Catalytic Preparation of 1-Aryl-Substituted 1,2,4-Triazolium Salts

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Supporting Information

ABSTRACT: 1,4-Diaryl- and 1-aryl-4-alkyl-substituted 1,2,4-triazolium salts are convenient air-stable precursors to carbenes used both as organocatalysts or as ligands for transition metal complexes. Beyond the ﬁeld of catalysis, these 1,2,4-triazole-based ligands form phosphorescent cyclometalated complexes with the substituents on the carbone ligand being key to their tunable emission wavelengths. While other late transition metal complexes containing 1,2,4-triazole ligands have shown promising in vitro anticancer activity in studies involving breast, colon, lung, skin, liver, and cervical cancer as well as leukemias. The use of diaryliodonium salts is well established for the catalytic arylation of monocyclic triazoles with diaryliodonium salts; however, the preparation of 1,4-diaryl- and 1-aryl-4-alkyl-substituted 1,2,4-triazolium salts has been quantitatively, we were never able to isolate more than 8% of the 3-mesityl-1,3,4-oxadiazolium intermediate derived from the electron-rich mesityl hydrazine. We therefore decided to investigate alternative routes to 1,4-diaryl- and 1-aryl-4-alkyl-substituted 1,2,4-triazolium salts. Scheme 1b shows our approach in which the primary amine RNH₂ is ﬁrst converted to the 4-R-4-aryltriazolium or 3-arylimidazolium salts via similar methods while other late transition metal complexes containing 1,2,4-triazole ligands have shown promising in vitro anticancer activity in studies involving breast, colon, lung, skin, liver, and cervical cancer as well as leukemias.

INTRODUCTION

Mostly known as convenient, air-stable precursors to N-heterocyclic carbenes (NHCs) used in organocatalytic transformations, 1,2,4-triazolium salts also form upon deprotonation of NHC ligands for transition metal catalysts. Beyond the ﬁeld of catalysis, these 1,2,4-triazole-based ligands form phosphorescent cyclometalated complexes with the substituents on the carbone ligand being key to their tunable emission wavelengths, while other late transition metal complexes containing 1,2,4-triazole ligands have shown promising in vitro anticancer activity in studies involving breast, colon, lung, skin, liver, and cervical cancer as well as leukemias.

Traditionally, 1-aryl-substituted 1,2,4-triazolium salts are prepared in three steps via a condensation reaction between an oxadiazolium intermediate derived from an aryl hydrazine and a primary amine (Scheme 1a). There are several disadvantages of this synthetic route: First, the oxadiazolium intermediates are not only highly water-sensitive and decompose within minutes upon exposure to air but their formation also requires perchloric acid, thus raising safety concerns regarding the scaling up of the procedure. Second, many aryl hydrazines are either not readily available or very expensive. Third, while phenyl hydrazine proved to be unproblematic and yielded the desired intermediates nearly quantitatively, we were never able to isolate more than 8% of the 3-mesityl-1,3,4-oxadiazolium intermediate derived from the electron-rich mesityl hydrazine. We therefore decided to investigate alternative routes to 1,4-diaryl- and 1-aryl-4-alkyl-substituted 1,2,4-triazolium salts. Scheme 1b shows our approach in which the primary amine RNH₂ is ﬁrst converted to the 4-R-4-aryltriazolium or 3-arylimidazolium salts via similar methods.

The use of diaryliodonium salts is well established for the arylation of a wide range of oxygen and nitrogen nucleophiles both with and without a copper catalyst. Chen and co-workers have described a copper-free route to N-aryl pyridinium species from diaryliodonium salts and pyridinium N-oxides or sulphonamides via a radical rearrangement; however, the N-arylation of pyridines themselves requires a copper catalyst. Most similar to this work describing the 1-arylation of triazoles is a recent report by Kumar et al. investigating a copper-catalyzed N-arylation of [1,2,4]triazolo[4,3-a]pyridines leading to fused triazolium salts. To our knowledge, there have been no examples described in the literature for the copper-catalyzed 1-arylation of monocyclic triazoles with diaryliodonium salts; however, the preparation of 4-aryltriazolium or 3-arylimidazolium salts via similar methods has been reported before.

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We were aiming to find the mildest conditions to carry out the copper-catalyzed quaternization within short reaction times. To optimize the copper-catalyzed 1-arylation of 4-R-4H-1,2,4-triazoles, we initially carried out a series of reactions on a 0.5 mmol scale with 4-benzyl-4H-1,2,4-triazole (1a) and diphenyliodonium tetrafluoroborate, which we monitored by LC-MS (Table 1). We found that at 100 °C, >95% conversion was achieved in the presence of all copper(I) and copper(II) catalysts except CuI after 4 h in DMF and acetonitrile, while reactions in water required prolonged reaction times (entries 1–13). When lowering the reaction temperature to 80 °C in acetonitrile, copper(I) proved to be superior to copper(II): After 4 h, 100% conversion was observed with CuOAc but only 87 and 88% were found with anhydrous Cu(OAc)2 and Cu(OAc)2·H2O, respectively (entries 1–13). Without the addition of a copper catalyst, the conversion dropped to 17% after 4 h of reaction time (entry 17). When shortening the reaction time to 1 h, the presence of CuOAc led to 97% conversion, while anhydrous Cu(OAc)2 and Cu(OAc)2·H2O showed significantly lower conversions (entries 18–20), thus being consistent with CuOAc being the most efficient catalyst. Since no unwanted side reactions were observed under these conditions, we decided to carry out the copper-catalyzed 1-arylation of triazoles with CuOAc in acetonitrile at 80 °C.

To explore the scope of the copper-catalyzed N-arylation, we prepared a variety of 4-R-4H-1,2,4-triazoles 1a−1m from the corresponding primary amines R-NH2 as described in Scheme 1b.50-54 Table 2 summarizes the results of the 1-arylation of 1a−1m with diphenyliodonium tetrafluoroborate using our previously optimized conditions. Based on NMR studies, 100% conversion was observed with all 4-R-4H-1,2,4-triazoles 1a−1m, and the corresponding 1-phenyl-4-R-4H-1,2,4-triazolium salts 2a−2m were obtained as sole products in good to excellent yields (Figures S002−S015). While this was not surprising with simple alkyl (2a−2c), aryl (2d and 2e), or haloaryl substituents (2g−2k), the copper-catalyzed arylation of 1f gave 2f cleanly without any arylation of the para-methoxy-substituted sulﬁde. Likewise, although 1l and 1m contain several heteroaryl nitrogen atoms that could be quaternized, 2l and 2m form preferentially and none of the other possible arylation products were observed under the chosen reaction conditions despite the presence of an excess of diaryliodonium tetrafluoroborate. The isolated yields were generally within 5−10% of the NMR yields. However, signiﬁcantly lower isolated yields were obtained with the heteroaryl-substituted triazolium salts 2l, which was strongly retained on silica, and 2m, which decomposed on silica and had to be puriﬁed by recrystallization.

Since the 1-aryl substituent governs the electronic properties of 1,2,4-triazolium salts used for organocatalytic transformations, a late stage introduction of the aryl group appears to be of general interest to the organic community. We found that with our N-arylation method, we were able to introduce a variety of aryl groups in the last synthetic step, using triazole 1d to investigate the scope of diaryliodonium salts in the copper-catalyzed quaternization of triazoles (Table 3). We observed that both the use of diaryliodonium tetraﬂuoroborates and triflates resulted in complete conversion to the corresponding 1-aryl-4-phenyltriazolium salts (2d−9d) within 4 h of reaction time. Unhindered electron-rich (e.g., 6d) and electron-poor (e.g., 7d) aryl groups were introduced with high yields, whereas a decreased isolated yield was observed for ortho-substituted aryl groups (3d−5d). Although LC-MS indicated complete conversion, we were unable to isolate 9d.

### Table 1. Optimization of Reaction Conditions

| entry | Cu catalyst | catalyst loading | Ph2I(BF4) (equiv)\(^b\) | solvent | temperature | time | conversion\(^c\) |
|-------|-------------|------------------|-----------------------|--------|-------------|-----|----------------|
| 1     | Cu(OAc)2·H2O | 5 mol%           | 1.5                   | DMF    | 100 °C     | 4 h | >95%          |
| 2     | Cu(OAc)2     | 5 mol%           | 1.5                   | DMF    | 100 °C     | 4 h | >95%          |
| 3     | Cu(OAc)      | 5 mol%           | 1.5                   | DMF    | 100 °C     | 4 h | >95%          |
| 4     | Cu(OAc)      | 5 mol%           | 1.5                   | H2O    | 100 °C     | 4 h | >80%          |
| 5     | Cu(OAc)      | 5 mol%           | 1.5                   | H2O    | 100 °C     | 4 h | >80%          |
| 6     | Cu(OAc)2·H2O | 5 mol%           | 1.5                   | MeCN   | 100 °C     | 4 h | >95%          |
| 7     | Cu(OAc)      | 5 mol%           | 1.5                   | MeCN   | 100 °C     | 4 h | >95%          |
| 8     | Cu(OAc)      | 5 mol%           | 1.5                   | MeCN   | 100 °C     | 4 h | >95%          |
| 9     | Cu(OTf)·0.5 toluene | 5 mol% | 1.5 | MeCN | 100 °C | 4 h | >95% |
| 10    | Cu(TC)       | 5 mol%           | 1.5                   | MeCN   | 100 °C     | 4 h | >95%          |
| 11    | Cu(OTf)2     | 5 mol%           | 1.5                   | MeCN   | 100 °C     | 4 h | >95%          |
| 12    | Cu(acac)2    | 5 mol%           | 1.5                   | MeCN   | 100 °C     | 4 h | >95%          |
| 13    | CuI          | 5 mol%           | 1.5                   | MeCN   | 100 °C     | 4 h | <30%          |
| 14    | Cu(OAc)2·H2O | 5 mol%           | 1.5                   | MeCN   | 100 °C     | 4 h | 88%           |
| 15    | Cu(OAc)      | 5 mol%           | 1.5                   | MeCN   | 100 °C     | 4 h | 87%           |
| 16    | Cu(OAc)      | 5 mol%           | 1.5                   | MeCN   | 100 °C     | 4 h | 100%          |
| 17    | none         | 5 mol%           | 1.5                   | MeCN   | 100 °C     | 4 h | 17%           |
| 18    | Cu(OAc)2·H2O | 5 mol%           | 1.5                   | MeCN   | 100 °C     | 1 h | 80%           |
| 19    | Cu(OAc)      | 5 mol%           | 1.5                   | MeCN   | 100 °C     | 1 h | 79%           |
| 20    | Cu(OAc)      | 5 mol%           | 1.5                   | MeCN   | 100 °C     | 1 h | 97%           |

\(^a\)Reaction conditions: triazole 1a (0.5 mmol), Ph2IBF4, Cu catalyst (relative to 1a), solvent (2 mL), and reaction time. \(^b\)Relative to 1a. \(^c\)Conversion based on LC-MS analysis. \(^d\)After 18 h, >95% conversion.
In the hope to find a way to isolate 9d, we decided to investigate the use of unsymmetrical diaryliodonium salts for the quaternization of triazole 1d (Scheme 2).不幸地，与mesityl(perfluorophenyl)iodonium triflate的使用相比，更难分离出所需的化合物9d，只有5%的副产物4d被分离出来。剩余的混合物由未反应的起始材料组成，包括未反应的mesityl(perfluorophenyl)iodonium triflate。然而，当mesityl(phenyl)iodonium triflate被用于N-arylation时，更多的电子缺陷基团被转移，正如预期的那样，给2d带来了95%的选择性。有效的分离2d的副产品4d是可能的，只要适用大规模的色谱柱，这使得使用对称的三芳基碘化物盐对三唑的选择性更好。由于它们的极低产率通过传统路线（Scheme 1a），我们特别感兴趣的是应用我们的N-arylation方法到1-mesityl-substituted 1,2,4-triazolium salts (Table 4)。尽管完全的几乎一般更低，因为对应三唑基质（Table 3）导致更困难的分离。
the reaction temperature might allow the use of triazoles containing sensitive functional groups. Indeed, further investigation of the reaction temperature (Figure 1) indicated that although the reaction rate decreases significantly below 60 °C, prolonged reaction times led to complete conversion.

Similarly, lowering the catalyst loading from 5 to 1 mol% or 0.5 mol%, resulted in slower but complete product formation within 4 h with the chosen test substrates (Figure 2).

Accordingly, while quaternization was still observed without the addition of the copper catalyst at 80 °C, N-arylation occurred at significantly lower rates, and 82% conversion was obtained after 23 h.

Since all reactions proceeded cleanly to the desired products, we rationalized that addition of stoichiometric quantities of diaryliodonium salt should lead to complete product formation. Indeed, when the loading of diaryliodonium salt was decreased to either 1.25 or 1.1 equivalents, the reaction still went to completion but required more time (Figure 3). With 1.0 equivalents of diaryliodonium salt complete conversion was observed after 24 h.

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**Table 4. Synthesis of 1-Mesityl Triazolium Salts**

| Triazole | Reaction Conditions |
|---------|---------------------|
| 1a-1l   | Mes$_2$IOTf (1.5 mmol), CuOAc (0.05 mmol, 5 mol%), MeCN (4 mL), 80 °C, and 4 h. |

**Table 5. Variation of Steric and Electronic Parameters**

| Triazole | Reaction Conditions |
|---------|---------------------|
| 1a-1m   | Ar$_2$IOTf (1.5 mmol), CuOAc (0.05 mmol, 5 mol%), MeCN (4 mL), 80 °C, and 4 h. |
Although the reaction proceeds slowly without a copper catalyst (Figure 2), we propose in analogy to the related literature a Cu(I)/Cu(III) mechanism to be operative in the presence of a copper salt. This is supported by our own findings that copper(I) proved to be more efficient than the corresponding copper(II) salt in catalyzing the N-arylation.

## CONCLUSIONS

In summary, we have demonstrated an efficient alternative route for the preparation of 1-aryl-substituted 4R-4H-1,2,4-triazolium salts from 4-R-4H-1,2,4-triazoles via a copper-catalyzed quaternization using diaryliodonium salts. Key features of this pathway are a uniformly applicable protocol, short reaction times, complete conversions, and clean product formation.

## EXPERIMENTAL SECTION

### General Information

Most reagents and solvents were obtained from commercial sources and used as supplied unless otherwise noted. Acetonitrile used for catalytic reactions was obtained from commercial sources and used as supplied unless otherwise noted. Acetonitrile used for catalytic reactions was obtained from commercial sources and used as supplied unless otherwise noted. Acetonitrile used for catalytic reactions was obtained from commercial sources and used as supplied unless otherwise noted. Acetonitrile used for catalytic reactions was obtained from commercial sources and used as supplied unless otherwise noted. Acetonitrile used for catalytic reactions was obtained from commercial sources and used as supplied unless otherwise noted.

### Analytical Data

1H NMR, 13C{1H} NMR spectra, and 19F{1H} NMR spectra were all recorded on a 400 MHz Bruker Avance III spectrometer with a 5 mm liquid-state Smart Probe. Chemical shifts (δ) are expressed in parts per million (ppm) and reported relative to the resonance of the residual protons of the DMSO-d6 (δH = 2.50 ppm) or CDCl3 (δH = 7.26 ppm) or in 13C{1H} NMR spectra relative to the resonance of the deuterated solvent DMSO-d6 (δC = 39.52 ppm) or CDCl3 (δC = 77.16 ppm). Chemical shifts in 19F{1H} NMR spectra are reported relative to the internal standard fluorobenzene (δF = −113.15). Coupling constants (J) are given in Hz. All measurements were carried out at 298 K. Abbreviations used in the description of NMR data are as follows: s, singlet; d, doublet; t, triplet; q, quartet; sept, septet; m, multiplet. High-resolution mass spectrometry (HRMS) data were obtained on an LTQ Orbitrap XL in FT Orbitrap mode at a resolution of 100,000.

### General Procedure 1a for the Synthesis of Triazoles 1a−1m

The amine (1 equiv) and the dihydrochloride of N,N-dimethylformamide azine (1.5 equiv) were ground together in a mortar until the mixture liquefied or became a homogeneous solid and then transferred to a round-bottom flask equipped with a stir bar. The reaction mixture was basified with water (2 × 50 mL), dried over MgSO4, filtered, and evaporated. The crude product was purified by column chromatography (5% methanol in dichloromethane) yielded the product as either hexanes or diethyl ether from a concentrated dichloromethane solution.

### General Procedure 1b for the Synthesis of Triazoles 1a−1m

The amine (1 equiv) and the dihydrochloride of N,N-dimethylformamide azine (1.5 equiv), and para-toluene sulfonic acid (0.05 equiv) were ground together in a mortar until the mixture liquefied or became a homogeneous solid and then transferred to a round-bottom flask equipped with a stir bar. The reaction mixture was layered with xylene, a reflux condenser was placed on the round-bottom flask, and the mixture was heated under argon in an oil bath to 150 °C for 16 h. After cooling to room temperature, the crude product was purified as described in procedure 1a.

### 4-Benzyl-4H-1,2,4-triazole (1a)

The title compound was prepared on a 50 mmol scale according to general procedure 1b. Purification by column chromatography (silica, 5% methanol in dichloromethane) yielded the product as a colorless powder in 42% yield (3.31 g, 20.8 mmol). The measured analytical data are in agreement with their literature values.

### 4-Cyclohexyl-4H-1,2,4-triazole (1b)

The title compound was prepared on a 100 mmol scale according to general procedure 1b. Purification with hexanes from a concentrated dichloromethane solution gave the pure pale yellow product in 15% yield (2.19 g, 14.5 mmol). The measured analytical data are in agreement with their literature values.

### 4-(35,5,7S)-Adamantan-1-y1-4H-1,2,4-triazole (1c)

The title compound was prepared on a 100 mmol scale according to general procedure 1b. The crude product was dissolved in a minimal amount of 5% methanol in dichloromethane and precipitated with toluene, which gave the pure product as a colorless powder in 31% yield (6.38 g, 31.4 mmol). The measured analytical data are in agreement with their literature values.

### 4-Phenyl-4H-1,2,4-triazole (1d)

The title compound was prepared according to general procedure 1a on a 50 mmol scale. The pure light brown product was obtained by precipitation with hexanes from a concentrated solution of dichloromethane. Yield: 73% (5.29 g, 36.5 mmol). The measured analytical data are in agreement with their literature values.

### 4-(2,6-Diisopropylphenyl)-4H-1,2,4-triazole (1e)

The title compound was prepared according to general procedure 1a on a 50 mmol scale. Purification by column chromatography (silica, 5% methanol in dichloromethane) yielded the product as an off-white powder in 37% yield (4.20 g, 18.3 mmol). The measured analytical data are in agreement with their literature values.

### 4-(2-(4-Methoxybenzylthio)phenyl)-4H-1,2,4-triazole (1f)

The title compound was prepared in 69% yield according to a literature procedure on a 100 mmol scale. The measured analytical data are in agreement with their literature values.

### 4-(2-Fluorophenyl)-4H-1,2,4-triazole (1g)

The title compound was prepared on a 50 mmol scale according to general procedure 1a. Purification by column chromatography (silica, 5% methanol in dichloromethane) yielded the product as an off-white powder in 48% yield (1.96 g, 12.0 mmol). 1H NMR (400 MHz, CDCl3, 298 K): δ 8.49 (s, 2H), 7.55-7.50 (m, 1H), 7.23-14 (m, 3H). 13C{1H} NMR (100 MHz, CDCl3, 298 K): δ 163.3 (d, JCF = 250.7 Hz), 141.3, 135.1 (d, JCF = 9.7 Hz), 132.0 (d, JCF = 9.1 Hz), 117.9 (d, JCF = 3.5 Hz), 116.2 (d, JCF = 210.0 Hz), 110.1 (d, JCF = 25.2 Hz). 19F{1H} NMR (376 MHz, CDCl3, 298 K, referenced to CF3H): δ −110.21.

## References

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(d, J_C-F = 12.3 Hz), 117.6 (d, J_C-F = 19.3 Hz). 19F{1H} NMR (376 MHz, CDCl₃, 298 K, referenced to C₆H₅F): δ = -123.56.

4-(Fluorophenyl)-4H-1,2,4-triazole (1i). The title compound was prepared on a 25 mmol scale according to general procedure 1a. Purification by column chromatography (silica, 5% methanol in dichloromethane) yielded the product as an off-white powder in 28% yield (1.16 g, 7.1 mmol). 1H NMR (400 MHz, CDCl₃, 298 K): δ 8.45 (s, 2H), 7.43–7.38 (m, 2H), 7.28–7.22 (m, 2H). 13C{1H} NMR (100 MHz, CDCl₃, 298 K): δ 162.6 (d, J_C-F = 250.1 Hz), 141.8, 130.0 (d, J_C-F = 11.0 Hz), 132.4 (d, J_C-F = 3.6 Hz), 124.5 (d, J_C-F = 8.8 Hz), 117.4 (d, J_C-F = 23.4 Hz). 19F{1H} NMR (376 MHz, CDCl₃, 298 K, referenced to C₆H₅F): δ = -110.10.

4-(2-Chlorophenyl)-4H-1,2,4-triazole (1j). The title compound was prepared on a 25 mmol scale according to general procedure 1a. Purification by column chromatography (silica, 5% methanol in dichloromethane) yielded the product as an off-white powder in 51% yield (2.31 g, 12.9 mmol). 1H NMR (400 MHz, CDCl₃, 298 K): δ 10.98 (s, 1H), 9.52 (s, 1H), 7.92 (d, J = 7.7 Hz, 2H), 7.72–7.68 (m, 2H), 7.64 (t, J = 7.3 Hz, 1H), 7.56 (d, J = 7.6 Hz, 2H), 7.50–7.44 (m, 3H), 5.59 (s, 2H). 13C{1H} NMR (100 MHz, CDCl₃, 298 K): δ 142.9, 131.5, 131.3, 131.2, 129.9, 128.5, 127.6.

4-(Chlorophenyl)-4H-1,2,4-triazole (1k). The title compound was prepared on a 25 mmol scale according to general procedure 1a. Purification by column chromatography (silica, 5% methanol in dichloromethane) yielded the product as an off-white powder in 34% yield (1.51 g, 12.0 mmol). 1H NMR (400 MHz, CDCl₃, 298 K): δ 8.46 (s, 2H), 7.62–7.60 (m, 1H), 7.51–7.39 (m, 3H). 13C{1H} NMR (100 MHz, CDCl₃, 298 K): δ 141.5, 135.2, 132.4, 130.6, 123.7.

4-(4-Chlorophenyl)-4H-1,2,4-triazole (1l). The title compound was prepared on a 25 mmol scale according to general procedure 1a. Purification by column chromatography (silica, 5% methanol in dichloromethane) yielded the product as a pale yellow powder in 51% yield (2.22 g, 15.2 mmol). The measured analytical data are in agreement with their literature values. 3,5,6

4-(2-Chloro-4H-1,2,4-triazol-4-yl)pyridine (1m). The title compound was prepared on a 100 mmol scale according to general procedure 1a. Purification by column chromatography (silica, 5% methanol in dichloromethane) yielded the product as a pale yellow powder in 74% yield (1.09 g, 7.4 mmol). The measured analytical data are in agreement with their literature values. 3,5,6

General Procedure 2a for the Catalytic Arylation of Triazoles 1a–1m. A 10 mL Schlenk flask equipped with a stir bar was loaded with the triazole (1 mmol, 1.0 equiv), diiodomalonitrile salt (1.5 mmol, 1.5 equiv), and copper(I) acetate (0.05 mmol, 5 mol%), sealed with a PTFE screwcap, and filled with argon. Dry acetonitrile (4 mL) was added under a stream of argon, and the flask was sealed, then placed into an oil bath, and stirred for 4 h at 80 °C. After the reaction mixture was cooled to room temperature, the solvent was evaporated. NMR yields and conversion were determined by addition of mesitylene (1 mmol, 1 equiv) in DMSO-d₆ to the crude reaction mixture. The pure triazolium salts were obtained either by recrystallization or column chromatography (dichloromethane/acetone, 4:1) as described below.

General Procedure 2b for the Catalytic Arylation of Triazoles 1a–1m. A 5 mL microwave tube equipped with a stir bar was loaded inside a glovebox with the triazole (0.5 mmol, 1.0 equiv) and the diiodomalonitrile salt (0.75 mmol, 1.5 equiv). After sealing the microwave tube and removing it from the glovebox, the catalyst (copper(I) acetate (0.025 mmol, 0.05 equiv, 5 mol%) in 2 mL of acetonitrile) was added via syringe to the reaction mixture. The reaction mixture was then stirred for 4 h in an oil bath at 80 °C, cooled to room temperature, and concentrated. NMR yields and conversion were determined by addition of mesitylene (0.5 mmol, 1 equiv) in DMSO-d₆ to the crude reaction mixture. The pure triazolium salts were obtained either by recrystallization or column chromatography (dichloromethane/acetone, 4:1) as described below.
The title compound was prepared according to general procedure 2b. Purification by column chromatography (silica; 1. dichloromethane; 2. dichloromethane/acetone, 4:1; Rf = 0.19) yielded the product as an off-white powder in 95% yield (154 mg, 0.474 mmol).1 H NMR (400 MHz, DMSO-d6, 298 K): δ 11.41 (s, 1H), 9.95 (s, 1H), 8.04 (d, J = 7.7 Hz, 2H), 7.79–7.75 (m, 4H), 7.72–7.67 (m, 2H). 13C{1H} NMR (100 MHz, DMSO-d6, 298 K): δ 148.42. HRMS (ESI) calcd for [C14H12N3]+, 223.0973; observed, 223.0972.

4-(2,6-Diisopropylphenyl)-1-phenyl-1,2,4-triazol-1-ium Tetrafluoroborate ([2]BF4). The title compound was prepared according to general procedure 2b. Purification by column chromatography (silica; 1. dichloromethane; 2. dichloromethane/acetone, 4:1; Rf = 0.17) yielded the product as a white powder in 95% yield (176 mg, 0.473 mmol).1 H NMR (400 MHz, DMSO-d6, 298 K): δ 11.43 (s, 1H), 10.01 (s, 1H), 8.04 (d, J = 7.7 Hz, 2H), 7.94 (d, J = 7.7 Hz, 2H), 7.79–7.75 (m, 4H), 7.72–7.67 (m, 2H). 13C{1H} NMR (100 MHz, DMSO-d6, 298 K): δ 143.3, 140.5, 134.9, 132.1, 130.8, 130.3, 126.6, 120.7. HRMS (ESI) calcd for [C14H12N3][BF4]−, 222.1026; observed, 222.1022.

5F{1H} NMR (376 MHz, DMSO-d6, 298 K). The title compound was prepared according to general procedure 2b. Purification by column chromatography (silica; 1. dichloromethane; 2. dichloromethane/acetone, 4:1; Rf = 0.19) yielded the product as an off-white powder in 95% yield (154 mg, 0.470 mmol).1 H NMR (400 MHz, DMSO-d6, 298 K): δ 11.42 (s, 1H), 9.96 (s, 1H), 8.04–7.98 (m, 4H), 7.78–7.75 (m, 2H), 7.71–7.64 (m, 3H). 13C{1H} NMR (100 MHz, DMSO-d6, 298 K): δ 162.9 (d, Jc-F = 249.9 Hz), 143.5, 140.7, 134.9, 130.8, 130.4, 128.5 (d, Jc-F = 2.9 Hz), 125.4 (d, Jc-F = 9.6 Hz), 120.7, 117.4 (d, Jc-F = 23.6 Hz). 5F{1H} NMR (376 MHz, DMSO-d6, 298 K, referenced to C6H5F): δ −109.92, −148.41. HRMS (ESI) calcd for [C14H12N3][F5]−, 256.0636; observed, 256.0627.

4-(2-Chlorophenyl)-1-phenyl-1,2,4-triazol-1-ium Tetrafluoroborate ([2]BF4). The title compound was prepared according to general procedure 2b. Purification by column chromatography (silica; 1. dichloromethane; 2. dichloromethane/acetone, 4:1; Rf = 0.19) yielded the product as an off-white powder in 95% yield (154 mg, 0.474 mmol).1 H NMR (400 MHz, DMSO-d6, 298 K): δ 11.41 (s, 1H), 9.95 (s, 1H), 8.04 (d, J = 7.7 Hz, 2H), 7.79–7.72 (m, 2H), 7.81–7.68 (m, 5H). 13C{1H} NMR (100 MHz, DMSO-d6, 298 K): δ 158.5, 145.5, 141.8, 134.7, 133.8, 132.2, 131.2, 130.2, 130.9, 130.3, 129.9, 128.9, 128.3, 127.2, 120.6, 113.9, 54.9, 38.4. HRMS (ESI) calcd for [C22H12F2N4OS]+, 374.3222; observed, 274.1305.

5F{1H} NMR (376 MHz, DMSO-d6, 298 K). The title compound was prepared according to general procedure 2b. Purification by column chromatography (silica; 1. dichloromethane; 2. dichloromethane/acetone, 4:1; Rf = 0.17) yielded the product as a white powder in 95% yield (155 mg, 0.491 mmol).1 H NMR (400 MHz, DMSO-d6, 298 K): δ 11.45 (s, 1H), 10.00 (s, 1H), 8.03 (d, J = 7.7 Hz, 2H), 7.98 (d, J = 9.0 Hz, 2H), 7.89 (d, J = 9.0 Hz, 2H), 7.79–7.75 (m, 2H), 7.69 (t, J = 7.3 Hz, 1H), 7.62–7.57 (m, 1H). 13C{1H} NMR (100 MHz, DMSO-d6, 298 K): δ 162.2 (d, Jc-F = 245.1 Hz), 143.3, 140.7, 134.8, 133.2 (d, Jc-F = 11.0 Hz), 132.4 (d, Jc-F = 8.8 Hz), 130.9, 130.4, 120.7, 118.7 (d, Jc-F = 3.3 Hz), 117.7 (d, Jc-F = 20.7 Hz), 110.4 (d, Jc-F = 27.1 Hz). 5F{1H} NMR (376 MHz, DMSO-d6, 298 K, referenced to C6H5F): δ −109.97, −148.42. HRMS (ESI) calcd for [C14H12F2N4][F5]−, 256.0932; observed, 204.0922.

4-(3-Fluorophenyl)-1-phenyl-1,2,4-triazol-1-ium Tetrafluoroborate ([2]BF4). The title compound was prepared according to general procedure 2b. Purification by column chromatography (silica; 1. dichloromethane; 2. dichloromethane/acetone, 4:1; Rf = 0.22) yielded the product as a white powder in 95% yield (127 mg, 0.410 mmol).1 H NMR (400 MHz, DMSO-d6, 298 K): δ 11.68 (s, 1H), 10.24 (s, 1H), 8.77–8.75 (m, 1H), 8.37–8.32 (m, 1H), 8.15 (d, J = 8.1 Hz, 1H), 8.05 (d, J = 7.7 Hz, 2H), 7.78 (m, 3H), 7.69 (t, J = 7.3 Hz, 1H). 13C{1H} NMR (100 MHz, DMSO-d6, 298 K): δ 149.5, 144.7, 142.0, 140.9, 139.7, 134.9, 130.9, 130.28, 126.2, 120.9, 115.4. HRMS (ESI) calcd for [C14H12N4][F5]−, 223.0978; observed, 223.0973.

1-Phenyl-4-(pyrimidin-2-yl)-1,2,4-triazol-1-ium Tetrafluoroborate ([2]BF4). The title compound was prepared according to general procedure 2b. Purification by column chromatography (silica; 1. dichloromethane; 2. dichloromethane/acetone, 4:1; Rf = 0.19) yielded the product as a white powder in 95% yield (154 mg, 0.474 mmol).1 H NMR (400 MHz, DMSO-d6, 298 K): δ 11.83 (s, 1H), 10.33

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(s, 1H), 9.19 (d, J = 4.9 Hz, 2H), 8.14 (d, J = 7.7 Hz, 2H), 7.91 (t, J = 4.9 Hz, 1H), 7.77–7.68 (m, 3H). 13C{1H} NMR (100 MHz, DMSO-d6, 298 K): δ 160.4, 151.0, 142.2, 140.1, 134.8, 131.0, 130.2, 132.4, 121.2. HRMS (ESI) calc'd for [C20H19N3]+, 224.0931; observed, 224.0929.

4-Phenyl-1-[(toly1)]-4H,1,2,4-triazol-1-ium Trifluoromethanesulfonate ([4d]OTf). The title compound was prepared according to general procedure 2b. Purification by column chromatography (silica; 1. dichloromethane; 2. dichloromethane/acetone, 4:1; Rf = 0.17) yielded the product as an off-white powder in 81% yield (155 mg, 0.404 mmol). 1H NMR (400 MHz, DMSO-d6, 298 K): δ 11.17 (s, 1H), 10.03 (s, 1H), 7.94 (d, J = 7.7 Hz, 2H), 7.79–7.53 (m, 7H), 2.40 (s, 3H). 13C{1H} NMR (100 MHz, DMSO-d6, 298 K): δ 143.0, 142.8, 134.1, 133.8, 132.1, 132.0, 131.6, 130.7, 130.7, 127.3, 126.3, 122.6, 17.3. HRMS (ESI) calc'd for [C17H16N3]+, 236.1182; observed, 236.1174.

8 mmol Scale. After evaporation of the reaction solvent, the crude product was dissolved in dichloromethane (50 mL), filtered, and washed with a hexane (70 mL), which yielded the pure product as a colorless powder in 77% yield (2.89 g, 6.13 mmol). 1H NMR (400 MHz, DMSO-d6, 298 K): δ 10.65 (s, 1H), 9.81 (s, 1H), 7.18 (s, 1H), 2.35 (s, 3H), 2.28 (bs, 9H), 2.05 (s, 6H), 1.79–1.71 (m, 6H). 13C{1H} NMR (100 MHz, DMSO-d6, 298 K): δ 143.3, 142.7, 141.4, 134.8, 131.3, 129.4, 60.9, 41.3, 34.7, 28.9, 20.7, 16.9. HRMS (ESI) calc'd for [C17H16N3]+, 222.2278; observed, 222.2273.

1-Mesityl-4-phenyl-4H,1,2,4-triazol-1-ium Tetrafluoroborate ([4d][BF4]). The title compound was prepared according to general procedure 2b. Purification by column chromatography (silica; 1. dichloromethane; 2. dichloromethane/acetone, 4:1; Rf = 0.36) yielded the product as an off-white powder in 52% yield (91 mg, 0.266 mmol). 1H NMR (400 MHz, DMSO-d6, 298 K): δ 11.10 (s, 1H), 10.11 (s, 1H), 7.97 (d, J = 8.0 Hz, 2H), 7.78–7.74 (m, 2H), 7.69 (t, J = 7.4 Hz, 1H), 7.21 (s, 2H), 2.37 (s, 3H), 2.16 (s, 6H). 13C{1H} NMR (100 MHz, DMSO-d6, 298 K): δ 1143.8, 143.2, 141.6, 134.9, 132.2, 131.0, 130.7, 130.2, 129.5, 122.5, 20.7, 17.0. HRMS (ESI) calc'd for [C17H16N3]+, 264.1495; observed, 264.1490.

1-Mesityl-4-phenyl-4H,1,2,4-triazol-1-ium Trifluoromethanesulfonate ([4d][OTf]). The title compound was prepared according to general procedure 2b. Purification by column chromatography (silica; 1. dichloromethane; 2. dichloromethane/acetone, 4:1; Rf = 0.19) yielded the product as an off-white powder in 74% yield (153 mg, 0.372 mmol). 1H NMR (400 MHz, DMSO-d6, 298 K): δ 11.10 (s, 1H), 10.11 (s, 1H), 7.96 (d, J = 8.0 Hz, 2H), 7.78–7.74 (m, 2H), 7.69 (t, J = 7.4 Hz, 1H), 7.21 (s, 2H), 2.37 (s, 3H), 2.16 (s, 6H). 13C{1H} NMR (100 MHz, DMSO-d6, 298 K): δ 1143.8, 143.2, 141.6, 134.9, 132.2, 131.0, 130.6, 129.5, 122.5, 20.7, 17.0. HRMS (ESI) calc'd for [C17H16N3]+, 264.1495; observed, 264.1485.

1-Mesityl-4-(2-(4-methoxybenzyl)thio)phenyl-4H,1,2,4-triazol-1-ium Trifluoromethanesulfonate ([4f][OTf]). The title compound was prepared according to general procedure 2b. Purification by column chromatography (silica; 1. dichloromethane; 2. dichloromethane/acetone, 4:1; Rf = 0.48) yielded the product as a light brown oil (which solidified upon standing) in 59% yield (166 mg, 0.229 mmol). 1H NMR (400 MHz, DMSO-d6, 298 K): δ 10.95 (s, 1H), 9.68 (s, 1H), 7.91 (dd, J = 7.9, 1.3 Hz, 1H), 7.88 (dd, J = 7.9, 1.3 Hz, 1H), 7.74 (td, J = 7.7, 1.3 Hz, 1H), 7.66 (td, J = 7.7, 1.3 Hz, 1H), 7.22 (s, 2H), 7.10 (d, J = 8.7 Hz, 2H), 6.83 (d, J = 8.7 Hz, 2H), 4.20 (s, 2H), 3.72 (s, 3H), 2.37 (s, 3H), 2.13 (s, 6H). 13C{1H} NMR (100 MHz, DMSO-d6, 298 K): δ 158.6, 146.0, 145.6, 141.7, 134.8, 133.1, 132.7, 132.2, 131.8, 130.8, 129.5, 129.5, 128.8, 128.2, 127.7, 55.1, 38.3, 20.7, 17.0. HRMS (ESI) calc'd for [C23H20NO3S]+, 416.1791; observed, 416.1766.

4-(4-Fluorophenyl)-1-mesityl-4H,1,2,4-triazol-1-ium Trifluoromethanesulfonate ([4f][OTf]). The title compound was prepared according to general procedure 2b. Purification by column chromatography (silica; 1. dichloromethane; 2. dichloromethane/acetone, 4:1; Rf = 0.47) yielded the product as a white powder in 54% yield (117 mg, 0.277 mmol). 1H NMR (400 MHz, DMSO-d6, 298 K): δ 11.05 (s, 1H), 10.06 (s, 1H), 8.04–8.01 (m, 2H), 7.68–7.63 (m, 2H), 7.20 (s, 1H), 2.37 (s, 3H), 2.15 (s, 6H). 13C{1H} NMR (100 MHz, DMSO-d6, 298 K): δ 162.7 (d, J = 248.6 Hz), 144.0, 143.3, 141.6, 134.9, 131.0, 129.5, 128.7 (d, J = 3.0 Hz), 125.3 (d, J = 9.3 Hz), 117.1 (d, J = 23.8 Hz), 20.7, 17.0.
The title compound was prepared according to general procedure 2b. Purification by column chromatography (silica; 1. dichloromethane; 2. dichloromethane/acetonitrile, 4:1; Rf = 0.43) yielded the product as an off-white powder in 58% yield (130 mg, 0.291 mmol). 1H NMR (400 MHz, DMSO-d6, 298 K): δ 11.10 (s, 1H), 10.10 (s, 1H), 8.00 (d, J = 8.9 Hz, 2H), 7.88 (d, J = 8.9 Hz, 2H), 7.20 (s, 2H), 2.37 (s, 3H), 2.15 (s, 6H). 13C{1H} NMR (100 MHz, DMSO-d6, 298 K): δ 143.9, 143.3, 241.6, 135.2, 134.9, 131.2, 131.0, 129.5, 124.5, 20.7, 17.0. HRMS (ESI) calcd for [C16H14ClN3]+, 298.1106; observed, 298.1101.

1-Mesityl-4-(pyridin-2-yl)-4H-1,2,4-triazol-1-ium Tetrafluoroborate ([5b][BF4]). The title compound was prepared according to general procedure 2b. Purification by column chromatography (silica; 2. dichloromethane/acetonitrile, 192 mg, 0.478 mmol). HRMS (ESI) calcd for [C16H14BF4N5]+, 265.1448; observed, 265.1444.

1-Cyclohexyl-1-(naphthalen-1-yl)-4H-1,2,4-triazol-1-ium Tetrafluoroborate ([5a][BF4]). The title compound was prepared according to general procedure 2b. Purification by column chromatography (silica; 1. dichloromethane; 2. dichloromethane/acetonitrile, 4:1; Rf = 0.41) yielded the product as an off-white powder in 96% yield (175 mg, 0.478 mmol). 1H NMR (400 MHz, DMSO-d6, 298 K): δ 10.78 (s, 1H), 9.69 (s, 1H), 8.32 (d, J = 8.3 Hz, 1H), 8.20–8.18 (m, 1H), 7.97–7.95 (m, 1H), 7.86–7.69 (m, 4H), 4.52 (tt, J = 11.6, 3.9 Hz, 1H), 2.37–2.33 (m, 2H), 1.94–1.70 (m, 5H), 1.51–1.44 (m, 2H), 1.30–1.20 (m, 1H). 13C{1H} NMR (100 MHz, DMSO-d6, 298 K): δ 144.0, 143.7, 133.7, 130.0, 132.3, 128.5, 128.3, 127.6, 127.1, 125.3, 125.1, 122.1, 58.4, 31.9, 24.4, 24.2. HRMS (ESI) calcd for [C14H14BF4N5]+, 278.1652; observed, 278.1647.

1-(Naphthalen-1-yl)-4-phenyl-4H-1,2,4-triazol-1-ium Tetrafluoroborate ([5d][BF4]). The title compound was prepared according to general procedure 2b. Purification by column chromatography (silica; 1. dichloromethane; 2. dichloromethane/acetonitrile, 4:1; Rf = 0.19) yielded the product as a brown powder in 81% yield (145 mg, 0.406 mmol). 1H NMR (400 MHz, DMSO-d6, 298 K): δ 11.36 (s, 1H), 10.15 (s, 1H), 8.37 (d, J = 8.4 Hz, 1H), 8.24–8.20 (m, 1H), 8.06–8.02 (m, 2H), 7.98 (d, J = 8.0 Hz, 2H), 7.85–7.70 (m, 6H). 13C{1H} NMR (100 MHz, DMSO-d6, 298 K): δ 143.7, 143.4, 133.7, 132.2 (2 signals), 131.0, 130.7, 130.3, 128.5, 128.4, 128.7, 127.1, 125.4, 125.2, 122.6, 122.3. HRMS (ESI) calcd for [C15H14BF4N5]+, 272.1182; observed, 272.1173.

1-(4-Methoxyphenyl)-4-phenyl-4H-1,2,4-triazol-1-ium Tetrafluoroborate ([5e][BF4]). The title compound was prepared according to general procedure 2b. Purification by column chromatography (silica; 1. dichloromethane; 2. dichloromethane/acetonitrile, 4:1; Rf = 0.19) yielded the product as a brown powder in 91% yield (155 mg, 0.456 mmol). 1H NMR (400 MHz, DMSO-d6, 298 K): δ 11.30 (s, 1H), 9.97 (s, 1H), 7.96–7.91 (m, 4H), 7.86–7.74 (m, 2H), 7.68 (t, J = 7.3 Hz, 1H), 7.29 (d, J = 9.1 Hz, 2H), 3.88 (s, 3H). 13C{1H} NMR (100 MHz, DMSO-d6, 298 K): δ 160.7, 143.1, 139.7, 132.1, 130.7, 130.3, 128.0, 122.5, 115.2, 55.8. HRMS (ESI) calcd for [C15H14BF4O]+, 252.1131; observed, 252.1124.

1-(4-Fluorophenyl)-4-phenyl-4H-1,2,4-triazol-1-ium Tetrafluoroborate ([5f][BF4]). The title compound was prepared according to general procedure 2b. Purification by column chromatography (silica; 1. dichloromethane; 2. dichloromethane/acetonitrile, 4:1; Rf = 0.11) yielded the product as an off-white powder in 74% yield (144 mg, 0.369 mmol). 1H NMR (400 MHz, DMSO-d6, 298 K): δ 11.41 (s, 1H), 10.02 (s, 1H), 8.11–8.06 (m, 2H), 7.94–7.92 (m, 2H), 7.93 (d, J = 7.7 Hz, 2H), 7.79–7.75 (m, 2H), 7.70 (t, J = 7.3 Hz, 1H), 7.66–7.62 (m, 2H). 13C{1H} NMR (100 MHz, DMSO-d6, 298 K): δ 162.8 (d, J = 247.9 Hz), 143.3, 140.7, 132.0, 131.4 (d, J = 17931

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3.0 Hz), 130.8, 130.3, 123.5 (d, J = 9.3 Hz), 122.5, 117.4 (d, J = 24.0 Hz). $^{19}$F$^1$(H) NMR (376 MHz, DMSO-d$_6$ 298 K, referenced to C$_6$H$_5$F): $\delta$ −77.85, −109.86. HRMS (ESI) calcld for [C$_4$H$_4$N$_3$O$^+$]: 240.0932; observed, 240.0925.

4-(2,6-Diisopropylphenyl)-1-(4-fluorophenyl)-4H-1,2,4-triazol-1-ium Trifluoromethanesulfonate (8bEOTf). The title compound was prepared according to general procedure 2b. Purification by column chromatography (silica; 1: dichloromethane; 2: dichloromethane/acetic acid, 4:1; R$_f$ = 0.44) yielded the product as an off-white solid in 91% yield (216 mg, 0.456 mmol). $^1$H NMR (400 MHz, DMSO-d$_6$ 298 K): $\delta$ 11.34 (s, 1H), 9.93 (s, 1H), 8.13 $\delta$ = 6.7 Hz, 2H), 1.20 (d, $J$ = 24.0 Hz). $^{19}$F$^1$(H) NMR (376 MHz, DMSO-d$_6$ 298 K): $\delta$ 162.8 (d, $J$ = 248.9 Hz), 114.60, 145.5, 142.2, 132.4, 131.7 ($J$ = 3.0 Hz), 127.1, 124.9, 123.7 (d, $J$ = 9.0 Hz), 122.3, 119.1, 117.0 (d, $J$ = 24.0 Hz).

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**ASSOCIATED CONTENT**

**Supporting Information**
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NMR spectra used for calculating NMR yields and conversion and NMR spectra of the isolated triazolium salts (PDF)

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All authors have contributed to the work presented in this article and have given approval to the final version of the manuscript.

**Notes**
The authors declare no competing financial interest.

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