL) at RT. The resulting yellow mixture was stirred for 1 h, followed by the dropwise addition of trimethyl(phenylethynyl)silane (49) (8.10 mL, 41.5 mmol, 1.1 equiv) (slightly exothermic). The resulting suspension was stirred for 6 h at RT,
during this time a white solid was formed. A saturated solution of NaHCO$_3$ (100 mL) was then added and the mixture was stirred vigorously. The resulting suspension was filtered on a glass filter of porosity 4. The two layers of the mother liquors were separated and the organic layer was washed with sat. NaHCO$_3$ (100 mL), dried over MgSO$_4$, filtered and evaporated under reduced pressure. The resulting mixture was combined with the solid obtained by filtration and boiled in CH$_3$CN (300 mL). The mixture was cooled down, filtered and dried under high vacuum to afford 1o (6.08 g, 17.4 mmol, 46 %) as a colorless solid. Mp (Dec.) 155 – 160°C (lit 153-155°C). $^1$H NMR (400 MHz, CDCl$_3$) (ca 0.03 mmol/ml) δ 8.46 (m, 1 H, ArH), 8.28 (m, 1 H, ArH), 7.80 (m, 2 H, ArH), 7.63 (m, 2 H, ArH), 7.48 (m, 3 H, ArH). $^{13}$C NMR (101 MHz, CDCl$_3$) δ 163.9, 134.9, 132.9, 132.5, 131.6, 131.3, 130.8, 128.8, 126.2, 120.5, 116.2, 106.6, 50.2. Consistent with reported data.$^{16}$
4. Preparation of Substrates

2-((S)-2-(((benzyloxy)carbonyl)amino)-3-(1H-indol-3-yl)propanamido)-3-mercapto propanoate) (16a)

To a mixture of L-cysteine ethyl ester hydrochloride (51) (1.90 g, 10.0 mmol, 1.00 eq.), N-carbobenzyloxy-L-tryptophan (50) (4.06 g, 12.0 mmol, 1.20 eq.) and HOBt hydrate (2.37 g, 15.0 mmol, 1.50 eq.) in CH$_2$Cl$_2$ (100 mL) was added at 0 °C EDC hydrochloride (2.30 g, 12.0 mmol, 1.20 eq.) in one portion. The resulting suspension was stirred for 10 minutes at 0 °C, after which DIPEA (5.24 mL, 30.0 mmol, 3.00 eq.) was slowly added. The ice bath was removed and the reaction mixture was stirred at room temperature for 17 h. Next, the solvent was evaporated under reduced pressure. The resulting oil was dissolved in EtOAc (250 mL) and extracted with 5% aq. KHSO$_4$ (3 x 75 mL), 5% aq. NaHCO$_3$ (2 x 50 mL) and brine (50 mL). The organic layer was dried over MgSO$_4$, filtered and concentrated in vacuo. The crude white solid was purified by flash chromatography (pentane:EtOAc 2:1 to 3:2) to afford 16a as a white solid (1.32 g, 2.81 mmol, 28%). Rf (EtOAc:pentane 1:1) = 0.81. $^1$H NMR (CDCl$_3$, 400 MHz): δ 8.11 (s, 1 H), 7.65 (d, 1 H, $J = 7.9$ Hz), 7.40 -7.28 (m, 6 H), 7.23-7.17 (m, 1 H), 7.11 (t, 1 H, $J = 7.5$ Hz), 7.07 (d, 1 H, $J = 2.2$ Hz), 6.60 (d, 1 H, $J = 6.3$ Hz), 5.45 (d, 1 H, $J = 7.5$ Hz), 5.13 (s, 2 H), 4.67 (dt, $J = 7.0$, 4.0 Hz, 1H), 4.61-4.51 (m, 1 H), 4.24-4.05 (m, 2 H), 3.42 (dd, 1 H, $J = 14.7$, 5.4 Hz), 3.18 (1 H, $J = 14.6$, 7.0 Hz), 2.96-2.68 (m, 2 H), 1.24 (t, 3 H, $J = 7.1$ Hz, CO$_2$CH$_2$CH$_3$) 1.02 (t, 1 H, $J = 8.8$ Hz, SH). $^{13}$C NMR (CDCl$_3$, 100 MHz): δ 171.3, 169.5, 156.1, 136.3, 136.1, 128.7, 128.4, 128.3, 127.5, 123.4, 122.6, 120.0, 118.9, 111.4, 110.2, 67.3, 62.1, 55.6, 53.9, 28.4, 26.7, 14.3. The characterization data is in accordance with reported literature values.\textsuperscript{17}

\textsuperscript{17} Frei, R.; Waser, J. J. Am. Chem. Soc. 2013, 135, 9620.
3-Methoxybenzothioic S-acid (22b)

Following a slightly modified reported procedure, \textsuperscript{18} thioacetamide (0.380 g, 5.00 mmol, 1.00 eq.) and chloride 52 (3.54 mL, 5.00 mmol, 1.00 eq.) were dissolved in dry benzene (4 mL). The resulting mixture was stirred for 3 h at 30 °C. Then, 10% NaOH (6 mL) was added to the mixture, the resulting biphasic mixture was stirred for 30 minutes and subsequently acidified by adding 1 M aq. KHSO\textsubscript{4}. The emulsion was extracted with EtOAc (80 mL) and brine (100 mL). The organic phase was dried over MgSO\textsubscript{4}, filtered and concentrated under reduced pressure. The crude oil was finally pushed through a small plug of silica gel (pentane/EtOAc 5:1 to 1:1) to yield a second crude mixture, which was concentrated under reduced pressure and then, dissolved in DCM. The organic layer was extracted with sat. aq. NaHCO\textsubscript{3} (2 x 15 mL) and the combined aq. layers were acidified by adding aq. 1 M HCl. The resulting mixture was extracted with EtOAc (3 x 30 mL), after which the combined organic layers were dried over MgSO\textsubscript{4}, filtered and concentrated under reduced pressure to afford 22b (0.270 g, 1.60 mmol, 32%) as a yellow oil. Rf (pentane/EtOAc 1:1, a smear) = 0.57. \textsuperscript{1}H NMR (CDCl\textsubscript{3}, 400 MHz): δ 7.49 (ddd, J = 7.7, 1.6, 0.9 Hz, 1 H, ArH), 7.38 (dd, J = 2.6, 1.6 Hz, 1 H, ArH), 7.35 (t, J = 7.9 Hz, 1 H, ArH), 7.13 (ddd, J = 8.3, 2.6, 1.0 Hz, 1 H, ArH), 5.38 (s, 1 H, SH), 3.83 (s, 3 H, OCH\textsubscript{3}). \textsuperscript{13}C NMR (CDCl\textsubscript{3}, 100 MHz): δ 190.1, 159.8, 137.9, 129.8, 120.7, 120.4, 111.9, 115.9, 55.5. IR ν 2963 (w), 2943 (w), 2836 (w), 2565 (w), 2255 (w), 1675 (m), 1584 (m), 1486 (m), 1261 (s), 909 (m), 780 (s), 731 (s), 696 (s). HRMS (ESI) C\textsubscript{8}H\textsubscript{8}O\textsubscript{2}S\textsuperscript{+} [M+] calc. = 168.0245; [M+] obs. = 167.0180.

4-Methoxybenzothioic S-acid (22c)

\textsuperscript{18} Toriyama, M.; Kamijo, H.; Motohashi, S.; Takido, T.; Itabashi, K. Phosphorus, Sulfur, Silicon Relat. Elem. 2003, 178, 1661.
Following a slightly modified reported procedure, 18 4-methoxybenzoyl chloride (53) (2.08 g, 12.0 mmol, 1.00 eq.) and dry toluene (10.0 mL) were added in an under vacuum flame-dried 25 mL round bottom flask at room temperature. To this clear colorless solution was added thioacetamide (0.924 g, 12.1 mmol, 1.00 eq.) in one portion. The reaction mixture was then stirred at 30 °C for 3 h. The oil bath was then removed and 10 minutes later, 10% (w/w) aq. NaOH (9 mL) was added in one portion. The bi-phasic mixture was stirred for 30 minutes at room temperature and then acidified with 1.0 M aq. KHSO₄. The mixture was then extracted with EtOAc (2 x 10 mL). The combined organic layers were dried over MgSO₄, filtered and concentrated in vacuo. The crude yellow oil was then purified by flash column chromatography (Pentane:EtOAc 9:1) to afford 22c (0.493 g, 2.93 mmol, 25%) as a yellow light crystals. ¹H NMR (CDCl₃, 400 MHz) δ 7.89-7.83 (m, 2 H, ArH), 6.96-6.88 (m, 2 H, ArH), 4.47 (bs, 1 H, S-H), 3.86 (s, 3 H, OCH₃). ¹³C NMR (CDCl₃, 100 MHz) δ 188.7, 164.3, 130.3, 129.6, 114.0, 55.7. The ¹³C NMR data is in accordance with reported literature values.¹⁸

4-Nitrobenzothioic S-acid (22d)

Following a slightly modified reported procedure, 18 4-nitrobenzoyl chloride (54) (5 g, 26.4 mmol, 1.00 eq.) was added in an under vacuum flame dried 25 mL round bottom flask to a suspension of thioacetamide (2.02 g, 24.4 mmol, 1.00 eq.) and dry toluene (20.0 mL) at room temperature. The light yellow reaction mixture was stirred at 30 °C for 3 h and then cooled to 0 °C. At 0 °C, 10% (w/w) aq. NaOH (14 mL) was added in one portion. The bi-phasic mixture was stirred for 30 minutes at 0 °C and then acidified with 1.0 M aq. KHSO₄. The mixture was diluted with water then extracted with EtOAc (3 x 10 mL). The combined organic layers were dried over MgSO₄, filtered and concentrated in vacuo. The crude yellow oil was then purified by flash column chromatography using pentane:EtOAc 4:1. ¹H NMR (CDCl₃, 400 MHz) δ 8.35-8.30 (m, 2 H, ArH), 8.10-8.04 (m, 2 H, ArH), 4.82 (bs, 1 H, S-H). ¹³C NMR (CDCl₃, 100 MHz) δ 188.6, 151.0, 141.1, 129.0, 124.2. The ¹³C NMR data is in accordance with reported literature values.¹⁸
5. Alkynylation Reaction

**General Procedure A (GPA): 2-Bromothiophenol Alkynylation**

![Chemical reaction of 2-bromothiophenol alkynylation](image)

The following general procedure was utilized to determine the representative thiophenol scope for the thiol-alkynylation reaction with R-EBX reagents (1b to 1l). A 25 mL round bottom flask was charged with a magnetic stirring bar, 2-bromothiophenol (0.300 to 0.800 mmol, 1.00 eq.) and triazabicyclodecene (TBD, 0.300 to 0.800 mmol, 1.00 eq.). The mixture was dissolved in THF (3.75 to 10.0 mL) to achieve a thiol concentration of 80 mM. Upon dissolution, the corresponding R-EBX reagents (1b to 1l, 0.330 to 0.880 mmol, 1.10 eq.) were added as a solid in one portion. The resulting reaction mixture was stirred with an open flask for 5 minutes at room temperature and worked-up and purified as indicated.

**General Procedure B (GPB): Benzene-1,3,5-trithiol Alkynylation**

![Chemical reaction of benzene-1,3,5-trithiol alkynylation](image)

The following general procedure was utilized to alkynylate benzene-1,3,5-trithiol using R-EBX reagents (1a, 1g, and 1k). A 25 mL round bottom flask was charged with a magnetic stirring bar, benzene-1,3,5-trithiol (10) (52.3 mg, 0.300 mmol, 1.00 eq.) and triazabicyclodecene (TBD, 125 mg, 0.900 mmol, 3.00 eq.). The mixture was dissolved in THF (5.0 mL) and water (0.5 mL). Upon dissolution, the corresponding R-EBX reagents (11a-c, 0.990 mmol, 3.30 eq.) were added as a solid in one portion. The resulting reaction mixture was stirred with an open flask for 5 minutes at room temperature and then quenched by adding water (10 mL). The mixture was extracted with EtOAc (3 x 10 mL) and the combined organic layers were dried over MgSO₄, filtered and concentrated in vacuo. The resulting crude product was purified as indicated.
General Procedure C (GPC): Alknylation of Protected Thioglycosides

A 25 mL round bottom flask was charged with a magnetic stirring bar, thiosugar 15a (146 mg, 0.400 mmol, 1.00 eq.), TMG (60.0 μL, 0.480 mmol, 1.20 eq.) and THF (5.0 mL). After stirring the resulting solution for 5 minutes at room temperature, R-EBX (1) (0.440 mmol, 1.10 eq.) was added as a solid in one portion. The resulting reaction mixture was stirred for 5 minutes at room temperature. Next, the mixture was diluted with water (10 mL) and extracted with EtOAc (3 x 15 mL). The combined organic layers were dried over MgSO₄, filtered and concentrated in vacuo. The crude reaction mixture was purified by flash chromatography.

General Procedure D (GPD): Alknylation of Unprotected Thioglycosides

A 25 mL round bottom flask was charged with a magnetic stirring bar, thiosugar 15b (87.0 mg, 0.400 mmol, 1.00 eq.) and THF (5.0 mL). After stirring the resulting solution for 5 minutes at room temperature, R-EBX (1) (0.440 mmol, 1.10 eq.) was added as a solid in one portion. The resulting reaction mixture was stirred for 5 minutes at room temperature. Next, the reaction mixture was evaporated under reduced pressure and then crude mixture was washed with 5% aq. NaHCO₃ (15 mL) and extracted with EtOAc (3 x 15 mL). The combined organic layers were dried over MgSO₄, filtered and concentrated in vacuo. The crude reaction mixture was purified by flash chromatography.
General Procedure E (GPE): Alkynylation of Cysteine Containing Dipeptide 16

A 25 mL round bottom flask was charged with a magnetic stirring bar, TrpCys dipeptide 16 (94.0 mg, 0.200 mmol, 1.00 eq.), TMG (30.0 μL, 0.240 mmol, 1.20 eq.) and THF (5.0 mL). After stirring the resulting solution for 5 minutes at room temperature, R-EBX (1) (0.220 mmol, 1.10 eq.) was added as a solid in one portion. The resulting reaction mixture was stirred for 5 minutes at room temperature. Next, the mixture was diluted with water (10 mL) and extracted with EtOAc (3 x 15 mL). The combined organic layers were dried over MgSO₄, filtered and concentrated in vacuo. The crude reaction mixture was purified by flash chromatography.

General Procedure F (GPF): Alkynylation of Sodium Hydrogen Sulfide (23)

A 25 mL round bottom flask was charged with a magnetic stirring bar, sodium hydrogen sulfide (23) (11.2 mg, 0.200 mmol, 1.00 eq.), TMG (60.0 μL, 0.480 mmol, 2.40 eq.) and MeOH (5.0 mL). After stirring the resulting solution for 5 minutes at room temperature, R-EBX (1) (0.440 mmol, 2.20 eq.) was added as a solid in one portion. The resulting reaction mixture was stirred for 5 minutes at room temperature. Next, the reaction mixture was evaporated under reduced pressure and then crude mixture was washed with 5% aq. NaHCO₃ (15 mL) and extracted with EtOAc (3 x 15 mL). The combined organic layers were dried over MgSO₄, filtered and concentrated in vacuo. The crude reaction mixture was purified by flash chromatography.
Benzyl(prop-1-yn-1-yl)sulfane (3b)

A 25 mL round bottom flask was charged with a magnetic stirring bar, benzylmercaptane (2) (50 mg, 0.40 mmol, 1.00 eq.), TMG (60.0 μL, 0.480 mmol, 1.20 eq.) and THF (5.0 mL). After stirring the resulting solution for 5 minutes at room temperature, Me-EBX (1b) (126 mg, 0.440 mmol, 1.10 eq.) was added as a solid in one portion. The resulting reaction mixture was stirred for 5 minutes at room temperature. Next, the mixture was diluted with water (10 mL) and extracted with EtOAc (3 x 15 mL). The combined organic layers were dried over MgSO₄, filtered and concentrated in vacuo. The crude reaction mixture was purified by flash chromatography using pentane as mobile phase affording 3b (45 mg, 0.28 mmol, 70%) as a colorless oil. Rf (pentane, KMnO₄ staining) = 0.47. ¹H NMR (CDCl₃, 400 MHz): δ 7.38-7.26 (m, 5 H, ArH), 3.90 (s, 2 H, ArCH₂), 1.93 (s, 3 H, CCCH₃). ¹³C NMR (CDCl₃, 100 MHz): δ 137.1, 129.1, 128.6, 127.7, 91.4, 67.4, 40.2, 5.1. IR ν 3062 (w), 3031 (m), 2919 (m), 2850 (w), 1606 (w), 1495 (m), 1450 (s), 1240 (m), 1072 (w), 1028 (w), 768 (s). The characterization data is in accordance with reported literature values.¹⁹

(E)-2-((2-(benzylthio)-2-(triisopropylsilyl)vinyl)iodonio)benzoate (6)

A 25 mL round bottom flask was charged with a magnetic stirring bar, benzylthiol (2) (47.0 μL, 0.400 mmol, 1.00 eq.), TMG (5.0 μL, 0.040 mmol, 0.1eq.) and THF (5.0 mL). After stirring the resulting reaction mixture for 5 minutes at room temperature, Me-EBX (126 mg, 0.440 mmol, 1.10 eq.) was added as a solid in one portion. The resulting solution was stirred for 1 h at room temperature. Next, the obtained precipitate was collected and washed several times with hexane and dried under vacuum to afford 6 in 20% yield as a white solid. Melting

¹⁹ Levanova, E. P.; Grabel’nykh, V. A.; Vakhrina, V. S.; Russavskaya, N. V.; Albanov, A. I.; Rozentsveig, I. B.; Korchevin, N. A. Russ. J. Gen. Chem. 2014, 84, 439.
point = 154.1-158.0 °C  

\[ \delta = 8.47 \text{ (dd, 1 H, } J = 7.5, 1.8 \text{ Hz, ArH),} \]

7.62 (td, 1 H, \( J = 7.3, 1.0 \text{ Hz, ArH}) \], 7.52 (ddd, 1 H, \( J = 8.1, 7.1, 1.8 \text{ Hz, ArH} \), 7.31-7.23 (m, 6 H, ArH)), 6.46 (q, 1 H, \( J = 1.3 \text{ Hz, alkene H}) \], 4.10 (s, 2 H, ArCH\(_2\)) \], 2.53 (d, 3 H, \( J = 1.3 \text{ Hz, } \text{CH}_3 \)).  

\( ^{13}\text{C NMR (CDCl}_3, 100 MHz): \delta 166.9, 159.5, 135.9, 133.5, 133.3, 130.8, 129.1, 128.8, 128.1, 125.6, 113.9, 98.1, 37.2, 25.2. \text{ IR } \nu 3430 \text{ (w), 3060 (w), 1602 (s), 1550 (m), 1435 (w), 1359 (m), 1227 (w), 1096 (w), 1004 (w), 831 (w), 747 (s). HRMS (ESI) C}_{17}H_{16}O\_2S^+ [M+H]^+ \text{ calc.} = 410.9910; \text{ obs.} = 410.9928. \)

**(2-Bromophenyl)(prop-1-yn-1-yl)sulfane (9a)**

Following general procedure GPA, the reaction was carried out using 2-bromothiophenol (8, 119 mg, 0.600 mmol). Upon reaction completion, the mixture was concentrated \( \text{in vacuo} \) and purified by flushing the crude oil dissolved in minimum amounts of CH\(_2\)Cl\(_2\) through a small plug of silica gel using pentane:EtOAc 199:1 as mobile phase affording 9a (126 mg, 0.555 mmol, 93%) as a clear colorless oil. \( R_f \) (pentane) = 0.61.  

\( ^1\text{H NMR (CDCl}_3, 400 MHz): \delta 7.70 \text{ (dd, 1 H, } J = 8.0, 1.6 \text{ Hz, ArH),} \]

7.47 (dd, 1 H, \( J = 7.9, 1.3 \text{ Hz, ArH}) \], 7.34 (ddd, 1 H, \( J = 8.0, 7.4, 1.3 \text{ Hz, ArH} \), 7.06 (ddd, 1 H, \( J = 7.9, 7.4, 1.6 \text{ Hz, ArH} \), 2.14 (s, 3 H, CCC\(_3\)H\(_2\)).  

\( ^{13}\text{C NMR (CDCl}_3, 100 MHz): \delta 135.4, 132.6, 128.1, 127.1, 126.8, 119.2, 97.5, 63.7, 5.4. \text{ IR } \nu 3059 \text{ (w), 2913 (w), 1563 (w), 1447 (s), 1430 (s), 1104 (w), 1019 (s). HRMS (ESI) C}_{9}H_{8}BrS^+ [M+H]^+ \text{ calc.} = 226.9525; [M+H]^+ \text{ obs.} = 226.9519. \)

**(2-Bromophenyl)(oct-1-yn-1-yl)sulfane (9b)**

Following general procedure GPA, the reaction was carried out using 2-bromothiophenol (8, 159 mg, 0.800 mmol). Upon reaction completion, the mixture was concentrated \( \text{in vacuo} \) and purified by flushing the crude oil dissolved in minimum amounts of CH\(_2\)Cl\(_2\) through a small plug of silica gel using pentane:EtOAc 199:1 as mobile phase affording 9b (233 mg, 0.784 mmol, 98%) as a clear colorless oil. \( R_f \) (pentane) = 0.64.  

\( ^1\text{H NMR (CDCl}_3, 400 MHz): \delta 7.71 \text{ (dd, 1 H, } J = 8.0, 1.6 \text{ Hz, ArH),} \]

7.48 (dd, 1 H, \( J = 7.9, 1.3 \text{ Hz, ArH}) \], 7.35 (ddd, 1 H, \( J = 8.0, 7.4, 1.3 \text{ Hz, ArH} \), 7.06 (ddd, 1 H, \( J = 7.7, 7.6, 1.6 \text{ Hz, ArH} \), 2.49 (t, 2 H, \( J = 7.1 \text{ Hz, CCCH}_2 \)), 1.68-1.58 (m, 2 H), 1.52-1.42 (m, 2 H), 1.41-1.26 (m, 4 H), 0.93 (t, 3 H, \( J = 6.9 \text{ Hz,} \]

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CH₂CH₃). ¹³C NMR (CDCl₃, 100 MHz): δ 135.6, 132.6, 128.0, 127.0, 126.7, 119.2, 102.1, 64.5, 31.4, 28.7, 28.6, 22.7, 20.4, 14.2. IR ν 2930 (m), 2858 (w), 1740 (m), 1712 (s), 1447 (s), 1373 (s), 1286 (m), 1253 (m), 1123 (m), 1020 (s), 909 (w). HRMS (ESI) C₁₄H₁₈BrS⁺ [M+H]⁺ calc. = 297.0307; [M+H]⁺ obs. = 297.0297.

(2-Bromophenyl)(hexadec-1-yn-1-yl)sulfane (9c)

Following general procedure GPA, the reaction was carried out using 2-bromothiophenol (8, 100 mg, 0.500 mmol). Upon reaction completion, the mixture was concentrated in vacuo and purified by flushing the crude oil dissolved in minimum amounts of CH₂Cl₂ through a small plug of silica gel using pentane:EtOAc 499:1 as mobile phase affording 9c (201 mg, 0.490 mmol, 98%) as a clear colorless oil. Rₐ (pentane) = 0.71. ¹H NMR (CDCl₃, 400 MHz): δ 7.70 (dd, 1 H, J = 8.0, 1.6 Hz, ArH), 7.47 (dd, 1 H, J = 7.9, 1.3 Hz, ArH), 7.34 (td, 1 H, J = 7.7, 1.4 Hz, ArH), 7.06 (td, 1 H, J = 7.7, 1.6 Hz, ArH), 2.48 (t, 2 H, J = 7.1 Hz, CCCH₂CH₂), 1.63 (p, 2 H, J = 7.1 Hz, CCCH₂CH₂), 1.51-1.40 (m, 2 H), 1.39-1.20 (m, 20 H), 0.90 (t, 3 H, J = 6.8 Hz, CH₂CH₃). ¹³C NMR (CDCl₃, 100 MHz): δ 135.7, 132.6, 128.1, 127.1, 126.8, 119.3, 102.1, 64.5, 32.1, 29.9, 29.8, 29.7, 29.5, 29.3, 29.1, 28.7, 22.9, 20.5, 14.3. IR ν 2968 (w), 1575 (m).

(2-Bromophenyl)(3,3-dimethylbut-1-yn-1-yl)sulfane (9d)

Following general procedure GPA, the reaction was carried out using 2-bromothiophenol (8, 100 mg 0.500 mmol). Upon reaction completion, the mixture was concentrated in vacuo and purified by flushing the crude oil dissolved in minimum amounts of CH₂Cl₂ through a small plug of silica gel using pentane:EtOAc 499:1 as mobile phase affording 9d (134 mg, 0.498 mmol, quant.) as a clear colorless oil. Rₐ (pentane) = 0.85. ¹H NMR (CDCl₃, 400 MHz): δ 7.65 (dd, 1 H, J = 8.0, 1.6 Hz, ArH), 7.47 (dd, 1 H, J = 7.9, 1.3 Hz, ArH), 7.36 (ddd, 1 H, J = 8.0, 7.4, 1.3 Hz, ArH), 7.10-7.02 (m, 1 H, ArH), 1.36 (s, 9 H, tBu). ¹³C NMR (CDCl₃, 100 MHz): δ 135.7, 132.6, 128.1, 127.1, 126.5, 119.3, 109.7, 63.5, 31.0, 29.2. IR ν 2968 (w), 1575...
(2-Bromophenyl)(oct-7-en-1-yn-1-yl)sulfane (9e)

Following general procedure GPA, the reaction was carried out using 2-bromothiophenol (8, 100 mg, 0.500 mmol). Upon reaction completion, the mixture was concentrated in vacuo and purified by flushing the crude oil dissolved in minimum amounts of CH2Cl2 through a small plug of silica gel using pentane:EtOAc 299:1 as mobile phase affording 9e (137 mg, 0.465 mmol, 93%) as a clear colorless oil. Rf (pentane) = 0.69. 1H NMR (CDCl3, 400 MHz): δ 7.68 (dd, 1 H, J = 8.0, 1.6 Hz, ArH), 7.48 (dd, 1 H, J = 7.9, 1.3 Hz, ArH), 7.34 (ddd, 1 H, J = 8.0, 7.4, 1.3 Hz, ArH), 7.06 (ddd, 1 H, J = 7.7, 7.6, 1.6 Hz, ArH), 5.83 (ddt, 1 H, J = 16.9, 10.2, 6.7 Hz, CHCH2), 5.09-4.95 (m, 2 H, CHCH2), 2.50 (t, 2 H, J = 6.8 Hz, CCCH2CH2), 2.16-2.06 (m, 2 H, CH2), 1.72-1.50 (m, 4 H, CH2). 13C NMR (CDCl3, 100 MHz): δ 138.5, 135.6, 132.6, 128.1, 127.1, 126.8, 119.3, 114.9, 101.8, 64.7, 33.3, 28.2, 28.1, 20.3. IR ν 3062 (w), 2859 (w), 1736 (w), 1706 (m), 1447 (m), 1430 (m), 1174 (w), 1019 (m), 912 (m), 745 (s). HRMS (ESI) C14H14BrS+ [M+H]+ calc. = 268.9994; [M+H]+ obs. = 268.9986.

(2-Bromophenyl)(4-(prop-2-yn-1-yloxy)but-1-yn-1-yl)sulfane (9f)

Following general procedure GPA, the reaction was carried out using 2-bromothiophenol (8, 60 mg, 0.30 mmol). Upon reaction completion, the mixture was concentrated in vacuo and purified by flushing the crude oil dissolved in minimum amounts of CH2Cl2 through a small plug of silica gel using pentane:EtOAc 99:1 as mobile phase affording 9f (84.1 mg, 0.285 mmol, 95%) as a clear colorless oil. Rf (pentane:EtOAc 25:1) = 0.49. 1H NMR (CDCl3, 400 MHz): δ 7.71 (dd, 1 H, J = 8.0, 1.5 Hz, ArH), 7.47 (dd, 1 H, J = 7.9, 1.3 Hz, ArH), 7.35 (ddd, 1 H, J = 7.9, 7.4, 1.4 Hz, ArH), 7.06 (ddd, 1 H, J = 7.9, 7.4, 1.6 Hz, ArH), 4.22 (d, 2 H, J = 2.4 Hz, OCH2CCCH), 3.74 (t, 2 H, J = 6.7 Hz, CCCH2CH2O), 2.79 (t, 2 H, J = 6.8 Hz, CCCH2CH2O), 2.47 (t, 1 H, J = 2.4 Hz, OCH2CCCH). 13C NMR (CDCl3, 100 MHz): δ 135.1, 132.6, 128.2, 127.3, 127.0, 119.4, 98.2, 79.5, 74.9, 67.9, 66.3, 58.4, 21.7. IR ν 3294 (w), 2912
(w), 2869 (w), 1735 (w), 1611 (w), 1447 (m), 1357 (w), 1250 (w), 1102 (s), 1018 (m), 747 (s). HRMS (ESI) C_{13}H_{12}BrOSS^{+} [M+H]^+ calc. = 294.9787; [M+H]^+ obs. = 294.9783.

(2-Bromophenyl)(5-chloropent-1-yn-1-yl)sulfane (9g)

Following general procedure GPA, the reaction was carried out using 2-bromo thiophenol (8, 100 mg, 0.500 mmol). Upon reaction completion, the mixture was concentrated in vacuo and purified by flushing the crude oil dissolved in minimum amounts of CH$_2$Cl$_2$ through a small plug of silica gel using pentane:EtOAc 299:1 as mobile phase affording 9g (126 mg, 0.436 mmol, 87%) as a clear colorless oil. $R_f$ (pentane) = 0.51. $^1$H NMR (CDCl$_3$, 400 MHz): $\delta$ 7.66 (dd, 1 H, $J = 8.0, 1.5$ Hz, ArH), 7.48 (dd, 1 H, $J = 7.9, 1.3$ Hz, ArH), 7.36 (ddd, 1 H, $J = 8.0, 7.4, 1.4$ Hz, ArH), 7.07 (ddd, 1 H, $J = 8.0, 7.4, 1.6$ Hz, ArH), 3.70 (t, 2 H, $J = 6.3$ Hz, CH$_2$CH$_2$Cl), 2.70 (t, 2 H, $J = 6.8$ Hz, CCCCH$_2$), 2.11-2.02 (m, 2 H, CCCH$_2$C). $^{13}$C NMR (CDCl$_3$, 100 MHz): $\delta$ 135.1, 132.7, 128.2, 127.3, 126.8, 119.4, 99.7, 66.1, 43.7, 31.2, 17.8. IR $\nu$ 2959 (w), 1574 (w), 1446 (s), 1301 (w), 1194, 99.7, 66.1, 43.7, 31.2, 17.8. IR $\nu$ 2959 (w), 1574 (w), 1446 (s), 1301 (w), 1194, 99.7, 66.1, 43.7, 31.2, 17.8. IR $\nu$ 2959 (w), 1574 (w), 1446 (s), 1301 (w), 1194, 99.7, 66.1, 43.7, 31.2, 17.8. IR $\nu$ 2959 (w), 1574 (w), 1446 (s), 1301 (w), 1194, 99.7, 66.1, 43.7, 31.2, 17.8. IR $\nu$ 2959 (w), 1574 (w), 1446 (s), 1301 (w), 1194, 99.7, 66.1, 43.7, 31.2, 17.8. IR $\nu$ 2959 (w), 1574 (w), 1446 (s), 1301 (w), 1194, 99.7, 66.1, 43.7, 31.2, 17.8.

(4-Azidobut-1-yn-1-yl)(2-bromophenyl)sulfane (9h)

Following general procedure GPA, the reaction was carried out using 2-bromo thiophenol (8, 119 mg, 0.600 mmol). Upon reaction completion, the mixture was concentrated in vacuo and purified by flushing the crude oil dissolved in minimum amounts of CH$_2$Cl$_2$ through a small plug of silica gel using pentane:EtOAc 199:1 as mobile phase affording 9h (153 mg, 0.542 mmol, 90%) as a clear colorless oil. $R_f$ (pentane:EtOAc 30:1) = 0.48. $^1$H NMR (CDCl$_3$, 400 MHz): $\delta$ 7.68 (dd, 1 H, $J = 8.0, 1.5$ Hz, ArH), 7.49 (dd, 1 H, $J = 7.9, 1.3$ Hz, ArH), 7.36 (ddd, 1 H, $J = 8.0, 7.4, 1.3$ Hz, ArH), 7.08 (ddd, 1 H, $J = 8.0, 7.4, 1.6$ Hz, ArH), 3.51 (t, 2 H, $J = 6.8$ Hz, CCCCH$_2$N$_3$), 2.77 (t, 2 H, $J = 6.8$ Hz, CCCCH$_2$N$_3$). $^{13}$C NMR (CDCl$_3$, 100 MHz): $\delta$ 134.7, 132.8, 128.2, 127.5, 127.0, 119.5, 97.4, 67.8, 49.9, 21.5. IR $\nu$ 2932 (w), 2103 (s), 1574 (w), 1447 (s), 1429 (m), 1301 (w), 1257 (m), 1105 (w), 1018 (m), 744 (s). HRMS (ESI) C$_{10}$H$_8$AgBrN$_3$S$^+$ [M+Ag]$^+$ calc. = 387.8668; [M+Ag]$^+$ obs. = 387.8661.

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7-((2-Bromophenyl)thio)hept-6-yn-1-ol (9i)

Following general procedure GPA, the reaction was carried out using 2-bromothiophenol (8, 119 mg, 0.600 mmol). Upon reaction completion, the mixture was concentrated in vacuo and purified by flushing the crude oil dissolved in minimum amounts of CH₂Cl₂ through a small plug of silica gel using pentane:EtOAc 7:2 as mobile phase affording 9i (175 mg, 0.585 mmol, 98%) as a light yellow oil. R_f (pentane:EtOAc 7:3) = 0.33. ¹H NMR (CDCl₃, 400 MHz): δ 7.66 (d, 1 H, J = 7.6 Hz, ArH), 7.45 (dd, 1 H, J = 7.7 Hz, ArH), 7.33 (t, 1 H, J = 7.6 Hz, ArH), 7.04 (td, 1 H, J = 7.4 Hz, ArH), 3.65 (t, 2 H, J = 5.6 Hz, CH₂OH), 2.48 (t, 2 H, J = 6.7 Hz, CCC₂H₂), 1.99 (bs, 1 H, CH₂O), 1.70-1.45 (m, 6 H). ¹³C NMR (CDCl₃, 100 MHz) δ 135.4, 132.5, 128.0, 127.1, 126.7, 119.2, 101.7, 64.7, 62.7, 32.2, 28.4, 25.1, 20.4. IR ν 3366 (w), 2938 (w), 2861 (w), 1447 (m), 1430 (w), 1019 (m), 730 (s). HRMS (ESI) C₁₃H₁₅BrNaOS⁺ [M+Na]⁺ calc. = 320.9919; [M+Na]⁺ obs. = 320.9928.

(2-Bromophenyl)(mesitylethynyl)sulfane (9j)

Following general procedure GPA, the reaction was carried out using 2-bromothiophenol (8, 100 mg, 0.500 mmol). Upon reaction completion, the mixture was concentrated in vacuo and purified by flushing the crude oil dissolved in minimum amounts of CH₂Cl₂ through a small plug of silica gel using pentane:EtOAc 499:1 as mobile phase affording 9j (165 mg, 0.499 mmol, quant.) as a light brown oil. R_f (pentane) = 0.47. ¹H NMR (CDCl₃, 400 MHz): δ 7.88 (d, 1 H, J = 7.9 Hz, ArH), 7.55 (d, 1 H, J = 7.8 Hz, ArH), 7.39 (t, 1 H, J = 7.6 Hz, ArH), 7.18-7.07 (m, 1 H, J = 7.4 Hz, ArH), 6.96 (s, 2 H, ArH), 2.52 (s, 6 H, CH₃), 2.36 (s, 3 H, CH₃). ¹³C NMR (CDCl₃, 100 MHz) δ 140.9, 138.6, 135.4, 132.7, 128.1, 127.8, 127.2, 126.9, 119.4, 119.3, 97.6, 81.2, 21.4, 21.2. IR ν 2914 (w), 2153 (w), 1610 (w), 1574 (w), 1446 (s), 1429 (m), 1019 (s), 852 (m), 744 (s). HRMS (ESI) C₁₇H₁₆BrS⁺ [M+H]⁺ calc. = 331.0151; [M+H]⁺ obs. = 331.0149.
Phenyl(oct-1-yn-1-yl)sulfane (9k)

Benzenethiol (0.522 mL, 5.10 mmol, 1.00 eq.) was dissolved in dry THF (64 mL). Next, TBD (0.700 g, 5.10 mmol, 1.00 eq.) was added and the mixture was stirred for 5 min at room temperature, after which Hex-EBX (1d) (2.00 g, 5.61 mmol, 1.10 eq.) was added and the resulting mixture was stirred for 10 min at room temperature. The mixture was concentrated under reduced pressure and the crude product was purified by flash chromatography (pentane/EtOAc 1:0 to 100:1) to afford 9k (0.670 g, 3.08 mmol, 60%) as colorless oil. Rf (pentane/EtOAc 100:1, KMnO₄) = 0.98. ¹H NMR (CDCl₃, 400 MHz): δ 7.47-7.41 (m, 2 H, ArH), 7.39-7.30 (m, 2 H, ArH), 7.25-7.17 (m, 1 H, ArH), 2.48 (t, J = 7.0 Hz, 2 H, CCCH₂), 1.70-1.57 (m, 2 H, CH₂), 1.55-1.42 (m, 2 H, CH₂), 1.42-1.27 (m, 4 H, CH₂), 0.94 (t, 3 H, CH₂CH₃). ¹³C NMR (CDCl₃, 100 MHz): δ 133.9, 129.1, 126.1, 125.8, 100.2, 64.6, 31.4, 28.7, 28.6, 22.6, 20.4, 14.1. IR v 2957 (w), 2932 (w), 2859 (w), 2249 (w), 1584 (w), 1479 (w), 1442 (w), 1025 (w), 907 (s), 730 (s), 689 (w). HRMS (ESI) C₁₄H₁₉S⁺ [M+H]⁺ calc. = 219.1202; [M+H]⁺ obs. = 219.1199.

1,3,5-Tris(((triisopropylsilyl)ethynyl)thio)benzene (11a)

Following our recently developed thiol-alkynylation procedure for TIPS-EBX (1a),¹⁷ a 25 mL round bottom flask was charged with a magnetic stirring bar, benzene-1,3,5-trithiol (52.3 mg, 0.300 mmol, 1.00 eq.) and 1,1,3,3-tetramethylguanidine (TMG, 137 µL, 1.08 mmol, 3.60 eq.). The mixture was dissolved in THF (5.0 mL) and water (0.5 mL). Upon dissolution, TIPS-EBX (1a, 424 mg, 0.990 mmol, 3.30 eq.) was added as a solid in one portion. The resulting reaction mixture was stirred with an open flask for 5 minutes at room temperature and then quenched by adding water (10 mL). The mixture was extracted with EtOAc (3 x 10 mL) and the combined organic layers were dried over MgSO₄, filtered and concentrated in vacuo. The
resulting crude product was purified by column chromatography (pentane) affording 11a (205 mg, 0.287 mmol, 96%) as a white solid. Rf (pentane) = 0.81. Melting point = 109.1-111.6 °C. 

$^1$H NMR (CDCl$_3$, 400 MHz): $\delta$ 7.39 (s, 3 H, ArH), 1.21-1.09 (m, 63 H, TIPS). $^{13}$C NMR (CDCl$_3$, 100 MHz): $\delta$ 136.1, 120.9, 105.5, 89.8, 18.8, 11.5. IR $\nu$ 2943 (m), 2865 (m), 2095 (w), 1557 (w), 1463 (w), 996 (w), 882 (s), 858 (s). HRMS (APPI) C$_{39}$H$_{66}$S$_3$Si$_3$ $^+$ [M]$^+$ calc. = 714.3634; [M]$^+$ obs. = 714.3616.

1,3,5-Tris(oct-7-en-1-yn-1-ylthio)benzene (11b)

Following general procedure GPB, the crude product was purified by column chromatography (pentane:EtOAc 199:1) affording 11b (128 mg, 0.260 mmol, 87%) as a colorless oil. Rf (hexane) = 0.79. $^1$H NMR (CDCl$_3$, 400 MHz): $\delta$ 7.23 (s, 3 H, ArH), 5.81 (ddt, 3 H, $J$ = 16.9, 10.2, 6.7 Hz, CH$_2$CHCH$_2$), 5.09-4.93 (m, 6 H, CH$_2$CHCH$_2$), 2.47 (t, 6 H, $J$ = 6.8 Hz, CCCCH$_2$), 2.15-2.05 (m, 6 H, CH$_2$), 1.68-1.49 (m, 12 H, CH$_2$). $^{13}$C NMR (CDCl$_3$, 100 MHz): $\delta$ 138.4, 136.5, 120.2, 114.9, 101.4, 63.9, 33.3, 28.2, 28.1, 20.4. IR $\nu$ 3075 (w), 2937 (m), 2862 (m), 2094 (w), 1556 (s), 1411 (m), 994 (m), 912 (s), 840 (m), 786 (m). HRMS (APPI) C$_{30}$H$_{36}$S$_3$ $^+$ [M]$^+$ calc. = 492.1979; [M]$^+$ obs. = 492.1977.
Following general procedure GPB, the crude product was purified by column chromatography (EtOAc to EtOAc:MeOH 98:2) affording 11c (133 mg, 0.264 mmol, 88%) as a colorless oil. \( R_f \) (EtOAc) = 0.26. \(^1\)H NMR (CDCl\(_3\), 400 MHz): \( \delta \) 7.22 (s, 3 H, Ar\( H \)), 3.64 (t, 6 H, \( J = 6.4 \) Hz, \( \text{CH}_2\text{OH} \)), 2.46 (t, 6 H, \( J = 7.0 \) Hz, \( \text{CCCH}_2\)), 1.97 (bs, 3 H, \( \text{OH} \)), 1.69-1.44 (m, 18 H, \( \text{CH}_2\)). \(^{13}\)C NMR (CDCl\(_3\), 100 MHz): \( \delta \) 136.4, 120.3, 101.4, 63.9, 62.7, 32.3, 28.5, 25.3, 20.5. IR \( \nu \) 3337 (w), 2937 (w), 2861 (w), 1556 (m), 1411 (w), 1057 (w), 903 (w), 732 (s). HRMS (ESI) \( C_{27}H_{36}NaO_3S_3^{+} \) [M+Na]\(^+\) calc. = 527.1719; [M+H]\(^+\) obs. = 527.1711.

Alkynylation of (4-methoxyphenyl)methanethiol (14)

\[
\begin{align*}
\text{14} & \quad \text{O} \quad \text{SH} & \quad \text{O} \quad \text{I} \quad \text{3} \quad \text{C} \quad \text{R} \\
& \quad \text{base} & \quad \text{THF, 5-10 min} & \quad \text{17}
\end{align*}
\]

(4-Methoxybenzyl)(prop-1-yn-1-yl)sulfane (17a)

A 25 mL round bottom flask was charged with a magnetic stirring bar, 4-methoxybenzylmercaptane (14) (79.0 mg, 0.500 mmol, 1.00 eq.) and dry THF (6.25 mL) at room temperature. The flask was capped with a glass stopper and heated at 40 °C. After 1
minute, the glass stopper was quickly removed and TMG (63.5 μL, 0.500 mmol, 1.00 eq.) was added. The mixture was stirred (capped again) for 30 seconds, after which Me-EBX (1b) (157 mg, 0.549 mmol, 1.10 eq.) was added in one portion. The resultant mixture was stirred at 50 °C for exactly 2 minutes. Next, the mixture was diluted with water (10 mL) and extracted with EtOAc (3 x 10 mL). The combined organic layers were dried over MgSO₄, filtered and concentrated in vacuo. The crude was then purified by flash column chromatography using EtOAc:pentane 1:99 as mobile phase affording 17a (72.8 mg, 0.379 mmol, 77%) as a colorless oil. Rf (EtOAc:pentane 1:24, KMnO₄ staining) = 0.24. ¹H NMR (CDCl₃, 400 MHz): δ 7.31-7.23 (m, 2 H, ArH), 6.93-6.83 (m, 2 H, ArH), 3.88 (s, 2 H, ArCH₂), 3.81 (s, 3 H, OCH₃), 1.95 (s, 3 H, CCCH₃). ¹³C NMR (CDCl₃, 100 MHz): δ 159.2, 130.2, 129.1, 114.0, 91.2, 67.6, 55.3, 39.7, 5.1. IR ν 2913 (w), 1610 (m), 1510 (s), 1463 (w), 1302 (w), 1248 (s), 1177 (m), 1034 (m), 832 (m). HRMS (ESI) C₁₁H₁₃OS⁺ [M+H]⁺ calc. = 193.0682; [M+H]⁺ obs. = 193.0684.

(4-Methoxybenzyl)(oct-1-yn-1-yl)sulfane (17b)

A 25 mL round bottom flask was charged with a magnetic stirring bar, 4-methoxybenzylmercaptane (44) (79.0 mg, 0.500 mmol, 1.00 eq.) and dry THF (6.25 mL) at room temperature. The flask was capped with a glass stopper and heated at 40 °C. After 1 minute, the glass stopper was quickly removed and TMG (63.5 μL, 0.500 mmol, 1.00 eq.) was added. The mixture was stirred (capped again) for 30 seconds, after which Hex-EBX (1d) (196 mg, 0.550 mmol, 1.10 eq.) was added in one portion. The resultant mixture was stirred at room temperature for 5 minutes. Next, the mixture was diluted with water (10 mL) and extracted with EtOAc (3 x 10 mL). The combined organic layers were dried over MgSO₄, filtered and concentrated in vacuo. The crude was then purified by flash column chromatography using EtOAc:pentane 1:99 as mobile phase affording 17b (111 mg, 0.422 mmol, 84%) as a colorless oil. Rf (pentane, KMnO₄ staining) = 0.31. ¹H NMR (CDCl₃, 400 MHz ): δ 7.26-7.19 (m, 2 H, ArH), 6.87-6.80 (m, 2 H, ArH), 3.84 (s, 2 H, ArCH₂), 3.77 (s, 3 H, OCH₃), 2.25 (t, 2 H, J = 7.0 Hz, CCCH₂), 1.50-1.40 (m, 2 H), 1.36-1.18 (m, 6 H), 0.88 (t, 3 H, J = 6.9 Hz, CH₂CH₂). ¹³C NMR (CDCl₃, 100 MHz): δ 159.2, 130.2, 129.2, 114.0, 96.0, 68.3, 55.3, 39.9, 31.5, 28.8, 28.6, 22.7, 20.2, 14.2. IR ν 2934 (m), 2857 (w), 1611 (w), 1511
(5-Chloropent-1-yn-1-yl)(4-methoxybenzyl)sulfane (17c)

A 25 mL round bottom flask was charged with a magnetic stirring bar, 4-methoxybenzylmercaptane (44) (79.0 mg, 0.500 mmol, 1.0 eq.), DBU (75.0 μL, 0.500 mmol, 1.00 eq.) and dry THF (6.25 mL) at room temperature. After stirring the reaction mixture for 30 seconds at room temperature, ClC\(_3\)-EBX (1j) (192 mg, 0.550 mmol, 1.10 eq.) was added as a solid in one portion. The resulting reaction mixture was stirred for 5 minutes at room temperature. Next, the mixture was diluted with water (10 mL) and extracted with EtOAc (3 x 15 mL). The combined organic layers were dried over MgSO\(_4\), filtered and concentrated in vacuo. The crude was then purified by flash column chromatography using EtOAc:pentane 1:99 as mobile phase affording 17c (97.1 mg, 0.381 mmol, 76%) as a colorless oil. Rf (EtOAc:pentane 1:19, KMnO\(_4\) staining) = 0.68. \(^1\)H NMR (CDCl\(_3\), 400 MHz): \(\delta\) 7.32-7.21 (m, 2 H, ArH), 6.97-6.82 (m, 2 H, ArH), 3.87 (s, 3 H, OC\(_3\)H\(_3\)), 3.82 (s, 2 H, ArCH\(_2\)), 3.55 (t, 2 H, J = 6.4 Hz, ClCH\(_2\)), 2.48 (t, 2 H, J = 6.7 Hz, C\(_2\)CH\(_3\)), 1.91 (p, 2 H, J = 6.5 Hz, ClCH\(_2\)CH\(_2\)). \(^{13}\)C NMR (CDCl\(_3\), 100 MHz): \(\delta\) 159.2, 130.2, 128.9, 114.0, 93.8, 69.7, 55.3, 43.7, 39.6, 31.4, 17.6. IR ν 2942 (w), 2865 (w), 2104 (w), 1703 (w), 1600 (m), 1510 (m), 1463 (w), 1255 (s), 1214 (m), 1168 (s), 1032 (m), 886 (s). HRMS (ESI) C\(_{16}\)H\(_{23}\)O\(_2\)S\(_{1}\) [M+H]\(^+\) calc. = 263.1464; [M+H]\(^+\) obs. = 263.1461.

4-((4-Methoxybenzyl)thio)but-3-yn-1-ol (17d)

A 25 mL round bottom flask was charged with a magnetic stirring bar, 4-methoxybenzylmercaptane (44) (79.0 mg, 0.500 mmol, 1.00 eq.) and dry THF (6.25 mL) at room temperature. The flask was capped with a glass stopper and heated at 40 °C. After 1 minute, the glass stopper was quickly removed and TMG (63.5 μL, 0.500 mmol, 1.00 eq.) was added. The mixture was stirred (capped again) for 30 seconds, after which OH-ethyl-EBX (1m) (174 mg, 0.550 mmol, 1.10 eq.) was added in one portion. It took 10 minutes for
all the OH-ethyl-EBX (1m) to dissolve and form a clear reaction mixture. The resultant mixture was stirred at room temperature for 10 minutes. Next, the mixture was diluted with water (10 mL) and extracted with EtOAc (3 x 10 mL). The combined organic layers were dried over MgSO₄, filtered and concentrated in vacuo. The crude was then purified by flash column chromatography using EtOAc:petane 3:7 as mobile phase affording 17d (64.8 mg, 0.291 mmol, 59%) as a colorless oil. Rf (EtOAc:petane 3:7, KMnO₄ staining) = 0.45. ¹H NMR (CDCl₃, 400 MHz): δ 7.29-7.22 (m, 2 H, ArH), 6.91-6.84 (m, 2 H, ArH), 3.88 (s, 2 H, ArCH₂), 3.81 (s, 3 H, OCH₃), 3.64 (t, 2 H, J = 6.1 Hz, CH₂CH₂OH), 2.54 (t, 2 H, J = 6.2 Hz, CCCH₂), 1.78 (bs, 1 H, CH₂O). ¹³C NMR (CDCl₃, 100 MHz): δ 159.3, 130.3, 128.9, 114.1, 92.3, 71.0, 61.2, 55.4, 39.6, 24.7. IR ν 3387 (w), 2910 (w), 1610 (m), 1510 (s), 1243 (s), 1177 (m), 1033 (s), 834 (m). HRMS (ESI) C₁₂H₁₅O₂S⁺ [M+H]⁺ calc. = 223.0787; [M+H]⁺ obs. = 223.0784.

(2R,3R,4S,5R,6S)-2-(Acetoxymethyl)-6-(((trimethylsilyl)ethynyl)thio)tetrahydro-2H-pyran-3,4,5-triyi triacetate (18a)

Following general procedure GPC, the crude reaction mixture was concentrated in vacuo and purified by flash chromatography using EtOAc:petane 2:5 as mobile phase affording 18a (183 mg, 0.336 mmol, 84%) as a white solid. Rf (EtOAc:petane 2:5, KMnO₄ staining) = 0.7. Melting point = 87.2-89.6 °C. ¹H NMR (CDCl₃, 400 MHz ) : δ 5.30-5.17 (m, 2 H, H₂ & H₃), 5.09 (dq, 1 H, J = 9.6, 5.1, 4.6 Hz, H₄), 4.61-4.51 (m, 1 H, H₁), 4.26 (dd, 1 H, J = 12.5, 4.8 Hz, H₆), 4.13 (dd, 1 H, J = 12.5, 2.1 Hz, H₅), 3.76 (ddd, 1 H, J = 10.1, 4.7, 2.2 Hz, H₃), 2.08 (s, 3 H, COCH₃), 2.02 (s, 3 H, COCH₃), 2.01 (s, 3 H, COCH₃), 1.12-1.07 (m, 21 H, TIPS). ¹³C NMR (CDCl₃, 100 MHz): δ 170.8, 170.4, 169.4, 169.0, 102.4, 89.0, 85.1, 76.6, 74.0, 70.0, 67.9, 62.1, 20.9, 20.8, 20.8, 20.7, 18.7, 11.4. IR ν 2923 (w), 2863 (w), 2102 (w), 1756 (s), 1742 (s), 1365 (w), 1362 (w), 1231 (s), 1207 (s), 1103 (m), 1053 (s), 914 (w), 884 (w), 860 (w). HRMS (ESI) C₂₅H₄₀NaO₉SSi⁺ [M+Na]⁺ calc. = 567.2055; [M+Na]⁺ obs. = 567.2034.

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²⁰ Hydrogens were assigned by analogy with similar compounds reported in the literature: Floyd, N.; Vijayakrishnan, B.; Koepppe, J. R.; Davis, B. G. Angew. Chem., Int. Ed. 2009, 48, 7798.
(2R,3R,4S,5R,6S)-2-(acetoxymethyl)-6-((4-azidobut-1-yn-1-yl)thio)tetrahydro-2H-pyran-3,4,5-triyl triacetate (18b)

Following general procedure GPC, the crude reaction mixture was concentrated in vacuo and purified by flash chromatography using EtOAc:pentane 1:2 as mobile phase affording **18b** (81.0 mg, 0.177 mmol, 45%) as a colorless oil. Rf (EtOAc:pentane 1:2, KMnO₄ staining) = 0.35. ¹H NMR (CDCl₃, 400 MHz): δ 5.27-5.18 (m, 2 H, H₃ & H₂), 4.54-4.45 (m, 1 H, H₄), 4.24 (dd, 1 H, J = 12.5, 4.9 Hz, H₆), 4.13 (dd, 1 H, J = 12.5, 2.3 Hz, H₆), 3.74 (ddd, 1 H, J = 10.0, 4.9, 2.3 Hz, H₅) 3.42 (t, 2 H, J = 6.7 Hz, CH₂CH₂N₃), 2.62 (t, 2 H, J = 6.7 Hz, CCCH₂), 2.07 (s, 3 H, COC₃H), 1.99 (s, 3 H, COCH₃). ¹³C NMR (CDCl₃, 100 MHz): δ 170.7, 170.3, 169.4, 169.1, 95.2, 84.1, 76.5, 74.0, 69.6, 67.9, 65.2, 62.1, 49.6, 21.4, 20.8, 20.7, 20.7, 20.7. IR ν 2360 (w), 2111 (w), 1751 (s), 1433 (w), 1370 (m), 1228 (m). HRMS (ESI) C₁₈H₂₃N₃NaO₉S⁺ [M+Na]⁺ calc. = 480.1047; [M+Na]⁺ obs.= 480.1051.

(2R,3R,4S,5R,6S)-2-(acetoxymethyl)-6-((7-hydroxyhept-1-yn-1-yl)thio)tetrahydro-2H-pyran-3,4,5-triyl triacetate (18c)

Following general procedure A, the crude reaction mixture was concentrated in vacuo and purified by flash chromatography using EtOAc: pentane 1:2 as mobile phase affording **18c** (156 mg, 0.328 mmol, 82%) as colorless oil. Rf (EtOAc:pentane 2:1, KMnO₄ staining) = 0.5. ¹H NMR (CDCl₃, 400 MHz): δ 5.25 (dt, 2 H, J = 18.6, 9.3 Hz, H₃ & H₂), 4.44 (d, 1 H, J = 9.3 Hz, H₄), 4.26 (dd, 1 H, J = 12.4, 4.9 Hz, H₆), 3.76 (ddd, 1 H, J = 12.4, 2.2 Hz, H₅), 2.37 (t, 2 H, J = 6.4 Hz, CCCH₂), 2.08 (s, 3 H, COCH₃), 1.77 (bs, 1 H, CH₂OH), 1.65-1.46 (m, 6 H, CH₂). ¹³C NMR (CDCl₃, 100 MHz): δ 170.8, 170.4, 169.7, 169.4, 99.4, 83.9, 76.4, 74.1. S62
68.0, 62.8, 62.2, 32.4, 28.1, 25.1, 20.9, 20.8, 20.8, 20.8, 20.8, 20.3. IR ν 2942 (w), 2196 (w), 1756 (s), 1373 (m), 1229 (s), 1053 (m), 915 (w). HRMS (ESI) C_{21}H_{31}O_{10}S \ [M+H]^+ \text{ calc.} = 475.1632; [M+H]^+ \text{ obs.} = 475.1624.

\( (2R,3S,4S,5R,6S)-2-\text{(hydroxymethyl)}-6-(((\text{trimethylsilyl})\text{ethynyl})\text{thio})\text{tetrahydro-2H-pyran-3,4,5-triol} \ (18d) \)

Following general procedure GPD, the crude reaction mixture was concentrated in vacuo and purified by flash chromatography using DCM:methanol 10:1 as mobile phase affording \( 18d \) (122 mg, 0.324 mmol, 81%) as a white solid. Rf (DCM:methanol 10:1, KMnO_4 staining) = 0.45. Melting point = 120.1-122.3 °C. \(^1\)H NMR (CD_3OD, 400 MHz ;\): \( \delta \) 4.36 (d, 1 H, \( J = 9.4 \) Hz, \( H_1 \)), 3.87 (dd, 1 H, \( J = 12.1, 2.0 \) Hz, \( H_6 \)), 3.63 (dd, 1 H, \( J = 12.1, 6.1 \) Hz, \( H_5 \)), 3.54 (t, 1 H, \( J = 9.1 \) Hz, \( H_2 \)), 3.40 (t, 1 H, \( J = 8.8 \) Hz, \( H_3 \)), 3.37-3.32 (m, 1 H, \( H_3 \)), 3.29-3.22 (m, 1 H, \( H_4 \)), 1.17-1.07 (m, 21 H, TIPS). \(^{13}\)C NMR (CD_3OD, 400 MHz): \( \delta \) 100.9, 93.1, 88.3, 82.8, 79.3, 73.4, 71.3, 63.1, 19.1, 12.6. IR ν 3381 (s), 3256 (m), 2108 (w), 1464 (m), 1367 (w), 994 (s), 884 (s), 782 (m). HRMS (ESI) C_{17}H_{32}NaO_{5}S\text{Si}^+ \ [M+Na]^+ \text{ calc.} = 399.1632; [M+Na]^+ \text{ obs.} = 399.1632.

\( (2S,3R,4S,5S,6R)-2-\text{(hexadec-1-yn-1-thio)}-6-\text{(hydroxymethyl)}\text{tetrahydro-2H-pyran-3,4,5-triol} \ (18e) \)

Following general procedure GPD, the crude reaction mixture was concentrated in vacuo and purified by flash chromatography using EtOAc:pentane 10:1 to 20:1 as mobile phase affording \( 18e \) (100 mg, 0.240 mmol, 60%) as a white solid. Rf (EtOAc:pentane 10:1, KMnO_4 staining) = 0.22. Melting point = 74.5-77.2 °C. \(^1\)H NMR (CD_3OD, 400 MHz ;): \( \delta \) 4.28 (d, 1 H, \( J = 9.2 \) Hz, \( H_1 \)), 3.87 (dd, 1 H, \( J = 12.1, 2.0 \) Hz, \( H_6 \)), 3.66 (dd, 1 H, \( J = 12.1, 5.5 \) Hz, \( H_5 \)), 3.47 (t, 1 H, \( J = 9.0 \) Hz, \( H_2 \)), 3.39 (t, 1 H, \( J = 8.6 \) Hz, \( H_3 \)), 3.36-3.32 (m, 1 H, \( H_3 \)), 3.30-3.25 (m, 1
H, $H_d$ \(^{17}\), 2.32 (t, $J = 6.9$ Hz, 2H, CCCH\(_2\)CH\(_2\)), 1.52 (dt, 2 H, $J = 14.1$, 6.7 Hz, CCCH\(_2\)CH\(_2\)), 1.47-1.34 (m, 2 H), 1.36-1.22 (m, 20 H), 0.90 (t, 3 H, $J = 6.8$ Hz, CH\(_2\)CH\(_3\)). \(^{13}\)C NMR (CD\(_3\)OD, 400 MHz); \(\delta\) 98.2, 88.1, 82.6, 79.4, 73.3, 71.3, 65.0, 62.9, 33.1, 30.8, 30.8, 30.7, 30.5, 30.3, 30.0, 29.8, 23.8, 21.0, 14.4. IR \(\nu\) 3363 (m), 2937 (s), 2842 (m), 2189 (w), 1636 (w), 1455 (m), 1046 (s), 760 (s). HRMS (ESI) C\(_{22}\)H\(_{41}\)O\(_5\)S\(^+\) [M+H]\(^+\) calc. = 417.2669; [M+H]\(^+\) obs. = 417.2672.

Ethyl 2-((S)-2-(((benzyloxy)carbonyl)amino)-3-(1H-indol-3-yl)propanamido)-3-(hexadec-1-yn-1-ylthio)propanoate (19a)

Following general procedure GPE, the crude reaction mixture was concentrated in vacuo and purified by flash chromatography using EtOAc:pentane 2:5 as mobile phase affording 19a (114 mg, 0.165 mmol, 83%) as a white solid. Rf (EtOAc:pentane 2:5, KMnO\(_4\) staining) = 0.42. Melting point = 129.0-131.5 °C. \(^1\)H NMR (CDCl\(_3\), 400 MHz); \(\delta\) 8.09 (s, 1 H), 7.68 (d, 1 H, $J = 7.9$ Hz), 7.42-7.29 (m, 6 H), 7.19 (t, 1 H, $J = 7.6$ Hz), 7.15-7.01 (m, 2 H), 6.60 (d, 1 H, $J = 7.4$ Hz), 5.50 (d, 1 H, $J = 8.0$ Hz), 5.18-5.07 (m, 2 H), 4.80-4.70 (m, 1 H), 4.56 (s, 1 H), 4.28-4.00 (m, 2 H), 3.40 (d, 1 H, $J = 13.4$ Hz), 3.20 (dd, 1 H, $J = 14.6$, 7.4 Hz), 3.03 (d, 2 H, $J = 4.8$ Hz), 2.07 (t, 2 H, $J = 7.1$ Hz, CCCH\(_2\)CH\(_2\)), 1.44-1.35 (m, 2 H), 1.33-1.19 (m, 25 H), 0.88 (t, 3 H, $J = 6.6$ Hz, CH\(_2\)CH\(_2\)CH\(_3\)). \(^{13}\)C NMR (CDCl\(_3\), 100 MHz); \(\delta\) 171.1, 169.4, 156.0, 136.4, 136.3, 128.7, 128.3, 128.2, 127.6, 123.6, 122.5, 120.0, 118.9, 111.4, 110.4, 95.0, 67.2, 67.0, 62.0, 55.6, 52.4, 37.3, 32.1, 29.8, 29.8, 29.7, 29.7, 29.5, 29.3, 29.0, 28.8, 28.7, 22.8, 20.0, 14.3, 14.2. IR \(\nu\) 3300 (m), 2923 (s), 2853 (w), 1724 (m), 1652 (m), 1544 (s), 1461 (w), 1254 (m), 1043 (w). HRMS (ESI) C\(_{46}\)H\(_{56}\)N\(_3\)O\(_5\)S\(^+\) [M+H]\(^+\) calc. = 690.3935; [M+H]\(^+\) obs. = 690.3945.
Ethyl 2-((S)-2-(((benzoyloxy)carbonyl)amino)-3-(1H-indol-3-yl)propanamido)-3-((5-chloropent-1-yn-1-yl)(thio)propanoate (19b)

Following general procedure GPE, the crude reaction mixture was concentrated in vacuo and purified by flash chromatography using EtOAc:pentane 1:2 to 1:1 as mobile phase affording 19b (77.0 mg, 0.135 mmol, 68%) as a white solid. Rf (EtOAc:pentane 1:2, KMnO4 staining) = 0.2. Melting point = 141.3-143.0 °C. 1H NMR (CDCl3, 400 MHz): δ 8.27 (s, 1 H), 7.65 (d, 1 H, J = 7.9 Hz), 7.39-7.29 (m, 6 H), 7.18 (dd, 1 H, J = 8.1, 6.9, 1.2 Hz), 7.13-7.02 (m, 2 H), 6.67 (d, 1 H, J = 7.5 Hz), 5.56 (d, 1 H, J = 7.8 Hz), 5.15-5.09 (m, 2 H), 4.76 (dt, 1 H, J = 7.5, 4.9 Hz), 4.57 (d, 1 H, J = 7.5 Hz), 4.27-4.02 (m, 2 H), 3.53 (t, 2 H, J = 6.3 Hz, CH2CH2Cl), 3.38 (dd, 1 H, J = 14.9, 5.2 Hz), 3.20 (dd, 1 H, J = 14.5, 7.3 Hz), 3.07-2.95 (m, 2 H), 2.28 (t, 2 H, J = 6.8 Hz, CCCH2CH2), 1.82 (p, 2 H, J = 6.6 Hz, CCCH2CH2), 1.26 (t, 3 H, J = 7.1 Hz, CO2CH2CH3). 13C NMR (CDCl3, 100 MHz): δ 171.2, 169.4, 156.0, 136.4, 136.3, 128.6, 128.3, 128.2, 127.5, 123.6, 122.4, 119.9, 118.8, 111.4, 110.2, 92.7, 68.6, 67.2, 62.1, 55.6, 52.3, 43.7, 37.2, 31.2, 28.6, 17.4, 14.1. IR ν 3061 (w), 2955 (w), 1716 (s), 1672 (s), 1513 (s), 1453 (m), 1343 (m), 1223 (s), 1031 (m), 748 (s). HRMS (ESI) C29H32ClN3NaO5S+ [M+Na]⁺ clac. = 592.1643; [M+Na]⁺ obs.= 592.1637.
Ethyl 3-((3-(benzyloxy)-3-methylbut-1-yn-1-yl)thio)-2-((S)-2-(((benzyloxy)carbonyl)amino)-3-(1H-indol-3-yl)propanamido)propanoate (19c)

Following general procedure GPE, the crude reaction mixture was concentrated in vacuo and purified by flash chromatography using EtOAc:pentane 1:3 as mobile phase affording **19c** (104 mg, 0.162 mmol, 81%) as a light yellow oil. Rf (EtOAc:pentane 2:5, KMnO₄ staining) = 0.24. ¹H NMR (CDCl₃, 400 MHz): δ 8.18 (s, 1 H), 7.66 (d, 1 H, J = 7.9 Hz), 7.43-7.25 (m, 11 H), 7.20 (t, 1 H, J = 7.4, 1.2 Hz), 7.12 (t, 1 H, J = 7.5 Hz), 7.05 (s, 1 H), 6.62 (d, 1 H, J = 7.6 Hz), 5.55 (d, 1 H, J = 7.0 Hz), 5.18-5.11 (m, 2 H), 4.75 (dt, 1 H, J = 7.3, 5.2 Hz), 4.62-4.51 (m, 3 H), 4.24-4.10 (m, 2 H), 3.45-3.30 (m, 1 H), 3.21 (dd, 1 H, J = 14.6, 7.3 Hz), 3.15-3.00 (m, 2 H), 1.53 (s, 6 H, 2 x C₆H₃), 1.25 (t, 3 H, J = 7.2 Hz, CO₂CH₂CH₃). ¹³C NMR (CDCl₃, 100 MHz): δ 171.3, 169.3, 156.0, 139.0, 136.3, 136.2, 128.6, 128.4, 128.3, 128.2, 127.8, 127.5, 123.5, 122.4, 119.9, 118.8, 111.4, 110.1, 96.4, 73.2, 71.4, 67.2, 66.5, 62.1, 55.6, 51.9, 37.6, 28.9, 28.8, 28.5, 14.1. IR ν 3322 (m), 3061 (w), 2984 (m), 2935 (w), 2167 (w), 1709 (s), 1668 (s), 1498 (s), 1457 (m), 1232 (s), 1149 (s), 1051 (s), 746 (s). HRMS (ESI) C₃₆H₄₀N₃O₆S⁺ [M+H]⁺ calc. = 642.2632; [M+H]⁺ obs. = 642.2610.
Ethyl 3-((4-azidobut-1-yn-1-yl)thio)-2-((S)-2-(((benzyloxy)carbonyl)amino)-3-(1H-indol-3-yl)propanamido)propanoate (19d)

Following general procedure **GPE**, the crude reaction mixture was concentrated in vacuo and purified by flash chromatography using EtOAc:pentane 2:3 as mobile phase affording 19d (67 mg, 0.12 mmol, 60%) as a light yellow color solid. Rf (EtOAc:pentane 2:3, KMnO₄ staining) = 0.5. Melting point = 112.1-115.3 °C. \(^1\)H NMR (CDCl₃, 400 MHz): δ 8.13 (s, 1 H), 7.68 (d, 1 H, J = 7.2 Hz), 7.42-7.28 (m, 6 H), 7.19 (ddd, 1 H, J = 8.2, 7.1, 1.2 Hz), 7.15-7.05 (m, 2 H), 6.59 (d, 1 H, J = 7.5 Hz), 5.54 (d, 1 H, J = 7.9 Hz), 5.17-5.07 (m, 2 H), 4.78 (dt, 1 H, J = 7.5, 4.9 Hz), 4.57 (d, 1 H, J = 7.0 Hz), 4.25-4.03 (m, 2 H), 3.45-3.35 (m, 1 H), 3.26-3.16 (m, 3 H), 3.13-2.96 (m, 2 H), 2.33 (t, 2 H, J = 6.7 Hz, CCCH₂CH₂N₃), 1.26 (t, 3 H, J = 7.1 Hz, CO₂CH₂CH₃). \(^1^3\)C NMR (CDCl₃, 100 MHz): δ 171.2, 169.3, 156.0, 136.4, 136.3, 128.6, 128.3, 128.2, 127.6, 123.7, 122.4, 119.9, 118.8, 111.4, 110.2, 90.6, 70.4, 67.2, 62.1, 55.6, 52.5, 49.7, 36.9, 28.7, 20.9, 14.2. IR ν 3324 (w), 2929 (w), 2076 (w), 1718 (m), 1672 (m), 1512 (m), 1220 (m), 778 (s). HRMS (ESI) C₂₈H₃₀N₆NaO₂S⁺ [M+Na]⁺ calc. = 585.1891; [M+Na]⁺ obs. = 585.1897.
Ethyl 2-((S)-2-((benzyloxy)carbonyl)amino)-3-(1H-indol-3-yl)propanamido)-3-((7-hydroxyhept-1-yn-1-yl)thio)propanoate (19e)

Following general procedure GPE, the crude reaction mixture was concentrated in vacuo and purified by flash chromatography using EtOAc:pentane 2:1 as mobile phase affording 19e (84.0 mg, 0.145 mmol, 73%) as a white solid. Rf (EtOAc:pentane 2:1, KMnO₄ staining) = 0.59. Melting point = 123.5-124.0 °C. ¹H NMR (CDCl₃, 400 MHz): δ 8.25 (s, 1 H), 7.68 (d, 1 H, J = 7.9 Hz), 7.40-7.28 (m, 6 H), 7.18 (t, 1 H, J = 7.5 Hz), 7.15-7.05 (m, 2 H), 6.65 (d, 1 H, J = 7.1 Hz), 5.59 (d, 1 H, J = 7.9 Hz), 5.17-5.08 (m, 2 H), 4.76 (dt, 1 H, J = 7.5, 5.2 Hz), 4.56 (d, 1 H, J = 6.7 Hz), 4.23-4.08 (m, 2 H), 3.62 (t, 2 H, J = 6.2 Hz, CH₂OH), 3.44-3.28 (m, 1 H), 3.20 (dd, 1 H, J = 14.6, 7.5 Hz), 3.10-2.91 (m, 2 H), 2.22 – 2.05 (m, 2 H, CCCH₂), 1.77 (bs, 1 H, CH₂OH), 1.52 (p, 2 H, J = 6.6 Hz), 1.47-1.35 (m, 4 H), 1.25 (t, 3 H, J = 7.1 Hz, CO₂CH₂CH₃). ¹³C NMR (CDCl₃, 100 MHz): δ 171.3, 169.5, 156.1, 136.4, 136.3, 128.7, 128.3, 128.2, 127.6, 123.7, 122.4, 119.9, 118.9, 111.4, 110.3, 94.9, 67.4, 67.2, 62.7, 62.1, 55.6, 52.5, 37.1, 32.2, 28.7, 28.2, 25.0, 20.0, 14.2. IR ν 3340 (w), 2938 (w), 1731 (s), 1671 (s), 1571 (s), 1218 (m), 1032 (w), 752 (s). HRMS (ESI) C₃₁H₃₈N₃O₆S⁺ [M+H]⁺ calc. = 580.2476; [M+H]⁺ obs. = 580.2472.
Ethyl 2-((S)-2-(((benzyloxy)carbonyl)amino)-3-(1H-indol-3-yl)propanamido)-3-((mesitylethynyl)thio)propanoate (19f)

Following general procedure GPE, the crude reaction mixture was concentrated in vacuo and purified by flash chromatography using EtOAc:pentane 1:2 as mobile phase affording 19f (98 mg, 0.16 mmol, 80%) as a white solid. Rf (EtOAc:pentane 1:2, KMnO₄ staining) = 0.32. Melting point = 147.0-149.0 °C. ¹H NMR (CDCl₃, 400 MHz): δ 8.18 (s, 1 H), 7.61 (d, 1 H, J = 7.9 Hz), 7.39-7.29 (m, 6 H), 7.18 (ddd, 1 H, J = 8.1, 7.0, 1.2 Hz), 7.09 (t, 1 H, J = 7.5 Hz), 7.01 (s, 1 H), 6.83 (s, 2 H), 6.76 (d, 1 H, J = 7.3 Hz), 5.46 (d, 1 H, J = 7.7 Hz), 5.14-5.04 (m, 2 H), 4.81 (dt, 1 H, J = 7.3, 5.0 Hz), 4.57 (d, 1 H, J = 6.8 Hz), 4.18-3.85 (m, 2 H), 3.38-3.27 (m, 1 H), 2.34 (s, 6 H, 2 x ArCH₃), 2.26 (s, 3 H, ArCH₃), 1.17 (t, 3 H, J = 7.1 Hz, CO₂CH₂CH₃). ¹³C NMR (CDCl₃, 100 MHz): 171.3, 169.4, 156.0, 140.8, 138.1, 136.3, 136.3, 128.6, 128.3, 128.2, 127.8, 127.5, 123.4, 122.4, 119.9, 119.8, 118.8, 111.4, 110.2, 91.1, 84.4, 67.2, 62.1, 55.7, 52.2, 38.2, 28.4, 21.4, 21.1, 14.0. IR ν 3301 (m), 2161 (w), 1729 (m), 1692 (m), 1692 (s), 1536 (s), 1250 (s), 1041 (m), 904 (s), 853 (w). HRMS (ESI) C₃₅H₃₈N₅O₅S⁺ [M+H]⁺ calc. = 612.2527; [M+H]⁺ obs.= 612.2538.

(R)-2-Amino-1-((3,3-dimethylbut-1-yn-1-yl)thio)hexan-3-one (19g)

A 25 mL round bottom flask was charged with a magnetic stirring bar, L-cysteine ethyl ester hydrochloride (16b) (74.3 mg, 0.400 mmol, 1.00 eq.), TMG (110 μL, 0.880 mmol, 2.20 eq.),
THF (5.0 mL) and water (0.5 mL). After stirring the resulting solution for 5 minutes at room temperature, t-Bu-EBX (If) (131 mg, 0.400 mmol, 1.00 eq.) was added as a solid in one portion. The resulting reaction mixture was stirred for 10 minutes at room temperature. Next, the mixture was diluted with water (10 mL) and extracted with EtOAc (3 x 15 mL). The combined organic layers were dried over MgSO$_4$, filtered and concentrated in vacuo. The crude oil was purified by flash chromatography using EtOAc:pentane 1:1 as mobile phase affording 19g (86.0 mg, 0.375 mmol, 94%) as a colorless oil. Rf (EtOAc:pentane 1:1, KMnO$_4$ staining) = 0.48. $^1$H NMR (CDCl$_3$, 400 MHz): δ 4.20 (q, 2 H, $J$ = 7.1 Hz, COC$_2$H$_5$CH$_3$), 3.79 (dd, 1 H, $J$ = 8.2, 4.2 Hz, CHCH$_2$S), 3.12 (dd, 1 H, $J$ = 13.2, 4.2 Hz, CHCH$_2$S), 2.75 (dd, 1 H, $J$ = 13.2, 8.2 Hz, CHCH$_2$S), 1.88 (s, 2 H, NH$_2$), 1.28 (t, 3 H, $J$ = 7.1 Hz, CH$_2$CH$_3$), 1.20 (s, 9 H, C(CH$_3$)$_3$). $^{13}$C NMR (CDCl$_3$, 100 MHz): δ 173.4, 102.9, 66.0, 61.5, 54.2, 40.6, 31.0, 28.8, 14.3. IR 3386 (w), 2972 (m), 2869 (w), 2362 (w), 1738 (s), 1598 (w), 1459 (w), 1368 (w), 1251 (s), 1191 (s), 1107 (w), 1030 (m), 859 (w). HRMS (ESI) C$_{11}$H$_{20}$NO$_2$S$^+$ [M+H]$^+$ calc. = 230.1209; [M+H]$^+$ obs.= 230.1212.

(S)-1-((S)-3-(Hexadec-1-yn-1-ylthio)-2-methylpropanoyl)pyrrolidine-2-carboxylic acid (21)

A 25 mL round bottom flask was charged with a magnetic stirring bar, captopril (20) (130 mg, 0.600 mmol, 1.00 eq.) and triazabicyclodecene (TBD, 167 mg, 0.600 mmol, 1.00 eq.). The mixture was dissolved in THF (7.0 mL) and water (0.5 mL) to achieve a thiol concentration of 80 mM. Upon dissolution, the corresponding R-EBX reagent (1e, 309 mg, 0.660 mmol, 1.10 eq.) was added as a solid in one portion. The resulting reaction mixture was stirred in an open flask for 5 minutes at room temperature and then quenched by adding 1.0 M aq. HCl (15 mL). The mixture was extracted with EtOAc (3 x 15 mL) and the combined organic layers were dried over MgSO$_4$, filtered and concentrated in vacuo. The crude product was purified by column chromatography (pentane:EtOAc 20:1 to 7:3) affording 21 (247 mg, 0.563 mmol, 94%) as a white solid. R$_f$ (pentane:EtOAc 1:1 and 1% acetic acid) = 0.37. Melting point = 60.4-63.0 °C. $^1$H NMR (CDCl$_3$, 400 MHz): δ 11.0 (bs, 1 H, COOH), 4.58 (dd, 1 H, $J$ = 7.9, 3.5 Hz, NCH), 3.78-3.69 (m, 1 H, CH$_2$N), 3.68-3.59 (m, 1 H, CH$_2$N), 3.14-
3.03 (m, 1 H), 2.91 (dd, 1 H, J = 13.0, 8.8 Hz, CHCH₂S), 2.67 (dd, 1 H, J = 13.0, 5.4 Hz, CHCH₂S), 2.26 (t, 2 H, J = 7.0 Hz, CCCH₂CH₂), 2.23-1.96 (m, 4 H), 1.47 (p, 2 H, J = 7.0 Hz, CCCH₂CH₂), 1.40-1.14 (m, 25 H), 0.85 (t, 3 H, J = 6.7 Hz, CH₂CH₃). ¹³C NMR (CDCl₃, 100 MHz): δ 175.4, 174.5, 95.0, 68.0, 59.4, 47.6, 38.5, 32.0, 29.8, 29.7, 29.4, 29.2, 29.0, 28.9, 28.3, 24.9, 22.8, 20.2, 16.9, 14.2. IR ν 2927 (w), 2855 (w), 1722 (w), 1633 (w), 1465 (w), 1442 (w), 1195 (w), 908 (s), 732 (s). HRMS (ESI) C₂₅H₄₄NO₃S⁺ [M+H]⁺ calc. = 438.3036; [M+H]⁺ obs. = 438.3032.

**Alkynylation of Thioacids**

\[
\begin{align*}
\text{O} & \quad \text{O} \\
\text{R₁}^\text{SH} & \quad \text{O} \quad \text{Me₂N} \quad \text{NMe₂} \\
& \quad \text{MeOH, rt, 5 min} \\
& \quad \text{O} \quad \text{S} \quad \equiv \quad \text{R} \\
\end{align*}
\]

**S-((Triisopropylsilyl)ethynyl) benzothioate (24a)**

Benzothioic acid (22a) (100 mg, 0.707 mmol, 1.00 eq.) was dissolved in dry THF (9 mL) and TIPS-EBX (1c) (300 mg, 0.707 mmol, 1.00 eq.) was added to the solution. The resulting mixture was stirred for 20 minutes at room temperature. Next, the mixture was concentrated under reduced pressure. The crude oil was purified by flash chromatography (pentane) to afford 24a (213 mg, 0.668 mmol, 94%) as a yellow oil. Rf (pentane/EtOAc 10:1, KMN₃O₄) = 0.76. ¹H NMR (CDCl₃, 400 MHz): δ 7.96-7.79 (m, 1 H, ArH), 7.67-7.55 (m, 2 H, ArH), 7.52-7.38 (m, 2 H, ArH), 1.15 (m, 21 H, TIPS). ¹³C NMR (CDCl₃, 100 MHz): δ 187.5, 135.4, 134.3, 129.0, 127.4, 109.4, 85.8, 18.6, 11.3. IR ν 2943 (w), 2866 (w), 2105 (w), 1704 (m), 1462 (w), 1203 (m), 1178 (w), 884 (s), 859 (s), 735 (m), 675 (s). HRMS (ESI) C₁₈H₂₇OSSi⁺ [M+H]⁺ calc. =319.1546; [M+H]⁺ obs. = 319.1532.

**S-((Triisopropylsilyl)ethynyl) 3-methoxybenzothioate (24b)**

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S71
3-Methoxybenzothioic acid (22b) (100 mg, 0.594 mmol, 1.00 eq.) was dissolved in dry THF (8 mL) and TIPS-EBX (1a) (255 mg, 0.594 mmol, 1.00 eq.) was added to the solution. The resulting mixture was stirred for 4 h at room temperature. Next, the mixture was concentrated under reduced pressure. The crude oil was purified by flash chromatography (pentane/EtOAc 99:1 to 5:1) to afford 24b (167 mg, 0.479 mmol, 80%) as a colorless oil. Rf (pentane/EtOAc 5:1, KMnO₄) = 0.81. ¹H NMR (CDCl₃, 400 MHz): δ 7.49-7.41 (m, 1 H, ArH), 7.37 (t, J = 1.3 Hz, 1 H, ArH), 7.37-7.33 (m, 1 H, ArH), 7.13 (ddd, J = 8.3, 2.7, 1.1 Hz, 1 H, ArH), 3.82 (s, 3 H, OCH₃), 1.16 (m, 21 H, TIPS). ¹³C NMR (CDCl₃, 100 MHz): δ 187.2, 156.0, 136.6, 130.0, 120.8, 119.9, 111.5, 109.3, 86.0, 55.4, 18.6, 11.3. IR ν 2945 (w), 2867 (w), 2255 (w), 2106 (w), 1702 (w), 1464 (w), 1264 (w), 906 (s), 728 (s). HRMS (ESI) C₁₉H₂₉O₂SSi⁺ [M+H]⁺ calc. = 349.1652; [M+H]⁺ obs. = 349.1655.

S-((Triisopropylsilyl)ethynyl) 4-methoxybenzothioate (24c)

4-Methoxybenzothioic acid (22c) (93.0 mg, 0.400 mmol, 1.00 eq.) was dissolved in dry THF (5.0 mL) and TIPS-EBX (1a) (171 mg, 0.400 mmol, 1.00 eq.) was added to the solution. The resulting mixture was stirred for 1 h at room temperature. Next, the mixture was concentrated under reduced pressure. The crude oil was purified by flash chromatography (pentane/EtOAc 99:1 to 5:1) to afford 24c (123 mg, 0.353 mmol, 88%) as a colorless oil. Rf (pentane/EtOAc 19:1, KMnO₄) = 0.8. ¹H NMR (CDCl₃, 400 MHz): δ 7.87-7.79 (m, 2 H, ArH), 6.97-6.88 (m, 2 H, ArH), 3.85 (s, 3 H, OCH₃), 1.21-1.09 (m, 21 H, TIPS). ¹³C NMR (CDCl₃, 100 MHz): δ 185.6, 164.6, 129.8, 128.1, 114.3, 108.8, 86.4, 55.7, 18.7, 11.4. IR ν 2944 (w), 2866 (w), 2105 (w), 1703 (m), 1600 (m), 1508 (w), 1463 (w), 1265 (m), 1214 (m), 1168 (s), 1030 (w), 886 (s), 859 (s). HRMS (ESI) C₁₉H₂₇NaO₂SSi⁺ [M+Na]⁺ calc. = 371.1471; [M+Na]⁺ obs. = 371.1479.

S-((Triisopropylsilyl)ethynyl) 4-nitrobenzothioate (24d)
4-Nitrobenzothioic acid (22d) (81.0 mg, 0.400 mmol, 1.00 eq.) was dissolved in dry THF (5.0 mL) and TIPS-EBX (1a) (171 mg, 0.400 mmol, 1.00 eq.) was added to the solution. The resulting mixture was stirred for 1 h at room temperature. Next, the mixture was concentrated under reduced pressure. The crude oil was purified by flash chromatography (pentane/EtOAc 99:1 to 5:1) to afford 24d (135 mg, 0.371 mmol, 93%) as colorless oil. Rf (pentane/EtOAc 19:1, KMnO₄) = 0.81. $^1$H NMR (CDCl₃, 400 MHz): δ 8.36-8.30 (m, 2 H, Ar H), 8.07-8.00 (m, 2 H, Ar H), 1.20-1.05 (m, 21 H, TIPS). $^{13}$C NMR (CDCl₃, 100 MHz): δ 186.8, 151.0, 139.9, 128.5, 124.4, 111.4, 84.0, 18.7, 11.3. IR ν 2945 (w), 2866 (w), 2108 (w), 1705 (m), 1531 (m), 1351 (m), 1194 (m), 900 (m), 860 (s), 844 (s). HRMS (ESI) C₁₈H₂₅AgNO₃SSi⁺ [M+Ag]⁺ calc. = 470.0370; [M+Ag]⁺ obs. = 470.0385.

S-(2-oxooctyl) benzothioate (26)

Benzothioic acid (22a) (100 mg, 0.740 mmol, 1.00 eq.) was dissolved in dry THF (9.5 mL) and Hex-EBX (1d) (260 mg, 0.740 mmol, 1.00 eq.) was added. The resulting mixture was stirred for 20 minutes at room temperature. Next, the mixture was concentrated under reduced pressure and purified by column chromatography (pentane/EtOAc 99:1) to afford the 26 (90.0 mg, 0.330 mmol, 45%) as a yellow light oil. Rf = (pentane/EtOAc 9:1) = 0.4. $^1$H NMR (CDCl₃, 400 MHz): δ 8.06-7.88 (m, 2 H, Ar H), 7.64-7.49 (m, 1 H, Ar H), 7.50-7.37 (m, 2 H, Ar H), 3.91 (s, 2 H, SC₂H₂CO), 2.60 (t, J = 7.4 Hz, 2 H, COCH₂), 1.76-1.43 (m, 2 H), 1.39-1.15 (m, 6 H), 0.86 (t, 3 H, CH₃CH₂). $^{13}$C NMR (CDCl₃, 100 MHz): δ 204.2, 190.5, 136.2, 133.8, 128.7, 127.4, 41.8, 38.9, 31.5, 28.8, 23.8, 22.5, 14.0. IR ν 2925 (w), 2866 (w), 1719 (w), 1664 (s), 1450 (w), 1208 (s), 1177 (w), 914 (s), 774 (m), 688 (s), 649 (m). HRMS (ESI) C₁₅H₂₁O₂S⁺ [M+H]⁺ calc. = 265.1257; [M+H]⁺ obs. = 265.1256.

Bis((triisopropylsilyl)ethynyl)sulfane (25a)
Following general procedure GPF, the crude reaction mixture was concentrated in vacuo and purified by flash chromatography using pentane affording 25a (60.0 mg, 0.152 mmol, 76%) as a colorless oil. Rf (pentane, KMnO$_4$ staining) = 0.85. $^1$H NMR (CDCl$_3$, 400 MHz): δ 1.07 (s, 42 H, TIPS). $^{13}$C NMR (CDCl$_3$, 100 MHz): δ 100.6, 87.9, 18.7, 11.4. IR ν 2944 (m), 2862 (m), 2099 (w), 1464 (w), 989 (w), 883 (m), 844 (s). HRMS (ESI) C$_{22}$H$_{43}$SSi$_2$ $^{+}$ [M+H]$^+$ calc. = 395.2619; [M+H]$^+$ obs. = 395.2601.

Di(hexadec-1-yn-1-yl)sulfane (25b)

Following general procedure GPF, the crude reaction mixture was concentrated in vacuo and purified by flash chromatography using pentane affording 25b (62.0 mg, 0.131 mmol, 66%) as a white solid. Rf (pentane, KMnO$_4$ staining) = 0.8. Melting point = 35.2-37.5 °C. $^1$H NMR (CDCl$_3$, 400 MHz): δ 2.30 (t, 4 H, J = 7.1 Hz, CCCH$_2$CH$_2$), 1.52 (p, 4 H, J = 7.3 Hz, CCCH$_2$CH$_2$), 1.43-1.31 (m, 4 H), 1.29-1.22 (m, 40 H), 0.88 (t, 6 H, J = 6.8 Hz, CH$_2$CH$_2$). $^{13}$C NMR (CDCl$_3$, 100 MHz): δ 96.4, 62.6, 32.1, 29.9, 29.8, 29.8, 29.7, 29.5, 29.3, 29.0, 28.5, 22.9, 20.2, 14.3. IR ν 2931 (s), 2853 (s), 2200 (w), 1597 (w), 1489 (s), 1444 (m). The characterization data is in accordance with reported literature values.

Bis(phenylethynyl)sulfane (25c)

Following general procedure GPF, the crude reaction mixture was concentrated in vacuo and purified by flash chromatography using pentane affording 25c (14 mg, 0.060 mmol, 30%) as a colorless oil. Rf (pentane, KMnO$_4$ staining) = 0.77. $^1$H NMR (CDCl$_3$, 400 MHz): δ 7.52-7.43 (m, 4 H, ArH), 7.38-7.29 (m, 6 H, ArH). $^{13}$C NMR (CDCl$_3$, 100 MHz): δ 132.1, 129.2, 128.5, 122.3, 94.8, 72.1. IR ν 3060 (w), 2925 (s), 2854 (m), 2176 (w), 1597 (w), 1489 (s), 1444 (m). The characterization data is in accordance with reported literature values.

Bis(3-(benzyloxy)-3-methylbut-1-yn-1-yl)sulfane (25d)

21 Voets, M.; Smet, M.; Dehaen, W. J. Chem. Soc., Perkins Trans. 1 1999, 1473.
Following general procedure GPF, the crude reaction mixture was concentrated in vacuo and purified by flash chromatography using EtOAc:pentane 1:50 as mobile phase affording 25d (56.0 mg, 0.148 mmol, 74%) as a colorless oil. Rf (EtOAc:pentane 1:60 KMnO₄ staining) = 0.5. ¹H NMR (CDCl₃, 400 MHz): δ 7.32-7.23 (m, 8 H, ArH), 7.22-7.16 (m, 2 H, ArH), 4.54 (s, 4 H, 2 x ArCH₂), 1.59 (s, 12 H, 4 x CH₃). ¹³C NMR (CDCl₃, 100 MHz): δ 138.8, 128.5, 127.9, 127.6, 97.9, 71.5, 68.0, 66.9, 28.6. IR ν 2986 (m), 2170 (w), 1735 (w), 1470 (w), 1462 (w), 1382 (m), 1234 (m), 1156 (s), 1055 (s), 900 (m), 738 (s). HRMS (ESI) C₂₄H₂₆O₂S [M+] calc. = 378.1654; [M+] obs. = 378.1653.

7,7'-thiobis(hept-6-yn-1-ol) (25e)

Following general procedure GPF, the crude reaction mixture was concentrated in vacuo and purified by flash chromatography using EtOAc:pentane 1:1 as mobile phase affording 25e (41.0 mg, 0.162 mmol, 81%) as a light yellow solid. Rf (EtOAc:pentane 1:1, KMnO₄ staining) = 0.16. Melting point = 37.2-39.0 °C. ¹H NMR (CDCl₃, 400 MHz): δ 3.64 (t, 4 H, J = 6.4 Hz, CH₂OH), 2.33 (t, 4 H, J = 6.8 Hz, CCCCH₂CH₂), 1.64 (bs, 2 H, CH₂OH), 1.61-1.51 (m, 8 H), 1.51-1.42 (m, 4 H). ¹³C NMR (CDCl₃, 100 MHz): δ 96.1, 62.9, 62.9, 32.3, 28.1, 25.1, 20.2. IR ν 3350 (m), 2937 (s), 2862 (s), 2195 (w), 1731 (w), 1459 (m), 1329 (m), 1058 (s), 757 (m). HRMS (ESI) C₁₄H₂₂NaO₂S⁺ [M+Na]⁺ calc. = 277.1233; [M+Na]⁺ obs. = 277.1237.
7-(Phenylselanyl)hept-6-yn-1-ol (28)

A 25 mL round bottom flask was charged with a magnetic stirring bar, benzeneselenol (27) (42.0 μL, 0.400 mmol, 1.00 eq.), TMG (60.0 μL, 0.480 mmol, 1.20 eq.) and THF (5.0 mL). After stirring the resulting solution for 5 minutes at room temperature, C₅-OH-EBX (1k) (158 mg, 0.440 mmol, 1.10 eq.) was added as a solid in one portion. The resulting reaction mixture was stirred for 10 minutes at room temperature. Next, the mixture was diluted with water (10 mL) and extracted with EtOAc (3 x 15 mL). The combined organic layers were dried over MgSO₄, filtered and concentrated in vacuo. The crude oil was purified by flash chromatography using EtOAc:pentane 1:2 as mobile phase affording 28 (45.0 mg, 0.178 mmol, 45%) as a colorless oil. Rf (EtOAc:pentane 1:2, KMnO₄ staining) = 0.58. ¹H NMR (CDCl₃, 400 MHz): δ 7.48-7.40 (m, 2 H, ArH), 7.26-7.20 (m, 2 H, ArH), 7.20-7.13 (m, 1 H, ArH), 3.58 (t, 2 H, J = 6.4 Hz, CH₂CH₂OH), 2.40 (t, 2 H, J = 6.9 Hz, CCCCH₂CH₂), 1.60-1.48 (m, 4 H), 1.48-1.39 (m, 3 H). ¹³C NMR (CDCl₃, 100 MHz): δ 129.5, 129.4, 128.7, 126.9, 104.4, 62.9, 57.9, 32.3, 28.6, 25.1, 20.7. IR ν 3356 (m), 3066 (w), 2944 (m), 2861 (m), 2180 (w), 1583 (w), 1477 (m), 1438 (m), 1328 (w), 1068 (m), 1024 (m), 736 (s). HRMS (ESI) C₁₃H₁₇OSe⁺ [M+H]⁺ calc. = 269.0439; [M+H]⁺ obs. = 269.0445.
6. Transformation of Thioalkynes

3-Hexyl-benzo thiophene (12)

Following a slightly modified procedure,22 the bromide 9b (230 mg, 0.774 mmol, 1.00 eq.) was added to a flame-dried 25 mL round bottom flask and dissolved in dry THF (1.55 mL). To the clear colorless solution was added 2.0 M 1PrMgCl-LiCl in THF (426 μL) at room temperature under nitrogen and the light yellow reaction mixture was stirred at room temperature for 4 h. Next, a solution of the copper catalyst (1.0 M, 232 μL, 0.232 mmol, 0.300 eq. prepared from 66.6 mg of CuCN, 63.0 mg of LiCl in 0.74 mL of dry THF) was added dropwise via a syringe. The light yellow reaction mixture was further stirred for 24 h at room temperature under nitrogen. The reaction mixture was cooled to 0 °C using an ice/water bath and quenched with half sat. aq. NH4Cl (10 mL) and extracted with Et2O (3 x 10 mL). The combined organic layers were dried over MgSO4, filtered and concentrated in vacuo. The crude was purified by flash column chromatography using pentane affording 12 (140 mg, 0.642 mmol, 83%) as a colorless oil. Rf (pentane) = 0.75. 1H NMR (CDCl3, 400 MHz) δ 7.91-7.86 (m, 1 H, ArH), 7.80-7.75 (m, 1 H, ArH), 7.44-7.33 (m, 2 H, ArH), 7.09 (s, 1 H, ArH), 2.89-2.82 (m, 2 H, ArCH2), 1.82-1.72 (m, 2 H), 1.50-1.29 (m, 6 H), 0.97-0.89 (m, 3 H, CH2CH3). 13C NMR (CDCl3, 100 MHz) δ 140.6, 139.3, 137.4, 124.2, 123.8, 123.0, 121.9, 120.9, 31.9, 29.4, 29.3, 28.7, 22.8, 14.3. IR ν 2926 (s), 2856 (m), 1460 (m), 1429 (m), 843 (w). HRMS (ESI) C14H19S+ [M+H]+ calc. = 219.1202; [M+H]+ obs. = 219.1204.

S-phenyl octanethioate (13)

Following a reported procedure,23 octynyl(phenyl)sulfane (87.0 mg, 0.400 mmol, 1.00 eq.) and p-TsOH (84.0 mg, 0.440 mmol, 1.00 eq.) were dissolved in dry DCM (2 mL) to which

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22 Kunz, T.; Knochel, P. Angew. Chem., Int. Ed. 2012, 51, 1958.
23 Braga, A. L.; Martins, T. L. C.; Silveira, C. C.; Rodrigues, O. E. D. Tetrahedron 2001, 57, 3297.
0.4 g of silica gel was added. The resulting suspension was heated at 40 °C and stirred for 10 h (after 1 h the color of the mixture became orange). Then, DCM (5 mL) was added and the silica gel was removed by filtration and the mixture was concentrated under reduced pressure. The crude oil was purified by column chromatography (pentane/EtOAc 15:1) to afford 13 (97.0 mg, 0.411 mmol, 93%) as a colorless oil. \(^1\)H NMR (CDCl\(_3\), 400 MHz): \(\delta\) 7.63-7.42 (m, 5 H, ArH), 2.66 (t, 2 H, CH\(_2\)CO), 1.80-1.66 (m, 2 H), 1.49-1.15 (m, 8 H), 0.91 (t, 3 H, CH\(_2\)CH\(_3\)). \(^{13}\)C NMR (CDCl\(_3\), 100 MHz): \(\delta\) 197.5, 134.5, 129.3, 129.1, 128.0, 43.7, 31.6, 29.5, 28.5, 25.6, 22.6, 14.1. The characterization data is in accordance with reported literature values.\(^{24}\)

\(^{24}\) Gersch, M.; Gut, F.; Korotkov, V. S.; Lehmann, J.; Böttcher, T.; Rusch, M.; Hedberg, C.; Waldmann, H.; Klebe, G.; Sieber, S. A. Angew. Chem., Int. Ed. 2013, 52, 3009.
$^1$H-NMR (400 MHz, CDCl$_3$) of compound 1b

$^{13}$C-NMR (100 MHz, CDCl$_3$) of compound 1b
IR of compound 1b
$^1$H-NMR (400 MHz, CDCl$_3$) of compound 1d

$^{13}$C-NMR (100 MHz, CDCl$_3$) of compound 1d
IR of compound 1d
$^{1}\text{H-NMR}$ (400 MHz, CDCl$_3$) of compound $1e$

$^{13}\text{C-NMR}$ (100 MHz, CDCl$_3$) of compound $1e$
IR of compound 1e
$^1$H-NMR (400 MHz, CDCl$_3$) of compound 1f

$^{13}$C-NMR (100 MHz, CDCl$_3$) of compound 1f
IR of compound 1f
$^{1}\text{H-NMR}$ (400 MHz, CDCl$_3$) of compound 1g

$^{13}\text{C-NMR}$ (100 MHz, CDCl$_3$) of compound 1g
IR of compound 1g
$^{1}$H-NMR (400 MHz, CDCl$_3$) of compound 1h

$^{13}$C-NMR (100 MHz, CDCl$_3$) of compound 1h
IR of compound 1h
$^1$H-NMR (400 MHz, CDCl$_3$) of compound 1i

$^{13}$C-NMR (100 MHz, CDCl$_3$) of compound 1i
IR of compound 1i
$^1$H-NMR (400 MHz, CDCl$_3$) of compound 1j

$^{13}$C-NMR (100 MHz, CDCl$_3$) of compound 1j
IR of compound 1j
$^1$H-NMR (400 MHz, CDCl$_3$) of compound 1k

$^{13}$C-NMR (100 MHz, CDCl$_3$) of compound 1k
IR of compound 1k
$^1$H-NMR (400 MHz, (CD$_3$)$_2$SO) of compound 1m

$^{13}$C-NMR (100 MHz, (CD$_3$)$_2$SO) of compound 1m
IR of compound 1m
$^1$H-NMR (400 MHz, CDCl$_3$) of compound 1n

$^{13}$C-NMR (100 MHz, CDCl$_3$) of compound 1n
IR of compound 1n
$^1$H-NMR (400 MHz, CDCl$_3$) of compound 3b

$^{13}$C-NMR (100 MHz, CDCl$_3$) of compound 3b
IR of compound 3b
$^1$H-NMR (400 MHz, CDCl$_3$) of compound 6

$^{13}$C-NMR (100 MHz, CDCl$_3$) of compound 6
Irradiation of the Methyl at 2.52 ppm

Irradiation of the vinylic proton at 6.45 ppm
Irradiation of the benzylic protons at 4.09 ppm

IR of compound 6
\(^1\text{H}-\text{NMR}\) (400 MHz, CDCl\(_3\)) of compound 9a

\[^{13}\text{C}-\text{NMR}\) (100 MHz, CDCl\(_3\)) of compound 9a
IR of compound 9a
$^1$H-NMR (400 MHz, CDCl$_3$) of compound 9b

$^{13}$C-NMR (100 MHz, CDCl$_3$) of compound 9b
IR of compound 9b
$^1$H-NMR (400 MHz, CDCl$_3$) of compound 9c

$^{13}$C-NMR (100 MHz, CDCl$_3$) of compound 9c
IR of compound 9c
$^1$H-NMR (400 MHz, CDCl$_3$) of compound 9d

$^{13}$C-NMR (100 MHz, CDCl$_3$) of compound 9d
IR of compound 9d
$^1$H-NMR (400 MHz, CDCl$_3$) of compound 9e

$^{13}$C-NMR (100 MHz, CDCl$_3$) of compound 9e
IR of compound 9e
\(^1\text{H-NMR}\) (400 MHz, CDCl\(_3\)) of compound 9f

\(^{13}\text{C-NMR}\) (100 MHz, CDCl\(_3\)) of compound 9f
IR of compound 9f
$^1$H-NMR (400 MHz, CDCl$_3$) of compound 9g

$^{13}$C-NMR (100 MHz, CDCl$_3$) of compound 9g
IR of compound 9g
$^1$H-NMR (400 MHz, CDCl$_3$) of compound 9h

$^{13}$C-NMR (100 MHz, CDCl$_3$) of compound 9h
IR of compound 9h
$^1$H-NMR (400 MHz, CDCl$_3$) of compound 9i

$^{13}$C-NMR (100 MHz, CDCl$_3$) of compound 9i
IR of compound 9i
$^1$H-NMR (400 MHz, CDCl$_3$) of compound 9j

$^{13}$C-NMR (100 MHz, CDCl$_3$) of compound 9j
IR of compound 9j
$^1$H-NMR (400 MHz, CDCl$_3$) of compound 9k

$^{13}$C-NMR (100 MHz, CDCl$_3$) of compound 9k
IR of compound 9k
$^1$H-NMR (400 MHz, CDCl$_3$) of compound 11a

$^{13}$C-NMR (100 MHz, CDCl$_3$) of compound 11a
IR of compound 11a
$^1$H-NMR (400 MHz, CDCl$_3$) of compound 11b

$^{13}$C-NMR (100 MHz, CDCl$_3$) of compound 11b
IR of compound 11b
$^1$H-NMR (400 MHz, CDCl$_3$) of compound 11c

$^{13}$C-NMR (100 MHz, CDCl$_3$) of compound 11c
IR of compound 11c
$^1$H-NMR (400 MHz, CDCl$_3$) of compound 12

$^{13}$C-NMR (100 MHz, CDCl$_3$) of compound 12
IR of compound 12
$^{1}$H-NMR (400 MHz, CDCl$_3$) of compound 13

$^{13}$C-NMR (100 MHz, CDCl$_3$) of compound 13
$^1$H-NMR (400 MHz, CDCl$_3$) of compound 17a

$^{13}$C-NMR (100 MHz, CDCl$_3$) of compound 17a
IR of compound 17a
$^1$H-NMR (400 MHz, CDCl$_3$) of compound 17b

$^{13}$C-NMR (100 MHz, CDCl$_3$) of compound 17b
IR of compound 17b
$^1$H-NMR (400 MHz, CDCl$_3$) of compound 17c

$^{13}$C-NMR (100 MHz, CDCl$_3$) of compound 17c
IR of compound 17c
$^{1}$H-NMR (400 MHz, CDCl$_3$) of compound 17d

$^{13}$C-NMR (100 MHz, CDCl$_3$) of compound 17d
IR of compound 17d
$^1$H-NMR (400 MHz, CDCl$_3$) of compound 18a

$^{13}$C-NMR (100 MHz, CDCl$_3$) of compound 18a
IR of compound 18a
$^1$H-NMR (400 MHz, CDCl$_3$) of compound 18b

$^{13}$C-NMR (100 MHz, CDCl$_3$) of compound 18b
IR of compound 18b
$^{1}$H-NMR (400 MHz, CDCl$_3$) of compound 18c

$^{13}$C-NMR (100 MHz, CDCl$_3$) of compound 18c
IR of compound 18c
$^1$H-NMR (400 MHz, CD$_3$OD) of compound 18d

$^{13}$C-NMR (100 MHz, CD$_3$OD) of compound 18d
IR of compound 18d
$^1$H-NMR (400 MHz, CD$_3$OD) of compound 18e

$^{13}$C-NMR (100 MHz, CD$_3$OD) of compound 18e
IR of compound 18e
$^1$H-NMR (400 MHz, CDCl$_3$) of compound 19a

$^{13}$C-NMR (100 MHz, CDCl$_3$) of compound 19a
IR of compound 19a
$^1$H-NMR (400 MHz, CDCl$_3$) of compound 19b

$^{13}$C-NMR (100 MHz, CDCl$_3$) of compound 19b
IR of compound 19b
$^1$H-NMR (400 MHz, CDCl$_3$) of compound 19c

$^{13}$C-NMR (100 MHz, CDCl$_3$) of compound 19c
IR of compound 19c
\(^1\)H-NMR (400 MHz, CDCl\(_3\)) of compound 19d

\(^{13}\)C-NMR (100 MHz, CDCl\(_3\)) of compound 19d
IR of compound 19d
$^1$H-NMR (400 MHz, CDCl$_3$) of compound 19e

$^{13}$C-NMR (100 MHz, CDCl$_3$) of compound 19e
IR of compound 19e
\(^1\text{H-NMR}\) (400 MHz, CDCl\(_3\)) of compound \(19f\)

\(^{13}\text{C-NMR}\) (100 MHz, CDCl\(_3\)) of compound \(19f\)
IR of compound 19f
$^1$H-NMR (400 MHz, CDCl$_3$) of compound 19g

$^{13}$C-NMR (100 MHz, CDCl$_3$) of compound 19g
IR of compound 19g
$^1$H-NMR (400 MHz, CDCl$_3$) of compound 21

$^{13}$C-NMR (100 MHz, CDCl$_3$) of compound 21
IR of compound 21
$^1\text{H-NMR}$ (400 MHz, CDCl$_3$) of compound 22b

$^{13}\text{C-NMR}$ (100 MHz, CDCl$_3$) of compound 22b
IR of compound 22b
$^{1}\text{H-NMR}$ (400 MHz, CDCl$_3$) of compound 24a

$^{13}\text{C-NMR}$ (100 MHz, CDCl$_3$) of compound 24a
IR of compound 24a
$^{1}$H-NMR (400 MHz, CDCl$_3$) of compound 24b

$^{13}$C-NMR (100 MHz, CDCl$_3$) of compound 24b
IR of compound 24b
$^1$H-NMR (400 MHz, CDCl$_3$) of compound 24c

$^{13}$C-NMR (100 MHz, CDCl$_3$) of compound 24c
IR of compound $24c$
$^1$H-NMR (400 MHz, CDCl$_3$) of compound 24d

$^{13}$C-NMR (100 MHz, CDCl$_3$) of compound 24d
IR of compound 24d
$^{1}$H-NMR (400 MHz, CDCl$_3$) of compound 25a

$^{13}$C-NMR (100 MHz, CDCl$_3$) of compound 25a
IR of compound 25a
$^1$H-NMR (400 MHz, CDCl$_3$) of compound 25b

$^{13}$C-NMR (100 MHz, CDCl$_3$) of compound 25b
IR of compound 25b
$^{1}H$-NMR (400 MHz, CDCl$_3$) of compound 25c

$^{13}C$-NMR (100 MHz, CDCl$_3$) of compound 25c
IR of compound 25c
$^1$H-NMR (400 MHz, CDCl$_3$) of compound 25d

$^{13}$C-NMR (100 MHz, CDCl$_3$) of compound 25d
IR of compound 25d
$^1$H-NMR (400 MHz, CDCl$_3$) of compound 25e

$^{13}$C-NMR (100 MHz, CDCl$_3$) of compound 25e
IR of compound 25e
$^1\text{H-NMR}$ (400 MHz, CDCl$_3$) of compound 26

$^{13}\text{C-NMR}$ (100 MHz, CDCl$_3$) of compound 26
IR of compound 26
$^{1}$H-NMR (400 MHz, CDCl$_3$) of compound 28

$^{13}$C-NMR (100 MHz, CDCl$_3$) of compound 28
IR of compound 28