Topology and Excited State Multiplicity as Controlling Factors in the Carbazole-Photosensitized CPD Formation and Repair

Gemma M. Rodríguez-Muñiz, Miguel Gomez-Mendoza, Paula Miro, Pilar García-Orduña, German Sastre, Miguel A. Miranda,* and M. Luisa Marin*

ABSTRACT: Photosensitized thymine<>thymine (Thy<>Thy) formation and repair can be mediated by carbazole (Cbz). The former occurs from the Cbz triplet excited state via energy transfer, while the latter takes place from the singlet excited state via electron transfer. Here, fundamental insight is provided into the role of the topology and excited state multiplicity, as factors governing the balance between both processes. This has been achieved upon designing and synthesizing different isomers of trifunctional systems containing one Cbz and two Thy units covalently linked to the rigid skeleton of the natural deoxycholic acid. The results shown here prove that the Cbz photosensitized dimerization is not counterbalanced by repair when the latter, instead of operating through-space, has to proceed through-bond.

1. INTRODUCTION

Solar light arriving at Earth is essential for humans, but at the same time, it is responsible for serious deleterious effects. Although UVB radiation represents only a minor sunlight component, it is associated to melanoma skin cancer, since it can be absorbed by the thymine (Thy) or cytosine (Cyt) nucleobases. As a consequence, formation of cyclopyrimidine dimers, (CPDs) such as Thy<>Thy, Cyt<>Cyt, as well as pyrimidine (6−4) pyrimidone adducts and their related Dewar isomers, are observed.5,6 The Thy<>Thy dimers are the photoproducts obtained with higher yields (likely because Cyt exhibits the highest energy triplet among the DNA bases)6 and also the most biologically significant.7−9 In addition, the effects of UVA should not be disregarded, in particular when they can be mediated by photosensitizers absorbing in this region. A limited number of photosensitizers have been employed to investigate this DNA photodamage, including non-steroidal anti-inflammatory drugs, fluoroquinolones, ketones, pyridoporalenes, or p-aminobenzoic acid derivatives.10−15 The reported quantum yields for photosensitized dimerization range from 10−5 to 10−2. Formation of Thy<>Thy dimers is thought to proceed through an initial triplet−triplet energy transfer step (TTET).15,16 Efficient TTET requires, in principle, a donor chromophore with a high intersystem crossing quantum yield, a triplet energy above that of Thy, and a long triplet lifetime. In general, Thy<>Thy dimer formation follows an exponential distance dependence as expected from a Dexter-type TTET mechanism.15,16 Nevertheless, alternative mechanisms involving the participation of triplet triplexes have been demonstrated to play a role in the photosensitized formation of Thy<>Thy mediated by benzo-phenone (Bzp).17 Moreover, recent examples have demonstrated the generation of Thy+ at long (non-bonding) distance through-bond (TB), in intramolecular systems in which the photosensitizer and the nucleobase are separated by a rigid hydrocarbon bridge.18

In prokaryotes, yeast, and plants, CPDs are repaired by photolyases. They act through a light-dependent single-electron transfer mechanism19,20 with quantum yields for the repair of Thy<>Thy as high as 0.7−0.98.21 The redox-active flavin adenine dinucleotide (FAD) cofactor plays a pivotal role in the photorepair activity of photolyases, since its fully reduced and protonated form (FADH−) can be directly excited to reach its singlet excited state (1FADH−*) or, more efficiently, via energy transfer from an antenna chromophore present in the medium. Then, the excited 1FADH−* transfers one electron to the CPD and leads to the dimer radical anion, inducing the spontaneous cleavage of the cyclobutane, finally giving rise to the restored pyrimidines. The limiting factor for the repair efficiency seems to be the back electron transfer from the dimer radical anion and the electron donor.22 Model compounds, which mimic the performance of the CPD-photolyase, have been reported to achieve the CPD photosensitized repair.22−27 Among them, the activity of the carbazole (Cbz) chromophore has been tested upon incorporation of an artificial Cbz-nucleoside into a DNA
2. RESULTS AND DISCUSSION

2.1. Synthesis. Two new dyads derived from DCA have been synthesized (Scheme 1), containing the Cbz chromophore at the lateral chain and the Thy units at 3α + 12α (2) or the Cbz at 3α and two Thy moieties at 12α + the lateral chain (6). The developed synthetic strategy started with esterification of DCA with Cbz-CH₂CH₂OH to yield 1. Then, in the presence of an excess of Thy-CH₂CO₂H, the positions 3α and 12α were esterified providing 2. To prepare the derivative with the two Thy moieties at 12α and at the lateral chain, initially, the carboxyl group at DCA was reduced to the corresponding alcohol (3), and the Thy at the lateral chain was covalently attached using Thy-CH₂CO₂H to give 4. The following step was the introduction of the chromophore at 3α to yield 5. Subsequent treatment with ThyCH₂CO₂H provided 6. In summary, new derivatives in which different combinations of Thy units and distances to the chromophore have been designed, synthesized, and fully characterized (1H and 13C NMR and exact mass) to investigate the influence of the topology on the photosensitized formation of Thy<>Thy dimers and eventually in their photosensitized repair.

2.2. Photosensitized Thy<>Thy Dimer Formation. Initially, diluted anaerobic solutions (4.4 × 10⁻⁵ M in 4CH₃CN:1H₂O) of 2 or 6 were submitted to steady-state photolysis. Irradiation was performed at λ_max = 350 nm and monitored after different irradiation times attending at the changes in the spectra at 260 nm, where the Thy chromophore has a maximum (Figure 1 top for 2, middle for 6, and Figure S5.1 for the control experiments under aerobic conditions). The controls Thy (as ThyCH₂CO₂H), Cbz (as Cbz-CH₂CH₂OH), and the intermolecular 1Cbz:2Thy mixture showed a slight decrease in the absorbance at 260 nm (Figure 1 and Figure S5.1 bottom); nevertheless, the intramolecular systems were clearly more reactive, although their reaction pattern was slightly different.

For preparative purposes, more concentrated deaerated solutions of the two dyads (2 and 6) in acetonitrile (8.3 × 10⁻⁴ M and 1.7 × 10⁻³ M, respectively) were independently irradiated (λ_max = 350 nm), and only one Thy<>Thy dimer was isolated in each case, in 99 and 68% yields, respectively (Scheme 2). These photoproducts were characterized by 1H and 13C NMR spectroscopy, together with an exact mass. More
upon formation of the cyclobutane ring. The $^{13}$C NMR signals corresponding to the characteristic double bond of the Thys moved from 140.2 and 140.0 ppm to 66.3 and 65.9 ppm for the CHs and from 111.7 and 110.6 to 46.2 and 45.5 ppm for the quaternary carbons. We found difficulties in the NOEDIFF experiments due to the NOE zero zone fulfilled by these molecules as a result of their high molecular mass (917.46 g mol$^{-1}$). Nevertheless, the photoproduct was found to be a trans-syn Thy<>Thy, the structure of which was unambiguously established by crystal data (Figure 2, see also the video in the Supporting Information, section S3). A new compound analogous to 6 but without Cbz (11) was synthesized starting from 4 to evaluate the role of Cbz in the formation of Thy<>Thy upon 350 nm irradiation (see Sections S4 and S5). Analog 11 resulted to be unreactive upon prolonged irradiation times at 350 nm, under a deaerated atmosphere, confirming the active role of Cbz in the Thy<>Thy formation. Moreover, a compound analogous to 2 without Cbz has already been described and its irradiation only produced the Thy<>Thy dimer in the presence of the absorbing benzophenone ($^{15}$).

2.3. Photophysics of the TTET in the Photosensitized Thy<>Thy Dimer Formation. The feasibility of the intermolecular TTET from the triplet of Cbz to Thy was investigated by LFP.$^{12,13,18}$ The transient absorption spectrum obtained after laser pulse excitation ($\lambda_{\text{exc}} = 308$ nm) of Cbz$\text{H}_2\text{CO}_2\text{H}$ showed a maximum at 420 nm. Thus, the decay of the characteristic $^{3}\text{Cbz}\ast$ obtained upon excitation at 308 nm was recorded upon the addition of one, two, and three equivalents of thymidine (Thd) (to achieve the required concentration), and these data were fitted to a first-order exponential equation (Figure 3, top). The corresponding lifetimes were fitted to a Stern–Volmer relationship, and the value for the intermolecular quenching constant was obtained from the slope of the linear fitting ($k_{\text{q}} = 4.9 \times 10^9$ M$^{-1}$ s$^{-1}$). This low value for the quenching constant indicates that intermolecular TTET is efficient. Next, we investigated the TB vs TS nature of the TTET from Cbz to the Thy units in the dyads (Figure 3, bottom). This was done by comparing the lifetime of the signals recorded at 420 nm upon selective excitation of Cbz at 308 nm in 5, 2, and 6. The decay corresponding to 5 was fitted to a first-order exponential equation, and the determined lifetime was 4.7 µs; by contrast, the triplet lifetime of 2 and 6 could not be accurately determined. In fact, in both cases, the amplitude of the signal observed just after the laser pulse was very low compared to the one of 5, which could be attributed to a very efficient quenching of the singlet excited state (see below), together with very efficient TS-TTET, giving rise to the $^{3}\text{Thy}\ast$ that has a very low extinction coefficient at 420 nm.$^{18}$

2.4. Photosensitized Thy<>Thy Dimer Repair. The photosensitized dimer repair was investigated upon selective irradiation of the Cbz chromophore ($\lambda_{\text{max}} = 350$ nm) in the two dimers 7 and 8, by monitoring changes of UV–visible spectra, steady-state and time-resolved fluorescence spectroscopy, and HPLC analysis (Figures 4 and 5, top and bottom for 7 and 8, respectively). Furthermore, to avoid subsequent formation of Thy<>Thy dimers, the prevalence of the Cbz singlet excited state ($^{1}\text{Cbz}\ast$) was favored over the $^{3}\text{Cbz}\ast$ by performing the experiments under air, although the Thy<>Thy competes with O$_2$ for the $^{1}\text{Cbz}\ast$ (see Figure S6.2 for quenching by O$_2$, $k_{\text{q}} = 1.7 \times 10^{10}$ M$^{-1}$ s$^{-1}$).

When aerated solutions of 7 and 8 were independently irradiated ($\lambda_{\text{max}} = 350$ nm), a remarkable increase in the absorbance at ~260 nm was observed in both cases (Figure...
This increase could safely be attributed to the opening of the cyclobutane ring, giving rise to the two free Thy units. These changes were accompanied by a decrease in the fluorescence emission (steady-state and time-resolved, Figure 4B,C,E,F), which indicates that the free intramolecular Thy units have higher quenching capability of the singlet excited state of carbazole than the Thy<>Thy moieties. In fact, the efficiency of the TS intramolecular quenching of $^1$Cbz* by Thy at $12\alpha$ can be determined from the lifetimes of $^1$Cbz* in 2 (pink trace in Figure 4C) and 6 (green trace in Figure 4F), and the lifetime of $^1$Cbz* under air (Figure S6.2). From the corresponding values of 4.8 ns for 2, 1.7 ns for 6, and 11.4 ns for $^1$Cbz*, the intramolecular TS quenching values in 2 and 6 are $k_{sq} = 1.2 \times 10^8$ s$^{-1}$ and $5.0 \times 10^8$ s$^{-1}$, respectively, much higher than the intermolecular quenching of $^1$Cbz* by Thy at the employed concentration ($k_{sq} \times$ [Thy] ca. $2.1 \times 10^4$ s$^{-1}$, see Figure S6.3).

This is not surprising since quenching of $^1$Cbz* by Thy<>Thy is likely happening TS since the probability of the three units being together TS is very low, while as soon as the Thy<>Thy are repaired, quenching of the Thy unit at $12\alpha$ happens TS.
Furthermore, the topology of the dimers plays again a role in the quenching of $^1$Cbz*, and therefore, in the efficiency of the photosensitized repair, with 8 being more reactive than 7.

A further piece of evidence for the photosensitized Thy<>Thy repair was obtained by monitoring in parallel the evolution of the irradiation by HPLC (Figure 5A,C). Interestingly, in both cases, irradiation of 7 or 8 led to the opening of the cyclobutane ring; however, while for 8 the conversion was practically quantitative (Figure 5D), for 7, it seems that a photoequilibrium was obtained, likely due to the concomitant photosensitized dimer formation (Figure 5B).

2.5. Computational Results. The participation of a TS mechanism in the formation of $^1$Thy* vs TB mechanism in the photosensitized repair was further investigated upon determining the chromophore—chromophore distances in compounds 2, 6, 7, and 8 by using molecular dynamics at 298 K (see Section S7 and geometries file in the Supporting Information). Since in a previous study the effect of solvent was demonstrated to be crucial, here, the simulations include explicit solvent molecules, that is, a 4:1 mixture of acetonitrile:water. For each compound, 300,000 configurations were produced and their chromophore—chromophore distances employed to prepare the histograms are shown in Figure 6, and the configuration of the analyzed molecules is presented in Figure 7. The conformational analysis of 2 and 6 shows that the distances Cbz-Thy are lower than 10 Å (ca. 90% frequencies) in the case of 2, while for 6, only ca. 50% of dyads show distances <10 Å (Figure 6 left). These results support the TS-TTET proposed mechanism in the photo-
sensitized dimerization and are in agreement with the higher reactivity observed for 2 vs 6 (see Figure 1). Moreover, the chromophore−chromophore (Thy<>Thy-Cbz) distances <10 Å in 7 and 8 have frequencies lower than 16% (Figure 6 right), in agreement with the likely TB mechanism operating for the photosensitized repair. Moreover, the higher speed of the photosensitized TB-repair found in the case of 8 compared to 7 (Figure 5) could be the result of a more favored overlap between the LUMO of the CBz* and the σ* of the spacer bonds.

Overall, opening of Thy<>Thy in 8 in aerated 4CH₃CN:1H₂O results quantitatively into 6, due to the high distance between Thy-Cbz in 6 that prevents the subsequent TS-TTET in an aerated atmosphere. Conversely, opening of Thy<>Thy in 7 results into 2, in which the low distance Cbz-Thy allows an efficient TS-TTET even under an aerated atmosphere. As a result of the opposite trends, different equilibrium compositions are found as observed in Figure 5, upon 180 min irradiation.

2.6. Mechanistic Proposal. We have demonstrated that Cbz covalently attached to the skeleton of DCA together with two Thy units can act as an efficient photosensitizer to produce Thy<>Thy dimers that could be repaired depending on the reaction conditions (Scheme 3). Thus, Cbz can be selectively excited, in the presence of Thy, to its singlet excited state, which is efficiently quenched by O₂ and by TS electron transfer to the Thy unit in 12α. The thermodynamics of this electron transfer is favorable (E,Thy/Thy*=−1.34 V, E,Cbz*/Cbz= 1.12 V vs SCE, E₁,Cbz*= 3.63 eV). Nevertheless, this pathway would be an energy-wasting channel, which regenerates the initial dyad upon back electron transfer. Still, the Cbz* is reached upon intersystem crossing. In the absence of oxygen, this excited

Figure 5. HPLC Chromatograms (top) and conversion rate (bottom) for 7 (left) or 8 (right) upon increasing irradiation times (λ exc = 350 nm), at 0.2 mM in aerated 4CH₃CN:1H₂O. The chromatograms corresponding to 2 (pink trace, left) and 6 (green trace, right) are shown for comparison.

Figure 6. Left: Histogram of chromophore−chromophore distances of 2 and 6. Right: Histogram of chromophore−chromophore Thy-Cbz distances of 7 and 8. Results were in all cases obtained from molecular dynamics during 3 ns at 298 K in a 4:1 acetonitrile:water solvent. Each plot has been calculated using 300,000 configurations.

Figure 7. Configuration of molecules 2, 6, 7, and 8 showing the distances between chromophore groups (dotted lines).
species lives longer; thus, it is quenched by the Thy at 12α to give 3Thy* (TS-TTET is much more efficiently than TTET). The 3Thy* gives rise to the Thy<>Thy upon [2 + 2] cycloaddition with the second intramolecular unit. The yield of the Thy<>Thy is enhanced in a deaerated atmosphere and is dependent on the topology of the three units.

Photosensitized repair starts with selective irradiation of Cbz in the presence of the Thy<>Thy. To enhance the prospects of the e− transfer from the singlet, the experiments were performed under air. The electron transfer to the Thy<>Thy necessarily happens TB, since the probability of the three units being together is quite low. Once the e− transfer has happened, opening of the dimer regenerates the initial systems. The formation of Thy<>Thy is disfavored in the presence of air. The calculated distances between chromophore units support the postulated mechanism.

3. CONCLUSIONS

In rigid bile acid-derived systems, TS triplet energy transfer from 3Cbz* to Thy gives rise to photosensitized Thy<>Thy formation. In general, when photorepair can also occur TS, e− happens TB, since the probability of the three units being together is quite low. Once the e− transfer has happened, opening of the dimer regenerates the initial systems. The formation of Thy<>Thy is disfavored in the presence of air. The calculated distances between chromophore units support the postulated mechanism.

4. EXPERIMENTAL SECTION

4.1. Chemicals. Deoxycholic acid (DCA), 9-carbazoleacetic acid (Cbz-CH2-COOH), 9H-carbazole-9-ethanol (Cbz-CH2-OH), thymine 1-acetic acid (Thy-CH2-COOH), benzyl bromide, 1,8-diazabicyclo[5.4.0]undec-7-ene (DBU), N,N-disopropylethylamine (DIEA), 4-dimethylaminopyridine (4-DMAP), lithium aluminum hydride (LiAlH4), O-(benzotriazol-1-yl)-N,N,N′,N′-tetramethyluronium tetrafluoroborate (TBTU), 2,4,6-trichlorobenzoyl chloride, benzyl alcohol, titanium(IV) isopropoxide, triethylamine, acetonitrile, dimethylformamide (DMF), and tetrahydrofuran (THF) were purchased from Sigma-Aldrich. Experimental procedures and methods for characterization are reported in the Supporting Information. Structural assignments were made with additional information from 1D and 2D NMR experiments ([M + H]+ calcd for C35H36N4O4S, 586.3896; found, 586.3881. The 1H NMR (300 MHz, CDCl3) δ (ppm) 10.16 (s, 1H, Thy-NH), 10.02 (s, 1H, Thy-NH), 7.90 (d, J = 7.8 Hz, 2H, arom), 7.39–7.56 (m, 4H, arom), 7.22–7.32 (m, 2H, arom), 3.61 (m, 1H, 3J−H), 0.91 (s, 3H, CH3), 0.87 (d, J = 6.3 Hz, 3H, 21-CH3), 0.80–2.29 (complex signal, 26H), 0.62 (s, 3H, CH3), 13C(1H) NMR (75 MHz, CDCl3) δ (ppm) 174.2 (C), 140.5 (2xC), 125.9 (2xCH2), 123.1 (2xC), 120.4 (2xCH), 119.3 (2xCH2), 108.7 (2xCH), 73.2 (CH), 48.3 (CH), 36.5 (CH2), 36.1 (CH), 35.3 (CH2), 35.1 (CH), 34.2 (C), 33.7 (CH), 31.2 (CH2), 30.7 (CH2), 30.6 (CH2), 28.7 (CH2), 27.5 (CH2), 27.2 (CH2), 26.2 (CH2), 23.7 (CH2), 23.2 (CH3), 17.3 (CH3), 12.8 (CH3), HRMS (ESI) m/z: [M + H]+ calcld for C35H36N4O4S, 586.3896; found, 586.3881.

4.2. Synthesis of 1. To a stirred solution of Cbz-(CH2)2-COOH (0.42 g, 2.31 mmol) in anhydrous THF (10 mL) was added tert-BuONa (0.64 mL) and 2,4,6-trichlorobenzoyl chloride (0.43 mL, 2.77 mmol) followed by DIEA (1.17 mL, 6.75 mmol) were added dropwise, and then, the reaction mixture was allowed to react overnight. Afterward, it was poured into brine and extracted with CH2Cl2, the combined organic layers were washed with brine, dried over MgSO4, and concentrated under reduced pressure. Purification by column chromatography (SiO2, EtOAc:hexane, 1:3) gave 1 as a white solid (0.93 g, 2.36 mmol).

4.3. Synthesis of 2. A stirred suspension of Thy-CH2-COOH (0.42 g, 2.31 mmol) in anhydrous THF (10 mL) was added with Et3N (0.64 mL) and 2,4,6-trichlorobenzyl chloride (0.43 mL, 2.77 mmol), and the resulting mixture was allowed to react for 1.5 h. Then, a solution of 4-DMAP (0.11 g, 0.91 mmol) and 1 (0.45 g, 0.77 mmol) in anhydrous THF (10 mL) was added and stirred overnight. Afterward, the reaction mixture was poured into brine, extracted with CH2Cl2, and the combined extracts were washed with brine, dried over MgSO4, and concentrated under vacuum. Purification by column chromatography (SiO2, EtOAc:hexane, 9:1) gave 2 as a yellow oil (0.54 g, 77%). The 1H NMR (300 MHz, CDCl3) δ (ppm) 10.36 (s, 1H, Thy-NH), 10.19 (s, 1H, Thy-NH), 8.10 (d, J = 7.8 Hz, 2H, arom), 7.39–7.56 (m, 4H, arom), 7.22–7.32 (m, 2H, arom), 6.98 (s, 1H, Thy-CH3), 5.11 (br s, 1H, 12β-H), 4.72 (m, 2H, 3J−H), 4.28–4.65 (m, 8H, 2xThy-CH2 + 2xCH3), 1.90 (br s, 3H, Thy-CH3), 1.86 (br s, 3H, Thy-CH3), 0.88 (s, 3H, CH3), 0.82–2.25 (complex signal, 26H), 0.72 (d, J = 5.7 Hz, 3H, 21-CH3), 0.65 (s, 3H, CH3); 13C(1H) NMR (75 MHz, CDCl3) δ (ppm) 173.9 (C), 167.2 (C), 166.5 (C), 164.7 (C), 114.39 (C), 111.0 (C), 110.5 (C), 108.0 (2xCH2), 77.7 (CH), 76.4 (CH2), 62.1 (CH2), 49.2 (CH + 2xCH2), 47.2 (CH), 41.8 (C), 41.6 (CH2 + CH), 35.4 (CH), 34.5 (CH2), 34.5 (CH), 34.1 (CH), 31.7 (CH3), 30.9 (CH3), 30.4 (CH2), 27.1 (CH2), 26.7 (CH2), 25.9 (2xCH2), 25.2
4.4. Synthesis of 3. A stirred solution of DCA was converted into DCA-Bn following the procedure previously described in the literature. Then, a stirred suspension of LiAlH4 (0.33 g, 9.13 mmol) in anhydrous THF (8.5 mL) was cooled to −10 °C, treated with a solution of DCA-Bn (1.54 g, 3.19 mmol) and the resulting mixture was refluxed overnight (70 °C). Afterward, the reaction was quenched with saturated aqueous NH4Cl solution (5 mL), redissolved with EtOAc, and extracted with water. The combined organic layers were washed with water, dried over MgSO4, and evaporated under vacuum. Purification by column chromatography (SiO2, EtOAc:hexane, 1:1) gave 6 as a colorless solid (0.267 g, 60%).

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4.5. Synthesis of 4. A solution of Tyr-CN (0.34 g, 0.45 mmol) in anhydrous THF (11 mL) was added and stirred overnight. Afterward, the reaction mixture was poured into water, extracted with CH2Cl2 and the combined extracts were washed with water, dried over MgSO4, and concentrated under vacuum. Purification by column chromatography (SiO2, EtOAc:hexane, 1:1) gave 6 as a colorless oil (0.25 g, 60%).

4.6. Synthesis of 5. To a stirred solution of 4 (0.23 g, 0.41 mmol) and TBTU (0.45 g, 1.41 mmol) and NMM (0.44 g, 1.17 mmol) were added, followed by DIEA (0.61 mL, 3.51 mmol), and the resulting reaction mixture was allowed to react at rt for 7 h. Then, it was poured into water and extracted with CH2Cl2. The combined organic extracts were washed with water, dried over MgSO4, and concentrated under reduced pressure. Purification by column chromatography (SiO2, CH2Cl2:MeOH, 5:0.2) gave 5 as a yellowish solid (0.353 g, 56%).

4.7. Synthesis of 6. A stirred suspension of Tyr-CN (0.64 g, 1.7 mmol) in anhydrous THF (15 mL) was treated with EtN (0.76 mL) and 2,4,6-trichlorobenzyl chloride (0.51 mL, 3.29 mmol), and the resulting mixture was allowed to react for 90 min. Then, a solution of 4-DMAP (0.064 g, 0.53 mmol) and S (0.34 g, 0.45 mmol) in anhydrous THF (11 mL) was added and stirred overnight. Afterward, the reaction mixture was poured into water, extracted with CH2Cl2 and the combined extracts were washed with water, dried over MgSO4, and concentrated under vacuum. Purification by column chromatography (SiO2, EtOAc:hexane, 1:1) gave 6 as a colorless oil (0.267 g, 60%).
0.82–1.91 (complex signal, 2H); 0.78 (s, 3H, CH); 13C{1H} NMR (75 MHz, CDCl3, 6 (ppm) 171.2 (C), 170.8 (C), 169.4 (2xC), 168.3 (C), 151.3 (C), 150.3 (C), 140.8 (2xC), 125.9 (2xCH), 123.3 (2xC), 120.5 (2xCH), 119.6 (2xC), 108.6 (2xC), 74.2 (CH), 67.7 (CH), 66.6 (CH2), 66.3 (CH), 65.9 (CH), 50.9 (CH2), 50.3 (CH), 49.2 (CH), 46.8 (C), 46.7 (CH), 46.2 (C), 45.3 (C), 42.2 (CH), 36.5 (CH), 35.6 (CH), 35.0 (CH2), 34.8 (CH), 34.6 (C), 33.7 (CH), 32.7 (CH2), 27.4 (CH2), 27.0 (CH), 26.6 (CH), 26.4 (CH2), 25.9 (CH), 25.6 (CH2), 23.5 (CH2), 23.4 (CH), 22.3 (CH), 22.2 (CH2), 16.4 (CH), 14.4 (CH3), HRMS (ESI) m/z: [M + H]+ calc'd for C29H45N4O5 918.4653; found, 918.4662.

ASSOCIATED CONTENT

Supporting Information

The Supporting Information is available free of charge at https://pubs.acs.org/doi/10.1021/acs.joc.2c00942.

1H NMR, and 13C{1H} NMR and bidimensional spectra, X-ray details, additional photophysical experiments, computational methods (PDF)

Geometries: Coordinates of all species calculated in Figure 7 (MOV)

Videos of the crystal structure of 8 and computational structures of molecules 2, 6, 7, and 8 (ZIP)

Accession Codes

CCDC 2159900 contains the supplementary crystallographic data for this paper. These data can be obtained free of charge via www.ccdc.cam.ac.uk/data_request/cif, or by emailing data_request@ccdc.cam.ac.uk, or by contacting The Cambridge Crystallographic Data Centre, 12 Union Road, Cambridge CB2 1EZ, UK; fax: +44 1223 336033.

AUTHOR INFORMATION

Corresponding Authors

Miguel A. Miranda – Instituto de Tecnología Química, Universitat Politècnica de Valencia-Consejo Superior de Investigaciones Científicas, 46022 Valencia, Spain; orcid.org/0000-0002-7717-8750; Email: mmiranda@qim.upv.es

M. Luisa Marin – Instituto de Tecnología Química, Universitat Politècnica de Valencia-Consejo Superior de Investigaciones Científicas, 46022 Valencia, Spain; orcid.org/0000-0002-9789-8894; Email: marmarin@qim.upv.es

Authors

Gemma M. Rodríguez-Muníz – Instituto de Tecnología Química, Universitat Politècnica de Valencia-Consejo Superior de Investigaciones Científicas, 46022 Valencia, Spain; orcid.org/0000-0001-8989-2401

Miguel Gomez-Mendoza – Instituto de Tecnología Química, Universitat Politècnica de Valencia-Consejo Superior de Investigaciones Científicas, 46022 Valencia, Spain; Present Address: Present address: Photoactivated Processes Unit, IMDEA Energy Institute, Aveda Ramon de la Sagra 3, 28935 Mostoles, Madrid, Spain (M.G.-M.)

Paula Miro – Instituto de Tecnología Química, Universitat Politècnica de Valencia-Consejo Superior de Investigaciones Científicas, 46022 Valencia, Spain

Pilar García-Orduña – Dpto. Química Inorgánica, ISQCH-Instituto de Síntesis Química y Catalisis Homogénea, Facultad de Ciencias, CSIC-Universidad de Zaragoza, 50009 Zaragoza, Spain

German Sastre – Instituto de Tecnología Química, Universitat Politècnica de Valencia-Consejo Superior de Investigaciones Científicas, 46022 Valencia, Spain

German Sastre – Instituto de Tecnología Química, Universitat Politècnica de Valencia-Consejo Superior de Investigaciones Científicas, 46022 Valencia, Spain

Científicas, 46022 Valencia, Spain; orcid.org/0000-0003-0496-6331

Complete contact information is available at: https://pubs.acs.org/doi/10.1021/acs.joc.2c00942

Notes

The authors declare no competing financial interest.

ACKNOWLEDGMENTS

Financial support from the Spanish Government (grant SEV-2016-0683), Generalitat Valenciana (PROMETEO/2017/075 and PROMETEO/2021/077), and Technical University of Valencia (Predoctoral FPI fellowship for P.M.) is gratefully acknowledged. G.S. thanks CTI-CSIC for the use of computational facilities.

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