Photocyclization Reactions of Epoxy Nitriles *via* Carbonyl Ylides. Formation of Spiroketals, Spiroethers, and a Spirolactone[1]

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Photocyclization reactions ($\lambda = 254$ nm) of γ-methyl δ-(4-hydroxybutyl) and δ-(4-hydroxypentyl) α,β-unsaturated γ,δ-epoxy nitriles gave spiroketals and spiroethers diastereoselectively, whereas reaction of δ-(6-hydroxyhexyl) nitrile afforded no cyclization product. In addition, photocyclization of nitrile bearing a carboxyl group in the δ-side-chain afforded spirolactone.

Key words carbonyl ylide; epoxy nitrile; spiroketal; photochemistry; anomeric effect; diastereoselectivity

In earlier studies[1] we have shown that, on irradiation ($\lambda = 254$ nm), δ-(4-hydroxybutyl) α,β-unsaturated γ,δ-epoxy nitriles (*E*/*Z*)-**1a, b** undergo C, C-bond cleavage of the oxirane leading to the carbonyl ylide **X**, followed by an intramolecular nucleophilic addition of the hydroxy group to afford the spiroketals (*E*/*Z*)-**2a, b** and **3a, b**. Compound **3b** is transformed to the spiroether **4b** diastereoselectively by an acid-catalyzed [1,3]-sigmatropic rearrangement. Consequently, we are interested in probing the scope and limitations of the photocyclization reaction for the formation of spiroketals. In this paper we report on the photoreactions of various epoxy nitriles possessing a γ-methyl substituent (*E*/*Z*)-**1c**, a secondary alcohol group in the δ-side-chain (*E*/*Z*)-**1dA+B**,[3] longer δ-side-chains (5 and 6 C atoms) (*E*/*Z*)-**1e** and (*E*/*Z*)-**1f**, and a carboxy group in the δ-side-chain (*E*/*Z*)-**1g**.[4]

Preparation of Epoxy Nitriles (*E*/*Z*)-1c—g Epoxy nitriles (*E*/*Z*)-**1c**—**g** were synthesized as follows. The reactions of β-ethoxyenones **5**[5] or **6**[6] with Grignard reagents prepared from tetrahydro-2-pyranylethers **7c**—**f**[6,7] and magnesium followed by an acid treatment gave the corresponding enones **8c**—**f**. Epoxidations of **8c**—**f** with 35% H_2O_2 and 20% aqueous NaOH afforded the epoxy ketones **9c**—**f**. Subsequent Horner–Emmons reactions of **9c**—**f** with diethyl cyanomethylphosphonate gave epoxy nitriles (*E*/*Z*)-**10c**—**f**, which were treated with oxalic acid in methanol to give deprotected hydroxy epoxides (*E*/*Z*)-**1c**—**f**. The hydroxy epoxide **1d** was obtained as a mixture of diastereomers (*E*/*Z*)-**1dA** and (*E*/*Z*)-**1dB** (1 : 1), and used in the photolysis without further separation. The yields and the (*E*/*Z*)-ratios of **8**—**10** and **1** are summarized in Table 1. The transformation of (*E*/*Z*)-**1b**[1] to the epoxy carboxylic acid (*E*/*Z*)-**1g** was accomplished by means of pyridinium dichromate (PDC) oxidation in *N*,*N*-dimethylformamide (DMF)[8] in 75% yield.

The structures of all compounds were deduced from the spectral data. The (*E*) and (*Z*) configurations of **1c**—**g** and **10c**—**f** were determined from a comparison of their spectral data with those of (*E*/*Z*)-**1a, b**.[1]

Photocyclization Reactions of Epoxy Nitriles (*E*/*Z*)-1c—g Preparative irradiations of (*E*/*Z*)-**1c**—**g** were performed under conditions optimized on the basis of the results of the cyclization of (*E*/*Z*)-**1b**.[1] Irradiation of (*E*/*Z*)-**1c** in the presence of 1 eq of triethylamine (TEA) in CH_2Cl_2 with low-pressure mercury lamp (quartz filter) at room temperature gave the spiroketal (*E*)-**2c** (9%) and the spiroether **4c** (40%).[9,10] Compounds (*E*)-**2c** and **4c** were each isolated as a single stereoisomer. Similar reaction of (*E*/*Z*)-**1dA+B** afforded (*E*)-**2d** (9%), (*Z*)-**2d** (8%), and **4d** (16%), diastereoselectively.

The total yield of the photocyclization products of (*E*/*Z*)-**1c** was not very different from that of (*E*/*Z*)-**1b** (see Table 2). However, the ratio of (*E*/*Z*)-**2**:**4** derived from

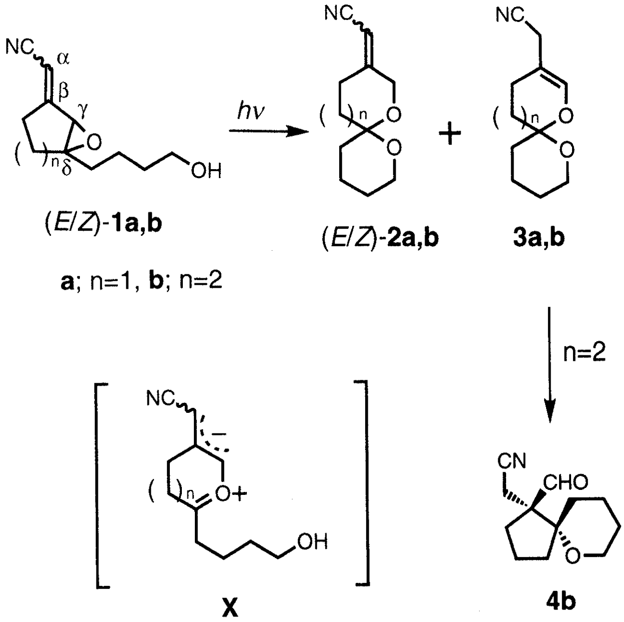
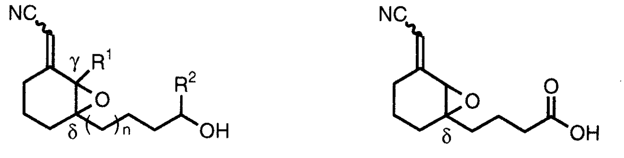


Chart 1



(*E*/*Z*)-**1c**	n=1, R^1=Me, R^2=H	(*E*/*Z*)-**1g**
(*E*/*Z*)-**1dA+B**	n=1, R^1=H, R^2=Me	
(*E*/*Z*)-**1e**	n=2, R^1=H, R^2=H	
(*E*/*Z*)-**1f**	n=3, R^1=H, R^2=H	

Fig. 1

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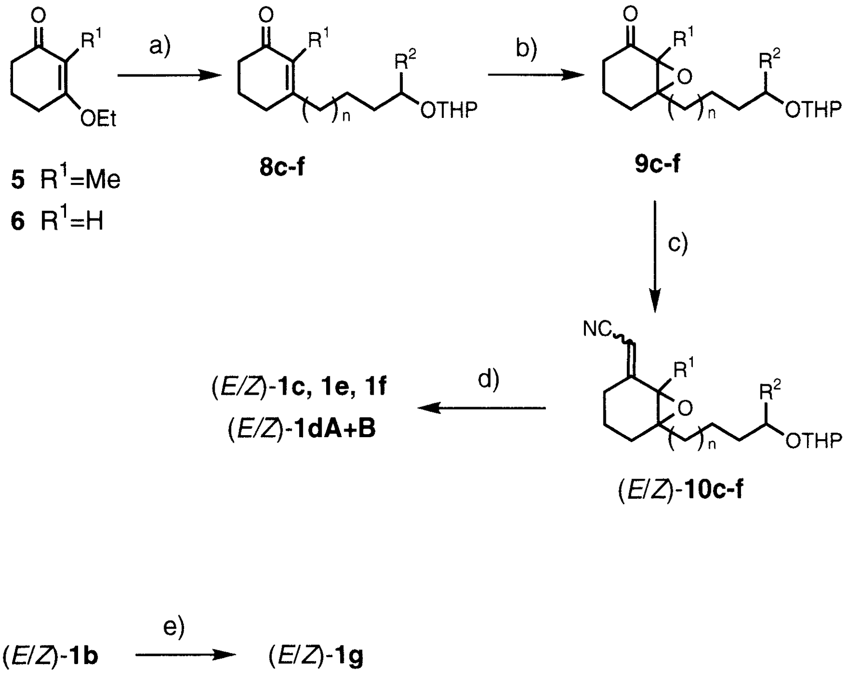


a) $Cl(CH_2)_nCH_2CH_2CH(R^2)OTHP$ **7c** (n = 1, R^2 = H), **7d** (n = 1, R^2 = Me), **7e** (n = 2, R^2 = H), **7f** (n = 3, R^2 = H), Mg, THF. b) 35% H_2O_2, 20% NaOH. c) $(EtO)_2P(O)CH_2CN$, NaH, DMF. d) Oxalic acid, MeOH. e) 3.5 equiv. PDC, DMF.

Chart 2

Table 1. Yields of Compounds **8**—**10** and **1**

	n	R^1	R^2	Yields (%)$^{a)}$ **8**	**9**	**10**	**1**	$(E/Z)^{b)}$
c	1	Me	H	70	84	88	61	(4:1)
d	1	H	Me	73	73	85	65	(4:3)$^{c)}$
e	2	H	H	45	74	88	26	(6:5)
f	3	H	H	88	68	Quantitative	52	(7:5)

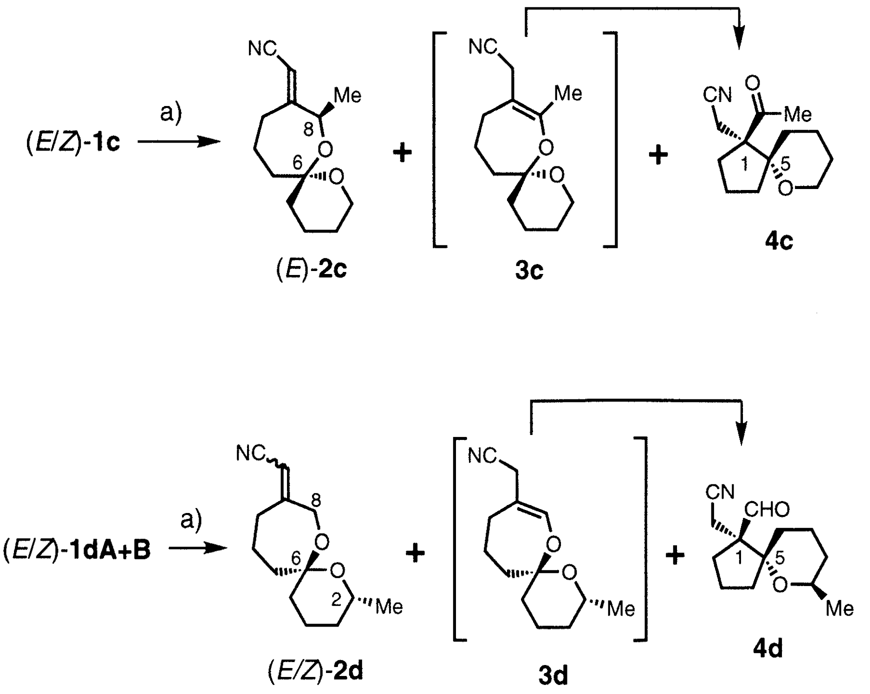
a) Isolated yields. *b)* The ratio of (*E*/*Z*) was determined from ^{1}H-NMR analysis. *c)* A mixture of (*E*/*Z*)-**1dA** and (*E*/*Z*)-**1dB** (1 : 1).

(*E*/*Z*)-**1c** was significantly lower than that from (*E*/*Z*)-**1b**.[11] In the case of the photocyclization of (*E*/*Z*)-**1dA**+**B**, the total yield of the photocyclization products was decreased in comparison with that of the primary alcohol (*E*/*Z*)-**1b**, owing to a decrease of the steric hindrance of the hydroxyl group.[13]

The structures of these photoproducts were determined mainly from spectral data. In particular, the significant signals in the ^{13}C-NMR spectra of (*E*)-**2c**, (*E*)-**2d**, and (*Z*)-**2d** were the singlets at 99.3, 99.9, and 100.0 ppm due to the spiro carbon, respectively. The (*E*) and (*Z*) configurations of **2c, d** were deduced from a comparison of the chemical shifts of the olefinic proton and 8-H with those of (*E*/*Z*)-**2b**[1] and the NOE enhancement between 8-H and the olefinic proton (5.3%) and between the olefinic proton and the methyl protons (3.3%) in (*E*)-**2c** (Fig. 2). The stereochemistry at C-6 and C-8 in (*E*)-**2c** was assigned as (6*R**,8*R**) based on the significant NOE enhancement between 2-H and 8-H (3.8%). In the case of (*E*)-**2d**, the relative configuration (2*R**,6*S**) was also indicated by the significant NOE enhancement between 2-H and 8-H (4.6%) and the lack of NOE between 8-H and the methyl protons. The conformations of (*E*)-**2c** and (*E*)-**2d** depicted in Fig. 2 were considered to be preferred, owing to two anomeric effects.

The structures of **4c, d** were deduced from the spectral data. An IR band (ν = 1707 cm^{-1}) and a signal in the ^{1}H-NMR spectrum (2.30 ppm) of **4c** were characteristic of the acetyl moiety. The ^{13}C-NMR spectrum of **4c** showed two singlets at 64.5 and 83.7 ppm due to C-1 and C-5, respectively. As characteristic signals for **4d**, the ^{1}H-NMR spectrum showed a singlet at 9.73 ppm due to the aldehyde moiety and the ^{13}C-NMR spectrum had singlets at 60.7 and 87.5 ppm due to C-1 and C-5, respectively. We will discuss the stereochemistry of **4** later in this paper.

The reaction mechanisms proposed for the formation of (*E*/*Z*)-**2d**, **3d**, and **4d** are depicted in Chart 4. The two diastereomers (*E*/*Z*)-**1dA** and (*E*/*Z*)-**1dB** underwent C(γ), C(δ)-bond cleavage of the oxirane, leading to the same carbonyl ylide intermediate **Y**. Subsequently, the hydroxyl group attacked the ylide **Y** from the top or bottom face to give the spiroketal (*E*/*Z*)-**2d′** or (*E*/*Z*)-**2d**, respectively. The formation of (*E*/*Z*)-**2d**, having two anomeric effects, is presumably kinetically and thermodynamically favored.[14,15] AM 1 calculations with the CAChe system[16] suggested that the heat of formation of (*E*)-**2d** (−74.4 kcal/mol) was lower than that of (*E*)-**2d′** (−69.6 kcal/mol). Similarly, the spiroketal **3d** having two anomeric effects was preferentially formed and underwent an acid-catalyzed rearrangement leading to **4d**.[1] For the same reason, the photoreaction of (*E*/*Z*)-**1c** gave the single



a) λ = 254 nm, 1 equiv. Et_3N, CH_2Cl_2.

Chart 3

Table 2. Yields of Photocyclization Products **2** and **4**

Substrate	Yields (%)			
	2	(*E*/*Z*)	**4**	Total
1b	18	(2.6 : 1)	28	46[a)]
1c	9	(*E* only)	40	49
1d	17	(1.1 : 1)	16	33
1e	1	(*Z* only)	4	5
1f	—	(—)	—	—

a) Ref. 1.

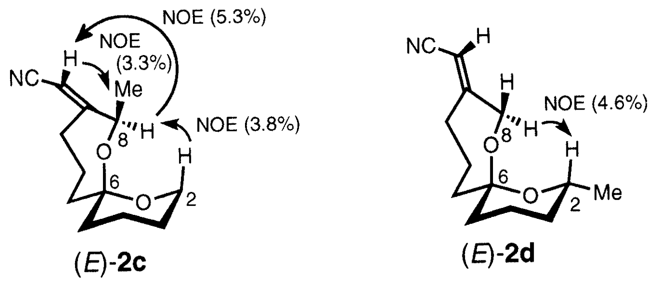


Fig. 2

stereoisomer (*E*)-**2c**.

Preparative irradiation of (*E*/*Z*)-**1e** under the same conditions gave (*Z*)-**2e** (1%), (1*R**,5*R**)-**4e** (*cis*-**4e**) (1%), and (1*R**,5*S**)-**4e** (*trans*-**4e**) (3%) (Chart 5). However, the reaction of (*E*/*Z*)-**1f** afforded no photocyclized product. The main products of both reactions were intractable materials (mainly polymers).

The structure of the spiroketal (*Z*)-**2e** was assigned from a comparison of the spectral data with those of (*Z*)-**2b**.[1)] The structures of the spiroethers *cis*- and *trans*-**4e** were deduced from spectral data. An IR band (1720 cm^{-1}), a singlet [9.60 for *cis* and 9.73 ppm for *trans*] in the ^1H-NMR spectrum, and a doublet [201.4 for *cis* and 203.6 ppm for *trans*] in the ^{13}C-NMR spectrum were characteristic of an aldehyde group. Singlets at 60.3 and 62.4 ppm due to C-1 and at 93.4 and 89.4 ppm due to C-5 in the ^{13}C-NMR spectrum also supported the *cis*- and *trans*-**4e** structures, respectively.

The relative configurations at C-1 and C-5 of the spiroethers **4c**—**e** were inferred from a comparison of the chemical shifts of the α-protons to the cyano group with those of **4b**[1)] (see Table 3), whose structure has been determined by X-ray analysis. In particular, the ^1H-NMR spectrum of *trans*-**4e** showed two doublets due to the α-protons at lower field than those of *cis*-**4e**, because of the deshielding effect of an oxygen atom in the ether ring. Consequently, the configurations of **4c** and **4d** were presumed to be (1*R**,5*R**), (*trans*) and these may be formed exclusively from the preferred conformations of the spiroketals **3c** and **3d** (see Chart 4), respectively, similar to the formation of **4b** from **3b**.[1)] In the 1,8-dioxaspiro[6.6]tridecane system **3e**, however, the difference of the relative stabilities between the possible conformations is presumably not so large as those of **3b**—**d**, and therefore, both spiroethers, *cis*- and *trans*-**4e**, were formed.

Irradiation of the epoxy carboxylic acid (*E*/*Z*)-**1g** and 1 eq of TEA in acetonitrile at room temperature gave the spirolactone **3g** (23%). The structure of **3g** was assigned on the basis of spectral data. In particular, the significant signal in the ^{13}C-NMR spectrum of **3g** was a singlet at 107.0 ppm due to the spiro carbon. An IR band at 1740 cm^{-1} and a singlet at 170.4 ppm in the ^{13}C-NMR spectrum were characteristic of a δ-lactone moiety. This

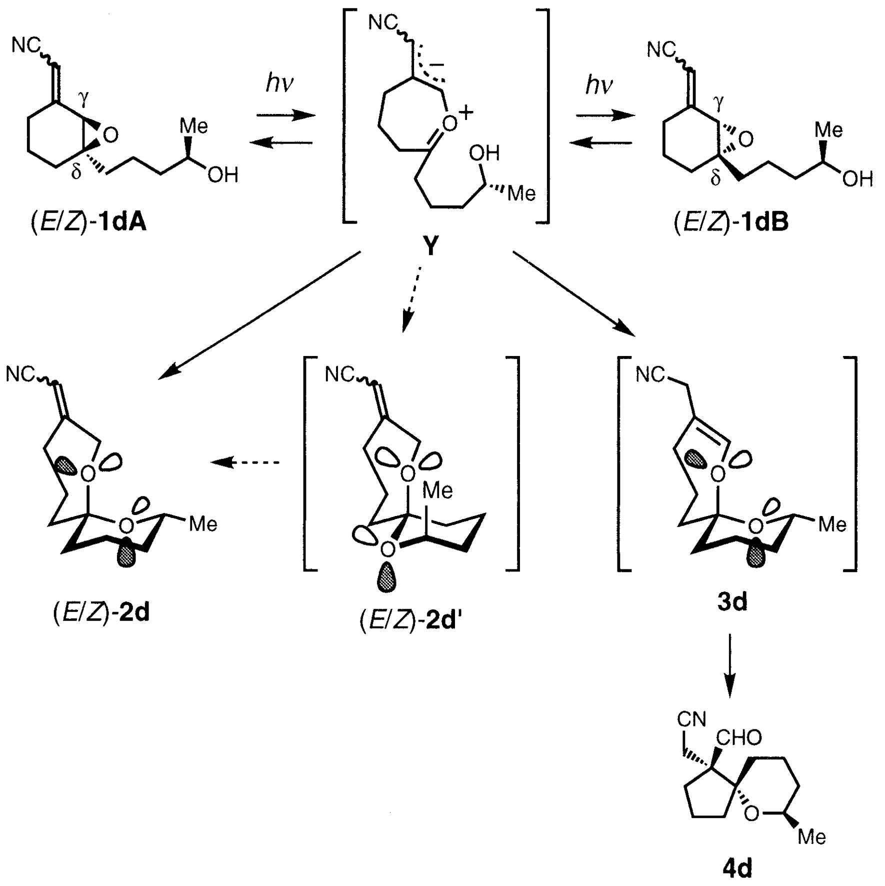
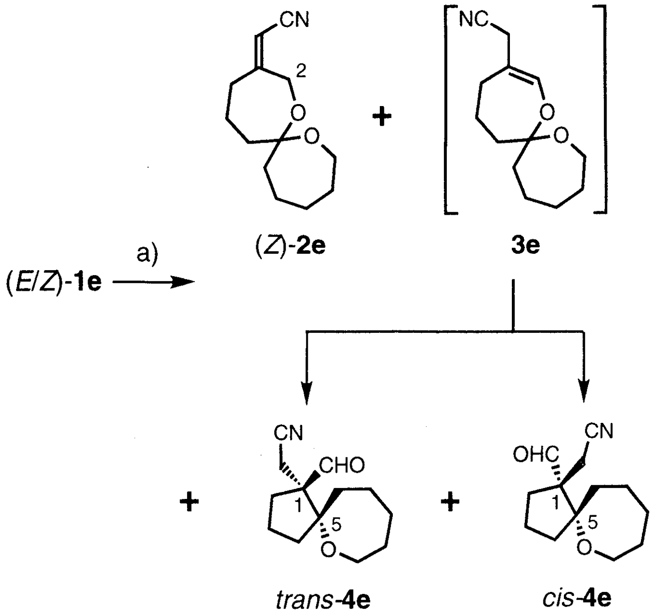


Chart 4



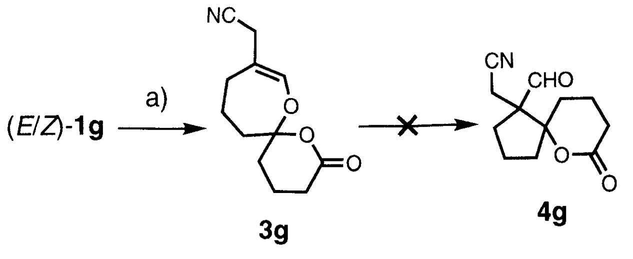
(E/Z)-**1f** $\xrightarrow{\text{a)}}$ no photocyclization product

a) $\lambda = 254$ nm, 1 equiv. Et_3N, CH_2Cl_2.

Chart 5

Table 3. ^{1}H-NMR Chemical Shifts (ppm) of α-Protons to the Cyano Group for the Spiroethers **4b**—**e**

4	*trans*	*cis*
b	2.66, 2.75	—
c	2.61, 3.02	—
d	2.54, 2.84	—
e	2.63, 2.83	2.25, 2.71



a) $\lambda = 254$ nm, 1 equiv. Et_3N, MeCN.

Chart 6

result proved that the nucleophilic addition to carbonyl ylide intermediates proceeds by attack of not only the hydroxyl but also the carboxyl group.

The spiroethers **4b**—**e** were formed from the corresponding spiroketals **3b**—**e**. However, **3g** was stable and was not transformed to the corresponding spiroether **4g** by treatment with SiO_2, because the electron-releasing effect of the O-1 atom of **3g** was smaller than that of **3b**—**e**.

In summary, the present work has demonstrated that epoxy nitriles (*E*/*Z*)-**1c**, **1dA**+**B**, and **1e** afford spiroketals (*E*)-**2c**, (*E*/*Z*)-**2d**, and (*Z*)-**2e** and spiroethers **4c**—**e** derived from **3c**—**e**, and the cyclization is limited to epoxy nitriles possessing less than five C-atoms in the δ-side chain. In particular, the photoproducts (*E*)-**2c** and **4c** and (*E*)-**2d**, (*Z*)-**2d**, and **4d** are diastereometically pure. The nucleophilic addition of the carboxyl group to the carbonyl ylide can also proceed, leading to the spirolactone **3g**.

Experimental

Melting points and boiling points are uncorrected. Melting points were measured with a Yanaco MP-J3 apparatus and boiling points were measured with Büchi Kugelrohr GKR-50 apparatus. IR spectra were recorded on a Hitachi 260-10 spectrometer. NMR spectra were obtained with a JEOL JNM-EX270 (270 MHz; EX) or a JEOL JNM-GX400 (400 MHz; GX) spectrometer in $CDCl_3$ solutions using tetramethylsilane as an internal standard. Mass spectra (MS) and high-resolution MS (HRMS) were taken on a JEOL JMS-DX 302 spectrometer. Column chromatography was performed with either Nakalai silica gel 60 (230—400 mesh (SiO_2 A)) or Kanto silica gel (100—200 mesh (SiO_2 B)).

An Eikosha 60 W (lamp A) and a Riko 32 W (lamp B) low-pressure mercury lamp were used for irradiation. The photolysis solutions were purged with argon both before and during irradiation.

Preparations of Epoxy Nitriles (*E*/*Z*)-1c—g. 2-Methyl-3-[4-(tetrahydro-2-pyranyloxy)butyl]-2-cyclohexen-1-one (8c) Ethyl bromide (125 mg, 1.15 mmol) was added dropwise to a mixture of magnesium (0.726 g, 29.9 mg-atom) in dry ether (2.6 ml) at room temperature. After the reaction had began, a solution of 4-(tetrahydro-2-pyranyloxy)butyl chloride **7c**$^{6)}$ (5.00 g, 25.9 mmol) in dry tetrahydrofuran (THF) (12 ml) was added dropwise at room temperature. The mixture was then heated under reflux for 3 h. After the mixture had cooled, a solution of 3-ethoxy-2-methyl-2-cyclohexenone **5**$^{5)}$ (2.00 g, 13.0 mmol) in dry THF (3.0 ml) was added at room temperature. The whole was heated under reflux for 45 min, poured into cold water, acidified with 5% aqueous HCl to pH 5, and extracted with diethyl ether. The ethereal extracts were washed with brine, dried over $MgSO_4$ and concentrated *in vacuo*, giving a residue that was subjected to flash chromatography (SiO_2 A; hexane–ethyl acetate (1 : 1)) to afford the enone **8c** (2.41 g, 70%) as a colorless oil, bp 185 °C (0.20 Torr). IR (film) cm^{-1}: 1667 (C=O), 1630 (C=C). ^{1}H-NMR (GX) δ: 1.52—1.86 (10H, m, 5CH_2), 1.78 (3H, s, CH_3), 1.90—1.96 (2H, m, CH_2), 2.27—2.30, 2.33—2.41 (6H, 2m, 4-H_2, 6-H_2, 1'-H_2), 3.38—3.44, 3.48—3.53, 3.74—3.80, 3.84—3.89 (4H, 4m, 4'-H_2, 6''-H_2), 4.57 (1H, t, J=3.5 Hz, 2''-H). MS m/z (rel. int. %): 266 (M^+, 1.7), 182 (70), 124 (39), 85 (100). *Anal.* Calcd for $C_{16}H_{26}O_3$: C, 72.14; H, 9.84. Found: C, 71.96; H, 10.27.

1-Methyl-6-[4-(tetrahydro-2-pyranyloxy)butyl]-7-oxabicyclo[4.1.0]-heptan-2-one (9c) A mixture of **8c** (1.31 g, 4.92 mmol), 20% aqueous NaOH (6 drops) and methanol (5.0 ml) was treated with 35% H_2O_2 (1.51 g) at 0 °C. The reaction mixture was stirred at 0 °C for 2 h and at room temperature for 1 h, then poured into cold brine and extracted with dichloromethane. The extracts were subjected to the same work-up as used for the synthesis of **8c**. Flash chromatography (SiO_2 A; hexane–ethyl acetate (4 : 1)) of the residue gave the epoxy ketone **9c** (1.10 g, 79%) as a colorless oil, bp 201 °C (0.35 Torr). IR (film) cm^{-1}: 1710 (C=O). ^{1}H-NMR (GX) δ: 1.42 (3H, s, CH_3), 1.45—1.85, 1.89—2.00, 2.04—2.13 (17H, 3m, 8CH_2, 3-H), 2.54—2.61 (1H, m, 3-H), 3.37—3.43, 3.48—3.53, 3.73—3.79, 3.84—3.89 (4H, 4m, 4'-H_2, 6''-H_2), 4.57 (1H, t, J=3.5 Hz, 2''-H). MS m/z (rel. int. %): 198 (M^+ − 84, 43), 111 (31), 85 (100), 55 (30), 43 (72). *Anal.* Calcd for $C_{16}H_{26}O_4$: C, 68.06; H, 9.28. Found: C, 67.93; H, 9.59.

(*E*/*Z*)-1-Methyl-6-[4-(tetrahydro-2-pyranyloxy)butyl]-7-oxabicyclo-[4.1.0]hept-2-ylideneacetonitrile ((*E*/*Z*)-10c) Diethyl cyanomethylphosphonate (705 mg, 3.98 mmol) was added dropwise to a suspension of 60% NaH (159 mg, 3.98 mmol) in dry DMF (6.9 ml) at room temperature. After stirring of the mixture for 20 min, **9c** (971 mg, 3.44 mmol) was added dropwise and stirring was continued at room temperature for 3 h. Ice/water was then added to the mixture, and the organic phase was extracted with diethyl ether and subjected to the same work-up as used for the synthesis of **8c**. Flash chromatography (SiO_2 A; cyclohexane–ethyl acetate (3 : 1)) of the residue yielded the epoxy nitrile (*E*/*Z*)-**10c** (*E* : *Z* = 4 : 1, 929 mg, 88%) as a colorless oil, bp 240 °C (0.30 Torr). IR (film) cm^{-1}: 2220 (C≡N), 1620 (C=C). ^{1}H-NMR (GX) δ: 1.41—1.92, 1.97—2.05, 2.41—2.48 (36H, 3m, 18CH_2 for *E* and *Z*), 1.47 (3H, s, CH_3 for *E*), 1.81 (3H, s, CH_3 for *Z*), 3.37—3.43, 3.48—3.53, 3.65—3.69, 3.73—3.79, 3.84—3.89 (8H, 5m, 4'-H_2, 6''-H_2 for *E* and *Z*), 4.56 (2H, t, J=3.7 Hz, 2''-H for *E* and *Z*), 5.40 (1H, t, J=1.2 Hz, HCCN for *Z*), 5.48 (1H, s, HCCN for *E*). MS m/z (rel. int. %): 221 (M^+ − 84, 25), 160 (28), 119 (32), 85 (100). *Anal.* Calcd for $C_{18}H_{27}NO_3$: C, 70.79; H, 8.91; N, 4.59. Found: C, 70.59; H, 9.18; N, 4.44.

(*E*/*Z*)-6-(4-Hydroxybutyl)-1-methyl-7-oxabicyclo[4.1.0]hept-2-ylideneacetonitrile ((*E*/*Z*)-1c) A solution of (*E*/*Z*)-**10c** (4.06 g, 13.3 mmol) and oxalic acid (2.51 g, 19.9 mmol) in methanol (364 ml) was stirred at room temperature for 25.5 h, then poured into a saturated aqueous $NaHCO_3$ solution and extracted with diethyl ether. The extracts were subjected to the same work-up and purification procedure as used for the synthesis of **8c**. The epoxy nitrile (*E*/*Z*)-**1c** (*E* : *Z* = 4 : 1, 1.78 g, 61%) was obtained as a colorless oil, bp 182 °C (0.52 Torr). IR (film) cm^{-1}: 3450 (O–H), 2220 (C≡N), 1620 (C=C). ^{1}H-NMR (GX) δ: 1.42—1.83, 1.84—1.93, 1.98—2.05, 2.41—2.48, 2.60—2.67 (26H, 5m, 12CH_2, 2OH for *E* and *Z*), 1.47 (3H, s, CH_3 for *E*), 1.81 (3H, s, CH_3 for *Z*), 3.66 (4H, t, J=6.0 Hz, 4'-H_2 for *E* and *Z*), 5.41 (1H, t, J=1.2 Hz, HCCN for *Z*), 5.49 (1H, s, HCCN for *E*). ^{13}C-NMR for *E* (GX) δ: 15.2 (q, CH_3), 20.0, 21.5, 27.6, 28.8, 32.6, 34.1 (6t, 6CH_2), 61.2, 68.8 (2s, C-1, C-6), 62.3 (t, C-4'), 96.8 (d, $\underline{C}$CN), 116.4 (s, CN), 165.7 (s, C-2). ^{13}C-NMR for *Z* (GX) δ: 16.4 (q, CH_3), 20.5, 21.5, 27.4, 32.6, 33.3, 33.8 (6t, 6CH_2), 61.0, 67.4 (2s, C-1, C-6), 62.3 (t, C-4'), 96.7 (d, $\underline{C}$CN), 116.8 (s, CN), 165.1 (s, C-2). MS m/z (rel. int. %): 221 (M^+, 8.2), 160 (86), 133 (58), 119 (100). HRMS m/z: 221.1403 (Calcd for $C_{13}H_{19}NO_2$: 221.1416).

3-[4-(Tetrahydro-2-pyranyloxy)pentyl]-2-cyclohexen-1-one (8d) By analogy with the synthesis of **8c**, 3-ethoxy-2-cyclohexenone **6**$^{6)}$ (11.9 g, 84.9 mmol) was stirred with Grignard reagent (prepared from magnesium (2.97 g, 122 mg-atom) and 4-(tetrahydro-2-pyranyloxy)pentyl chloride **7d**$^{7a)}$ (21.0 g, 102 mmol) at 40 °C for 2 h) at room temperature for 40 h. Flash chromatography [SiO_2 A; hexane–ethyl acetate (2 : 1)] of the reaction mixture gave the enone **8d** (a mixture of two diastereomers, 16.5 g, 73%) as an oil. IR (film) cm^{-1}: 1673 (C=O), 1630 (C=C). ^{1}H-NMR (EX) δ: 1.11, 1.23 (6H, 2d, J=6 Hz, 2(5'-H_3)), 1.41—1.89, 1.94—2.04 (24H, 2m, 12CH_2), 2.20—2.38 (12H, m, 2(4-H_2, 6-H_2, 1'-H_2)), 3.45—3.59, 3.70—3.96 (6H, 2m, 2(4'-H, 6''-H_2)), 4.62, 4.68 (2H, 2t, J=3.7 Hz, 2(2''-H)), 5.88 (2H, t, J=1.5 Hz, 2(2-H)). MS m/z (rel. int. %): 266 (M^+, 5.5), 165 (100), 97 (69), 85 (92). HRMS m/z: 266.1881 (Calcd for $C_{16}H_{26}O_3$: 266.1882).

6-[4-(Tetrahydro-2-pyranyloxy)pentyl]-7-oxabicyclo[4.1.0]heptan-2-one (9d) By analogy with the synthesis of **9c**, **8d** (5.95 g, 22.3 mmol) was treated with 35% H_2O_2 (6.51 g) and 20% aqueous NaOH (0.720 g) in methanol (23 ml). The mixture was stirred at room temperature for 14 h. Distillation under reduced pressure afforded the epoxy ketone **9d** (a mixture of four diastereomers, 4.62 g, 73%) as a colorless oil, bp 160 °C (0.28 Torr). IR (film) cm^{-1}: 1718 (C=O). ^{1}H-NMR (EX) δ: 1.06—1.12, 1.19—1.25 (12H, 2m, 4(5'-H_3)), 1.41—2.19, 2.21—2.44, 2.48—2.56 (72H, 3m, 36CH_2), 3.08, 3.09 (4H, 2s, 4(1-H)), 3.45—3.53 (4H, m, 4(4'-H)), 3.64—3.96 (8H, m, 4(6''-H_2)), 4.59—4.64, 4.64—4.69 (4H, 2m, 4(2''-H)]. MS m/z (rel. int. %): 282 (M^+, 0.7), 181 (13), 163 (25), 145 (11), 113 (27), 85 (100). HRMS m/z: 282.1834 (Calcd for $C_{16}H_{26}O_4$: 282.1831).

(*E*)-6-[4-(Tetrahydro-2-pyranyloxy)pentyl]-7-oxabicyclo[4.1.0]hept-2-ylideneacetonitrile ((*E*)-10d) and (*Z*)-6-[4-(Tetrahydro-2-pyranyloxy)-pentyl]-7-oxabicyclo[4.1.0]hept-2-ylideneacetonitrile ((*Z*)-10d) By analogy with the synthesis of **10c**, **9d** (18.0 g, 63.7 mmol) was treated with 60% NaH (3.82 g, 95.5 mmol) and diethyl cyanomethylphosphonate (17.0 g, 96.0 mmol) in dry DMF (143 ml) at 0 °C. The mixture was stirred at 0 °C for 30 min. Flash chromatography (SiO_2 A; hexane–ethyl acetate (4 : 1)) of the reaction mixture gave the epoxy nitriles (*E*)-**10d** (a mixture of four diastereomers, 9.49 g, 49%) and (*Z*)-**10d** (a mixture of four diastereomers, 7.11 g, 36%).

(*E*)-**10d**: A colorless oil, bp 172 °C (0.20 Torr). IR (film) cm^{-1}: 2220 (C≡N), 1630 (C=C). ^{1}H-NMR (EX) δ: 1.11, 1.23 (12H, 2d, J=6 Hz, 4(5'-H_3)), 1.39—1.86, 1.98—2.07 (64H, 2m, 32CH_2), 2.25—2.37 (4H, m, 4(3-H)), 2.60 (4H, m with dtd character, J=14.9, 3.6, 1.2 Hz, 4(3-H)), 3.23 (4H, s, 4(1-H)), 3.44—3.52 (4H, m, 4(4'-H)), 3.73—3.91 (8H, m, 4(6''-H_2)), 4.60—4.68 (4H, m, 4(2''-H)), 5.47 (4H, t, J=1.8 Hz, 4HCCN). MS m/z (rel. int. %): 221 (M^+ − 84, 5.7), 204 (22), 136 (24), 85 (100). HRMS m/z: 221.1411 (Calcd for $C_{13}H_{19}NO_2$ ($M^+ - C_5H_8O$): 221.1416).

(*Z*)-**10d**: A colorless oil, bp 170 °C (0.21 Torr). IR (film) cm^{-1}: 2220 (C≡N), 1630 (C=C). ^{1}H-NMR (EX) δ: 1.12, 1.23 (12H, 2d, J=6 Hz, 4(5'-H$_3$)), 1.36—1.92, 1.93—2.01 (64H, 2m, 32CH$_2$), 2.05—2.16, 2.37—2.47 (8H, 2m, 4(3-H$_2$)), 3.47—3.53 (4H, m, 4(4'-H)), 3.67—3.96 (8H, m, 4(6''-H$_2$)), 3.70 (4H, s, 4(1-H)), 4.63, 4.68 (4H, 2t, J=3.5 Hz, 4(2''-H)), 5.40 (4H, t, J=1.5 Hz, 4HCCN). MS m/z (rel. int. %): 221 (M^+-84, 5.3), 204 (22), 136 (31), 85 (100). HRMS m/z: 221.1440 (Calcd for $C_{13}H_{19}NO_2$ ($M^+-C_5H_8O$): 221.1416).

***(E)*-6-(4-Hydroxypentyl)-7-oxabicyclo[4.1.0]hept-2-ylideneacetonitrile ((*E*)-1dA+B) and (*Z*)-6-(4-Hydroxypentyl)-7-oxabicyclo[4.1.0]hept-2-ylideneacetonitrile ((*Z*)-1dA+B)** By analogy with the synthesis of **1c**, (*E*/*Z*)-**10d** (15.1 g, 49.4 mmol) was treated with oxalic acid (1.56 g, 12.4 mmol) in methanol (1.42 l). The mixture was stirred at room temperature for 17 h. Flash chromatography (SiO$_2$ A; hexane–ethyl acetate (1 : 1)) of the reaction mixture afforded the epoxy nitriles (*E*)-**1dA+B** (a mixture of two diastereomers, 4.07 g, 37%) and (*Z*)-**1dA+B** (a mixture of two diastereomers, 3.06 g, 28%).

(*E*)-**1dA+B**: A colorless oil, bp 155 °C (0.23 Torr). IR (film) cm^{-1}: 3460 (O–H), 2220 (C≡N), 1630 (C=C). ^{1}H-NMR (EX) δ: 1.19 (6H, d, J=6.3 Hz, 2(5'-H$_3$)), 1.40—2.08 (22H, m, 10CH$_2$, 2OH), 2.26—2.37 (2H, m, 2(3-H)), 2.60 (2H, m with dtd character, J=16.8, 5.4, 1.3 Hz, 2(3-H)), 3.24 (2H, s, 2(1-H)), 3.76—3.83 (2H, m, 2(4'-H)), 5.48 (2H, t, J=1.8 Hz, 2HCCN). ^{13}C-NMR (EX) δ: 18.6, 20.6, 20.8, 26.7, 26.7, 27.1, 36.3, 36.4, 38.8, 38.9 (10t, 12CH$_2$), 23.5, 23.6 (2q, 2(C-5')), 59.6, 59.7, 67.6, 67.7 (4d, 2(C-1, C-4')), 63.7 (s, 2(C-6)), 98.8 (s, 2$\underline{\mathrm{C}}$CN), 115.7 (s, 2CN), 161.0 (s, 2(C-2)). MS m/z (rel. int. %): 221 (M^+, 4.5), 161 (100), 136 (90), 67 (69). HRMS m/z: 221.1404 (Calcd for $C_{13}H_{19}NO_2$: 221.1416).

(*Z*)-**1dA+B**: A colorless oil, bp 150 °C (0.19 Torr). IR (film) cm^{-1}: 3472 (O–H), 2222 (C≡N), 1630 (C=C). ^{1}H-NMR (EX) δ: 1.20 (6H, d, J=6.3 Hz, 2(5'-H$_3$)), 1.39—1.70, 1.73—1.88, 1.97—2.17 (24H, 3m, 10CH$_2$, 2(3-H), 2OH), 2.41 (2H, dddd, J=15.5, 7.9, 4.1, 1.5 Hz, 2(3-H)), 3.71 (2H, s, 2(1-H)), 3.76—3.83 (2H, m, 2(4'-H)), 5.42 (2H, t, J=1.7 Hz, 2HCCN). ^{13}C-NMR (EX) δ: 19.6, 20.6, 20.7, 26.4, 26.5, 29.2, 36.6, 38.8 (8t, 12CH$_2$), 23.4, 23.4 (2q, 2(C-5')), 57.2, 57.3, 67.4 (3d, 2(C-1, C-4')), 64.1 (s, 2(C-6)), 98.6 (d, 2$\underline{\mathrm{C}}$CN), 115.7 (s, 2CN), 161.2, 161.3 (2s, 2(C-2)). MS m/z (rel. int. %): 221 (M^+, 4.1), 161 (100), 136 (96), 67 (69). HRMS m/z: 221.1398 (Calcd for $C_{13}H_{19}NO_2$: 221.1416).

3-[5-(Tetrahydro-2-pyranyloxy)pentyl]-2-cyclohexen-1-one (8e) By analogy with the synthesis of **8c**, 3-ethoxy-2-cyclohexenone **6**$^{6)}$ (27.5 g, 196 mmol) was heated under reflux with Grignard reagent (prepared from magnesium (4.76 g, 196 mg-atom) and 5-(tetrahydro-2-pyranyloxy)pentyl chloride **7e**$^{7b,c)}$ (33.7 g, 163 mmol) under reflux for 15 h) for 11 h. Flash chromatography (SiO$_2$ A; hexane–ethyl acetate (1 : 2)) of the reaction mixture gave the enone **8e** (23.6 g, 54%) as an oil. IR (film) cm^{-1}: 1670 (C=O), 1626 (C=C). ^{1}H-NMR (EX) δ: 1.25—1.84, 1.94—2.03 (14H, 2m, 7CH$_2$), 2.20—2.38 (6H, m, 4-H$_2$, 6-H$_2$, 1'-H$_2$), 3.34—3.43, 3.47—3.54, 3.61—3.78, 3.82—3.90 (4H, 4m, 5'-H$_2$, 6''-H$_2$), 4.57 (1H, t, J=3.3 Hz, 2''-H), 5.88 (1H, s, 2-H). ^{13}C-NMR (EX) δ: 19.7, 22.7, 25.5, 26.0, 26.8, 29.5, 29.7, 30.8, 37.4, 38.0 (10t, 10CH$_2$), 62.5, 67.3 (2t, C-5', C-6''), 99.0 (d, C-2''), 125.7 (d, C-2), 166.5 (s, C-3), 200.0 (s, C-1). MS m/z (rel. int. %): 266 (M^+, 2.6), 182 (35), 123 (77), 110 (53), 85 (100). HRMS m/z: 266.1882 (Calcd for $C_{16}H_{26}O_3$: 266.1882).

6-[5-(Tetrahydro-2-pyranyloxy)pentyl]-7-oxabicyclo[4.1.0]heptan-2-one (9e) By analogy with the synthesis of **9c**, **8e** (23.6 g, 88.6 mmol) was treated with 35% H$_2$O$_2$ (24.5 g) and 20% aqueous NaOH (2.71 g) in methanol (85 ml). The mixture was stirred at room temperature for 28.5 h. Distillation under reduced pressure afforded the epoxy ketone **9e** (18.5 g, 74%) as a colorless oil, bp 200 °C (0.30 Torr). IR (film) cm^{-1}: 1705 (C=O). ^{1}H-NMR (EX) δ: 1.34—2.15 (19H, m, 9CH$_2$, 3-H), 2.46—2.56 (1H, m, 3-H), 3.07 (1H, s, 1-H), 3.38, 3.73 (2H, each dt, J=9.6, 6.6 Hz, 5'-H$_2$), 3.46—3.54, 3.82—3.90 (2H, 2m, 6''-H$_2$), 4.56 (1H, t, J=3.5 Hz, 2''-H). ^{13}C-NMR (EX) δ: 17.3, 19.6, 24.4, 25.4, 26.1, 26.3, 29.5, 30.7, 35.9 (10t, 2t at 35.9, 10CH$_2$), 61.1 (d, C-1), 62.3, 67.2 (2t, C-5, C-6''), 65.3 (s, C-6), 98.9 (d, C-2''), 206.8 (s, C-2). MS m/z (rel. int. %): 198 (M^+-84, 8.1), 101 (34), 85 (100). HRMS m/z: 198.1234 (Calcd for $C_{11}H_{18}O_3$ ($M^+-C_5H_8O$): 198.1256).

(*E*/*Z*)-6-[5-(Tetrahydro-2-pyranyloxy)pentyl]-7-oxabicyclo[4.1.0]-hept-2-ylideneacetonitrile ((*E*/*Z*)-10e) By analogy with the synthesis of **10c**, **9e** (17.5 g, 62.0 mmol) was treated with 60% NaH (3.23 g, 80.8 mmol) and diethyl cyanomethylphosphonate (14.3 g, 80.7 mmol) in dry DMF (105 ml) at −50 °C. The mixture was stirred at −50 °C for 20 min. Flash chromatography (SiO$_2$ A; hexane–ethyl acetate (5 : 2)) of the reaction mixture gave the epoxy nitrile (*E*/*Z*)-**10e** (*E* : *Z*=6 : 5, 16.6 g, 88%) as a colorless oil, bp 210 °C (0.21 Torr). IR (film) cm^{-1}: 2218 (C≡N), 1630 (C=C). ^{1}H-NMR (EX) δ: 1.33—1.86, 1.96—2.16, 2.24—2.47, 2.55—2.66 (40H, 4m, 20CH$_2$ for *E* and *Z*), 3.22 (1H, s, 1-H for *E*), 3.38, 3.73 (2H, each dt, J=9.6, 6.6 Hz, 5'-H$_2$ for *E*), 3.39, 3.74 (2H, each dt, J=9.6, 6.6 Hz, 5'-H$_2$ for *Z*), 3.46—3.54, 3.82—3.91 (4H, 2m, 6''-H$_2$ for *E* and *Z*), 3.71 (1H, s, 1-H for *Z*), 4.56 (1H, t, J=3.6 Hz, 2''-H for *E*), 4.58 (1H, t, J=3.5 Hz, 2''-H for *Z*), 5.39 (1H, t, J=1.5 Hz, HCCN for *Z*), 5.47 (1H, t, J= 1.7 Hz, HCCN for *E*). ^{13}C-NMR for *E* (EX) δ: 18.7, 19.7, 24.4, 25.5, 26.3, 26.8, 27.2, 29.6, 30.8, 36.5 (10t, 10CH$_2$), 59.8 (d, C-1), 62.5, 67.3 (2t, C-5', C-6''), 63.8 (s, C-6), 98.8, 99.0 (2d, C-2'', $\underline{\mathrm{C}}$CN), 115.8 (s, CN), 161.2 (s, C-2). ^{13}C-NMR for *Z* (EX) δ: 19.7, 19.9, 24.5, 25.5, 26.3, 26.6, 29.4, 29.6, 30.7, 36.9 (10t, 10CH$_2$), 57.5 (d, C-1), 62.4, 67.3 (2t, C-5', C-6''), 64.3 (s, C-6), 98.6, 98.9 (2 d, C-2'', $\underline{\mathrm{C}}$CN), 115.8 (s, CN), 161.4 (s, C-2). MS m/z (rel. int. %): 221 (M^+-84, 17), 136 (15), 85 (100). *Anal.* Calcd for $C_{18}H_{27}NO_3$: C, 70.79; H, 8.91; N, 4.59. Found: C, 70.62; H, 9.17; N, 4.48.

(*E*/*Z*)-6-(5-Hydroxypentyl)-7-oxabicyclo[4.1.0]hept-2-ylideneacetonitrile ((*E*/*Z*)-1e) By analogy with the synthesis of **1c**, (*E*/*Z*)-**10e** (10.1 g, 33.1 mmol) was treated with oxalic acid (1.04 g, 8.25 mmol) in methanol (950 ml). The mixture was stirred at room temperature for 22 h. Flash chromatography (SiO$_2$ A; hexane–ethyl acetate (1 : 1→1 : 2)) of the reaction mixture afforded recovered (*E*/*Z*)-**10e** (3.40 g, 34%) and the epoxy nitrile (*E*/*Z*)-**1e** (*E* : *Z*=6 : 5, 1.91 g, 26%) as a colorless oil, bp 170 °C (0.13 Torr). IR (film) cm^{-1}: 3406 (O–H), 2218 (C≡N), 1627 (C=C). ^{1}H-NMR (EX) δ: 1.32—1.86, 1.97—2.16, 2.27—2.46, 2.56—2.66 (30H, 4m, 14CH$_2$, 2OH for *E* and *Z*), 3.22 (1H, s, 1-H for *E*), 3.65 (1H, t, J=6.4 Hz, 5'-H$_2$ for *Z*), 3.65 (1H, t, J=6.4 Hz, 5'-H$_2$ for *E*), 3.72 (1H, s, 1-H for *Z*), 5.40 (1H, t, J= 1.6 Hz, HCCN for *Z*), 5.47 (1H, t, J= 1.8 Hz, HCCN for *E*). ^{13}C-NMR for *E* (EX) δ: 18.7, 24.3, 25.8, 26.8, 27.2, 32.5, 36.5 (7t, 7CH$_2$), 59.8 (d, C-1), 62.7 (t, C-5'), 63.8 (s, C-6), 98.9 (d, $\underline{\mathrm{C}}$CN), 115.8 (s, CN), 161.2 (s, C-2). ^{13}C-NMR for *Z* (EX) δ: 19.8, 24.2, 25.6, 26.5, 29.3, 32.4, 36.7 (7t, 7CH$_2$), 57.4 (d, C-1), 62.5 (t, C-5'), 64.2 (s, C-6), 98.5 (d, $\underline{\mathrm{C}}$CN), 115.8 (s, CN), 161.4 (s, C-2). MS m/z (rel. int. %): 221 (M^+, 46), 149 (78), 79 (77), 67 (100). HRMS m/z: 221.1420 (Calcd for $C_{13}H_{19}NO_2$: 221.1416).

3-[6-(Tetrahydro-2-pyranyloxy)hexyl]-2-cyclohexen-1-one (8f) By analogy with the synthesis of **8c**, 3-ethoxy-2-cyclohexenone **6**$^{6)}$ (9.87 g, 70.4 mmol) was heated under reflux with Grignard reagent (prepared from magnesium (2.75 g, 113 mg-atom) and 6-(tetrahydro-2-pyranyloxy)-hexyl chloride **7f**$^{7d)}$ (20.2 g, 91.5 mmol) at room temperature for 14 h) for 1.5 h. Flash chromatography (SiO$_2$ A; hexane–ethyl acetate (2 : 1)) of the reaction mixture gave the enone **8f** (17.4 g, 88%) as an oil. IR (film) cm^{-1}: 1671 (C=O), 1630 (C=C). ^{1}H-NMR (EX) δ: 1.24—1.89, 1.94—2.03 (16H, 2m, 8CH$_2$), 2.18—2.41 (6H, m, 4-H$_2$, 6-H$_2$, 1'-H$_2$), 3.38, 3.73 (2H, each dt, J=9.6, 6.6 Hz, 6'-H$_2$), 3.46—3.54, 3.83—3.91 (2H, 2m, 6''-H$_2$), 4.57 (1H, t, J=3.5 Hz, 2''-H), 5.87 (1H, s, 2-H). ^{13}C-NMR (EX) δ: 19.7, 22.7, 25.4, 26.0, 26.8, 29.0, 29.5, 29.6, 30.7, 37.3, 37.9 (11t, 11CH$_2$), 62.3, 67.4 (2t, C-6', C-6''), 98.9 (d, C-2''), 125.6 (d, C-2), 166.5 (s, C-3), 199.8 (s, C-1). MS m/z (rel. int. %): 280 (M^+, 14), 123 (100), 110 (91), 85 (59). HRMS m/z: 281.2121 (Calcd for $C_{17}H_{29}O_3$ (M^++H): 281.2117).

6-[6-(Tetrahydro-2-pyranyloxy)hexyl]-7-oxabicyclo[4.1.0]heptan-2-one (9f) By analogy with the synthesis of **9c**, **8f** (16.9 g, 60.3 mmol) was treated with 35% H$_2$O$_2$ (17.6 g) and 20% aqueous NaOH (1.95 g) in methanol (61 ml). The mixture was stirred at room temperature for 14 h. Distillation under reduced pressure afforded the epoxy ketone **9f** (12.1 g, 68%) as a colorless oil, bp 165 °C (0.20 Torr). IR (film) cm^{-1}: 1715 (C=O). ^{1}H-NMR (EX) δ: 1.30—2.15 (21H, m, 10CH$_2$, 3-H), 2.46—2.56 (1H, m, 3-H), 3.07 (1H, s, 1-H), 3.38, 3.73 (2H, each dt, J=9.6, 6.6 Hz, 6'-H$_2$), 3.46—3.54, 3.82—3.91 (2H, 2m, 6''-H$_2$), 4.57 (1H, t, J=3.5 Hz, 2''-H). ^{13}C-NMR (EX) δ: 17.3, 19.6, 24.5, 25.4, 26.0, 26.3, 29.3, 29.5, 30.7, 35.9 (11t, 2t at 35.9, 11CH$_2$), 61.1 (d, C-1), 62.3, 67.4 (2t, C-6', C-6''), 65.4 (s, C-6), 98.8 (d, C-2''), 206.9 (s, C-2). MS m/z (rel. int. %): 296 (M^+, 0.21), 101 (54), 85 (100). HRMS m/z: 296.1994 (Calcd for $C_{17}H_{28}O_4$: 296.1987).

(*E*)-6-[6-(Tetrahydro-2-pyranyloxy)hexyl]-7-oxabicyclo[4.1.0]hept-2-ylideneacetonitrile ((*E*)-10f) and (*Z*)-6-[6-(Tetrahydro-2-pyranyloxy)-hexyl]-7-oxabicyclo[4.1.0]hept-2-ylideneacetonitrile ((*Z*)-10f) By analogy with the synthesis of **10c**, **9f** (4.00 g, 13.5 mmol) was treated with 60% NaH (0.703 g, 17.6 mmol) and diethyl cyanomethylphosphonate (3.11 g, 17.6 mmol) in dry DMF (25 ml) at −50 °C. The mixture was stirred at −50 °C for 30 min. Flash chromatography (SiO$_2$ A; hexane–ethyl acetate (5 : 2)) of the reaction mixture gave the epoxy nitriles (*E*)-**10f** (2.41 g, 56%) and (*Z*)-**10f** (1.73 g, 40%).

(*E*)-**10f**: A colorless oil, bp 190 °C (0.19 Torr). IR (film) cm^{-1}: 2220 (C≡N), 1630 (C=C). ^{1}H-NMR (EX) δ: 1.36—1.89, 1.95—2.06 (20H, 2m, 10CH$_2$), 2.25—2.39, 2.55—2.65 (2H, 2m, 3-H$_2$), 3.21 (1H, s, 1-H), 3.38, 3.73 (2H, each dt, $J=9.6$, 6.6 Hz, 6′-H$_2$), 3.46—3.54, 3.82—3.91 (2H, 2m, 6″-H$_2$), 4.57 (1H, t, $J=3.5$ Hz, 2″-H), 5.47 (1H, t, $J=1.8$ Hz, HCCN). ^{13}C-NMR (EX) δ: 18.7, 19.7, 24.4, 25.4, 26.1, 26.7, 27.2, 29.3, 29.5, 30.7, 36.5 (11t, 11CH$_2$), 59.7 (d, C-1), 62.4, 67.4 (2t, C-6′, C-6″), 63.8 (s, C-6), 98.7, 98.9 (2d, C-2″, $\underline{C}$CN), 115.8 (s, CN), 161.2 (s, C-2). MS *m/z* (rel. int. %): 319 (M$^+$, 0.21), 85 (100). HRMS *m/z*: 319.2122 (Calcd for $C_{19}H_{29}NO_3$: 319.2147).

(*Z*)-**10f**: A colorless oil, bp 195 °C (0.18 Torr). IR (film) cm^{-1}: 2225 (C≡N), 1630 (C=C). ^{1}H-NMR (EX) δ: 1.36—1.87, 1.95—2.01 (20H, 2m, 10CH$_2$), 2.03—2.15, 2.27—2.48 (2H, 2m, 3-H$_2$), 3.38, 3.73 (2H, each dt, $J=9.6$, 6.6 Hz, 6′-H$_2$), 3.46—3.54, 3.83—3.91 (2H, 2m, 6″-H$_2$), 3.71 (1H, s, 1-H), 4.57 (1H, t, $J=3.6$ Hz, 2″-H), 5.39 (1H, t, $J=1.5$ Hz, HCCN). ^{13}C-NMR (EX) δ: 19.6, 19.9, 24.5, 25.4, 26.1, 26.6, 29.4, 29.6, 30.7, 36.9 (11t, 2t at 29.4, 11CH$_2$), 57.4 (d, C-1), 62.3, 67.4 (2t, C-6′, C-6″), 64.3 (s, C-6), 98.6, 98.8 (2d, C-2″, $\underline{C}$CN), 115.8 (s, CN), 161.4 (s, C-2). MS *m/z* (rel. int. %): 319 (M$^+$, 0.32), 101 (19), 85 (100). HRMS *m/z*: 319.2125 (Calcd for $C_{19}H_{29}NO_3$: 319.2147).

(*E*)-6-(6-Hydroxyhexyl)-7-oxabicyclo[4.1.0]hept-2-ylideneacetonitrile ((*E*)-1f) and (*Z*)-6-(6-Hydroxyhexyl)-7-oxabicyclo[4.1.0]hept-2-ylideneacetonitrile ((*Z*)-1f) By analogy with the synthesis of **1c**, (*E*/*Z*)-**10f** (4.50 g, 14.1 mmol) was treated with oxalic acid (0.888 g, 7.04 mmol) in methanol (405 ml). The mixture was stirred at room temperature for 66 h. Flash chromatography (SiO$_2$ A; hexane–ethyl acetate (1 : 1)) of the reaction mixture afforded the epoxy nitriles (*E*)-**1f** (0.997 g, 30%) and (*Z*)-**1f** (0.713 g, 22%).

(*E*)-**1f**: A colorless oil, bp 140 °C (0.19 Torr). IR (film) cm^{-1}: 3442 (O–H), 2220 (C≡N), 1628 (C=C). ^{1}H-NMR (EX) δ: 1.36—1.84, 1.96—2.07 (15H, 2m, 7CH$_2$, OH), 2.25—2.37 (1H, m, 3-H), 2.60 (1H, m with dt character, $J=16.8$, 4.9 Hz, 3-H), 3.21 (1H, s, 1-H), 3.64 (2H, t, $J=6.6$ Hz, 6′-H$_2$), 5.47 (1H, t, $J=1.7$ Hz, HCCN). ^{13}C-NMR (EX) δ: 18.7, 24.5, 25.6, 26.8, 27.2, 29.3, 32.6, 36.5 (8t, 8CH$_2$), 59.8 (d, C-1), 62.8 (t, C-6′), 63.9 (s, C-6), 98.8 (d, $\underline{C}$CN), 115.8 (CN), 161.2 (s, C-2). MS *m/z* (rel. int. %): 235 (M$^+$, 16), 149 (100). HRMS *m/z*: 235.1558 (Calcd for $C_{14}H_{21}NO_2$: 235.1572).

(*Z*)-**1f**: A colorless oil, bp 140 °C (0.12 Torr). IR (film) cm^{-1}: 3442 (O–H), 2220 (C≡N), 1628 (C=C). ^{1}H-NMR (EX) δ: 1.36—1.86, 1.96—2.01 (15H, 2m, 7CH$_2$, OH), 2.09 (1H, m with ddd character, $J=8.6$, 4.0, 1.7 Hz, 3-H), 2.42 (1H, dddd, $J=15.5$, 8.3, 4.0, 1.7 Hz, 3-H), 3.65 (2H, t, $J=6.6$ Hz, 6′-H$_2$), 3.71 (1H, s, 1-H), 5.39 (1H, t, $J=1.7$ Hz, HCCN). ^{13}C-NMR (EX) δ: 20.0, 24.5, 25.6, 26.7, 29.3, 29.4, 32.6, 36.8 (8t, 8CH$_2$), 57.5 (d, C-1), 62.9 (t, C-6′), 64.4 (s, C-6), 98.6 (d, $\underline{C}$CN), 115.8 (s, CN), 161.5 (s, C-2). MS *m/z* (rel. int. %): 235 (M$^+$, 17), 149 (98), 67 (97), 55 (100), 41 (98). HRMS *m/z*: 235.1569 (Calcd for $C_{14}H_{21}NO_2$: 235.1572).

(*E*/*Z*)-4-(5-Cyanomethylidene-7-oxabicyclo[4.1.0]hept-1-yl)butyric Acid ((*E*/*Z*)-1g) The epoxy nitrile (*E*/*Z*)-**1b**[1)] (3.00 g, 14.5 mmol) was added dropwise to a solution of PDC (19.1 g, 50.8 mmol) in dry DMF (38 ml) at room temperature . The mixture was then stirred at room temperature for 20 h, poured into water, and extracted with diethyl ether 3 times. The extracts were subjected to the same work-up as used for the synthesis of **8c**. Flash chromatography (SiO$_2$ A; hexane–ethyl acetate (1 : 4)) of the residue yielded the epoxy carboxylic acid (*E*/*Z*)-**1g** (2.42 g, 75%) as an oil. IR (film) cm^{-1}: 3650—2800 (COOH), 2210 (C≡N), 1710 (C=O), 1630 (C=C). ^{1}H-NMR (EX) δ: 1.43—1.58, 1.63—1.91, 1.96—2.16, 2.25—2.48, 2.55—2.65 (24H, 5m, 12CH$_2$ for *E* and *Z*), 3.25 (1H, s, 6-H for *E*), 3.73 (1H, s, 6-H for *Z*), 5.41 (1H, t, $J=1.5$ Hz, HCCN for *Z*), 5.49 (1H, t, $J=1.8$ Hz, HCCN for *E*), 8.57 (2H, br s, COOH for *E* and *Z*). ^{13}C-NMR (EX) δ: 18.6, 19.5, 19.6, 19.8, 26.5, 26.6, 27.1, 29.3, 33.5, 35.7, 36.0 (11t, 12CH$_2$ for *E* and *Z*), 57.2 (d, C-6′ for *Z*), 59.5 (d, C-6′ for *E*), 63.3 (s, C-1′ for *E*), 63.7 (s, C-1′ for *Z*), 98.9 (d, $\underline{C}$CN for *Z*), 99.0 (d, $\underline{C}$CN for *E*), 115.7 (s, 2CN for *E* and *Z*), 160.7 (s, C-5′ for *E*), 161.0 (s, C-5′ for *Z*), 178.9 (s, 2(C-1) for *E* and *Z*). MS *m/z* (rel. int. %): 221 (M$^+$, 27), 161 (94), 125 (58), 97 (100), 55 (74). HRMS *m/z*: 221.1048 (Calcd for $C_{12}H_{15}NO_3$: 221.1052).

Photocyclizations of Epoxy Nitriles (*E*/*Z*)-1c—g. Irradiation of (*E*/*Z*)-1c A solution of the epoxy nitrile (*E*/*Z*)-**1c** (*E* : *Z* = 4 : 1, 47.0 mg, 0.212 mmol) in dry CH$_2$Cl$_2$ (9.4 ml) with TEA (21.5 mg, 0.212 mmol) was irradiated with a low-pressure mercury lamp (lamp B) in a quartz test tube (95% conversion) at room temperature for 1.5 h. After removal of the solvent, chromatography (SiO$_2$ B; hexane–ethyl acetate (1 : 4)) of the residue yielded several fractions; the following product distribution was determined by ^{1}H-NMR analysis: the spiroketal (*E*)-**2c** (3.9 mg, 9%), the spiroether **4c** (18.0 mg, 40%), and intractable material (mainly polymers).

(*E*,6*R,8*R**)-8-Methyl-1,7-dioxaspiro[5.6]dodec-9-ylideneacetonitrile ((*E*,6*R**,8*R**)-2c)** Colorless crystals, mp 68.5—69.5 °C. IR (CHCl$_3$) cm^{-1}: 2222 (C≡N), 1625 (C=C). ^{1}H-NMR (GX) δ: 1.25—1.41, 1.49—1.89 (10H, 2m, 5CH$_2$), 1.32 (3H, d, $J=6.6$ Hz, CH$_3$), 2.60—2.66, 2.71—2.78 (2H, 2m, 10-H$_2$), 3.61—3.65 (1H, m, 2-H), 3.71 (1H, td, $J=11.5$, 3.4 Hz, 2-H), 4.52 (1H, q, $J=6.6$ Hz, 8-H), 5.15 (1H, s, HCCN). ^{13}C-NMR (GX) δ: 18.6, 19.4, 25.3, 30.1, 34.5, 37.7 (6t, 6CH$_2$), 21.1 (q, CH$_3$), 61.7 (t, C-2), 67.4 (d, C-8), 93.0 (d, $\underline{C}$CN), 99.3 (s, C-6), 116.7 (s, CN), 171.8 (s, C-9). MS *m/z* (rel. int. %): 221 (M$^+$, 37), 206 (60), 121 (50), 111 (43), 101 (100). HRMS *m/z*: 221.1429 (Calcd for $C_{13}H_{19}NO_2$: 221.1416).

(1*R,5*R**)-1-Acetyl-6-oxaspiro[4.5]dec-1-ylacetonitrile ((1*R**,5*R**)-4c)** Colorless crystals, mp 72—74 °C. IR (CHCl$_3$) cm^{-1}: 2250 (C≡N), 1707 (C=O). ^{1}H-NMR (GX) δ: 1.21—1.38, 1.44—1.59, 1.69—1.83, 1.92—2.00, 2.26—2.39 (12H, 5m, 6CH$_2$), 2.30 (3H, s, CH$_3$), 2.61 (1H, d, $J=17.1$ Hz, HCCN), 3.02 (1H, dd, $J=17.1$, 0.9 Hz, HCCN), 3.48—3.55, 3.76—3.81 (2H, 2m, 7-H$_2$). ^{13}C-NMR (GX) δ: 18.9, 20.0, 20.6, 25.5, 30.2, 30.3, 30.5 (7t, 7CH$_2$), 28.1 (q, CH$_3$), 63.5 (t, C-7), 64.5 (s, C-1), 83.7 (s, C-5), 118.8 (s, CN), 208.0 (s, C=O). MS *m/z* (rel. int. %): 221 (M$^+$, 15), 178 (8.5), 111 (100), 98 (10). HRMS *m/z*: 221.1432 (Calcd for $C_{13}H_{19}NO_2$: 221.1416).

Irradiation of (*E*/*Z*)-1dA+B By analogy with the photolysis of **1c**, (*E*/*Z*)-**1dA+B** (*E* : *Z* = 4 : 3, 1.58 g, 7.14 mmol) in dry CH$_2$Cl$_2$ (316 ml) with TEA (723 mg, 7.14 mmol) was irradiated (lamp A; conversion 35%) for 1.5 h. After removal of the solvent, flash chromatography (SiO$_2$ A; hexane–ethyl acetate (3 : 1→1 : 4)) of the residue yielded the spiroketals (*E*)-**2d** (51.1 mg, 9%) and (*Z*)-**2d** (43.7 mg, 8%), the spiroether **4d** (89.0 mg, 16%), compounds of unknown structure (52.6 mg), and intractable material (mainly polymers).

(*E*,2*R,6*S**)-2-Methyl-1,7-dioxaspiro[5.6]dodec-9-ylideneacetonitrile ((*E*,2*R**,6*S**)-2d)** Colorless oil, bp 105 °C (0.18 Torr). IR (film) cm^{-1}: 2220 (C≡N), 1625 (C=C). ^{1}H-NMR (EX) δ: 1.15 (3H, d, $J=6$ Hz, CH$_3$), 1.19—1.40, 1.53—1.91 (10H, 2m, 5CH$_2$), 2.58—2.66, 2.72—2.83 (2H, 2m, 10-H$_2$), 3.68 (1H, dqd, $J=11.4$, 6, 2.1 Hz, 2-H), 3.87 (1H, d, $J=14.5$ Hz, 8-H), 4.50 (1H, dd, $J=14.5$, 1.3 Hz, 8-H), 5.19 (1H, t, $J=1.2$ Hz, HCCN). ^{13}C-NMR (EX) δ: 19.0, 19.5, 32.5, 33.4, 34.2, 40.9 (6t, 6CH$_2$), 21.8 (q, CH$_3$), 63.6 (t, C-8), 66.7 (d, C-2), 95.1 (d, $\underline{C}$CN), 99.9 (s, C-6), 116.4 (s, CN), 166.6 (s, C-9). MS *m/z* (rel. int. %): 221 (M$^+$, 27), 152 (100), 125 (49), 97 (34). HRMS *m/z*: 221.1428 (Calcd for $C_{13}H_{19}NO_2$: 221.1416).

(*Z*,2*R,6*S**)-2-Methyl-1,7-dioxaspiro[5.6]dodec-9-ylideneacetonitrile ((*Z*,2*R**,6*S**)-2d) (Contaminated with *ca.* 35% of (*E*)-2d)** Colorless oil, bp 105 °C (0.17 Torr). IR (film) cm^{-1}: 2220 (C≡N), 1625 (C=C). ^{1}H-NMR (EX) δ: 1.16 (3H, d, $J=6.3$ Hz, CH$_3$), 1.20—1.40, 1.52—1.91 (10H, 2m, 5CH$_2$), 2.33—2.42, 2.56—2.65 (2H, 2m, 10-H$_2$), 3.73 (1H, dqd, $J=11.2$, 6.3, 2.3 Hz, 2-H), 4.39 (1H, dd, $J=16.0$, 1.3 Hz, 8-H), 4.55 (1H, d, $J=16.0$ Hz, 8-H), 5.14 (1H, t, $J=1.3$ Hz, HCCN). ^{13}C-NMR (EX) δ: 18.8, 20.1, 32.4, 33.9, 34.9, 39.7 (6t, 6CH$_2$), 21.7 (q, CH$_3$), 61.4 (t, C-8), 66.6 (d, C-2), 93.1 (d, $\underline{C}$CN), 100.0 (s, C-6), 115.8 (s, CN), 168.0 (s, C-9). MS *m/z* (rel. int. %): 221 (M$^+$, 31), 152 (100), 125 (38), 97 (31). HRMS *m/z*: 221.1414 (Calcd for $C_{13}H_{19}NO_2$: 221.1416).

(1*R,5*R**,7*S**)-1-Formyl-7-methyl-6-oxaspiro[4.5]dec-1-ylacetonitrile ((1*R**,5*R**,7*S**)-4d)** Colorless oil, bp 140 °C (0.20 Torr). IR (film) cm^{-1}: 2220 (C≡N), 1628 (C=O). ^{1}H-NMR (EX) δ: 1.09 (3H, d, $J=6$ Hz, CH$_3$), 1.12—1.29, 1.32—1.59, 1.71—1.91, 1.96—2.17, 2.29—2.40 (12H, 5m, 6CH$_2$), 2.54, 2.83 (2H, each d, $J=17.1$ Hz, H$_2$CCN), 3.34 (1H, dqd, $J=10.4$, 6, 2.3 Hz, 7-H), 9.73 (1H, s, CHO). ^{13}C-NMR (EX) δ: 18.7, 18.9, 21.0, 31.1, 31.1, 31.3, 42.1 (7t, 7CH$_2$), 21.9 (q, CH$_3$), 60.7 (s, C-1), 69.3 (d, C-7), 87.5 (s, C-5), 118.4 (s, CN), 202.8 (d, CHO). MS *m/z* (rel. int. %): 221 (M$^+$, 8.5), 161 (100), 136 (95), 97 (76), 55 (75). HRMS *m/z*: 221.1404 (Calcd for $C_{13}H_{19}NO_2$: 221.1416).

Irradiation of (*E*/*Z*)-1e By analogy with the photolysis of **1c**, (*E*/*Z*)-**1e** (*E* : *Z* = 6 : 5, 2.34 g, 10.6 mmol) in dry CH$_2$Cl$_2$ (468 ml) with TEA (1.07 g, 10.6 mmol) was irradiated (lamp A; conversion 100%) for 25 h. After removal of the solvent, flash chromatography (SiO$_2$ A; hexane–ethyl acetate (1 : 1→1 : 2)) of the residue yielded the spiroketal (*Z*)-**2e** (14.8 mg, 1%), the spiroether (1*R**,5*R**)/(1*R**,5*S**)-**4e** (104 mg, 4%, (1*R**,5*R**)/(1*R**,5*S**) = 1 : 3), compounds of unknown structure (69.8 mg), and intractable material (mainly polymers).

(*Z*)-1,8-Dioxaspiro[6.6]tridec-3-ylideneacetonitrile ((*Z*)-2e) Oil. IR (CHCl$_3$) cm^{-1}: 2200 (C≡N), 1636 (C=C). ^{1}H-NMR (EX) δ: 1.25—1.42, 1.48—2.03, 2.17—2.66 (14H, 3m, 7CH$_2$), 3.47—3.87 (2H, m, 9-H$_2$), 4.33 (1H, dd, $J=16.2$, 1.3 Hz, 2-H), 4.56 (1H, d, $J=16.2$ Hz, 2-H), 5.13 (1H, t, *J*=1.3 Hz, HCCN). ^{13}C-NMR (EX) δ: 20.9, 22.8, 29.8, 30.6, 35.1, 36.5, 38.1 (7t, 7CH$_2$), 62.0, 62.5 (2t, C-2, C-9), 93.4 (d, $\underline{\text{C}}$CN), 105.2 (s, C-7), 115.9 (s, CN), 167.5 (s, C-3). MS *m/z* (rel. int. %): 221 (M$^+$, 24), 152 (53), 125 (100), 97 (27), 55 (39). HRMS *m/z*: 221.1419 (Calcd for C$_{13}$H$_{19}$NO$_2$: 221.1416).

((1*R,5*R**)/(1*R**,5*S**))-1-Formyl-6-oxaspiro[4.6]undec-1-ylacetonitrile ((1*R**,5*R**)/(1*R**,5*S**)-4e)** Oil. IR (CHCl$_3$) cm^{-1}: 2253 (C≡N), 1717 (C=O). ^{1}H-NMR (GX) δ: 1.42—2.07, 2.17—2.22 (14H, 2m, 7CH$_2$), 2.25 (1H, d, *J*=16.6 Hz, HCCN for (1*R**,5*R**)), 2.64, 2.83 (2H, each d, *J*=16.7 Hz, H$_2$CCN for (1*R**,5*S**)), 2.71 (1H, dd, *J*=16.6, 0.7 Hz, HCCN for (1*R**,5*R**)), 3.51—3.56 (2H, m, 7-H$_2$ for (1*R**,5*S**)), 3.63—3.67 (2H, m, 7-H$_2$ for (1*R**,5*R**)), 9.60 (1H, s, CHO for (1*R**,5*S**)), 9.73 (1H, s, CHO for (1*R**,5*R**)). ^{13}C-NMR (GX) for (1*R**,5*R**)-**4e** δ: 20.5, 21.5, 23.8, 29.2, 31.5, 32.2, 34.0, 37.9 (8t, 8CH$_2$), 60.3 (s, 1-C), 64.5 (t, 7-C), 93.4 (s, C-5), 118.1 (s, CN), 203.6 (d, CHO). ^{13}C-NMR (GX) for (1*R**,5*S**)-**4e** δ: 18.7, 20.3, 24.0, 29.1, 31.6, 32.0, 34.8, 38.2 (8t, 8CH$_2$), 62.4 (s, 1-C), 65.1 (t, 7-C), 89.4 (s, C-5), 118.7 (s, CN), 201.4 (d, CHO). MS *m/z* (rel. int. %): 221 (M$^+$, 2.4), 125 (100), 55 (23). HRMS *m/z*: 221.1420 (Calcd for C$_{13}$H$_{19}$NO$_2$: 221.1416).

Irradiation of (*E*/*Z*)-1f By analogy with the photolysis of **1c**, (*E*/*Z*)-**1f** (*E*:*Z*=7:5, 1.26 g, 5.35 mmol) in dry CH$_2$Cl$_2$ (237 ml) with TEA (0.542 g, 5.36 mmol) was irradiated (lamp A; conversion 54%) for 5.5 h. After removal of the solvent, flash chromatography (SiO$_2$ A; hexane–ethyl acetate (1:2)) of the residue yielded compounds of unknown structure (68.4 mg) and intractable material (mainly polymers).

Irradiation of (*E*/*Z*)-1g A solution of the epoxy carboxylic acid (*E*/*Z*)-**1g** (*E*:*Z*=7:4, 645 mg, 2.92 mmol) in dry acetonitrile (122 ml) with TEA (295 mg, 2.92 mmol) was irradiated with a low-pressure mercury lamp (lamp A) in a quartz test tube (conversion 100%) at room temperature for 3 h. After removal of the solvent, flash chromatography (SiO$_2$ A; hexane–ethyl acetate (1:4)) of the residue yielded the spirolactone **3g** (147 mg, 23%), compounds of unknown structure (37.2 mg), and intractable material (mainly polymers).

2-Oxo-1,7-dioxaspiro[5.6]dodec-8-en-9-ylacetonitrile (3g) Oil. IR (film) cm^{-1}: 2250 (C≡N), 1743 (C=O), 1670 (C=C). ^{1}H-NMR (EX) δ: 1.65—2.24, 2.34—2.55, 2.66—2.73 (12H, 3m, 6CH$_2$), 2.99 (2H, s, H$_2$CCN), 6.15 (1H, d, *J*=1.7 Hz, 8-H). ^{13}C-NMR (EX) δ: 15.4, 18.5, 22.8, 29.2, 30.5, 32.3, 39.3 (7t, 7CH$_2$), 107.0 (s, C-6), 117.1, 118.0 (2s, C-9, CN), 139.3 (d, C-8), 170.4 (s, C-2). MS *m/z* (rel. int. %): 221 (M$^+$, 3.9), 149 (52), 125 (100), 97 (88), 55 (74). HRMS *m/z*: 221.1052 (Calcd for C$_{12}$H$_{15}$NO$_3$: 221.1052).

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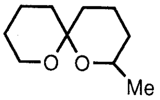

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Fig. 3

15) After analytical irradiation of (*E*/*Z*)-**1d** in acetonitrile, the ^{1}H-NMR spectrum of the crude photoproduct failed to show the characteristic signals of (*E*/*Z*)-**2d′**. Thus, in methylene chloride (*E*/*Z*)-**2d** was also formed presumably not from (*E*/*Z*)-**2d′** by an acid-catalyzed (hydrogen chloride photochemically generated from methylene chloride) recyclization, but directly from the ylide **Y**.
16) Tektronix Corp. (Beaverton, Oregon, U.S.A.). CAChe MOPAC version 94. All orbital energies were obtained from AM1-optimized geometries.