JOC*Note*

Bis(*o*-nitrophenyl)ethanediol: A Practical Photolabile Protecting Group for Ketones and Aldehydes

Aurélien Blanc and Christian G. Bochet*,[1]

Department of Organic Chemistry, University of Geneva, 30, quai Ernest-Ansermet, CH-1211 Geneva 4, Switzerland

christian.bochet@unifr.ch

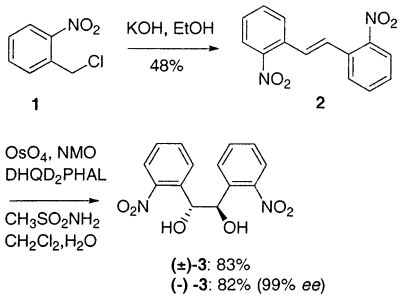
Received August 23, 2002

Abstract: The ketals of bis(*o*-nitrophenyl)ethanediol and ketones or aldehydes are smoothly deprotected in neutral conditions by irradiation with 350 nm light. The chemical stability in basic, acidic, and oxidizing media makes this form of protection orthogonal to classical protecting groups. Both racemic and enantiopure forms are readily available in two steps from inexpensive starting materials.

Photochemical lability is an attractive feature for a protecting group, since it allows deprotection without the requirement of any reagent. This permits the handling of compounds very sensitive to acids, bases, or other chemical conditions. Many photolabile protecting groups are known, mainly for the protection of carboxylic acids (as esters or amides), amines (as carbamates), and alcohols (as carbonates).[2] On the other hand, there are very few of such groups for ketones and aldehydes.[3,4] This is quite surprising, since carbonyl compounds are among the most commonly protected functions in organic synthesis. In this work, we describe a new photosensitive group, highly labile under photochemical conditions, but otherwise very robust in many chemical conditions.

Upon excitation by UV-light (λ < 400 nm), *o*-nitrobenzylic derivatives are capable of intramolecular hydrogen abstraction, followed by oxygen transfer from the nitro group.[5] The formal result is the oxidation of the benzylic center. If this position is functionalized with an alkoxy group, a hemiketal is formed, which spontaneously decomposes into the corresponding ketone, and liberates the other half as a free OH group. This strategy has been utilized with the *o*-nitrophenylethylene glycol as a protecting group for ketones and aldehydes.[4] However, several drawbacks limit its general use in organic synthesis. The presence of a chiral center leads to the formation of two diastereoisomers when used with another chiral molecule,[4] making already complicated NMR signal patterns (two sets of signals) more difficult to interpret. Purification of the resulting pair of compounds can also be cumbersome. These issues were addressed by using two units of *o*-nitrobenzyl alcohol instead of a diol.[6] Nevertheless, an excess of diol in the ketalization and significant lability in acidic media are other drawbacks that render their application useful in only very specific cases.

SCHEME 1



As an alternative, we have prepared the more robust diol **3**, symmetrical and easily accessible in its enantiopure form (Scheme 1). It was prepared by simple treatment of inexpensive *o*-nitrobenzyl chloride **1** with potassium hydroxide,[7] followed by osmium-catalyzed dihydroxylation (1 mol % OsO_4, NMO, water/CH_2Cl_2, 83%) of the *trans*-stilbene **2**. The asymmetric version was also carried out by using a slightly modified Sharpless dihydroxylation (1 mol % of $DHQD_2PHAL$, 1 mol % of OsO_4, 1.25 equiv of NMO, 1 equiv of $MeSO_2NH_2$, water/CH_2Cl_2).[8] The crude enantiomeric excess (93% ee, measured by chiral SFC) was increased by a recrystallization (82%, 99% ee). The absolute configuration of (−)-**3** was tentatively assigned to (*R*,*R*), by analogy to stilbene.[8b] Standard conditions with AD-mix-α in ^{t}BuOH/water gave poor or no conversion, presumably due to the poor solubility of the substrate.

To test this new photosensitive group, the protection of various types of ketones and aldehydes was carried out in refluxing benzene with a Dean−Stark apparatus (10 mol % PPTS). Deprotection was performed by exposing the ketals to UV-light (350 nm) for 1−2 h. Yields were high, in both protection and deprotection (Scheme 2, Table 1). It is worth mentioning the absence of double

(1) Present address: Department of Chemistry, University of Fribourg, Chemin du Musée 9, CH-1700 Fribourg, Switzerland. E-mail: Christian.Bochet@unifr.ch. Fax: +41−26−300 9738.

(2) For reviews on photolabile protecting groups, see: (a) Pillai, V. N. R. *Synthesis* **1980**, 1−26. (b) Pillai, V. N. R. *Org. Photochem.* **1987**, *9*, 225−321. (c) Bochet, C. G. *J. Chem. Soc., Perkin 1* **2002**, 125−142.

(3) McHale, W. A.; Kutateladze, A. G. *J. Org. Chem.* **1998**, *63*, 9924−9931.

(4) (a) Gravel, D.; Hebert, J. *Can. J. Chem.* **1974**, *52*, 187−189. (b) Sam, D. J. U.S. Patent 4,111,960, **1978**. (c) Gravel, D.; Hebert, J.; Thoraval, D. *Can. J. Chem.* **1983**, *61*, 400−410. (d) Aurell, M. J.; Boix, C.; Ceita, M. L.; Llopis, C.; Tortajada, A.; Mestres, R. *J. Chem. Res. (S)* **1995**, 452−453. (e) Ceita, L.; Mestres, R.; Tortajada, A. *Bol. Soc. Quim. Perú* **1998**, *64*, 55−61. (f) Ceita, L.; Maiti, A. K.; Mestres, R.; Tortajada, A. *J. Chem. Res. (S)* **2001**, 403−404.

(5) (a) Ciamician, G.; Silber, P. *Chem. Ber.* **1901**, *34*, 2040−2046. (b) Patchornik, A.; Amit, B.; Woodward, R. B. *J. Am. Chem. Soc.* **1970**, *92*, 6333−6335. For more recent mechanistic work, see: (c) Yip, R. W.; Sharma, D. K.; Giasson, R.; Gravel, D. *J. Phys. Chem.* **1985**, *89*, 5328−5330. (d) Walker, J. W.; Reid, G. P.; McCray, J. A.; Trentham, D. R. *J. Am. Chem. Soc.* **1988**, *110*, 7170−7177. (e) Yip, R. W.; Wen, Y. X.; Gravel, D.; Giasson, R.; Sharma, D. K. *J. Phys. Chem.* **1991**, *95*, 6078−6081. (f) Il'Ichev, Y. V.; Wirz, J. *J. Phys. Chem. (A)* **2000**, *104*, 7856−7870. For additional references, see ref 2.

(6) Gravel, D.; Murray, S.; Ladouceur, G. *J. Chem. Soc., Chem. Commun.* **1985**, 1828−1829.

(7) (a) Bischoff, C. A. *Ber. Deutsch. Chem. Ges.* **1888**, *21*, 2071−2078. (b) Ehrensperger, C. P.; Heberlein, M.; Skrabal, P. *Helv. Chim. Acta* **1978**, *61*, 2813−2822.

(8) (a) Kolb, H. C.; Van Nieuwenzhe, M. S.; Sharpless, K. B. *Chem. Rev.* **1994**, *94*, 2483−2547. (b) Sharpless, K. B.; Amberg, W.; Bennani, Y. L.; Crispino, G. A.; Hartung, J.; Jeong, K. S.; Kwong, H. L.; Morikawa, K.; Wang, Z. M.; Xu, D.; Zhang, X. L. *J. Org. Chem.* **1992**, *57*, 2768−2771. (c) Wang, Z. M.; Sharpless, K. B. *J. Org. Chem.* **1994**, *59*, 8302−8303.

10.1021/jo026347x CCC: $25.00
Published on Web 12/24/2002

SCHEME 2

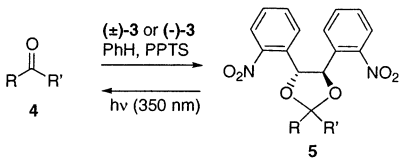
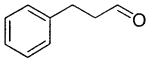
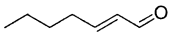


TABLE 1

entry	substrate		ketal	%	Photolysis[a]
1	**4a**		**5a**	92	87 (83)
2	**4b**		**5b**	75	90 (73)
3	**4c**		**5c**	90	97 (60)
4	**4d**		**5d**	85	69 (62)
5	**4e**		**5e**	83	84 (52)[b]
6	**4f**		**5f**	88	85 (38)[b]
7	**4g**	4-Cholesten-3-one	**5g**	67	(76)

[a] Yield determined by GC or NMR (isolated yield). [b] Volatile products.

TABLE 2

solvent	reagent	conditions	**5b**	**4b**
CH_2Cl_2	NaH, 5 equiv	25 °C, 10 h	100	0
THF	NaH, 5 equiv	25 °C, 10 h	92	trace
DME	NaH, 5 equiv	25 °C, 10 h	100	0
DMF	NaH, 5 equiv	25 °C, 10 h	80	17
DMSO	NaH, 5 equiv	25 °C, 10 h	59	trace
PhMe	NaH, 5 equiv	25 °C, 10 h	97	trace
Et_2O	NaH, 5 equiv	25 °C, 10 h	100	0
MeCN	NaH, 5 equiv	25 °C, 10 h	100	0
PhH	NaH, 5 equiv	reflux, 10 h	99	0
DMSO	NaH, 5 equiv	110 °C, 14 h	0	0
H_2O[a]	NaOH 2N	reflux, 24 h	91	9
EtOH[a]	EtONa	25 °C, 24 h	100	0
EtOH[a]	EtONa	reflux, 24 h	51	29
^{t}BuOH	^{t}BuOK	25 °C, 24 h	12	6
THF	LDA	−78 to 25 °C, 10 h	92	8

[a] With 50% dioxane.

bond isomerization in unsaturated ketones or aldehydes (entries 5−7). In the latter case, the use of 4 Å molecular sieves was essential to avoid deconjugation during the formation of the ketal.

Stability against a broad variety of chemical conditions is critical to a protecting group. We tested the stability of ketal **5b** in basic conditions (Table 2), acidic conditions (Table 3), and other commonly used reagents (Table 4).

Strong bases did not decompose the ketal, unless in the presence of nucleophilic solvents (DMSO, alcohols). It is worth pointing out that the stability in basic media is markedly higher than that with previously known ketone photolabile groups.[4,6]

The stability in acidic media is also significantly better, even in the presence of aqueous strong acids (such as sulfuric acid). On the other hand, neat trifluoroacetic acid should be avoided.

TABLE 3

solvent	reagent	conditions	**5b**	**4b**
THF	HCl 5%[a]	25 °C, 16 h	100	0
THF	HCl 10%[a]	25 °C, 16 h	100	0
THF	AcOH 10%[a]	25 °C, 16 h	100	0
THF	*p*-TsOH 3 mol %	25 °C, 16 h	96	trace
THF	oxalic acid 2 mol %	25 °C, 16 h	98	trace
THF	H_2SO_4 10%[a]	25 °C, 72 h	99	trace
TFA		25 °C, 1 h	68	30

[a] THF/aqueous solution (1:1 v/v).

TABLE 4

solvent	reagent	conditions	**5b**	**4b**
THF	TBAF, 1 equiv	25 °C, 16 h	75	13
MeCN[a]	CAN, 4 equiv	25 °C, 16 h	97	3
MeCN	DDQ, 4 equiv	25 °C, 18 h	90	8
piperidine		25 °C, 24 h	100	0
MeOH	$NaBH_4$	25 °C, 1 h	98	trace
Et_2O	$LiAlH_4$	25 °C, 1 h	0	0

[a] With 50% water.

Finally, conditions used to hydrolyze other protecting groups showed that the compatibility is also satisfactory, except for fluoride source and strongly reducing agents (reactive against the nitro groups of **5b**).

In conclusion, we have developed a symmetrical, enantiopure photolabile protecting group for ketones and aldehydes. Its improved stability ensures real orthogonality with respect to other existing groups. We are currently examining the possibility of tuning its reactivity according to the wavelength.[9]

Experimental Section

All reactions were carried out under argon, with magnetic stirring, unless otherwise specified. Purchased chemicals were used without further purification, unless otherwise specified. Solvents were dried by distillation from drying agents as follows: Et_2O and THF (Na/benzophenone); toluene and benzene (Na); MeCN and CH_2Cl_2 (CaH_2); MeOH ($Mg(OMe)_2$). Flash column chromatography (FC): SiO_2. Melting points were uncorrected.

***trans*-2,2′-Dinitrostilbene (2).** KOH (4.17 g, 74.5 mmol) dissolved in 40 mL of EtOH was slowly added to a solution of *o*-nitrobenzyl chloride **1** (4.26 g, 24.8 mmol) in 10 mL of EtOH. The mixture was stirred at room temperature for 4 h (formation of a yellow solid). The solid was filtered and washed several times with EtOH. The KCl remaining was removed by dissolution in hot AcOEt and filtration. Recrystallization (AcOEt) gave **2** (1.6 g, 48%) as a yellow solid: mp 204 °C; TLC R_f 0.42 (cyclohexane/AcOEt 3/2); IR ($CHCl_3$) ν_{max} 3020, 1525, 1345, 1275 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.48 (td, J = 7.8, 1.3 Hz, 2 H), 7.57 (s, 2 H), 7.67 (td, J = 7.7, 1.3 Hz, 2 H), 7.81 (dd, J = 7.8, 1.3 Hz, 2 H), 8.04 (dd, J = 8.1, 1.3 Hz, 2 H); ^{13}C NMR (100 MHz, $CDCl_3$) 124.9, 128.9, 129.0, 129.1, 132.6, 133.6, 147.9; MS (EI) *m*/*z* (%) 270 (2, $M^{+\bullet}$), 206 (4), 195 (7), 176 (21), 165 (46), 151 (56), 135 (75), 119 (52), 104 (58), 92 (100); HR-MS 270.0618 ($C_{14}H_{10}O_4N_2$ calcd 270.0606).

(1*R,2*R**)-1,2-Bis(2-nitrophenyl)ethane-1,2-diol (±3).** OsO_4 (96 μL, 0.015 mmol, 4% in water) was added to a solution of *trans*-stilbene **2** (405 mg, 1.5 mmol) and *N*-methylmorpholine *N*-oxide (NMO, 400 μL, 1.9 mmol, 50% in water) in 10 mL of CH_2Cl_2/H_2O (4/1). The reaction was vigorously stirred at room

(9) Blanc, A.; Bochet, C. G. *J. Org. Chem.* **2002**, *67*, 5567−5577.

temperature for 48 h (follow the reaction by TLC). The reaction was quenched with $Na_2S_2O_4$ (1.2 g in 10 mL of water). After 24 additional hours of stirring, the aqueous phase was extracted with AcOEt. The combined organic layers were washed with brine, dried over $MgSO_4$, filtered, and evaporated. The purification by FC (cyclohexane/AcOEt 2/1) gave (±**3**) (380 mg, 83%) as a white-gray solid: mp 142 °C; TLC R_f 0.29 (cyclohexane/AcOEt 3/2); IR ($CHCl_3$) ν_{max} 3500, 3020, 1530, 1350 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 3.37 (d, J = 4.5 Hz, 2 H), 5.60 (d, J = 4.5 Hz, 2 H), 7.45 (td, J = 8, 1.3 Hz, 2 H), 7.62 (td, J = 7.8, 1.3 Hz, 2 H), 7.78 (dd, J = 5, 1.3 Hz, 2 H), 7.80 (dd, J = 5.2, 1.3 Hz, 2 H); ^{13}C NMR (100 MHz, $CDCl_3$) 71.9, 124.5, 129.0, 129.5, 133.2, 134.8, 148.6; MS (EI) *m*/*z* (%) 152 (13), 135 (56), 121 (68), 93 (48), 77 (75), 65 (72), 51 (100); HR-MS 152.0334 ($C_7H_6O_3N$ calcd 152.0347).

(1*R*,2*R*)-1,2-Bis(2-nitrophenyl)ethane-1,2-diol ((−)-3). NMO (50% in water, 530 μL, 2.5 mmol) was added to a solution of *trans*-stilbene **2** (540 mg, 2 mmol), $(DHQD)_2PHAL$ (20 mg, 0.025 mmol), $CH_3SO_2NH_2$ (190 mg, 2 mmol), and OsO_4 (4% in water, 130 μL, 0.02 mmol). The mixture was stirred at 0 °C for 4 h. The enantiomeric excess was determined, after FC (cyclohexane/AcOEt 2/1), by SFC (Chiralcel ODH, 0.46 cm ∅ × 25 cm, 15% MeOH in CO_2, 200 bar CO_2, 30 °C, T_1 = 4.3 min (1*R*,2*R*), T_2 = 4.8 min (1*S*,2*S*); 93% ee). Recrystallization in toluene gave (−)-**3** (142 mg, 82%, 99% ee) as white-gray crystals: mp 172 °C; $[\alpha]^{17}_D$ −30.1 (4.7 mg·mL^{-1}, $CHCl_3$).

General Procedure for the Acetalization. In a flask under argon equipped with a Dean−Stark water separator, a solution of distilled aldehyde or ketone (1 mmol), 1,2-diol **3** (1.0−1.2 mmol) and pyridinium *p*-toluenesulfonate (PPTS, 25 mg, 0.1 mmol) in 10 mL of dry benzene were stirred at reflux. After completion of the reaction (monitored by TLC), the benzene was distilled and AcOEt was added. The organic phase was washed once with a satd $NaHCO_3$ solution and once with brine, dried over $MgSO_4$, filtered, and evaporated. The residue was purified by FC (silica gel, cyclohexane/AcOEt).

2-Decyl-2-methyl-4,5-bis(2-nitrophenyl)[1,3]dioxolane (5a). Following the general procedure, the dodecan-2-one **4a** (46 mg, 0.25 mmol) and the diol (±**3**) (91 mg, 0.3 mmol) in the presence of PPTS (7 mg, 0.025 mmol) gave **5a** (108 mg, 92%) as a pale yellow oil: TLC R_f 0.55 (cyclohexane/AcOEt 3/1); IR ($CHCl_3$) ν_{max} 2930, 2855, 1525, 1350 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 0.88 (t, J = 6.8 Hz, 3 H), 1.20−1.40 (m, 14 H), 1.58 (m, 2 H), 1.66 (s, 3 H), 1.94 (m, 2 H), 5.46 (ab, J_{ab} = 8.1 Hz, 2 H), 7.48 (m, 2 H), 7.73 (t, J = 7.6 Hz, 2 H), 7.79 (d, J = 8.3 Hz, 2 H), 7.97 (td, J = 8.1, 1.3 Hz, 2 H); ^{13}C NMR (100 MHz, $CDCl_3$) 14.1, 22.7, 24.2, 25.0, 29.3, 29.5, 29.6, 29.9, 31.9, 40.4, 79.4, 80.2, 111.4, 124.2, 128.9, 129.0, 129.1, 131.9, 132.3, 133.4, 148.9; MS (EI) *m*/*z* (%) 329 (35), 152 (11), 135 (100), 104 (15), 91 (40); HR-MS 329.0782 ($C_{16}H_{13}O_6N_2$ calcd 329.0774; $C_{26}H_{34}O_6N_2$-$C_{10}H_{21}$).

2,3-Bis(2-nitrophenyl)-1,4-dioxa-spiro[4.11]hexadecane (5b). Following the general procedure, the cyclododecanone **4b** (182 mg, 1 mmol) and the diol (±**3**) (304 mg, 1 mmol) in the presence of PPTS (25 mg, 0.1 mmol) gave **5b** (350 mg, 75%) as a white solid: mp 153−154 °C; TLC R_f 0.45 (cyclohexane/AcOEt 5%); IR ($CHCl_3$) ν_{max} 3020, 2935, 2850, 1525, 1470, 1360, 1220, 1115 cm^{-1}; UV (MeCN) λ_{max} (ϵ) 210 (20300), 252 (7500); ^1H NMR (400 MHz, $CDCl_3$) δ 1.40 (m, 14 H), 1.60 (m, 4 H), 1.98 (m, 4 H), 5.46 (s, 2 H), 7.47 (td, J = 8.0, 1.3 Hz, 2 H), 7.72 (td, J = 7.8, 1.3 Hz, 2 H), 7.78 (dd, J = 8.3, 1.3 Hz, 2 H), 7.95 (dd, J = 8.1, 1.3 Hz, 2 H); ^{13}C NMR (100 MHz, $CDCl_3$) 20.1, 22.2, 22.5, 25.8, 26.2, 33.4, 79.7, 114.1, 124.2, 129.0, 129.1, 132.0, 133.4, 149.0; MS (EI) *m*/*z* (%) 468 (1, $M^{+\bullet}$), 300 (1), 254 (3), 237 (5), 181 (3), 135 (100), 120 (13); HR-MS 300.1962 ($C_{19}H_{26}O_2N$ calcd 300.1963).

4,5-Bis(2-nitrophenyl)-2-undecyl[1,3]dioxolane (5c). Following the general procedure, the lauraldehyde **4c** (92 mg, 0.5 mmol) and the diol (±**3**) (182 mg, 0.6 mmol) in the presence of PPTS (12.5 mg, 0.05 mmol) gave **5c** (210 mg, 90%) as a pale yellow solid: mp 49−50 °C; TLC R_f 0.54 (cyclohexane/AcOEt 3/1); IR ($CHCl_3$) ν_{max} 2930, 2855, 1530, 1350, 1265, 1205, 1140, 1035 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 0.88 (t, J = 6.8 Hz, 3 H), 1.20−1.40 (m, 16 H), 1.56 (m, 2 H), 1.92 (m, 2 H), 5.48 (t, J = 4.6 Hz, 1 H), 5.61 (ab, J_{ab} = 6.6 Hz, 2 H), 7.50 (m, 2 H), 7.72 (m, 2 H), 7.83 (dd, J = 7.8, 1.3 Hz, 1 H), 7.90 (m, 3 H); ^{13}C NMR (100 MHz, $CDCl_3$) 14.1, 22.7, 23.9, 29.3, 29.6, 29.7, 31.9, 34.2, 80.3, 80.6, 106.2, 124.4, 124.7, 128.2, 128.7, 129.0, 129.1, 133.5, 133.7, 133.9, 134.6, 148.3, 148.4; MS (EI) *m*/*z* (%) 315 (41), 152 (17), 135 (100), 104 (15); HR-MS 315.0626 ($C_{15}H_{11}O_6N_2$ calcd 315.0617; $C_{26}H_{34}O_6N_2$-$C_{11}H_{23}$).

4,5-Bis(2-nitrophenyl)-2-phenethyl[1,3]dioxolane (5d). Following the general procedure, the hydrocinnamaldehyde **4d** (67 mg, 0.5 mmol) and the diol (±**3**) (167 mg, 0.55 mmol) in the presence of PPTS (12.5 mg, 0.05 mmol) gave **5d** (160 mg, 85%) as a yellow oil: TLC R_f 0.43 (cyclohexane/AcOEt 3/1); IR ($CHCl_3$) ν_{max} 3030, 2930, 2865, 1530, 1350, 1135, 1035 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 2.27 (m, 2 H), 2.93 (m, 2 H), 5.53 (t, J = 4.7 Hz, 1 H), 5.65 (ab, J_{ab} = 6.5 Hz, 2 H), 7.23−7.36 (m, 5 H), 7.52 (m, 2 H), 7.73 (m, 2 H), 7.82 (dd, J = 7.8, 1.3 Hz, 1 H), 7.93 (m, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) 30.0, 35.7, 80.4, 80.6, 105.2, 124.4, 124.7, 126.0, 128.2, 128.4, 128.5, 128.6, 129.0, 129.1, 133.4, 133.5, 133.6, 134.4, 141.0, 148.3, 148.4; MS (EI) *m*/*z* (%) 315 (3), 165 (3), 152 (13), 135 (100), 119 (14); HR-MS 315.0620 ($C_{15}H_{11}O_6N_2$ calcd 315.0617; $C_{23}H_{20}O_6N_2$-$PhCH_2CH_2$).

2,3-Bis(2-nitrophenyl)-1,4-dioxa-spiro[4.5]dec-6-ene (5e). Following the general procedure, the cyclohexenone **4e** (24 mg, 0.25 mmol) and the diol (±**3**) (76 mg, 0.25 mmol) in the presence of PPTS (7 mg, 0.025 mmol) gave **5e** (79 mg, 83%) as a yellow oil: TLC R_f 0.25 (cyclohexane/AcOEt 9/1); IR ($CHCl_3$) ν_{max} 2930, 2855, 1530, 1350, 1220, 1205, 1115 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 1.90 (m, 2 H), 2.13 (m, 4 H), 5.53 (ab, J_{ab} = 8.1 Hz, 2 H), 5.91 (d, J = 9.9 Hz, 1 H), 6.13 (dt, J = 10.1 Hz, 1 H), 7.48 (td, J = 8.1, 1.3 Hz, 2 H), 7.72 (td, J = 7.8, 1.3 Hz, 2 H), 7.81 (dd, J = 8.1, 1.3 Hz, 2 H), 7.97 (dd, J = 8.1, 1.3 Hz, 2 H); ^{13}C NMR (100 MHz, $CDCl_3$) 20.6, 24.8, 34.8, 79.4, 79.9, 106.9, 124.3, 127.5, 128.9, 129.1, 129.2, 132.1, 132.1, 133.4, 133.5, 134.1, 148.8; MS (EI) *m*/*z* (%) 354 (3), 135 (100), 97 (11), 91 (34); HR-MS 354.0857 ($C_{18}H_{14}O_6N_2$ calcd 354.0852; $C_{20}H_{18}O_6N_2$-C_2H_4).

2-Hex-1-enyl-4,5-bis(2-nitrophenyl)[1,3]dioxolane (5f). Following the general procedure, the *trans*-heptenal **4f** (28 mg, 0.25 mmol) and the diol (±**3**) (91 mg, 0.3 mmol) in the presence of PPTS (7 mg, 0.025 mmol) gave **5f** (88 mg, 88%) as a yellow oil: TLC R_f 0.31 (cyclohexane/AcOEt 3/1); IR ($CHCl_3$) ν_{max} 2930, 2855, 1530, 1350, 1130, 1035 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 0.92 (t, J = 7.2 Hz, 3 H), 1.25−1.50 (m, 4 H), 2.16 (q, J = 7.1 Hz, 2 H), 5.68 (ab, J_{ab} = 6.1 Hz, 2 H), 5.75−5.80 (m, 2 H), 6.12 (dt, J = 6.6 Hz, 1 H), 7.51 (td, J = 7.8, 1.0 Hz, 2 H), 7.71 (qd, J = 8.3, 1.0 Hz, 2 H), 7.74−7.94 (m, 4 H); ^{13}C NMR (100 MHz, $CDCl_3$) 13.9, 22.2, 30.6, 31.8, 80.1, 80.6, 105.8, 124.5, 124.8, 125.3, 128.2, 128.8, 129.1, 133.5, 133.7, 133.9, 134.2, 139.8, 148.3, 148.5; MS (EI) *m*/*z* (%) 287 (1), 152 (4), 135 (100), 91 (34), 79 (44); HR-MS 287.0643 ($C_{14}H_{11}O_5N_2$ calcd 287.0668; $C_{21}H_{22}O_6N_2$-$C_7H_{11}O$).

4-Cholesten-3-one, (1*R*,2*R*)-1,2-Bis(2-nitrophenyl)ethane-1,2-diol Ketal (5g). The 4-cholesten-3-one **4g** (58 mg, 0.15 mmol), the diol (−)-**3** (46 mg, 0.15 mmol), and PPTS (4 mg, 0.015 mmol) were stirred at 80 °C in dry benzene with molecular sieves 4 Å (at 110 °C in dry toluene only the deconjugated product was observed). The organic phase was washed once with a satd $NaHCO_3$ solution and once with brine, dried over $MgSO_4$, filtered, and evaporated. The purification by FC (cyclohexane/AcOEt 9/1) gave **5g** (68 mg, 67%) as a thick orange oil: $[\alpha]^{17}_D$ +158.3 (8.7 mg·mL^{-1}, $CHCl_3$); TLC R_f 0.48 (cyclohexane/AcOEt 3/1); IR ($CHCl_3$) ν_{max} 3025, 2950, 2870, 1705, 1655, 1610, 1580, 1525, 1465, 1350, 1100, 1010 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 0.70 (s, 3 H), 0.85−2.35 (m, 40 H), 5.55 (s, 2 H), 5.62 (s, 1 H), 7.47 (m, 2 H), 7.70−7.80 (m, 4 H), 7.96 (dd, J = 7.1, 1.0 Hz, 1 H), 8.05 (d, J = 7.0 Hz,1 H); ^{13}C NMR (125 MHz, $CDCl_3$) 12.0, 17.9, 18.6, 21.2, 22.5, 22.8, 23.8, 24.2, 28.0, 28.2, 28.9, 31.7, 32.3, 32.6, 34.2, 35.7, 35.8, 36.1, 38.7, 39.5, 39.8, 42.5, 53.4, 56.0, 56.1, 68.2, 79.7, 80.1, 107.4, 119.6, 124.2, 124.3, 128.8, 129.0, 129.1, 130.9, 132.3, 132.5, 133.4, 133.5, 148.9, 149.0, 153.5; MS (EI) *m*/*z* (%) 491 (1), 400 (26), 384 (44), 369 (9), 342 (17), 271 (13), 261 (23), 247 (22), 229 (47), 124 (83), 93 (65), 55 (100); HR-MS 384.3378 ($C_{27}H_{44}O$ calcd 384.3392; $C_{41}H_{54}O_6N_2$-$C_{14}H_{10}O_5N_2$).

General Procedure for the Photochemical Deprotection. The acetal (0.1 mmol) and an internal standard (tetrade-

cane) were dissolved in 10 mL of CH_3CN or Et_2O in a quartz vessel. The mixture was degassed by bubbling argon and stirred under irradiation at 350 nm for 1−2 h in a Rayonet apparatus (equipped with 16 RPR-3500 Å monochromatic lamps). Aliquots were taken after a given time and the yield was determined by GC or NMR. The solvent was evaporated and the residue was purified by FC (silica gel, cyclohexane/AcOEt).

General Procedure for Testing the Stability of Ketals. Samples of ketal **5b** (47 mg, 0.1 mmol) were submitted to the conditions described in the tables in a parallel reactor. The residues were analyzed by NMR after workup (in some cases after FC: silica gel, cyclohexane/AcOEt).

Acknowledgment. This work was supported by the Swiss National Science Foundation (grant 20-65047.01) and by the Fonds Frédéric Firmenich et Philippe Chuit. The authors thank Prof. Alexandre Alexakis for his generous support.

Supporting Information Available: Proton and carbon NMR spectra for all cited compounds and chiral SFC data for the diol **3**. This material is available free of charge via the Internet at http://pubs.acs.org.

JO026347X