Photoremovable Hydroxyl Group Protection. Use of the *p*-Tolylsulfonyl Protecting Group in β-Disaccharide Synthesis

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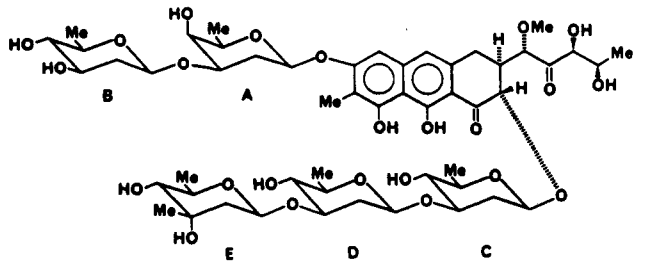
The *p*-tolylsulfonyl group has been shown to a photoremovable group effective for protection of carbohydrates during disaccharide synthesis. The formation of the versatile, *p*-tolylsulfonyl-protected disaccharide **13** [methyl 3-*O*-(4-*O*-benzoyl-3-*O*-benzyl-2,6-dideoxy-β-D-*arabino*-hexopyranosyl)-2,6-dideoxy-4-*O*-(*p*-tolylsulfonyl)-α-D-*arabino*-hexopyranoside] was accomplished by silver silicate catalyzed coupling of methyl 2,6-dideoxy-4-*O*-(*p*-tolylsulfonyl)-α-D-*arabino*-hexopyranoside (**7**) with 4-*O*-benzyl-2,6-dideoxy-α-D-*arabino*-hexopyranosyl bromide (**8**). Each of the three protecting groups (benzyl, benzoyl, and *p*-tolylsulfonyl) present in **13** was removed regioselectively under nonacidic conditions.

The *p*-tolylsulfonyl group has been recognized for more than 20 years as a photoremovable protecting group for carbohydrates.[1,2] *p*-Tolylsulfonyl protection is easily introduced and is stable under a wide variety of reaction conditions.[3] Use of this group in synthesis has been rare, however, because the strongly basic conditions (methanolic sodium hydroxide) under which deprotection occurs are unacceptable in most synthetic situations. In particular, these conditions lead to rapid removal of acetyl and benzoyl groups. Recent study of the mechanism of the photochemical reaction of *p*-toluenesulfonates has shown that the primary step in this process is the transfer of an electron from an electron donor (e.g., hydroxide ion) to the excited *p*-toluenesulfonate.[4] Since many amines are effective electron donors, replacement of sodium hydroxide with a tertiary amine should allow acyl groups to remain in place during photolysis. If regioselective *p*-tolylsulfonyl deprotection occurs, the number of situations in which this group can be used in synthesis would increase considerably.

One situation of particular interest to us involves work currently in progress in our laboratory on the preparation of analogues of the anticancer agent mithramycin (**1**).[5,6]



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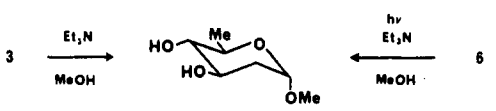
Considerable flexibility in group deprotection has been needed in the synthesis of a disaccharide essential to this project. The anticipated use of this disaccharide required it to be a fully protected compound in which each of three different protecting groups could be removed regioselectively. The choice of protecting groups was limited to those that did not require acidic conditions for group introduction or removal since glycosides of 2,6-dideoxy sugars undergo facile, acid-catalyzed hydrolysis. Benzyl ethers, cleaved by hydrogenolysis, and benzoyl esters, easily replaced by trans-esterification, were logical choices for two of the three groups. There was not, however, a clear choice for the third group. One possibility was the *p*-tolylsulfonyl group since potentially it could be introduced and removed under conditions that would leave the other protecting groups in place.

Scheme I



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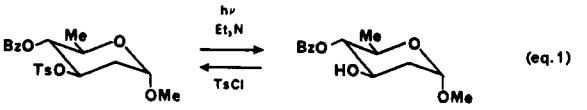
Results and Discussion

Initial experiments focused on testing the photochemical stability of the benzoyl and benzyl groups in compounds that also contained *p*-tolylsulfonyl protection. The first reaction conducted was photolysis of methyl 4-*O*-benzoyl-2,6-dideoxy-3-*O*-(*p*-tolylsulfonyl)-α-D-*arabino*-hexopyranoside (**2**) in methanol in the presence of triethylamine. This reaction resulted in formation of methyl 4-*O*-benzoyl-2,6-dideoxy-α-D-*arabino*-hexopyranoside (**3**) in 91% yield (eq 1). Even though the reaction conditions



2 **3**

were only mildly basic, care had to be taken to keep the reaction mixture at or below room temperature during photolysis and product isolation; otherwise, loss of the benzoyl group to give methyl 2,6-dideoxy-α-D-*arabino*-hexopyranoside (**4**) became a significant side reaction (Scheme I).

The second stability test conducted was the photolysis of methyl 3-*O*-benzyl-2,6-dideoxy-4-*O*-(*p*-tolylsulfonyl)-α-D-*arabino*-hexopyranoside (**5**) in methanol in the presence of triethylamine. This reaction initially did not appear promising since, in addition to the formation of the desired methyl 3-*O*-benzyl-2,6-dideoxy-α-D-*arabino*-hexopyranoside (**6**) in 34% yield, the fully deprotected methyl glycoside **4** was produced in 49% yield. The yield of **6** increased to 48% (and that of **4** dropped to 26%) when the concentration of triethylamine was raised from 0.001 to 0.003 M. When a much higher triethylamine concentration (0.02 M) was used, the yield of the desired glycoside **6** increased to 91% with only a trace of **4** being formed (Scheme II). Even with the higher triethylamine concentration, it was necessary to avoid extented irradiation since prolonged photolysis caused benzyl group loss. (This unexpected debenzylation reaction is currently being in-

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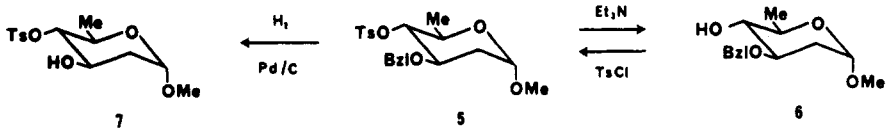
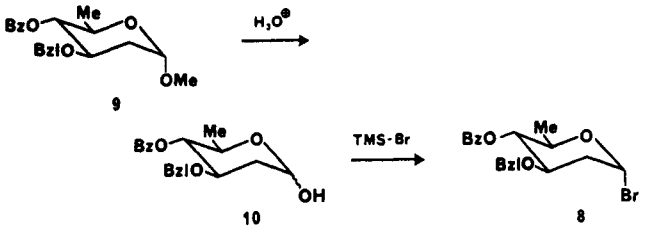
Scheme II



Scheme III

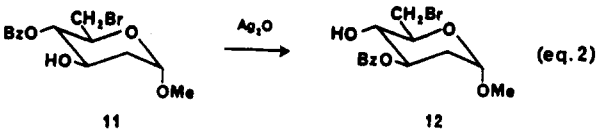


vestigated.) The results from irradiations of compounds 2 and 5 indicated that, as long as care was exercised in avoiding extended photolysis and unnecessary heating, the *p*-tolylsulfonyl group would be an effective third group for disaccharide protection.

The next decision to be made concerned the type of coupling reaction needed to maximize β-glycoside formation. Since the monosaccharides involved were 2,6-dideoxy sugars, the traditional approach, anchimeric assistance by a group attached to C-2, was not a possibility. Extension of the participation idea to a group attached to C-3 already had been tested and found to be unsatisfactory.[7] (The best β/α ratio obtained by C-3 benzoyloxy participation was 1/1.) The most attractive remaining possibility appeared to be the insoluble silver catalyst (silver silicate) method, developed by Paulsen and co-workers[8,9] for use in this type of situation (i.e., synthesis of β-glycosides in which no participating group is present to govern stereoselectivity).

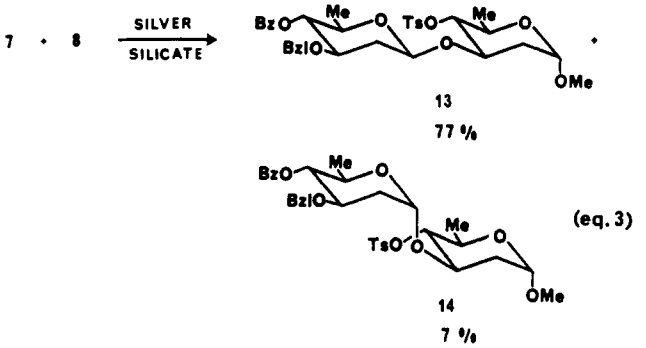
Before the monosaccharide coupling reaction could be conducted, it was necessary to decide how the protecting groups would be distributed between the glycosyl donor and acceptor. In making this decision the findings of van Boeckel and Beetz on the influence of remote substituents on glycoside formation provided valuable guidance. These workers had determined that the highest β/α ratio in the anomers produced during disaccharide formation using silver silicate occurred when there was an electron-withdrawing group at C-4 and electron-donating group at C-3 in the glycosyl donor.[10-12] Using this information, we selected methyl 2,6-dideoxy-4-*O*-(*p*-tolylsulfonyl)-α-D-*arabino*-hexopyranoside (7) as the glycosyl acceptor and 4-*O*-benzoyl-3-*O*-benzyl-2,6-dideoxy-D-*arabino*-hexopyranosyl bromide (8) as the glycosyl donor. The synthesis of these two compounds (7 and 8) is outlined in Schemes II and III, respectively.

Since *p*-tolylsulfonyl and benzoyl groups are both electron-withdrawing, their locations (one in the glycosyl donor and one in the acceptor) could have been interchanged and the directive influence of the O-4 substituents would have been qualitatively the same. Placing the *p*-tolylsulfonyl group in the glycosyl acceptor, however, did avoid a significant potential problem. Several years ago Yoshimure and co-workers[13] observed that methyl 4-*O*-benzoyl-6-bromo-2,6-dideoxy-α-D-*arabino*-hexopyranoside (11) experienced benzoyl migration in the presence of silver oxide to give the 3-*O*-benzoyl derivative 12 in 90% yield (eq 2).



If the *p*-tolylsulfonyl and benzoyl group positions had been interchanged, the glycosyl acceptor would have been compound 3 and a reaction similar to that shown in eq 2, catalyzed by silver silicate, would have been possible. Benzoyl migration during glycoside formation would have increased the complexity of the reaction mixutre and could have rendered the coupling reaction too complicated to be usable. Since *p*-tolylsulfonyl groups do not undergo the migration reaction characteristic of acyl groups, this problem was avoided by selecting 7 as the glycosyl acceptor. This situation illustrates an inherent advantage of *p*-tolylsulfonyl protection over that provided by acyl groups.

The process for selection of the reactants for glycoside formation proved to be effective. Silver silicate catalyzed coupling between compounds 7 and 8 produced the desired β-disaccharide 13 ($J_{1',2a'}$ = 9.9 Hz) in 77% yield along with a 7% yield of the α-anomer 14 ($J_{1',2a'}$ = 3.9 Hz) (eq 3); thus, the stereoselectivity in the coupling reaction was very good (β/α = 11/1).



Since the planned synthesis of mithramycin analogues required the ability to invert configuration at C-4 or C-4′ in the disaccharide 13 as well as selective deprotection at C-3′, it was necessary to be able to remove each of the three protecting groups regioselectively (Scheme IV). The benzoyl group was easily removed in the presence of methanolic sodium hydroxide; however, removal of the benzyl group by hydrogenolysis was less convenient. The reaction was slow, and sometimes additional catalyst was needed to cause the reaction to go to completion. Photochemical removal of the *p*-tolylsulfonyl group using triethylamine as the electron transfer agent was effective, although it was necessary to monitor the reaction carefully to prevent the loss of benzyl groups caused by extended irradiation.

In conclusion, the *p*-tolylsulfonyl group, when removed photochemically by electron transfer reaction, is an effective protecting group which should be suitable for a

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(12) Van Boeckel, C. A. A.; Beetz, T. *Recl. Trav. Chim. Pays-Bas* **1985**, *104*, 174.
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Scheme IV

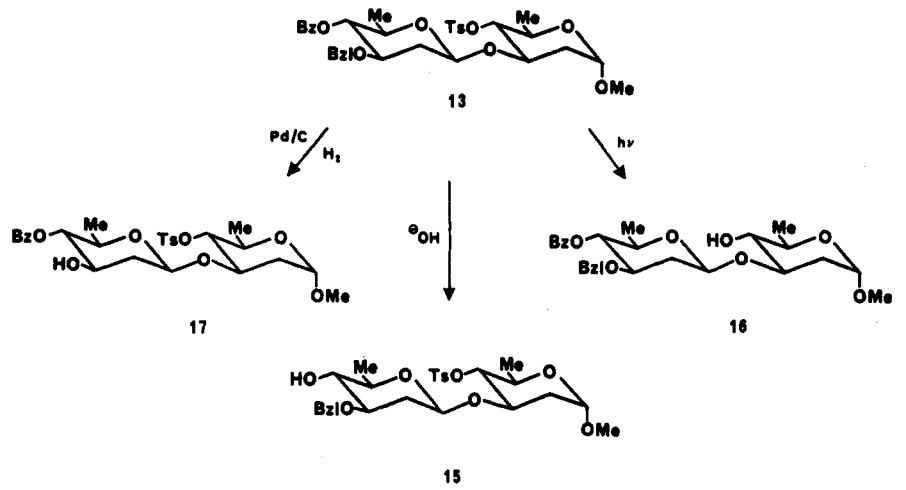

Table I. ^{13}C NMR Spectral Data

	2	5	7	8	9	10α	10β	13	14	15	16	17
C-1	97.89	97.90	97.93	89.08	98.37	91.89	94.09	97.71	97.86	97.73	98.17	97.69
C-2	36.98	35.82	37.55	41.23	35.53	35.73	38.12	35.27	35.08	35.24	36.91[b]	35.18
C-3	77.04[a]	73.98	66.72	74.05[a]	75.97[a]	73.63[a]	75.52[a]	75.36[a]	74.45[a]	75.56[a]	75.55[a]	78.63
C-4	74.17[a]	85.08	86.93	75.70[a]	76.87[a]	77.00[a]	76.17[a]	83.91	84.62	83.77	80.41	83.91
C-5	65.94	65.82	64.76	71.66	65.99	66.26	70.45	66.06	66.55	66.00	67.74	66.00
C-6	17.58	18.04	17.60	17.02	17.68	17.74	17.74	17.99	18.04	18.00	17.91	17.96
C-1′								95.00	99.75	95.05	99.93	94.99
C-2′								36.02	37.66	35.24	36.23[b]	38.68
C-3′								69.97[b]	73.81[a]	71.31[a]	76.80[a]	69.50
C-4′								76.00[a]	76.80[a]	78.82[a]	75.43[a]	70.09
C-5′								69.83[b]	65.43	69.89	70.62	69.50
C-6′								17.57	17.57	17.78	17.61	17.56
OMe	54.89	54.65	54.75		54.67			54.68	54.68	54.70	54.50	54.68
C=O	165.00				165.76	165.76	165.76	165.81	165.81		165.00	166.94
ArMe	21.54	21.55	21.64					21.58	21.58	21.56		21.57
ArCH2O		71.10		71.43	71.25	71.36	70.86	70.99	70.99	70.66	70.92	
Ar	133.11	144.21	145.28	137.31	138.34	133.25	138.25	144.71	144.64	144.00	137.85	144.48
Ar	129.96	138.23	133.43	132.92	133.51	133.10	133.10	138.13	138.46	138.09	135.76	135.06
Ar	129.84	135.00	129.89	129.92	133.01	130.09	130.09	135.09	135.31	129.28	133.21	133.62
Ar	129.57	129.39	129.57	128.36	130.17	129.79	129.79	133.13	132.99	128.57	129.81	133.44
Ar	128.33	128.16	128.66	128.23	129.76	128.41	128.41	130.06	130.21	128.41	128.75	129.76
Ar	128.23	127.78	128.42	127.57	128.36	128.28	128.28	129.73	129.78	127.94	128.44	129.58
Ar	127.49	127.37	128.00	127.51	128.17	127.54	127.46	129.46	128.34	127.68	128.37	129.42
Ar					127.44			129.04	128.14	127.48	127.61	129.01
								128.44	127.61			128.80
								128.25	127.39			128.46
								127.73				
								127.73				
								127.51				
								127.39				

[a,b] Assignments for absorptions with the same superscript in each column may be interchanged.

variety of synthetic situations. When used with the benzoyl and benzyl groups, the *p*-tolylsulfonyl group provides a valuable third member to this trio of groups, each of which can be removed regioselectively under nonacidic conditions.

Experimental Section

General Procedures. Unless otherwise noted, ^1H NMR and ^{13}C NMR spectra were determined by using a Varian FT-80A spectrometer with $CDCl_3$ as the solvent. Chemical shifts are relative to tetramethylsilane (δ 0.0). (The ^{13}C NMR spectra are given in tabular form in Table I). Column chromatography was conducted with a 2.5 × 15 cm column of Baker 240–400 mesh silica gel with hexane–ethyl acetate (3:1) as the developer. TLC was done with Whatmann silica gel 60 A plates developed with hexane–ethyl acetate (3:1). Photolyses were conducted with a water-cooled, Hanovia 450-W, mercury-vapor lamp or a Rayonet photochemical chamber equipped with 16 RPR2537 lamps. All photochemical reaction mixtures were purged with nitrogen for 1 h prior to photolysis, and the purge was continued during irradiation. Optical rotations were determined for solutions in chloroform at 22 °C using a Perkin-Elmer Model 241 spectrometer.

Methyl 4-*O*-Benzoyl-2,6-dideoxy-3-*O*-(*p*-tolylsulfonyl)-α-D-*arabino*-hexopyranoside (2). Methyl 4-*O*-benzoyl-2,6-dideoxy-α-D-*arabino*-hexopyranoside (3)[5] (22.0 g, 0.0826 mol) was dissolved in 200 mL of pyridine. To this stirred solution was added 35 g (0.18 mol) of *p*-toluenesulfonyl chloride. After standing for 14 h, the reaction mixture was added slowly to a stirred solution of 50 g of sodium bicarbonate in 800 mL of water. The precipitate that formed was collected, washed with 25 mL of cold ethanol, and recrystallized from the minimum amount of hot ethanol to give 31.2 g (0.074 mol, 90%) of compound 2: mp 129–30 °C; $[\alpha]_D$ +10° (*c* 1.08); ^1H NMR δ 1.16 (H_6, $J_{5,6}$ = 6.3 Hz), 2.12 (H_{2a}, $J_{1,2a}$ = 3.3 Hz), 2.51 (H_{2e}, $J_{1,2a}$ = 1.2 Hz, $J_{2a,3}$ = 5.0 Hz), 3.34 (OCH_3), 3.87 (H_5, $J_{4,5}$ = 9.3 Hz), 4.78 (H_1), 4.92–5.14 (H_3, H_5), 6.88, 6.98, 7.26–7.87 (aromatic). Anal. Calcd for $C_{21}H_{24}O_7S$: C, 59.98; H, 5.75. Found: C, 59.62; H, 5.61.

Photolysis of Methyl 4-*O*-Benzoyl-2,6-dideoxy-3-*O*-(*p*-tolylsulfonyl)-α-D-*arabino*-hexopyranoside (2). Compound 2 (10.36 g, 0.0246 mol) was stirred with 1000 mL of methanol to which 15 mL of freshly distilled triethylamine had been added.

This suspension was irradiated under standard conditions for 16 h with the Hanovia apparatus. After 8 h of irradiation, all material had dissolved. After photolysis, the solvent was distilled under reduced pressure to yield a yellow oil, which was chromatographed in the standard fashion to give 6.12 g (0.023, 93%) of the deprotected benzoate **3**, mp 60–61 °C (lit.[14] mp 61–62 °C). Care had to be taken during photolysis and solvent removal to keep the temperature of the reaction mixture at or below 25 °C to avoid loss of the benzoyl group from **3** by methanolysis.

Methyl 3-*O*-Benzyl-2,6-dideoxy-4-*O*-(*p*-tolylsulfonyl)-α-D-*arabino*-hexopyranoside (5). Methyl 3-*O*-benzyl-2,6-dideoxy-α-D-*arabino*-hexopyranoside (**6**), prepared by the method of Monneret et al.[15] (6.12 g, 0.0242 mol), and 6.92 g (0.0363 mol) of *p*-toluenesulfonyl chloride were dissolved in 150 mL of pyridine and heated to 55–60 °C for 13 h. After cooling, 2 mL of water was added slowly to the stirred reaction mixture, and the mixture was allowed to stand for 30 min. The reaction mixture then was added dropwise to a rapidly stirred solution of 30 g of sodium bicarbonate in 500 mL of water. The precipitate that formed was washed with 100 mL of water, air-dried, and chromatographed in the standard fashion to give 8.75 g (0.0215 mol, 89%) of compound **5**: mp 77–78 °C; $[\alpha]_D$ +72° (*c* 0.85); R_f 0.52; ^{1}H NMR δ 1.31 (H_6, $J_{5,6}$ = 6.3 Hz), 1.64 (H_{2a}, $J_{1,2a}$ = 3.6 Hz, $J_{2a,3}$ = 10.8 Hz), 2.18 (H_{2e}, $J_{1,2a}$ = 1.4 Hz, $J_{2e,3}$ = 5.2 Hz), 2.30 ($ArCH_3$), 3.61–3.95 (H_3, H_5), 4.14 and 4.29 ($ArCH_2O$, J_{CH_2} = 12.1 Hz), 4.40 (H_4, $J_{3,4}$ = $J_{4,5}$ = 9.4), 4.69 (H_1), 7.04–7.30, 7.68–7.81 (aromatic). Anal. Calcd for $C_{21}H_{26}O_6S$: C, 62.05; H, 6.45. Found: C, 62.01; H, 6.49.

Photolysis of Methyl 3-*O*-Benzyl-2,6-dideoxy-4-*O*-(*p*-tolylsulfonyl)-α-D-*arabino*-hexopyranoside (5). Compound **5** (300 mg, 0.74 mmol) was dissolved in 100 mL of a 0.02 M solution of triethylamine in methanol and irradiated for 12 h under standard conditions with the Rayonet photochemical chamber. After irradiation, the solvent was distilled under reduced pressure, and the residue was chromatographed in the standard fashion to give methyl 3-*O*-benzyl-2,6-dideoxy-α-D-*arabino*-hexopyranoside (**6**)[16] (212 mg, 0.67 mol, 90%, R_f 0.36).

Methyl 2,6-Dideoxy-4-*O*-(*p*-tolylsulfonyl)-α-D-*arabino*-hexopyranoside (7). Compound **5** (1.97 g, 4.84 mmol) was dissolved in 75 mL of methanol in which 0.8 g of 5% palladium on carbon was suspended. The reaction flask was purged with hydrogen, and the reaction mixture was stirred while a hydrogen pressure of 1 atm was maintained. After 24 h, the reaction mixture was filtered through a 1-cm layer of silica gel to remove most of the catalyst. The solvent was distilled from the filtrate under reduced pressure, the residue was shaken with 200 mL of ethyl ether, and the suspension was filtered through silica gel (1-cm layer) to give a colorless solution. The ether was evaporated to give 1.38 g (4.36 mmol, 90%) of compound **7**, mp 126 °C (lit.[17] mp 126 °C). The ^{1}H NMR spectrum was the same as that reported for the enantiomer of **7**.[18]

Methyl 4-*O*-Benzoyl-3-*O*-benzyl-2,6-dideoxy-α-D-*arabino*-hexopyranoside (9). Compound **6** (2.33 g, 9.2 mmol) was dissolved in 20 mL of pyridine, and 2.5 g (18 mmol) of benzoyl chloride was added. The reaction mixture was stirred for 2 h and then cooled while 2 mL of water was added in a dropwise manner. The entire solution was then added slowly to a stirred solution of 5 g of sodium bicarbonate in 200 mL of water. After stirring for 30 min, the aqueous solution was decanted from the yellow oil that had formed. The oil was chromatographed in the normal fashion to give 3.20 g (9.0 mmol, 97%) of compound **9**: R_f 0.59; ^{1}H NMR δ 1.22 (H_6, $J_{5,6}$ = 6.3 Hz), 1.80 (H_{2a}, $J_{1,2a}$ = 3.0 Hz, $J_{2a,3}$ = 11.3 Hz), 2.33 (H_{2e}, $J_{1,2e}$ = 1.4 Hz, $J_{2e,3}$ = 5.2 Hz), 3.33 (OCH_3), 3.78–4.15 (H_3, H_5), 4.41 and 4.61 ($ArCH_2O$), 4.81 (H_1), 5.06 (H_4, $J_{3,4}$ = $J_{4,5}$ = 9.5 Hz), 7.13, 7.57–7.39, 7.97–8.10 (aromatic). Anal. Calcd for $C_{21}H_{24}O_5$: C, 70.77; H, 6.79. Found: C, 70.40; H, 6.70.

4-*O*-Benzoyl-3-*O*-benzyl-2,6-dideoxy-α-D-*arabino*-hexopyranose (10). Compound **9** (2.50 g, 0.70 mmol) was combined with a solution of 24 mL of acetic acid and 8 mL of water and heated at 110 °C for 2 h. After cooling, the solution was added to 150 mL of water. The solution immediately became cloudy. Upon standing overnight, a clear oil separated. The aqueous solution was decanted, and the remaining yellow oil was chromatographed in the normal fashion to give **10** (2.01 g, 5.87 mmol, 84%, R_f 0.36). Compound **10** consisted of a 3:1 (α/β) mixture anomers. Anal. Calcd for $C_{20}H_{22}O_5$: C, 70.16; H, 6.48. Found: C, 70.44; H, 6.40.

Synthesis of Methyl 3-*O*-(4-*O*-Benzoyl-3-*O*-benzyl-2,6-dideoxy-β-D-*arabino*-hexopyranosyl)-2,6-dideoxy-4-*O*-(*p*-tolylsulfonyl)-α-D-*arabino*-hexopyranoside (13) and Methyl 3-*O*-(4-*O*-Benzoyl-3-*O*-benzyl-2,6-dideoxy-α-D-*arabino*-hexopyranosyl)-2,6-dideoxy-4-*O*-(*p*-tolylsulfonyl)-α-D-*arabino*-hexopyranoside (14). Compound **10** (1.01 g, 2.95 mmol) was dissolved in 10 mL of dry benzene to which 0.65 mL (3.0 mmol) of trimethylsilyl bromide in 5 mL of dry benzene was added in a dropwise manner. After 5 min, the benzene was removed under reduced pressure below room temperature. The moisture-sensitive glycosyl bromide **8** [^{1}H NMR δ 1.14 (H_6, $J_{5,6}$ = 6.3 Hz), 1.70 (H_{2a}, $J_{1,2a}$ = 3.7 Hz, $J_{2a,3}$ = 10.8 Hz), 2.23 (H_{2e}, $J_{1,2e}$ = 1.3 Hz, $J_{2e,3}$ = 4.9 Hz), 4.07–4.35 (H_3, H_5, $ArCH_2$), 5.23 (H_4, $J_{3,4}$ = $J_{4,5}$ = 9.5 Hz), 6.17 (H_1), 6.89, 7.18, 7.95–8.05 (aromatic)] thus produced was immediately dissolved in 5 mL of dry toluene, and the solution was added in a dropwise manner to a solution of 0.61 g (1.93 mmol) of **7** in which 3 g of silver silicate had been suspended by vigorous stirring. After stirring for 12 h, the suspension was filtered through a 1-cm pad of silica gel, the silica gel was washed with 30 mL of ethyl acetate, and the solvent was distilled under reduced pressure. The residue was chromatographed under the standard conditions to give 0.95 g (1.49 mmol, 77%) of compound **13**: $[\alpha]_D$ +24° (*c* 0.47); R_f 0.31; mp 169–69.5 °C; ^{1}H NMR (300 MHz) (toluene-d_8) δ 0.73 ($H_{2a'}$, $J_{1',2a'}$ = 11.6 Hz, $J_{2a',3'}$ = 9.9 Hz), 1.17 ($H_{6'}$, $J_{5',6'}$ = 6.2 Hz), 1.54 (H_{2a}, $J_{1,2a}$ = 3.6 Hz, $J_{2a,3}$ = 11.4 Hz), 1.77 (H_6, $J_{5,6}$ = 6.3 Hz), 1.82 ($H_{2e'}$, $J_{1',2e'}$ = 2.0 Hz, $J_{2e',3'}$ = 5.3 Hz), 2.10 (H_{2e}, $J_{1,2e}$ = 1.0 Hz, $J_{2e,3}$ = 9.3 Hz), 2.55 ($ArCH_3$), 3.22 (OCH_3), 3.16 ($H_{5'}$, $J_{3'4'}$ = 9.1 Hz, $J_{4',5'}$ = 9.5 Hz), 3.25 ($H_{3'}$), 3.88 (H_5, $J_{4,5}$ = 9.5z), 4.07 (H_3, $J_{3,4}$ = 9.3 Hz), 4.13 ($H_{1'}$), 4.35 and 4.41 ($ArCH_2O$), 4.55 (H_1), 4.88 ($H_{4'}$), 7.00–7.36 and 7.74–7.82 (aromatic). Anal. Calcd for $C_{34}H_{40}O_{10}S$: C, 63.73; H, 6.29. Found: C, 63.51; H, 6.31. Also isolated was 0.086 g (0.14 mmol, 7%) of compound **14**: [α] +58° (*c* 0.61); R_f 0.36; ^{1}H NMR (300 MHz) δ 1.12 ($H_{6'}$, $J_{5',6'}$ = 6.3 Hz), 1.18 (H_6, $J_{5,6}$ = 6.3 Hz), 1.63 ($H_{2a'}$, $J_{1',2a'}$ = 3.9 Hz, $J_{2a',3'}$ = 11.3 Hz), 1.84 (H_{2a}, $J_{1,2a}$ = 3.6 Hz, $J_{2a,3}$ = 11.3 Hz), 2.27 (H_{2e}, $J_{1,2e}$ = 0.0 Hz, $J_{2e,3}$ = 5.5 Hz), 2.35 ($H_{2e'}$, $J_{1',2e'}$ = 0.0 Hz, $J_{2e',3}$ = 5.0 Hz), 2.42 ($ArCH_3$), 3.28 (H_3), 3.77 (H_5, $J_{4,5}$ = 9.4 Hz), 3.93 ($H_{5'}$, $J_{4'5'}$ = 9.5 Hz), 4.00 ($H_{3'}$, $J_{3',4'}$ = 9.5 Hz), 4.05 (H_3), 4.41 (H_4), 4.37 and 4.68 ($ArCH_2O$), 4.70 (H_1), 5.00 ($H_{4'}$), 5.17 ($H_{1'}$), 7.00–7.36 and 7.74–7.82 (aromatic). Anal. Calcd for $C_{34}H_{40}O_{10}S$: C, 63.73; H, 6.29. Found: C, 63.43; H, 6.27.

Methyl 3-*O*-(3-*O*-Benzyl-2,6-dideoxy-β-D-*arabino*-hexopyranosyl)-2,6-dideoxy-4-*O*-(*p*-tolylsulfonyl)-α-D-*arabino*-hexopyranoside (15). Compound **13** (300 mg, 0.47 mmol) was dissolved in 10 mL of methanol containing 40 mg of sodium hydroxide. After 5 h, the methanol was distilled under reduced pressure, and the residue was extracted with ethyl acetate (30 mL). This solution was filtered through a 1-cm layer of silica gel, and the solvent was distilled under reduced pressure to give 245 mg (0.47 mmol, 100%) of compound **15**: R_f 0.07; ^{1}H NMR (acetone-d_6) δ 0.64 ($H_{2a'}$, $J_{1',2a'}$ = 10.0 Hz, $J_{2a',3'}$ = $J_{2a',2e'}$ = 11.9 Hz), 1.16 ($H_{6'}$, $J_{5',6'}$ = 6.3 Hz), 1.33 (H_6, $J_{5,6}$ = 6.0 Hz), 1.48 (H_{2a}, $J_{1,2a}$ = 3.6 Hz, $J_{2a,3}$ = 11.0 Hz, $J_{2a,2e}$ = 13.1 Hz), 1.82 ($H_{2e'}$, $J_{1',2e'}$ = 2.0 Hz, $J_{2e',3'}$ = 5.1 Hz), 2.21 (H_{2e}, $J_{1,2e}$ = 1.2z, $J_{2e,3}$ = 5.0 Hz), 2.38 ($ArCH_3$), 3.29 (OCH_3), 4.25 ($H_{1'}$), 4.25 ($H_{1'}$), 4.66 (H_1), 7.19–7.87 (aromatic). Compound **15** was judged to be >90% pure by ^{1}H and ^{13}C NMR spectral determination, and these spectra appear in the supplementary material. To confirm the structure of **15**, whose NMR spectra showed a loss of the benzoyl group, this compound was reacted with benzoyl chloride (according to the procedure used for formation of **9**) to regenerate **13**.

Methyl 3-*O*-(4-*O*-Benzoyl-3-*O*-benzyl-2,6-dideoxy-β-D-*arabino*-hexopyranosyl)-2,6-dideoxy-α-D-*arabino*-hexopyranoside (16). Compound **13** (330 mg, 0.51 mmol) was dissolved in 100 mL of a 0.02 M solution of triethylamine in methanol and irradiated under standard conditions using the Rayonet chamber. After 1 h, the solvent was distilled under reduced pressure and the residue was chromatographed in the standard

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manner to give 220 mg (0.20 mmol, 80% based of starting material reacted) of **16**: R_f 0.15; ^{1}H NMR δ 1.27 ($H_{6'}$, $J_{5',6'}$ = 6.1 Hz), 1.32 (H_6, $J_{5,6}$ = 6.1 Hz), 1.48–1.91 ($H_{2a,2a'}$), 2.09 ($H_{2e'}$, $J_{1',2e'}$ = 2.0 Hz, $J_{2e',3'}$ = 5.4 Hz), 2.38 (H_{2e}, $J_{1,2e}$ = 2.9 Hz, $J_{2e,3}$ = 5.0 Hz), 3.12 (H_4, $J_{3,4}$ = $J_{4,5}$ = 8.9 Hz), 3.32 (OCH_3), 3.37–3.85 (H_3, $H_{3'}$, H_5, $H_{5'}$), 4.55 and 4.60 ($ArCH_2$), 4.58 ($H_{1'}$, $J_{1',2a'}$ = 10 Hz), 4.76 (H_1), 5.03 ($H_{4'}$, $J_{4',5'}$ = $J_{3',4'}$ = 9.3 Hz), 7.16–7.56, 7.94–8.07 (aromatic). Anal. Calcd for $C_{27}H_{34}O_8$: C, 66.65; H, 7.04. Found: C, 66.81; H, 7.17. Compound **16** was reacted with *p*-toluenesulfonyl chloride, according to the procedure used for formation of **5**, to regenerate **13**.

Synthesis of Methyl 3-*O*-(4-*O*-Benzoyl-2,6-dideoxy-β-D-*arabino*-hexopyranosyl)-2,6-dideoxy-4-*O*-(*p*-tolylsulfonyl)-α-D-*arabino*-hexopyranoside (17). Compound **13** (210 mg, 0.33 mmol) and 1.05 g of 5% Pd on carbon was stirred in 25 mL of ethyl acetate under 1 atm of hydrogen for 48 h. The suspension was filtered, and the filtrate evaporated to give 145 mg (0.26 mmol, 79% yield) of **17**: mp 154–155 °C; R_f 0.05; ^{1}H NMR δ 1.12 ($H_{6'}$, $J_{5',6'}$ = 6.1 Hz), 1.43 (H_6, $J_{5,6}$ = 6.2 Hz), 2.52 ($ArCH_3$), 3.31 (OCH_3), 4.74 (H_1, $J_{1,2a}$ = 3.0 Hz, $J_{1,2e}$ = 1.0 Hz), 7.25–8.07 (aromatic). Anal. Calcd for $C_{27}H_{34}O_{10}S$: C, 58.89; H, 6.22. Found: C, 59.98; H, 6.23. Reaction of compound **17** with benzyl triflate regenerated **13**.

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Supplementary Material Available: ^{1}H and ^{13}C NMR spectra for compound **15** (7 pages). Ordering information is given on any current masthead page.

Solvent Effects on the Ability of Amines To Physically Quench Singlet Oxygen As Determined by Time-Resolved Infrared Emission Studies

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The rates of physical quenching of singlet oxygen by nine amines were determined by following the decrease in the singlet oxygen emission intensity at 1270 nm. The effect of solvents on these rates were shown to be related to the hydrogen bond donating ability of the solvent, α.

The ability of solvents to produce both subtle and dramatic effects in singlet oxygen reactions has been known for many years.[2] It was also recognized that analysis of these solvent effects was complicated by the multistep nature of singlet oxygen reactions. Solvent effects on the photophysics of the sensitizer[3] and lifetime of singlet oxygen[4] had to be separated from the solvent effect on the reaction of interest. Early reports were restricted to determining solvent effects on β[5] (rate of decay of $^1O_2$/rate of reaction with acceptor), and any successful study required a time-consuming and careful kinetic analysis.

In 1979 Krasnovskii[6] and Khan and Kasha[7] reported for the first time the observation of the phosphorescence from $^1O_2[^1\Delta_g(\nu = 0) \rightarrow {}^3\Sigma_g^-(\nu = 0)]$ in solution at 1270 nm. The technique of following the time rate of change of the $^1O_2$ phosphorescence intensity results in a simple, direct, and accurate measure of the $^1O_2$ lifetime in comparison to earlier indirect methods based on competitive kinetics. The lifetime of the $^1\Delta_g$ state is a function of competitive processes which include physical quenching, chemical quenching, and electronic to vibronic energy transfer to the solvent. Early studies by investigators[4,8] with this now popular and improved technique focused on examinations of the effect of solvents on the nonradiative lifetime of $^1O_2$.

Table I. Solvent Effects on Singlet Oxygen Lifetimes[a]

solvent	$1/(k_d + k_s[S])$[b]	$1/k_d$[b]
(±)-2-butanol	16.1 ± 0.2	19.7
2-propanol	22.4 ± 0.4	22.1
CF_3CH_2OH	24.3 ± 0.4	
benzene[c]	25.8 ± 0.7	31.2,[d] 32,[e] 28[f]
acetone	38.2 ± 1.1	40,[e] 46.5[f]
acetone[g]	43.4 ± 0.2	
$(CF_3)_2CHOH$	52.5 ± 0.3	
CH_3CN	55.3 ± 0.5	61,[e] 54.4[f]
acetone-d_6	585 ± 5.0	640,[d] 690[f]

[a] 9.0×10^{-5} to 1.0×10^{-6} M Rose Bengal. [b] In microseconds. [c] Sensitizer acridine. [d] Reference 4c. [e] Reference 4b. [f] Reference 4a. [g] 1×10^{-4} M tetraphenylporphyrin.

We report here a study of the physical quenching ability of several amines (Figure 1) using this technique. The quenching of singlet oxygen by amines has been extensively examined.[9] Several workers[10] have observed that

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