

GREEN PHOTOCHEMISTRY: SUN-INDUCED AROMATIC NUCLEOPHILIC SUBSTITUTION OF ALKOXY GROUPS BY ALKYLAMINES

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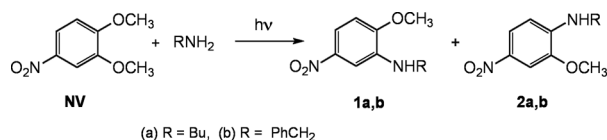
Abstract

Solar photochemistry was proved to be efficient for the nucleophilic substitution of alkoxy groups by amines in alkoxy nitrobenzenes. The results of the sun-induced photochemical substitution were comparable to the outcome of the same reaction under irradiation by a low-pressure mercury lamp. Using 4'-nitrobenzo-15-crown-5 as a starting material we obtained a polyether amino alcohol - a precursor for the regioselective synthesis of benzoazacrown ethers.

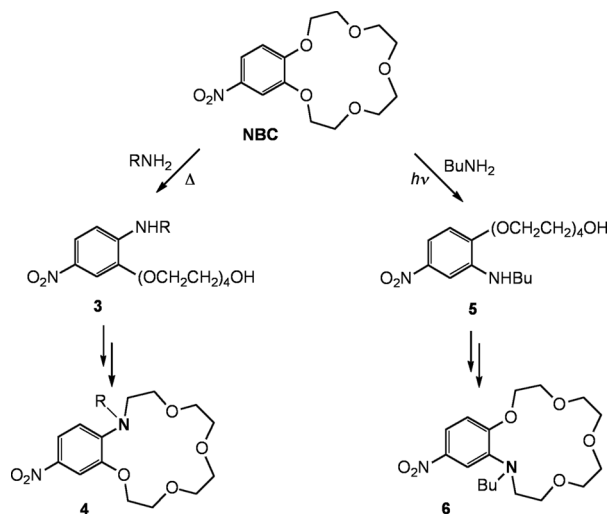
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Introduction

Many photochemical reactions have been performed using sun as a source of light ["green photochemistry" (1), "solar photochemistry" (2)]. However, to the best of our knowledge, the sun-induced substitution of alkoxy groups in alkoxy nitrobenzenes by amines has never been described



Scheme 1



Scheme 2

before. Photochemical aromatic substitution of alkoxy groups by amines is known to produce different regioisomers as compared to a thermal reaction (3-8). Thus, the irradiation of 4-nitroveratrole (NV) and excess butylamine with a mercury lamp resulted mostly in substitution of the methoxy group in *meta*-position to the nitro group (compound **1a**) (6,7), while a thermochemical substitution would occur predominantly at *para*-position producing the regioisomer **2a** (Scheme 1).

Aromatic substitution by alkyl amines was suggested by Gromov *et al.* (9) for cleavage of a polyether macrocycle in nitrobenzocrown ethers as a first step in their transformation into nitrobenzoazacrown analogs **4** (Scheme 2). The regioselectivity of such cleavage could be inverted by using the photoinduced substitution, thus providing an approach to different regioisomers of benzoazacrown ethers **6** (Scheme 2). An attempt of such a photochemical cleavage was one of the goals of the present study.

We report here the preliminary results of our studies on the sun-induced photochemical substitution of alkoxy groups by amines in alkoxy nitrobenzenes, and on the same reaction under irradiation by a low-pressure mercury lamp (Schemes 1, 2). Using 4'-nitrobenzo-15-crown-5 (NBC) as a starting material we obtained the compound **5**, which will be used for the synthesis of benzoazacrown ethers.

Experimental

Column chromatography was performed on silica gel (Sorbent Technologies, 40-75 μm). ^1H NMR and ^{13}C NMR spectra were acquired on a Varian Mercury

Table 1. Isolated yields in the nucleophilic aromatic photosubstitution of NV and NBC with amines and the data of mass spectra.

Conditions	Yields, %		
	NV + BuNH ₂		
	NV	1a	2a
Hg lamp (115 h)	31	25	5
Sunlight (80 h)	52	21	<10 ^a
[M+H] ⁺ /[M+Na] ⁺		225.1/247.1	225.1/247.1
[2M+H] ⁺ /[2M+Na] ⁺		449.2/471.2	449.2/471.2
(M = C ₁₁ H ₁₆ N ₂ O ₃)			
	NV + PhCH ₂ NH ₂		
	NV	1b	2b
Hg lamp (137 h)	65	30	<5 ^a
Sunlight (100 h)	59	33	<5 ^a
[M+H] ⁺ /[M+Na] ⁺		259.1/281.1	259.1/281.1
[2M+H] ⁺ /[2M+Na] ⁺		517.2/539.2	517.2/539.2
(M = C ₁₄ H ₁₄ N ₂ O ₃)			
	NBC + BuNH ₂		
	NBC	5	3
Hg lamp (135 h)	-	32	3
Sunlight (100 h)	-	53	4
[M+H] ⁺ / [M+Na] ⁺		387.2/409.2	387.1/409.2
(M = C ₁₈ H ₃₀ N ₂ O ₇)			

^a These samples were substantially contaminated by side products.

NMR-spectrometer (300 MHz, CDCl₃ solutions). The ESI mass spectra were recorded on a Varian 1200 LC triple-quad mass spectrometer in positive mode.

4-Nitroveratrol (NV) and 4'-nitrobenzo-15-crown-5 (NBC) were obtained from Aldrich Chemical Co. and used without purification. Solvents of HPLC grade were distilled prior to use.

General procedures for the photoreactions.

A solution (and/or suspension) of NV (0.70 g, 3.8 mmol), or NBC (0.31 g, 1.0 mmol) in 10 mL of BuNH₂ in a 20 mL quartz cuvette was flushed with argon for 30 min, then was sealed and irradiated with two 6 W low-pressure Hg lamps (G4T4/1) at 28-30°C at a distance 2 cm, or was immersed into water bath and exposed to sunlight outdoors [in California, at the latitude of San Francisco (37°46' North)]. In the latter case, the temperature of water varied during the day time within 20-30 °C. The same simple procedures were applied to the mixture of NV (0.70 g, 3.8 mmol) with PhCH₂NH₂ (1.30 mL, 1.28 g, 12.0 mmol) in 2 mL MeOH.

The reactions were monitored by TLC [250 μm silica gel, plates (8x2 cm) with UV-indicator (254 nm), from Analtech, Inc. (Uniplate)], and were stopped when a noticeable accumulation started of products other than 1 and 2 (R_f in toluene was 0.44 for 1a,b and 0.33 for 2a,b), or 3 and 5 (R_f in isopropanol 0.60 and 0.52, resp.). The excess amine was removed on a rotary evaporator. To complete the removal, toluene was added and evaporated three or more times in 10 mL portions. The residue was separated by column chromatography on silica gel

Table 2. Data of ^1H NMR: δ , ppm (J_{HH} , Hz)

Prods.	H-5, dd	H-3, d	H-6, d	OCH ₃ , OCH ₂	NH; OH	NR
1a	7.61 (8.8; 2.5)	7.37 (2.5)	6.74 (8.8)	3.94 s, 3H	4.37	3.18 br.q, CH ₂ N (6.4); 1.67 m, 2H; 1.46 m, 2H; 0.98 t (7.3)
1b	7.63 (8.8; 2.75)	7.41 (2.75)	6.76 (8.8)	3.94 s, 3H	4.84	7.39 m, 4H; 7.34 m, 1H; 4.39 d, 2H (4.7)
5	7.56 (8.8; 2.75)	7.36 (2.75)	6.75 (8.8)	4.24 m, 2H; 3.90 m, 2H; 3.7 m, 10H; 3.60 m, 2H	4.62; 1.8	3.18 br.q, CH ₂ N (6.4); 1.66 br.quin. (7.3), 1.45 br. sext. (7.4), 0.97 t (7.3)
2a	7.91 (8.8; 2.5)	7.61 (2.5)	6.48 (8.8)	3.93 s, 3H	5.00	3.23 br.q, CH ₂ N (6.5); 1.67 m, 2H; 1.45 m, 2H; 0.98 t (7.3)
2b	7.87 (8.8; 2.45)	7.65 (2.45)	6.49 (8.8)	3.94 s, 3H	5.42	7.35 m, 5H; 4.46 d, 2H (5.5)
3	7.90 (8.8; 2.45)	7.63 (2.45)	6.47 (8.9)	4.23 m, 2H; 3.89 m, 2H; 3.7 m, 10H; 3.61 m, 2H	5.50 br.t (5.2); 1.9	3.23 dt, CH ₂ N (5.7; 7.2); 1.66 m, 2H; 1.44 m, 2H; 0.97 t (7.3)

Table 3. Data of ^{13}C NMR: δ , ppm

Prods.	C-1	C-2	C-3	C-4	C-5	C-6	OCH ₃ , OCH ₂	NR
1a	151.58	128.49	103.70	138.86	107.98	112.93	56.13	43.27; 31.45; 20.45; 13.99
1b	151.65	138.32	103.97	142.53	108.04	113.43	56.09	138.27; 128.86; 127.68; 127.66; 47.75
5	150.72	139.14	103.76	142.90	109.35	112.61	72.66; 70.88; 70.77; 70.71; 70.44; 69.56; 68.38; 61.84	43.29; 31.41; 20.46; 14.02
2a	144.58	145.20	104.91	137.08	120.21	106.58	56.05	42.89; 31.37; 20.36; 13.92
2b	144.09	145.46	104.97	137.74	119.93	107.27	56.08	131.02; 129.06; 127.93; 127.51; 47.44
3	144.27	145.14	106.78	136.68	120.61	106.78	72.72; 70.85; 70.81; 70.74; 70.49; 69.67; 68.54; 61.90	42.90; 31.31; 20.38; 13.95

with toluene (for **1** and **2**), or isopropanol (for **3** and **5**) as an eluent.

The benzylamino derivative **1b** formed bright-yellow crystals with m.p. 93-94°C. All other products were dark-orange or orange-brown viscous oils. The isolated yields of the products and the recovered starting compounds, and the data of mass spectra are presented in Table 1.

The ^1H and ^{13}C NMR data are presented in Tables 2 and 3. The appropriate spectral parameters for compounds **1a**, **2a** and **3** are identical to those reported earlier (7,9,10). We obtained a sample of **2a** for comparison by refluxing **NV** in butylamine. A structural assignment of regioisomers was made by comparison of the experimental chemical shifts of the aromatic carbon atoms with the shifts calculated using the incremental shifts for monosubstituted benzenes according to (11).

Results and Discussion

In accordance with the previously published data (6,7), the photosubstitution of **NV** with amines under UV-radiation from the Hg lamp yielded compounds **1a,b** as the major products (Table 1). The ratio **NV:1a:2a** in the reaction mixture after evaporation of excess butylamine was found by ^1H NMR integration as approximately 55:36:9 (Hg lamp) and 63:30:7 (sunlight), which is fairly close to the isolated

yields of these compounds (Table 1) and to the previously published results (6,7). Interestingly, the Hg lamp irradiation and sunlight produced practically the same outcome. However, the proton signals of the major side products (not isolated) were different in the spectra of reaction mixtures from the experiments with Hg lamp and with sunlight.

Similar ratios of the isomeric products and the recovered starting material were obtained from the reactions of **NV** with benzylamine (Table 1).

In spite of the apparently similar isolated yields of the products in the photoreaction of **NBC** with butylamine (Table 1), the actual outcome of this reaction was different. In this case the product of *meta*-substitution, aminoalcohol **5**, was not only the major product, but practically the only significant component of the evaporated reaction mixtures. The ratio **NBC:5:3** was equal approximately 1:10:1 (^1H NMR) in both experiments. Thus, a conversion of **NBC** was fairly close to completion, and a potential yield of the valuable product **5** could be close to 90%. However, the column separation resulted in a rather moderate yield of 32-53% (Table 1). So, it may be advisable to use the synthetic intermediate **5** without purification for further transformations towards the nitrobenzocrown **6**.

The results of our experiments demonstrated an efficiency of solar photochemistry for the

nucleophilic substitution of alkoxy groups in alkoxy nitrobenzenes by amines. The light of the (Californian) sun proved to be at least as efficient for this reaction as the UV-irradiation at a short distance by a low pressure mercury lamp. We did not find any noticeable difference between the results of sun-induced reactions performed in summer and in winter time.

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