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Synthesis and Evaluation of a Photochromic Surfactant for Organic Reactions in Aqueous Media

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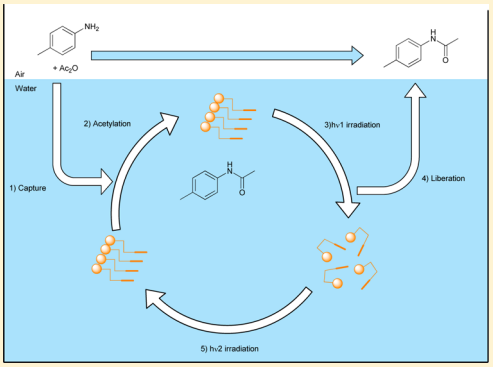
Supporting Information

ABSTRACT: A novel photochromic azobenzene-based surfactant was described for organic chemistry in water. The molecule 4-butylazobenzyl-4′-triazologlucuronic acid sodium salt thus synthesized can be isomerized from its trans to its cis form reversibly in solution by simple light irradiation. That property allowed the recyclability of a model acetylation reaction performed in the surfactant media, compared to the well-known, commercially available sodium dodecyl sulfate surfactant media.



INTRODUCTION

With the notion of green chemistry and its 12 principles,[1] organic chemists are strongly encouraged to use water as solvent, even for organic reactions. For this purpose, amphiphiles are one of many possibilities, because they are able to interact with both polar and nonpolar entities. Reactions that take place in micellar systems have been reviewed,[2] showing that surfactant assemblies lead to notable effects on the rate, recyclability, and selectivity of reactions.[3−6] It has been noticed that there are examples where surfactants can be used in substoichiometric quantities with respect to the substrate.

It is well-known that to control the molecular and supramolecular assemblies, and among various input sensors, photochromic cores, which have been drawing various attention for several decades, can operate a reversible control without any waste.[7−9] Among photochromic surfactant systems, azobenzene can modify its structure and this allows for various applications. Examples of those applications[10−16] show that the use of diazo compounds to modify media has already been widely discussed in the literature. Moreover, it was shown that the addition of an azo moiety to the hydrophobic tail of linear alkanesulfonates and alkanecarboxylates promotes adsorption and micellization.[17] In addition, it induces the preassociation of surfactant monomers below the critical micelle concentration (cmc) and improves the surfactant solubility in water. It was reported that the exposure of an azobenzene surfactant to UV or visible lights affected the cmc, the surface tension equilibrium, and the air−water interfacial composition.[18] Recently, it was demonstrated that UV illumination can induce the bursting of a significant fraction of cell-sized multicomponent lipid vesicles in a photosensitive surfactant solution containing an azobenzene moiety.[19] However, to the best of our knowledge, no report outlined the use of photochromic surfactant as chemical reactor for organic reactions in aqueous media to allow the reversible photo-organization and disorganization of the micelles formed and thus the possible recycling of the reaction mixture.

On the basis of those results, the main purpose of the present work was to focus on a photochromic surfactant for reactions in water. The molecule was designed (i) for its ability to organize and disorganize in solution, (ii) to facilitate the reactions taking place in an aqueous phase, (iii) to allow a better extraction of the product formed, and (iv) to enable the recyclability of the reaction phase. So, bearing an azobenzene moiety as photochromic core, an alkyl chain as hydrophobic tail, and a modified sugar as hydrophilic headgroup, 4-butylazobenzyl-4′-triazologlucuronic acid sodium salt (BABTGA, **1**) was chosen to be our best candidate (Figure 1). The chromophore and the hydrophilic head were linked together by a triazole moiety, giving the molecule many advantages, such as is its polarity and its ease of synthesis, implying an atom economy.

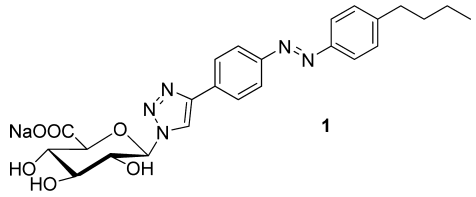


Figure 1. 4-Butylazobenzyl-4′-triazologlucuronic acid sodium salt (BABTGA).

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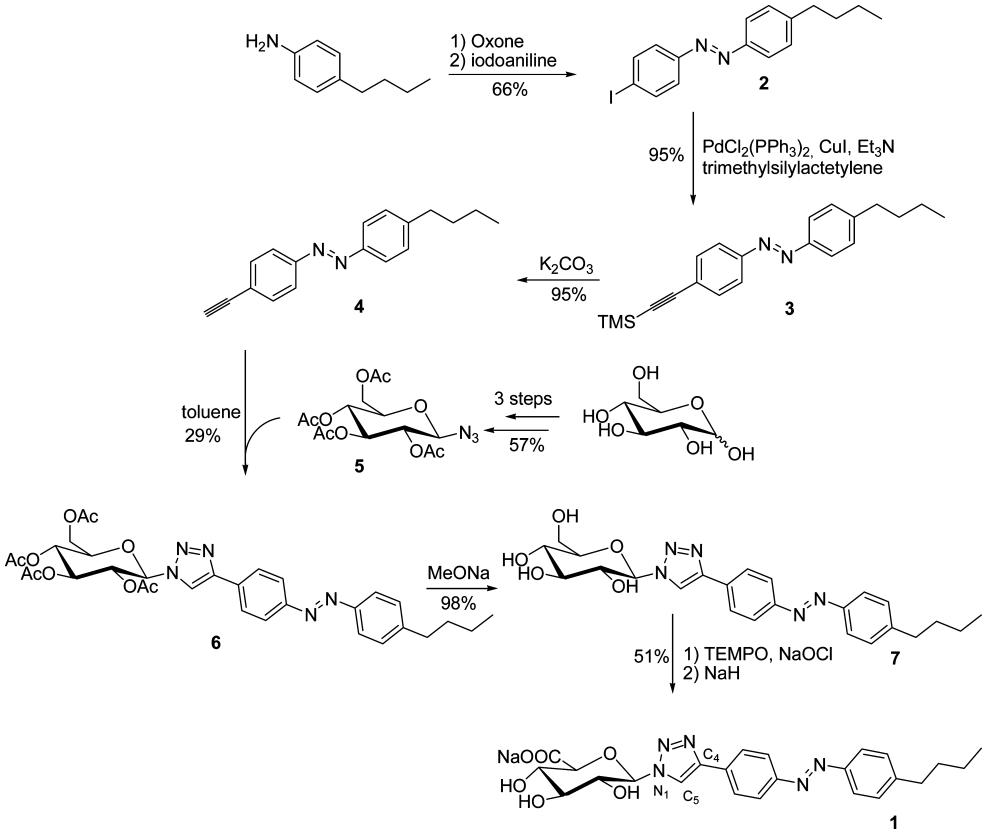
Scheme 1. Synthetic Pathway of 4-Butylazobenzyl-4′-triazologlucuronic Acid Sodium Salt (BABTGA, 1)

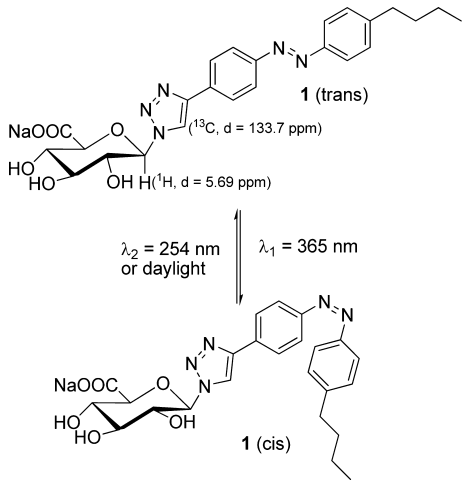


RESULTS AND DISCUSSION

Azobenzene **2** (Scheme 1) was synthesized by coupling the nitrosoarene (the oxidized form of butylaniline by oxone)[20] with iodoaniline. The butyl chain was chosen according to the results referred to above.[14] Then, a Sonogashira coupling[21] with trimethylsilylacetylene afforded the protected alkynylazobenzene **3**, which was deprotected[22] in basic media to obtain the surfactant precursor **4** with a yield of 90% over the two steps. In three steps, a mixture of D-glucose was transformed into its 2,3,4,6-tetra-*O*-acetyl-*β*-D-glucopyranosyl azide **5** with an overall yield of 57%,[23] which was coupled with **4** by performing a copper-free Huisgen's 1,3-dipolar cycloaddition to furnish successively the azobenzene product **6** and then the corresponding deprotected analogue **7** in 28% yield overall.[24−26] As the deprotected molecule **7** was not fully soluble in water, the selective oxidation of its primary alcohol into its carboxylic acid sodium salt by TEMPO as oxidant and sodium hypochlorite as co-oxidant was performed.[27] This was followed by an acid−base reaction to obtain the target compound **1** without need of any purification.

The literature clearly shows that the outcome of the addition of azides to unsymmetrical acetylenes without the addition of any copper catalyst is determined by steric and electronic factors.[28] Such an addition tends to give mainly the isomers with electron-withdrawing groups at the fourth position. On the other hand, the sterically less-hindered isomer tends to be the major one.[28] But in our hand, it is noticeable that even without copper only the 1,4-triazole isomer was obtained. This was confirmed by an NMR HMBC experiment (Scheme 2) showing a correlation peak between the anomeric proton (δ = 5.69 ppm) and the carbon (proved to be the tertiary carbon by DEPT 135) at the fifth position in the triazole moiety (δ = 133.7 ppm).

Scheme 2. NMR Chemical Shifts and Isomerization Equilibrium from *trans*- to *cis*-BABTGA (1)



In order to confirm the ability of the diazo function to isomerize under UV exposure (Scheme 2), BABTGA (**1**) has been analyzed by UV/vis absorption spectroscopy using a 500 W mercury lamp. As shown in Figure 2, UV irradiation at 365 nm of the sample containing **1** in pure water at room temperature causes a substantial change in the UV/vis spectra, allowing the compound **1** to switch from its trans to its cis form. The absorption band at around 340 nm decreases gradually as the irradiation goes on. At the same time, the bands at around 250 and 420 nm slightly increase. Because the

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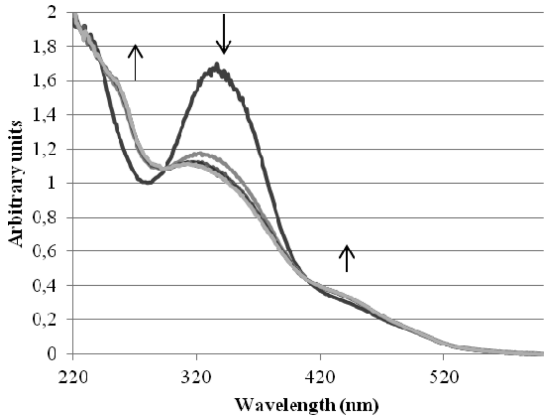


Figure 2. Overlaid UV spectra (1 scan per 30 s, from 0 to 4 min) during the isomerization of BABTGA (**1**) at 365 nm (500 W lamp). Sample concentration: 5×10^{-5} mol/L.

absorption bands at 340, 250, and 420 nm are ascribed to $\pi-\pi^*$ and $n-\pi^*$ of the trans form and the cis form of azo moiety, respectively,[29] this spectral variation clearly shows the isomerization of the azo groups from the trans photoisomer to the cis photoisomer. The maximum isomerization yield was obtained after 4 min of irradiation at 365 nm. The cis isomer of **1** was found to be stable when protected from the light for at least 18 h.

When irradiated at 254 nm (Figure 3), the cis isomer of **1** returned gradually to its trans form, and the maximum

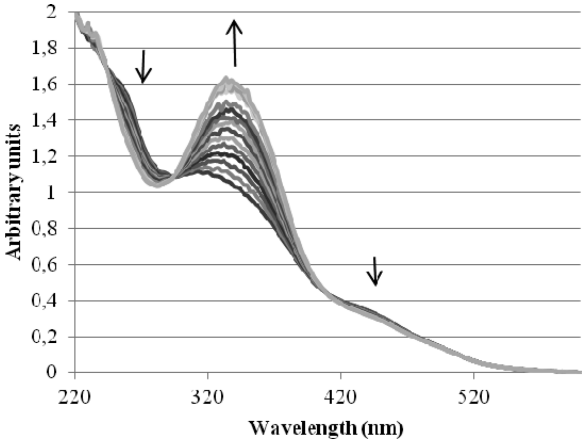


Figure 3. Overlaid UV spectra (1 scan per 30 s, from 0 to 6 min) during the isomerization of BABTGA (**1**) at 254 nm (500 W lamp). Sample concentration: 5×10^{-5} mol/L.

isomerization yield was obtained after 6 min of irradiation. It is noticeable that upon exposure to natural daylight, the cis form goes to its trans form in approximately 40 min. Finally, as already shown for numerous azo derivatives, it must be pointed out that the cis isomer could not be isolated in pure form.[30]

Repeating the irradiation of BABTGA (**1**) in solution from its trans to cis and then cis to trans forms several times did not yield any degradation of **1**, as the maximum UV spectra obtained after each irradiation was identical to the previous ones. At the equilibrium the amount of cis/trans isomers (10/90) was determined by a ^{1}H NMR experiment.

Surface tension measurements without and with photoisomerization of the compound in water were performed. Without isomerization, *trans*-BABTGA (**1**) reduces significantly the water surface tension from 72.6 to 29.9 mN/m. The rupture in the slope of the $\gamma = f([\text{BABTGA}])$ curves around a concentration of 3×10^{-3} mol/L of **1** could indicate an aggregation process rather than a cmc, as the product solubility limit in water has been reached (Figure 4). Four minutes of

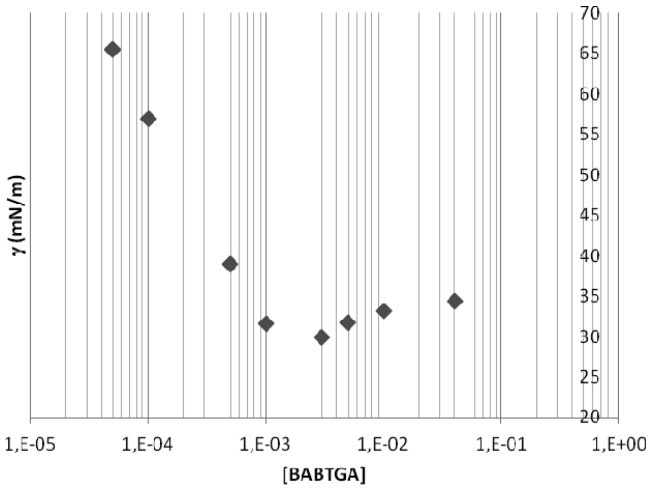
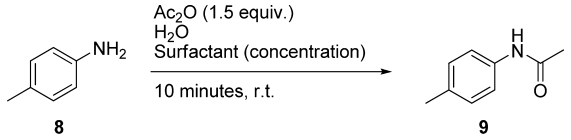


Figure 4. Surface tension curve of BABTGA (**1**) in water at 20 °C.

irradiation at 365 nm of **1** prior to surface tension measurement did not induce any major variation of these measures, despite the theoretic dipolar moment variation induced by the isomerization. So the tensioactivity variation from the trans to the cis form is very small.

To evaluate our system properties on a model reaction, the acetylation of anilines (Scheme 3) was chosen. Indeed, the

Scheme 3. Acetylation of *p*-Toluidine under Various Surfactant Conditions



8 **9**

acetylation of amines and anilines is an important and widely used transformation in organic synthesis, and a number of reagents coupled with promoters or catalysts have been put forth.[31−34] With the aim of performing microreactions in aqueous media, acid halides and acid anhydrides are usually employed.[35] Few other strategies have been reported in the literature, especially with acetic anhydride in sodium dodecyl sulfate (SDS) media.[36] However, in our hands (Scheme 3), and in contrast with the literature,[36] the solid obtained after filtration was not pure enough due to the remaining starting material, so after purification on a column chromatography, the target amide **9** was obtained in 74% isolated yield (Table 1, entry 3).

To optimize the reaction, the same process was repeated with a higher SDS concentration above the cmc (9×10^{-3} vs 3.5×10^{-3} mol/L) (Table 1, entry 4). The yield was still around 75%, but the recycling of the reaction at this concentration did not give any better result. So the initial conditions described in the literature (Table 1, entry 3) were used as our control test.

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Table 1. Optimization of the *p*-Toluidine Acetylation under Surfactant Conditions

entry	surfactant	concn (mol/L)	irradiation time[a] (min)	isolated yield of **9** (%)
1	none	–	–	61
2	none	–	10[b]	62
3	SDS	3.5×10^{-3}	–	74
4	SDS	9×10^{-3}	–	73
5	BABTGA	1.5×10^{-3}	5	69
6	BABTGA	3.5×10^{-3}	–	65
7	BABTGA	3.5×10^{-3}	5	77

[a]Irradiation time (in min) at 365 nm just before the product filtration in the dark. [b]Irradiation time (in min) at 365 nm during the reaction.

Without any surfactant (Table 1, entry 1), the toluidine **8** gave **9** in 61% yield. Under 365 nm light, the model acetylation proved that the reaction was not light-driven (Table 1, entry 2). At a lower concentration of 1.5×10^{-3} mol/L and when irradiated just before the filtration of the product, BABTGA (**1**) allowed the toluidine **8** to give the target product **9** in a low yield of 69% (Table 1, entry 5). When its concentration increased to 3.5×10^{-3} mol/L, the same as our control test using SDS, the product **9** was obtained in 77% yield (Table 1, entry 7). The same manipulation without any irradiation before the filtration gave a yield of 65% (Table 1, entry 6). The difference of 12% yield between entries 6 and 7 could be directly correlated to the photochromism ability of the molecule in water. However, and despite the lack of surface tension variation observed previously, the photoirradiation directly acts on the surfactant **1** for a better extraction of the amide **9** formed from the media. Taking the best results of the conditions described above (Table 1, entries 3 and 7), the recycling of the media was carried out. *p*-Toluidine and the acetic anhydride were added to each filtrate of the two reactions and the reactions were launched again. As shown in Figure 5,

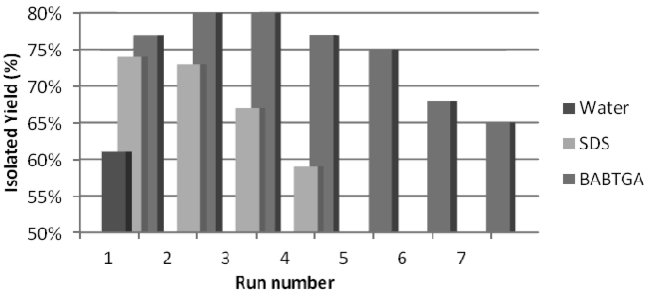

Figure 5. Recyclings of the reaction in SDS or BABTGA media compared to pure water only.

four runs were performed with SDS giving **9** from **8** with yields of 74%, 73%, 67%, and 59%, respectively. So after three recyclings, the amount of product **9** obtained may be compared to that without surfactant (Table 1, entry 1), whereas with BABTGA (**1**) the acetylated product was obtained with 77%, 80%, 80%, 77%, 75%, 68%, and 65%, respectively, allowing the media to be recycled six times until the surfactant effect was not noticeable anymore, leading to a real improvement of the media effect on the reaction tested. In both cases, however, the decreasing of reactivity may be correlated with the loss of surfactant molecules during the amide **9** extraction by filtration. The acidity of the acetic acid residue at the end of each reaction was measured by pH-metry and showed that the pH of the media before any reaction was launched was of 6.0 and it reached 2.7 at the end of the first run, being stable around 2.5 after that. So a reaction under acetic acid conditions (pH = 2.5) without surfactant was performed, and the yield obtained was identical to that in pure water.

To explore the versatility of the reaction, different reactions were carried out with various substrates and various anhydrides (Table 2).

By using BABTGA (**1**) instead of SDS, the chemoselectivity between a hydroxyl and an amino group is still observed, even with 4-aminobenzyl alcohol (Table 2, entries 1–4). These results were consistent with the literature.[36] It has been observed that in acetylation reactions electron-donating groups favor the reaction, whereas electron-withdrawing groups inhibit the reaction when performed in organic reaction media. Upon switching from a hydroxyl group to a strong electron-withdrawing group, the yield of the reaction fell drastically to 54% (Table 2, entry 6), as expected, and no reaction was observed with this moiety in the para-position, due to the mesomeric effect of the nitro group. To figure out the importance of the aromatic moiety substituent, 4-bromoaniline and the 4-aminobenzoic acid were tested as substrates and gave the corresponding target compounds **16** and **17** in 81% and 80%, respectively (Table 2, entries 7 and 8), so there is still a strong correlation between the moiety carried by the aniline substrate and the success of the reaction in our media.

Starting from *β*-naphtylamine or *N*-methylaniline as secondary arylamine, the acetylation gave the corresponding amides **18** and **19** in 88% and 86% yields (Table 2, entries 9 and 10).

Then the possible regioselectivity starting from *p*-phenylenediamine as substrate was tested (Table 2, entry 11). Using our optimized conditions, the acetylation of the diamine did not furnish the monoacetylated compound. The peracetylation was conducted to give the diacetylated compound **20** in 71% yield.

The aliphatic amine acetylation in the presence of acetic anhydride afforded the coformation of acetic acid, involving the protonation of the amino group. With regard to the literature, using SDS as surfactant,[25] the amine retained its nucleophilic character. In the presence of BABTGA (**1**) the aliphatic amines lost their activity upon an increase of the acetic acid concentration (Table 2, entries 12 and 13).

When switching from acetic anhydride to benzoic or hexanoic anhydride (Table 2, entries 14 and 15), the corresponding amides **23** and **24** were obtained in good yields of 80% and 73%, respectively, tending to demonstrate that the acylation reaction is not affected by sterically hindered or longer linear anhydrides.

■ CONCLUSION

To conclude, the synthesis and evaluation of a novel photochromic surfactant BABTGA (**1**) were descibed for organic chemistry in water. The photochromic surfactant was designed (i) to photo-organize and disorganize in aqueous solution [BABTGA (**1**) can isomerize reversibly from its trans to its cis form by light irradiation], (ii) to allow a better extraction of the product formed thanks to its photochromism ability, (iii) to facilitate the reactions taking place in an aqueous phase (decreasing substantially the water surface tension), and (iv) to enable the recycling of a model acetylation reaction.

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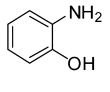
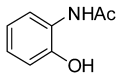
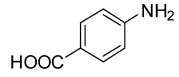
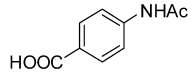
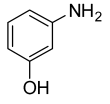
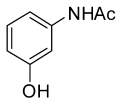
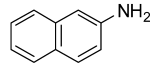
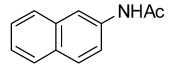
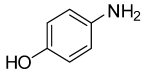
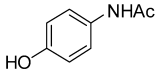
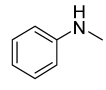
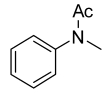
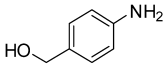
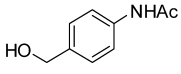
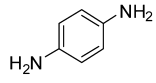
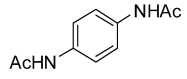
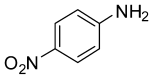
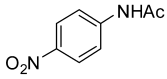
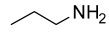
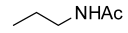
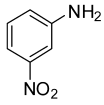
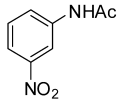
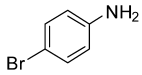
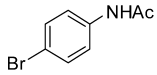
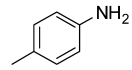
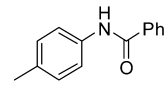
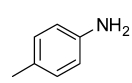
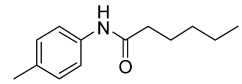
Table 2. Reaction of Various Substrates with Anhydrides[a]

Entry	Substrate	**Product**:Isolated Yield	Entry	Substrate	**Product**:Isolated Yield
1		 **10**:79%	8		 **17**:80%
2		 **11**:83%[b]	9		 **18**:88%
3		 **12**:79%[b]	10		 **19**:86%[b]
4		 **13**:71%[b]	11		 **20**:71%[c]
5		 **14**:0%	12		 **21**:50%[b]
6		 **15**:54%	13		 **22**:30%[b]
7		 **16**:81%	14		 **23**:80%
			15		 **24**:73%

[a]Typical procedure: To a solution of the amine (1 mmol, 1 equiv) and BABTGA (9.6 mg) in water (5 mL) was added the anhydride (1.5 mmol, 1.5 equiv). The mixture was stirred at room temperature for 10 min. The mixture was irradiated at 365 nm during 5 min. Then the mixture was filtered and the residue was purified using column chromatography on silica gel. A typical procedure used acetic anhydride (Ac), benzoic anhydride, or hexanoic anhydride. [b]Organic extraction with ethyl acetate was performed after the irradiation instead of the simple filtration described in the general procedure. [c]As no regioselectivity was observed, the reaction was carried out with 3 equiv of acetic anhydride.

EXPERIMENTAL SECTION

Materials. All starting materials were used without purification. All reactions were monitored by TLC with detection by UV light. Flash column chromatography was performed on silica gel SiOH 40−60 μm. UV analyses were performed on a UV/vis spectrophotometer coupled with an optic fiber. A 500 W mercuric lamp was used for the irradiation of the BABTGA solutions. Mass spectrometry analyses were performed on a mass spectrometer equipped with an electrospray source (ESCI). The structures were assigned by aid of the following techniques: ^{1}H and ^{13}C NMR and, if needed, HMBC and COSY H−H experiments. ^{1}H and ^{13}C NMR, HMBC, and COSY H−H spectra were recorded on a 400 MHz instrument. Chemical shifts (δ) are quoted in ppm and are referenced to TMS as an internal standard. Coupling constants (J) are quoted in Hz; common splitting patterns and their abbreviations are s (singulet), d (doublet), t (triplet), q (quartet), quin (quintet), sex. (sextet), and m (multiplet). Infrared spectra were measured on FT/IR instrument equipped with an ATR apparatus. Melting points were recorded without correction. High-resolution electrospray mass spectra (HR-ESI-MS) in the positive ion mode were obtained on a quadrupole/time-of-flight instrument, equipped with a pneumatically assisted electrospray (Z-spray) ion source. Surface tension was measured by a Wilhelmy plate technique using a tensiometer thermostated at 20 °C. The concentrations tested were of 5×10^{-5}, 10^{-4}, 5×10^{-4}, 10^{-3}, 3×10^{-3}, 5×10^{-3}, 10^{-2}, and 4×10^{-2} mol/L solution of **1**. α_D^{20} was recorded in methanol at 20 °C.

1-(4-Butylphenyl)-2-(4-iodophenyl)diazene (2). Following the method described in the literature,[20] to a solution of 4-butylaniline (3 mL, 18.9 mmol, 1 equiv) in CH_2Cl_2 (60 mL) under nitrogen atmosphere was added a solution of Oxone (23 g, 37.9 mmol, 2 equiv) in water (240 mL). The reaction mixture was stirred vigorously under nitrogen atmosphere at room temperature during 12 h. The layers were separated, and the aqueous layer was washed with CH_2Cl_2 (2 × 60 mL). The organic layer was washed successively by a solution of 1 N HCl (150 mL), a saturated solution of $NaHCO_3$ (150 mL), and brine (150 mL). The organic layer was dried over Na_2SO_4, filtered, and concentrated under vacuum. 1-Butyl-4-nitrosobenzene (2.26 g, 73% yield) was obtained as a green oil and used directly due to the instability of the compound. To a solution of 1-butyl-4-nitrosobenzene (2.26 g, 13.84 mmol, 1 equiv) in glacial acetic acid (110 mL) was added 4-iodoaniline (3.64 g, 16.61 mmol, 1.2 equiv). The reaction mixture was stirred for 24 h at room temperature. After addition of water (100 mL), the product was extracted with CH_2Cl_2 (2 × 200 mL) and washed with a solution of 1 N HCl (200 mL). The organic layer was dried over Na_2SO_4, filtered, and concentrated under vacuum. The product was purified using column chromatography on silica gel

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(cyclohexane/CH_2Cl_2 95:5) to obtain 1-(4-butylphenyl)-2-(4-iodophenyl)diazene (**2**) (3.31 g, 66% yield) as an orange solid. R_f = 0.4 (cyclohexane/CH_2Cl_2 95:5). Mp: 84−86 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) 0.95 (t, J = 7.6 Hz, 3H, CH_3), 1.38 (sex., J = 7.6 Hz, 2H, CH_2), 1.65 (quin, J = 7.6 Hz, 2H, CH_2), 2.69 (t, J = 7.6 Hz, 2H, CH_2), 7.32 (d, J = 8.4 Hz, 2H, CH^{Ar}), 7.63 (d, J = 8.4 Hz, 2H, CH^{Ar}), 7.83 (d, J = 8.4 Hz, 2H, CH^{Ar}), 7.85 (d, J = 8.4 Hz, 2H, CH^{Ar}). ^{13}C NMR (101 MHz, $CDCl_3$): δ (ppm) 13.9 (CH_3), 22.3 (CH_2), 33.4 (CH_2), 35.6 (CH_2), 97.2 (C^{Ar}), 122.9 (2 × CH^{Ar}), 124.4 (2 × CH^{Ar}), 129.2 (2 × CH^{Ar}), 138.3 (2 × CH^{Ar}), 147.0 (C^{Ar}), 150.7 (C^{Ar}), 152.0 (C^{Ar}). ESI-MS: $[M + H]^+$ calcd for $C_{16}H_{18}IN_2$ m/z = 365.05 found m/z = 365.00. HRMS: $[M + H]^+$ calcd for $C_{16}H_{18}IN_2$ m/z = 365.0509, found m/z = 365.0508. UV/vis (CH_3CN) (L mol^{-1} cm^{-1}): λ (ε_0) = 229 nm (75 800), 337 nm (60 533), 439 nm (7553).

1-(4-Butylphenyl)-2-(4-(2-(trimethylsilyl)ethynyl)-phenyl)-diazene (3). Following the method described in the literature,[21] under nitrogen atmosphere, 1-(4-butylphenyl)-2-(4-iodophenyl)-diazene (**2**) (0.67 g, 1.84 mmol, 1 equiv), $PdCl_2(PPH_3)_2$ (0.064 g, 0.092 mmol, 5 mol %), and copper iodide (0.024 g, 0.18 mmol, 10 mol %) were added successively. Then, anhydrous THF (11 mL) and Et_3N (2 mL, 14.72 mmol, 8 equiv) were added to the substrates. Finally, trimethylsilylacetylene (0.2 g, 2.02 mmol, 1.1 equiv) was added. The reaction mixture was stirred at room temperature under nitrogen atmosphere for 4 h. The reaction was quenched with a saturated solution of NH_4Cl. The product was extracted with CH_2Cl_2 (2 × 50 mL) and washed with a saturated solution of NH_4Cl (100 mL). The organic layer was dried over Na_2SO_4, filtered, and concentrated under vacuum. The product was purified using column chromatography on silica gel (cyclohexane/CH_2Cl_2 95:5) to obtain 1-(4-butylphenyl)-2-(4-(2-(trimethylsilyl)ethynyl)phenyl)diazene (**3**) (0.58 g, 95% yield) as an orange solid. R_f = 0.55 (cyclohexane/CH_2Cl_2 7:3). Mp: 78−80 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) 0.28 (s, 9H, Si-CH_3), 0.95 (t, J = 7.6 Hz, 3H, CH_3), 1.39 (sex., J = 7.6 Hz, 2H, CH_2), 1.65 (quin, J = 7.6 Hz, 2H, CH_2), 2.69 (t, J = 7.6 Hz, 2H, CH_2), 7.32 (d, J = 8 Hz, 2H, CH^{Ar}), 7.60 (d, J = 8 Hz, 2H, CH^{Ar}), 7.84 (d, J = 8 Hz, 2H, CH^{Ar}), 7.85 (d, J = 8 Hz, 2H, CH^{Ar}). ^{13}C NMR (101 MHz, $CDCl_3$): δ (ppm) 0 (3 × $SiCH_3$), 13.9 (CH_3), 22.3 (CH_2), 33.4 (CH_2), 35.6 (CH_2), 96.8 (C^{sp}), 104.7 (C^{sp}), 122.6 (2 × CH^{Ar}), 122.9 (2 × CH^{Ar}), 125.4 (C^{Ar}), 129.1 (2 × CH^{Ar}), 132.8 (2 × CH^{Ar}), 146.9 (C^{Ar}), 150.9 (C^{Ar}), 152.0 (C^{Ar}). ESI-MS: $[M + H]^+$ calcd for $C_{21}H_{27}N_2Si$ m/z = 335.19, found m/z = 335.15. HRMS: $[M + H]^+$ calcd for $C_{21}H_{27}N_2Si$ m/z = 335.1938, found m/z = 335.1944. UV/vis (CH_3CN) (L mol^{-1} cm^{-1}): λ (ε_0) = 229 nm (36 400), 349 nm (34 933), 442 nm (3687).

1-(4-Butylphenyl)-2-(4-ethynylphenyl)diazene (4). Following the method described in the literature,[22] to a solution of 1-(4-butylphenyl)-2-(4-(2-(trimethylsilyl)ethynyl)phenyl)diazene (**3**) (0.55 g, 1.64 mmol, 1 equiv) in methanol (130 mL) was added K_2CO_3 (0.22 g, 1.64 mmol, 1 equiv). The reaction mixture was stirred at room temperature for 3 h. The solvent was removed under vacuum. The residue was diluted in CH_2Cl_2 (100 mL) and washed with distillated water (2 × 100 mL) and brine (100 mL). The organic layer was dried over Na_2SO_4, filtered, and concentrated under vacuum. The product did not need further purification. 1-(4-Butylphenyl)-2-(4-ethynylphenyl)diazene (**4**) (0.41 g, 95% yield) was obtained as an orange solid. R_f = 0.47 (cyclohexane/CH_2Cl_2 7:3). Mp: 70−72 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) 0.97 (t, J = 7.6 Hz, 3H, CH_3), 1.40 (sex., J = 7.6 Hz, 2H, CH_2), 1.67 (quin, J = 7.6 Hz, 2H, CH_2), 2.70 (t, J = 7.6 Hz, 2H, CH_2), 3.24 (s, 1H, CH), 7.33 (d, J = 8.4 Hz, 2H, CH^{Ar}), 7.64 (d, J = 8.4 Hz, 2H, CH^{Ar}), 7.87 (d, J = 8.4 Hz, 2H, CH^{Ar}), 7.88 (d, J = 8.4 Hz, 2H, CH^{Ar}). ^{13}C NMR (101 MHz, $CDCl_3$): δ (ppm) 13.9 (CH_3), 22.3 (CH_2), 33.4 (CH_2), 35.6 (CH_2), 79.3 (C^{sp}), 83.3 (C^{sp}), 122.7 (2 × CH^{Ar}), 123.0 (2 × CH^{Ar}), 124.3 (C^{Ar}), 129.1 (2 × CH^{Ar}), 132.9 (2 × CH^{Ar}), 147.0 (C^{Ar}), 150.8 (C^{Ar}), 152.3 (C^{Ar}). ESI-MS: $[M + H]^+$ calcd for $C_{18}H_{19}N_2$ m/z = 263.15, found m/z = 263.10. HRMS: $[M + H]^+$ calcd for $C_{18}H_{19}N_2$ m/z = 263.1548, found m/z = 263.1545. UV/vis (CH_3CN) (L mol^{-1} cm^{-1}): λ (ε_0) = 231 nm (26 641), 339 nm (30 358), 445 nm (2433).

2,3,4,6-Tetra-*O*-acetyl-β-D-glucopyranosyl Azide (5). Following the method described in the literature,[23] 2,3,4,6-tetra-*O*-acetyl-β-D-glucopyranosyl azide was obtained starting from glucose in three steps.

First, acetic anhydride (75 mL) was added at 0 °C to a solution of D-glucose (17 g, 83.26 mmol, 1 equiv) in pyridine (150 mL). After stirring at room temperature for 2 days, the excess of acetic anhydride was quenched with methanol. The solvent was evaporated under vacuum. The product was precipitated in water and filtrated to obtain 1,2,3,4,6-penta-*O*-acetyl-D-glucopyranose (32 g, 94% yield) as a white solid. R_f = 0.18 (cyclohexane/EtOAc 7:3).

Second, 1,2,3,4,6-penta-*O*-acetyl-D-glucopyranose (8 g, 20.49 mmol, 1 equiv) was dissolved in CH_2Cl_2 (100 mL). A solution of hydrogen bromide (33% in acetic acid, 50 mL) was added at 0 °C. The reaction mixture was stirred at room temperature. After 3 h the reaction was quenched with a saturated solution of $NaHCO_3$. The product was extracted with CH_2Cl_2 (2 × 100 mL) and washed with a saturated solution of $NaHCO_3$ (2 × 100 mL). The organic layer was washed with Na_2SO_4, filtered, and concentrated under vacuum. 2,3,4,6-Tetra-*O*-acetyl-α-D-glucopyranosyl bromide (8.17 g, 97% yield) was obtained as a colorless paste and used directly without further purification. R_f = 0.5 (cyclohexane/EtOAc 7:3).

Third, to a solution of 2,3,4,6-tetra-*O*-acetyl-α-D-glucopyranosyl bromide (6.7g, 16.29 mmol, 1 equiv) in dry CH_3CN (70 mL) was added NaN_3 (3.8 g, 58.65 mmol, 3.6 equiv). The reaction mixture was stirred at 80 °C under nitrogen atmosphere overnight. The mixture was filtered through a Büchner apparatus and the solvent was removed under vacuum. The product 2,3,4,6-tetra-*O*-acetyl-β-D-glucopyranosyl azide (**5**) (3.83 g, 63% yield) was obtained after recrystallization from ethanol as white crystals. R_f = 0.31 (cyclohexane/EtOAc 7:3). ^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) 2.00 (s, 3H, OCH_3), 2.02 (s, 3H, OCH_3), 2.07 (s, 3H, OCH_3), 2.10 (s, 3H, OCH_3), 3.79 (ddd, J = 2.4, 4.8, 10 Hz, 1H, H-5), 4.16 (dd, J = 2.4, 12.4 Hz, 1H, H-6a), 4.27 (dd, J = 4.8, 12.4 Hz, 1H, H-6b), 4.64 (d, J = 8.8 Hz, 1H, H-1), 4.95 (dd, J = 8.8, 9.6 Hz, 1H, H-2), 5.11 (dd, J = 9.2, 10 Hz, 1H, H-4), 5.21 (dd, J = 9.2, 9.6 Hz, 1H, H-3). ^{13}C NMR (101 MHz, $CDCl_3$): δ (ppm) 20.5 (2 × $COCH_3$), 20.6 ($COCH_3$), 20.7 ($COCH_3$), 61.6 (CH_2), 67.8 (CH), 70.6 (CH), 72.6 (CH), 77.0 (CH), 87.9 (CH), 169.2 ($COCH_3$), 169.3 ($COCH_3$), 170.1 ($COCH_3$), 170.6 ($COCH_3$). ESI-MS: $[M + Na]^+$ calcd for $C_{14}H_{19}N_3NaO_9$ m/z = 396.10, found m/z = 396.00.

(1-((2,3,4,6-Tetra-*O*-acetyl)-1-β-D-glucopyranosyl)-(1,2,3-triazol-4-yl))-4′-butylazobenzene (6). Following the method described in the literature,[27] to a solution of 2,3,4,6-tetra-*O*-acetyl-β-D-glucopyranosyl azide (**5**) (2.20 g, 8.39 mmol, 1 equiv) in the minimum amount of toluene was added 1-(4-butylphenyl)-2-(4-ethynylphenyl)diazene (**4**) (3.13 g, 8.39 mmol, 1 equiv). The reaction mixture was stirred at reflux for 24 h. The solvent was concentrated under vacuum. The product was purified using column chromatography on silica gel (cyclohexane/EtOAc 9:1 to 7:3) to obtain (1-((2,3,4,6-tetra-*O*-acetyl)-1-β-D-glucopyranosyl)-(1,2,3-triazol-4-yl))-4′-butylazobenzene (**6**) (1.68 g, 29% yield) as an orange solid. R_f = 0.22 (cyclohexane/EtOAc 7:3). Mp: 120−122 °C. ^{1}H NMR (400 MHz, DMSO-d_6): δ (ppm) 0.92 (t, J = 7.6 Hz, 3H, CH_3), 1.34 (sex., J = 7.6 Hz, 2H, CH_2), 1.62 (quin, J = 7.6 Hz, 2H, CH_2), 1.80 (s, 3H, OCH_3), 1.97 (s, 3H, OCH_3), 2.02 (s, 3H, OCH_3), 2.11 (s, 3H, OCH_3), 2.7 (t, J = 7.6 Hz, 2H, CH_2), 4.15−4.26 (m, 2H, H-6a,b), 4.43−4.47 (m, 1H, H-5), 5.11 (t, J = 9.6 Hz, 1H, H-3), 5.61 (dd, J = 9.2, 9.6 Hz, 1H, H-4), 5.82 (dd, J = 9.2, 9.6 Hz, 1H, H-2), 6.32 (d, J = 9.2 Hz, 1H, H-1), 7.45 (d, J = 8.4 Hz, 2H, CH^{Ar}), 7.81 (d, J = 8.4 Hz, 2H, CH^{Ar}), 7.88 (d, J = 8.4 Hz, 2H, CH^{Ar}), 8.05 (d, J = 8.4 Hz, 2H, CH^{Ar}), 8.15 (s, 1H, CH). ^{13}C NMR (101 MHz, DMSO-d_6): δ (ppm) 13.7 (CH_3), 20.1 ($COCH_3$), 20.4 ($COCH_3$), 20.6 ($COCH_3$), 21.7 (CH_2), 22.2 ($COCH_3$), 32.8 (CH_2), 34.7 (CH_2), 61.7 (CH), 67.4 (CH), 69.2 (CH), 72.5 (CH), 73.02 (CH), 81.6 (CH), 122.8 (2 × CH^{Ar}), 123.0 (2 × CH^{Ar}), 127.8 (C^{Ar}), 129.4 (2 × CH^{Ar}), 130.0 (2 × CH^{Ar}), 133.6 (CH), 138.3 (CH), 147.2 (C^{Ar}), 150.1 (C^{Ar}), 152.3 (C^{Ar}), 168.1 ($COCH_3$), 169.0 ($COCH_3$), 170.0 ($COCH_3$), 170.2 ($COCH_3$). ESI-MS: $[M + Na]^+$ calcd for $C_{32}H_{37}N_5NaO_9$ m/z = 658.26, found m/z = 658.25. HRMS: $[M + H]^+$ calcd for $C_{32}H_{38}N_5O_9$ m/z = 636.2664, found m/z = 636.2666. UV/vis (CH_3CN) (L mol^{-1} cm^{-1}): λ (ε_0) = 228 nm (90 767), 337 nm (42 444), 440 nm (6378).

(1-(1-β-D-Glucopyranosyl)-(1,2,3-triazol-4-yl))-4′-butylazobenzene (7). Following the method described in the literature,[37] to a solution of (1-((2,3,4,6-tetra-*O*-acetyl)-1-β-D-glucopyranosyl)-(1,2,3-

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triazol-4-yl))-4′-butylazobenzene (**6**) (1.68 g, 2.64 mmol, 1 equiv) in methanol (300 mL) was added sodium methoxide (0.43 g, 7.93 mmol, 3 equiv). The reaction mixture was stirred at room temperature overnight. The reaction was quenched with an acidic resin Amberlist 15 dry to pH = 4−5. The resin was filtered and the filtrate was evaporated under vacuum. An orange solid of (1-(1-β-D-glucopyranosyl)-(1,2,3-triazol-4-yl))-4′-butylazobenzene (**7**) (1.21 g, 98% yield) was obtained and was directly oxidized without any further purification. R_f = 0.41 (CH_2Cl_2/MeOH 9:1). Mp: 88 −90 °C. ^{1}H NMR (400 MHz, MeOD- d_4): δ (ppm) 0.90 (t, J = 7.6 Hz, 3H, CH_3), 1.31 (sex., J = 7.6 Hz, 2H, CH_2), 1.58 (quin, J = 7.6 Hz, 2H, CH_2), 2.63 (t, J = 7.6 Hz, 2H, CH_2), 3.46−3.53 (m, 3H, CH), 3.69−3.73 (m, 1H, CH), 3.94−3.97 (m, 1H, CH), 4.35 (t, 1H, CH), 5.39 (d, J = 9.2 Hz, 1H, H-1), 7.29 (d, J = 8.4 Hz, 2H, CH^{Ar}), 7.78 (m, 4H, CH^{Ar}), 7.95 (s, 1H, CH), 7.97 (d, J = 8.4 Hz, 2H, CH^{Ar}). ^{13}C NMR (101 MHz, MeOD-d_4): δ (ppm) 14.1 (CH_3), 23.2 (CH_2), 34.4 (CH_2), 36.3 (CH_2), 62.5 (CH), 71.0 (CH), 72.6 (CH), 78.5 (CH), 81.0 (CH), 87.2 (CH), 123.9 (2 × CH^{Ar}), 124.2 (2 × CH^{Ar}), 129.0 (C^{Ar}), 130.1 (2 × CH^{Ar}), 131.1 (2 × CH^{Ar}), 133.3 (CH), 140.9 (CH), 148.5 (C^{Ar}), 151.9 (C^{Ar}), 154.3 (C^{Ar}). ESI-MS: $[M + Na]^+$ calcd for $C_{24}H_{29}N_5NaO_5$ m/z = 490.25, found m/z = 490.00. HRMS: $[M + H]^+$ calcd for $C_{24}H_{30}N_5O_5$ m/z = 468.2241, found m/z = 468.2253. UV/vis (CH_3CN) (L mol^{-1} cm^{-1}): λ (ε_0) = 233 nm (29 749), 345 nm (39 725), 440 nm (1884).

4-Butylazobenzyl-4′-triazologlucuronic Acid Sodium Salt (1). Following the method described in the literature,[27] a solution of (1-(1-β-D-glucopyranosyl)-(1,2,3-triazol-4-yl))-4′-butylazobenzene (**7**) (0.9 g, 1.93 mmol, 1 equiv), TEMPO (9.4 mg, 0.06 mmol, 3 mol %), and sodium bromide (24 mg, 0.23 mmol, 12 mol %) in a mixture of EtOAc (12 mL) and a saturated solution of $NaHCO_3$ (5 mL) was kept at 0 °C. A mixture of 13% sodium hypochlorite solution (4.5 mL), brine (9 mL), and a saturated solution of $NaHCO_3$ (4 mL) was added. The reaction mixture was stirred at 0 °C during 3 h and then diluted with water (25 mL) and EtOAc (25 mL). The organic layer was extracted with a saturated solution of $NaHCO_3$ (3 × 25 mL). The aqueous layer was acidified with a solution of HCl 2 M until pH = 3 and then extracted with EtOAc (5 × 25 mL), dried over $MgSO_4$, and evaporated under vacuum. An orange powder of 4-butylazobenzyl-4′-triazologlucuronic acid was obtained (0.472 g, 51% yield) without need of purification. The sodium salt of the molecule was obtained by adding NaH (24 mg, 0.98 mmol, 1 equiv) to a solution of 4-butylazobenzyl-4′-triazologlucuronic acid (0.472 g, 0.98 mmol, 1 equiv) in 10 mL of dry THF. The mixture was stirred at room temperature during 1 h and then solvent was removed under vacuum. The product did not need further purification. 4-Butylazobenzyl-4′-triazologlucuronic acid sodium salt (**1**) as an orange powder was obtained (0.493 g, 99% yield). Mp: 116−118 °C. $[\alpha]_D^{20}$ = −80° (c = 0.06 in MeOH). ^{1}H NMR (400 MHz, MeOD-d_4): δ (ppm) 0.94 (t, J = 7.2 Hz, 3H, CH_3), 1.37 (sex., J = 7.2 Hz, 2H, CH_2), 1.63 (quin, J = 7.2 Hz, 2H, CH_2), 2.68 (t, J = 7.2 Hz, 2H, CH_2), 3.58 (m, 1H, CH), 3.75 (m, 1H, CH), 4.14 (m, 1H, CH), 4.34 (m, 1H, CH), 5.57 (m, 1H, CH), 7.33 (m, 2H, CH^{Ar}), 7.75 (m, 2H, CH^{Ar}), 7.83 (m, 2H, CH^{Ar}), 7.94 (brs, 1H, CH), 7.99 (m, 2H, CH^{Ar}). ^{13}C NMR (101 MHz, MeOD-d_4): δ (ppm) 14.1 (CH_3), 18.8 (CH_2), 23.5 (CH_2), 41.7 (CH_2), 72.5 (CH), 72.6 (CH), 78.1 (CH), 78.9 (CH), 87.6 (CH), 124.2 (2 × CH^{Ar}), 124.4 (C^{Ar}), 124.8 (2 × CH^{Ar}), 130.4 (2 × CH^{Ar}), 130.7 (C^{Ar}), 131.6 (2 × CH^{Ar}), 134.4 (CH), 140.3 (CH), 154.4 (C^{Ar}), 156.2 (C^{Ar}), 201.8 (COOH). ESI-MS: $[M - H]$ calcd for $C_{24}H_{26}N_5O_6$ m/z = 480.19, found m/z = 480.15. HRMS: $[M - H + 2Na]^+$ calcd for $C_{24}H_{26}N_5Na_2O_6$ m/z = 526.1678, found m/z = 526.1674. UV/vis (water) (L mol^{-1} cm^{-1}): λ (ε_0) = 256 nm (17 400), 337 nm (23 828), 428 nm (3510). IR (KBr): 3416 cm^{-1} (ν_{OH}), 1681 cm^{-1} ($\nu_{C=O}$).

General Procedure for *N*-Acylation. To a solution of the amine (1 mmol, 1 equiv) and BABTGA (**1**) (9.6 mg) in water (5 mL) was added the anhydride (1.5 mmol, 1.5 equiv). The mixture was stirred at room temperature for 10 min. The mixture was irradiated at 365 nm during 5 min. Then the mixture was filtered and the residue was purified using column chromatography on silica gel.

General Procedure for Recycling. To the filtrate was added only the amine (1 mmol, 1 equiv) and the anhydride (1.5 mmol, 1.5 equiv). Then the general procedure for *N*-acylation was followed.

***N*-*p*-Tolylacetamide (9).** The general procedure for *N*-acylation using *p*-toluidine (0.107 g, 1 mmol) and acetic anhydride (0.14 mL, 1.5 mmol) was followed. After purification by column chromatography on silica gel (cyclohexane/EtOAc 7:3), *N*-*p*-tolylacetamide (**9**) was obtained as a white powder (0.115 g, 77% yield). Analyses are consistent with the literature.[37] ^{1}H NMR ($CDCl_3$, 400 MHz): δ (ppm) 2.12 (s, 3H, CH_3), 2.29 (s, 3H, $C(O)CH_3$), 7.08 (d, J = 8.4 Hz, 2H, CH^{Ar}), 7.36 (d, J = 8.4 Hz, 2H, CH^{Ar}), 7.74 (brs, 1H, NH). ^{13}C NMR ($CDCl_3$, 101 MHz): δ (ppm) 20.8 (CH_3), 24.3 ($C(O)CH_3$), 120.1 (2 × CH^{Ar}), 129.3 (2 × CH^{Ar}), 133.8 (C^{Ar}), 135.4 (C^{Ar}), 168.6 ($C(O)CH_3$).

***N*-(2-Hydroxyphenyl)acetamide (10).** The general procedure for *N*-acylation using 2-aminophenol (0.109 g, 1 mmol) and acetic anhydride (0.14 mL, 1.5 mmol) was followed. After purification by column chromatography on silica gel (cyclohexane/EtOAc 5:5), *N*-(2-hydroxyphenyl)acetamide (**10**) was obtained as a white powder (0.119 g, 79% yield). Analyses are consistent with the literature.[38] ^{1}H NMR (MeOD-d_4, 400 MHz): δ (ppm) 2.18 (s, 3H, $C(O)CH_3$), 6.79 (t, J = 8.4 Hz, 1H, CH^{Ar}), 6.86 (d, J = 8.4 Hz, 1H, CH^{Ar}), 6.99 (t, J = 8.4 Hz, 1H, CH^{Ar}), 7.60 (d, J = 8.4 Hz, 1H, CH^{Ar}). ^{13}C NMR (MeOD-d_4, 101 MHz): δ (ppm) 23.4 ($C(O)CH_3$), 117.2 (CH^{Ar}), 120.6 (CH^{Ar}), 123.9 (CH^{Ar}), 126.8 (CH^{Ar}), 127.1 (C^{Ar}), 149.8 (C^{Ar}), 172.2 ($C(O)CH_3$).

***N*-(3-Hydroxyphenyl)acetamide (11).** The general procedure for *N*-acylation using 3-aminophenol (0.109 g, 1 mmol) and acetic anhydride (0.14 mL, 1.5 mmol) was followed. At the end of the reaction the product was extracted with EtOAc (2 × 5 mL) instead being filtered. After purification by column chromatography on silica gel (cyclohexane/EtOAc 5:5), *N*-(3-hydroxyphenyl)acetamide (**11**) was obtained (0.125 g, 83% yield) as a white powder. Analyses are consistent with the literature.[38] ^{1}H NMR (MeOD-d_4, 400 MHz): δ (ppm) 2.10 (s, 3H, $C(O)CH_3$), 6.52 (d, J = 8.4 Hz, 1H, CH^{Ar}), 6.91 (d, J = 8.4 Hz, 1H, CH^{Ar}), 7.09 (t, J = 8.4 Hz, 1H, CH^{Ar}), 7.18 (s, 1H, CH^{Ar}). ^{13}C NMR (MeOD-d_4, 101 MHz): δ (ppm) 23.8 ($C(O)CH_3$), 108.4 (CH^{Ar}), 112.1 (CH^{Ar}), 112.3 (CH^{Ar}), 130.5 (CH^{Ar}), 140.9 (C^{Ar}), 158.9 (C^{Ar}), 171.6 ($C(O)CH_3$).

***N*-(4-Hydroxyphenyl)acetamide (12).** The general procedure for *N*-acylation using 4-aminophenol (0.109 g, 1 mmol) and acetic anhydride (0.14 mL, 1.5 mmol) was followed. At the end of the reaction, the product was extracted with EtOAc (2 × 5 mL) instead of the filtration. After purification by column chromatography on silica gel (cyclohexane/EtOAc 5:5), *N*-(4-hydroxyphenyl)acetamide (**12**) was obtained (0.120 g, 79% yield) as a white powder. Analyses are consistent with the literature.[37] ^{1}H NMR (MeOD-d_4, 400 MHz): δ (ppm) 2.09 (s, 3H, $C(O)CH_3$), 6.73 (d, J = 8.8 Hz, 1H, CH^{Ar}), 7.30 (d, J = 8.8 Hz, 1H, CH^{Ar}). ^{13}C NMR (MeOD-d_4, 101 MHz): δ (ppm) 23.5 ($C(O)CH_3$), 116.2 (2 × CH^{Ar}), 123.4 (2 × CH^{Ar}), 131.7 (C^{Ar}), 155.3 (C^{Ar}), 171.3 ($C(O)CH_3$).

***N*-(4-(Hydroxymethyl)phenyl)acetamide (13).** The general procedure for *N*-acylation using 4-aminobenzyl alcohol (0.123 g, 1 mmol) and acetic anhydride (0.14 mL, 1.5 mmol) was followed. At the end of the reaction, the product was extracted with EtOAc (2 × 5 mL) instead being filtered. After purification by column chromatography on silica gel (cyclohexane/EtOAc 7:3), *N*-(4-(hydroxymethyl)phenyl)-acetamide (**13**) was obtained (0.117 g, 71% yield) as a white powder. Analyses are consistent with the literature.[39] ^{1}H NMR (MeOD-d_4, 400 MHz): δ (ppm) 2.10 (s, 3H, $C(O)CH_3$), 4.54 (s, 2H, CH_2), 7.27 (d, J = 8.4 Hz, 2H, CH^{Ar}), 7.50 (d, J = 8.4 Hz, 2H, CH^{Ar}). ^{13}C NMR (MeOD-d_4, 101 MHz): δ (ppm) 23.9 ($C(O)CH_3$), 64.85 (CH_2), 121.1 (2 × CH^{Ar}), 128.6 (2 × CH^{Ar}), 138.4 (C^{Ar}), 139.0 (C^{Ar}), 171.6 ($C(O)CH_3$).

***N*-(3-Nitrophenyl)acetamide (15).** The general procedure for *N*-acylation using 3-nitroaniline (0.138 g, 1 mmol) and acetic anhydride (0.14 mL, 1.5 mmol) was used. After purification by column chromatography on silica gel (cyclohexane/EtOAc 7:3), *N*-(3-nitrophenyl)acetamide (**15**) was obtained (0.097 g, 54% yield) as a white powder. Analyses are consistent with the literature.[38] ^{1}H NMR (MeOD-d_4, 400 MHz): δ (ppm) 2.15 (s, 3H, $C(O)CH_3$), 7.50 (t, J = 8

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Hz, 1H, CH^{Ar}), 7.82 (d, J = 8 Hz, 1H, CH^{Ar}), 7.89 (d, J = 8 Hz, 1H, CH^{Ar}), 8.57 (s, 1H, CH^{Ar}). ^{13}C NMR (MeOD-d_4, 101 MHz): δ (ppm) 23.7 ($C(O)CH_3$), 115.0 (CH^{Ar}), 119.1 (CH^{Ar}), 126.1 (CH^{Ar}), 130.6 (CH^{Ar}), 141.1 (C^{Ar}), 149.7 (C^{Ar}), 171.8 ($C(O)CH_3$).

***N*-(4-Bromophenyl)acetamide (16).** The general procedure for *N*-acylation using 4-bromoaniline (0.171 g, 1 mmol) and acetic anhydride (0.14 mL, 1.5 mmol) was followed. After purification by column chromatography on silica gel (cyclohexane/EtOAc 7:3), *N*-(4-bromophenyl)acetamide (**16**) was obtained (0.172 g, 81% yield) as a white powder. Analyses are consistent with the literature.[40] ^{1}H NMR (MeOD-d_4, 400 MHz): δ (ppm) 2.11 (s, 3H, $C(O)CH_3$), 7.41 (d, J = 9 Hz, 2H, CH^{Ar}), 7.48 (d, J = 9 Hz, 2H, CH^{Ar}). ^{13}C NMR (MeOD-d_4, 101 MHz): δ (ppm) 23.9 ($C(O)CH_3$), 117.4 (C^{Ar}), 122.7 (2 × CH^{Ar}), 132.8 (2 × CH^{Ar}), 139.3 (C^{Ar}), 171.7 ($C(O)CH_3$).

4-Acetamidobenzoic Acid (17). The general procedure for *N*-acylation using 4-aminobenzoic acid (0.137 g, 1 mmol) and acetic anhydride (0.14 mL, 1.5 mmol) was followed. After purification by column chromatography on silica gel (cyclohexane/EtOAc 7:3), 4-acetamidobenzoic acid (**17**) was obtained (0.143 g, 80% yield) as a white powder. Analyses are consistent with the literature.[41] ^{1}H NMR (MeOD-d_4, 400 MHz): δ (ppm) 2.15 (s, 3H, $C(O)CH_3$), 7.65 (d, J = 8.8 Hz, 2H, CH^{Ar}), 7.95 (d, J = 8.8 Hz, 2H, CH^{Ar}). ^{13}C NMR (MeOD-d_4, 101 MHz): δ (ppm) 24.1 ($C(O)CH_3$), 120.1 (2 × CH^{Ar}), 126.9 (C^{Ar}), 131.8 (2 × CH^{Ar}), 144.4 (C^{Ar}), 169.5 ($C(O)CH_3$), 172.1 (COOH).

***N*-(Naphthalen-2-yl)acetamide (18).** The general procedure for *N*-acylation using 2-naphtylamine (0.143 g, 1 mmol) and 1.5 equiv of acetic anhydride (0.14 mL, 1.5 mmol) was followed. After purification by column chromatography on silica gel (EtOAc/cyclohexane 5:5), *N*-(naphthalen-2-yl)acetamide (**18**) was obtained (0.163 g, 88% yield) as a white powder. Analyses are consistent with the literature.[38] ^{1}H NMR ($CDCl_3$, 400 MHz): δ (ppm) 2.20 (s, 3H, $C(O)CH_3$), 7.40 (m, 3H, CH^{Ar}), 7.73 (m, 4H, CH^{Ar}), 8.17 (s, 1H, NH). ^{13}C NMR ($CDCl_3$, 101 MHz): δ (ppm) 24.6 ($C(O)CH_3$), 116.7 (CH^{Ar}), 119.9 (CH^{Ar}), 125.0 (CH^{Ar}), 126.5 (CH^{Ar}), 127.5 (CH^{Ar}), 127.6 (CH^{Ar}), 128.7 (CH^{Ar}), 130.6 (C^{Ar}), 133.7 (C^{Ar}), 135.3 (C^{Ar}), 168.7 ($C(O)CH_3$).

***N*-Methyl-*N*-phenylacetamide (19).** The general procedure for *N*-acylation using *N*-methylaniline (0.10 mL, 1 mmol) and 1.5 equiv of acetic anhydride (0.14 mL, 1.5 mmol) was followed. At the end of the reaction the product was extracted with EtOAc (2 × 5 mL) instead of being filtered. After purification by column chromatography on silica gel (EtOAc/cyclohexane 5:5), *N*-methyl-*N*-phenylacetamide (**19**) was obtained (0.128 g, 86% yield) as a white powder. Analyses are consistent with the literature.[42] ^{1}H NMR ($CDCl_3$, 400 MHz): δ (ppm) 1.87 (s, 3H, $C(O)CH_3$), 3.27 (s, 3H, $N-CH_3$), 7.18 (d, J = 8.4 Hz, 2H, CH^{Ar}), 7.40 (m, 3H, CH^{Ar}). ^{13}C NMR ($CDCl_3$, 101 MHz): δ (ppm) 22.4 ($C(O)CH_3$), 37.2 ($N-CH_3$), 127.1 (2 × CH^{Ar}), 127.7 (CH^{Ar}), 129.7 (2 × CH^{Ar}), 144.6 (C^{Ar}), 170.5 ($C(O)CH_3$).

***N*-(4-(Acetylamino)phenyl)acetamide (20).** The general procedure for *N*-acylation using 1,4-benzenediamine (0.108 g, 1 mmol) and 3 equiv of acetic anhydride (0.28 mL, 3 mmol) instead of 1 equiv was followed. After purification by column chromatography on silica gel (EtOAc/cyclohexane 8:2), *N*-(4-(acetylamino)phenyl)acetamide (**20**) was obtained (0.136 g, 71% yield) as a white powder. Analyses are consistent with the literature.[37] ^{1}H NMR (DMSO-d_6, 400 MHz): δ (ppm) 2.01 (s, 6H, $C(O)CH_3$), 7.47 (s, 4H, CH^{Ar}), 9.85 (s, 2H, NH). ^{13}C NMR (DMSO-d_6, 101 MHz): δ (ppm) 23.8 (2 × $C(O)CH_3$), 119.3 (4 × CH^{Ar}), 134.5 (2 × C^{Ar}), 167.8 (2 × $C(O)CH_3$).

***N*-Propylacetamide (21).** The general procedure for *N*-acylation using propylamine (0.08 mL, 1 mmol) and acetic anhydride (0.14 mL, 1.5 mmol) was followed. At the end of the reaction the product was extracted with EtOAc (2 × 5 mL) instead of being filtered. After purification by column chromatography on silica gel (EtOAc), *N*-propylacetamide (**21**) was obtained (0.05 g, 50% yield) a colorless oil. ^{1}H NMR ($CDCl_3$, 400 MHz): δ (ppm) 0.92 (t, J = 7.6 Hz, 3H, CH_3), 1.51 (dt, J = 7.6, 6.8 Hz, 2H, CH_2), 1.95 (s, 3H, $C(O)CH_3$), 3.18 (dd, J = 6.8, 6.4 Hz, 2H, CH_2). ^{13}C NMR ($CDCl_3$, 101 MHz): δ (ppm) 11.3 (CH_3), 22.8 (CH_2), 23.6 ($C(O)CH_3$), 41.3 (CH_2), 170.0 ($C(O)CH_3$). ESI-MS: $[M + H]^+$ calcd for $C_5H_{11}NO$ m/z = 102.08, found m/z = 102.15. IR (ATR): ν = 1751 (s).

1-Acetylpiperidine (22). The general procedure for *N*-acylation using piperidine (0.1 mL, 1 mmol) and acetic anhydride (0.14 mL, 1.5 mmol) was followed. At the end of the reaction, the product was extracted with EtOAc (2 × 5 mL) instead of being filtered. After purification by column chromatography on silica gel (cyclohexane/EtOAc 1:1), 1-acetylpiperidine (**22**) was obtained (0.038 g, 50% yield) as a light yellow oil. Analyses are consistent with the literature.[43] ^{1}H NMR (DMSO-d_6, 400 MHz): δ (ppm) 1.39 (m, 2H, CH_2), 1.48 (m, 2H, CH_2), 1.55 (m, 2H, CH_2), 1.96 (s, 3H, $C(O)CH_3$), 3.37 (m, 4H, CH_2). ^{13}C NMR (DMSO-d_6, 101 MHz): δ (ppm) 21.2 ($C(O)CH_3$), 23.9 (CH_2), 25.2 (CH_2), 25.9 (CH_2), 41.6 (CH_2), 46.6 (CH_2), 167.7 ($C(O)CH_3$).

***N*-*p*-Tolylbenzamide (23).** The general procedure for *N*-acylation using *p*-toluidine (0.107 g, 1 mmol) and benzoic anhydride (0.339 g, 1.5 mmol) was followed. After purification by column chromatography on silica gel (cyclohexane/EtOAc 9:1), *N*-*p*-tolylbenzamide (**23**) was obtained (0.168 g, 80% yield) as a white powder. Analyses are consistent with the literature.[36] ^{1}H NMR (MeOD-d_4, 400 MHz): δ (ppm) 2.32 (s, 3H, CH_3), 7.16 (d, J = 8.2 Hz, 2H, CH^{Ar}), 7.50 (t, J = 7.2 Hz, 2H, CH^{Ar}), 7.55 (d, J = 8.2 Hz, 3H, CH^{Ar}), 7.91 (d, J = 7.2 Hz, 2H, CH^{Ar}). ^{13}C NMR (MeOD-d_4, 101 MHz): δ (ppm) 21.0 (CH_3), 122.5 (2 × CH^{Ar}), 128.6 (2 × CH^{Ar}), 129.6 (2 × CH^{Ar}), 130.3 (2 × CH^{Ar}), 132.8 (CH^{Ar}), 135.4 (C^{Ar}), 136.4 (C^{Ar}), 137.2 (C^{Ar}), 168.9 ($C(O)Ph$).

***N*-*p*-Tolylhexanamide (24).** The general procedure for *N*-acylation using *p*-toluidine (0.107 g, 1 mmol) and hexanoic anhydride (0.35 mL, 1.5 mmol) was followed. After purification by column chromatography on silica gel (cyclohexane/EtOAc 9:1), *N*-*p*-tolylhexanamide (**24**) was obtained (0.150 g, 73% yield) as a white powder. Analyses are consistent with the literature.[44] ^{1}H NMR (MeOD-d_4, 400 MHz): δ (ppm) 0.91 (t, J = 6.6 Hz, 3H, CH_3), 1.33 (m, 4H, CH_2), 1.67 (quin, J = 7.6 Hz, 2H, CH_2), 2.54 (s, 3H, CH_3), 2.31 (t, J = 7.6 Hz, 2H, CH_2), 7.06 (d, J = 8.2 Hz, 2H, CH^{Ar}), 7.42 (d, J = 8.2 Hz, 2H, CH^{Ar}). ^{13}C NMR (MeOD-d_4, 101 MHz): δ (ppm) 14.4 (CH_3), 21.0 (CH_2), 23.5 (CH_3), 26.7 (CH_2), 32.6 (CH_2), 38.0 (CH_2), 121.3 (2 × CH^{Ar}), 130.2 (2 × CH^{Ar}), 136.7 (C^{Ar}), 137.3 (C^{Ar}), 174.5 ($C(O)C_5H_{11}$).

■ ASSOCIATED CONTENT

Ⓢ Supporting Information

^{1}H, ^{13}C, and 2D NMR experiments spectra are provided. This material is available free of charge via the Internet at http://pubs.acs.org.

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Notes

The authors declare no competing financial interest.

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