Control of the Regioselectivity in the Pauson−Khand Reaction of 7-Oxanorbornene Derivatives

Odón Arjona,* Aurelio G. Csákÿ, M. Carmen Murcia, and Joaquín Plumet*

Departamento de Química Orgánica I, Facultad de Química, Universidad Complutense, 28040 Madrid, Spain

Received February 18, 1999

The regiochemistry of the Pauson−Khand reaction of 7-oxanorbornene derivatives can be influenced by a remote substituent at carbon C-2. Furthermore, a remarkable effect on the regiochemical outcome of this reaction was observed by halide substituents in the olefin carbons, which may be utilized as an element of control of regioselectivity.

The Pauson−Khand reaction, a formal [2 + 2 + 1] cycloaddition between an alkyne, an alkene, and CO promoted by $Co_2(CO)_8$ has become one of the most versatile methods for the assembly of cyclopentenones due to the high degree of stereo- and regiochemical control usually attainable in the process.[1]

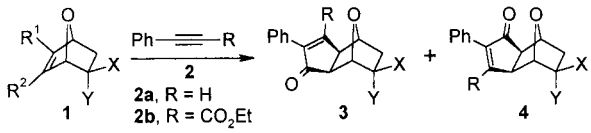
On the other hand, 7-oxanorbornenes (7-oxabicyclo-[2.2.1]-5-heptenes), easily derived from the cycloaddition reaction of furans with substituted alkenes, can be considered as chirons equivalent to hexoses. These can be transformed into a wide variety of both cyclic and open-chain targets with high level of sterocontrol.[2]

In connection with the utility of 7-oxanorbornene derivatives as starting materials in organic synthesis, we envisioned that the almost unexplored[3] Pauson−Khand reaction on these compounds should afford bicyclic cyclopentenones suitable for further transformation into more elaborated targets, if a satisfactory control of the regiochemistry were possible. In this context we wish to account for our results in this field.

Results and Discussion

At the onset of this study, only the 2-substituted 7-oxanorbornenes **1a**−**d** (Scheme 1) were chosen as starting materials for the Pauson−Khand cycloadditions. The control of the regioselectivity of different types of reactions performed on the endocyclic C=C bond in these systems by the substituent at C-2 appears to be different depending on the reaction to be considered. Thus, the regioselectivity of the electrophilic addition[4] is governed by the nature of the remote substituent at C-2, while 1,3-dipolar[5,6] and Diels−Alder reactions[7] do not display a similar remote-controlled regioselectivity.

Scheme 1



1a, X,Y = O, R^1 = H, R^2 = H
1b, X = CN, Y = OAc, R^1 = H, R^2 = H
1c, X,Y = OCH_2CH_2O, R^1 = H, R^2 = H
1d, X = H, Y = OH, R^1 = H, R^2 = H
1e, X,Y = O, R^1 = Br, R^2 = H
1f, X = CN, Y = OAc, R^1 = Br, R^2 = H
1g, X,Y = OCH_2CH_2O, R^1 = Br, R^2 = H
1h, X = H, Y = OH, R^1 = Br, R^2 = H
1i, X,Y = O, R^1 = H, R^2 = Br

3,4a, X,Y =O, R =H
3,4b, X = CN, Y =OAc, R =H
3,4c, X,Y =O, R = CO_2Et
3,4d, X = CN, Y =OAc, R = CO_2Et
3,4e, X,Y = OCH_2CH_2O, R = H
3,4f, X,Y = OCH_2CH_2O, R = CO_2Et
3,4g, X = H, Y = OH, R =H
3,4h, X = H, Y = OH, R = CO_2Et

Compounds **1a**−**d** were allowed to react with the preformed complexes between alkynes **2** and $Co_2(CO)_8$ under a variety of conditions: (a) toluene at reflux temperature (method A), (b) acetonitrile at reflux temperature (method B), and (c) CH_2Cl_2 at room temperature in the presence of NMO (method C). In all three cases, cyclopentenones **3** and **4** were obtained as the sole reaction products. In these reactions, complete regiochemistry with regard to the alkyne moiety was observed (CO and Ph in 1,2- relationship) as well as full exo diastereoselectivity.[8,9] The results are gathered in Table 1 (entries 1−16).

(1) Khand, I. U.; Knox, G. R.; Pauson, P. L.; Watts, W. E.; Foreman, M. I. *J. Chem. Soc., Perkin Trans. 1* **1973**, 977. For selected reviews, see: (a) Schore, N. E. *Chem. Rev.* **1988**, *88*, 1081. (b) Schore N. E. In *Comprehensive Organic Synthesis, Vol. 5*; Trost, B. M., Fleming, I., Eds.; Pergamon: Oxford, 1991; p 1037. (c) Geis, O.; Schmalz H−G. *Angew. Chem., Int. Ed. Engl.* **1998**, *37*, 911.

(2) For selected reviews, see: (a) Vogel, P. *Bull. Soc. Chim. Belg.* **1990**, *99*, 395. (b) Woo, S.; Keay, B. A. *Synthesis* **1996**, 669. (c) Chiu, P.; Lautens, M. *Topics Curr. Chem.* **1997**, *190*, 3. (d) Kappe, C. O.; Murphree, S.; Padwa, A. *Tetrahedron* **1997**, *53*, 14179.

(3) To the best of our knowledge, only one isolated example of the Pauson−Khand reaction of a bridgehead substituted 7-oxanorbornene derivative has been previously reported: de Meijere, A.; Wessjohan, L. *Synlett* **1990**, 20.

(4) (a) Vogel, P.; Fattori, D.; Gasparini, F.; le Drian, C. *Synlett* **1990**, 173. (b) Arjona, O.; de la Pradilla, R. F.; Pita-Romero, I.; Plumet, J.; Viso, A. *Tetrahedron* **1990**, *46*, 8199.

(5) Arjona, O.; Domínguez, C.; de la Pradilla, R. F.; Mallo, A.; Manzano, C.; Plumet, J. *J. Org. Chem.* **1989**, *54*, 5883.

(6) Arjona, O.; de Dios, A.; de la Pradilla, R. F.; Mallo, A.; Plumet, J. *Tetrahedron* **1990**, *46*, 8179.

(7) Black, K. A.; Vogel, P. *J. Org. Chem.* **1986**, *51*, 5341.

(8) The structural assignment of compounds **3a** and **4d** has been carried out by 1D NOE measurements. Thus, saturation of the H-2 signal of compound **3a** (δ = 2.85 ppm, d, J = 5.5 Hz) gave rise to a 4% NOE enhancement of the H-6 signal (δ = 3.30 ppm, dd, J = 5.5 Hz, 3.0 Hz) and a 9% NOE enhancement of the H-1 signal (δ = 4.60 ppm, s), and saturation of the methylene group of the $CO_2CH_2CH_3$ moiety (δ = 4.25 ppm, q, J = 7 Hz) of compound **4d** produced a 6% NOE enhancement of the H-7 signal (δ = 5.25 ppm, s). The ^{1}H NMR spectra of all compounds **3** showed a chemical shift difference between the signals of H-2 and H-6 of 0−0.6 ppm, while this value was of 0.7−1.2 ppm for the regioisomeric compounds **4**. The ^{13}C NMR spectra of all compounds **3** showed a chemical shift difference between the signals of C-2 and C-6 of 0.4−1.5 ppm, while this value was of 9−14 ppm for the regioisomeric compounds **4**.

(9) Compounds **3b**, **3d**−**h**, **4b**, and **4d**−**h** have been correlated with ketones **3a**,**c** and **4a**,**c** by chemical transformations. Thus, **3b**,**d** and **4b**,**d** have been converted into ketones **3a**,**c** and **4a**,**c** by reaction with NaOMe/MeOH and formaldehyde. See: Black, K. A.; Vogel, P. *Helv. Chim. Acta* **1984**, *67*, 1612. Compounds **3e**,**f** and **4e**,**f** have been transformed into ketones **3a**,**c** and **4a**,**c** by acid hydrolysis (HCl/H_2O). Finally, alcohols **3g**,**h** and **4g**,**h** have been oxidized to ketones **3a**,**c** and **4a**,**c** with PCC.

10.1021/jo9903095 CCC: $18.00
Published on Web 09/10/1999

Table 1. Pauson−Khand Reaction of Compound 1 with Alkyne 2

entry	1	2	X, Y	R	method[a]	**3**:**4** (ratio,[b] percent[c])
1	**1a**	**2a**	O	H	A	**3a**:**4a** (80:20, 70)[d]
2	**1a**	**2a**	O	H	B	**3a**:**4a** (75:25, 65)[d]
3	**1a**	**2a**	O	H	C	**3a**:**4a** (60:40, 80)[d]
4	**1b**	**2a**	X = CN, Y = OAc	H	A	**3b**:**4b** (60:40, 70)[d]
5	**1b**	**2a**	X = CN, Y = OAc	H	B	**3b**:**4b** (70:30, 75)[d]
6	**1b**	**2a**	X = CN, Y = OAc	H	C	**3b**:**4b** (70:30, 80)[d]
7	**1a**	**2b**	O	CO_2Et	A	**3c**:**4c** (70:30, 60)
8	**1a**	**2b**	O	CO_2Et	B	**3c**:**4c** (80:20, 55)
9	**1a**	**2b**	O	CO_2Et	C	**3c**:**4c** (85:15, 80)
10	**1b**	**2b**	X = CN, Y = OAc	CO_2Et	A	**3d**:**4d** (60:40, 70)[e]
11	**1b**	**2b**	X = CN, Y = OAc	CO_2Et	B	**3d**:**4d** (70:30, 60)[e]
12	**1d**	**2b**	X = CN, Y = OAc	CO_2Et	C	**3d**:**4d** (75:25, 80)[e]
13	**1c**	**2a**	OCH_2CH_2O	H	C	**3e**:**4e** (60:40, 80)[e]
14	**1c**	**2b**	OCH_2CH_2O	CO_2Et	C	**3f**:**4f** (50:50, 80)
15	**1d**	**2a**	X = H, Y = OH	H	C	**3g**:**4g** (60:40, 80)[e]
16	**1d**	**2b**	X = H, Y = OH	CO_2Et	C	**3h**:**4h** (50:50, 80)
17	**1e**	**2a**	O	H	C	**3a**:**4a** (20:80, 70)[d]
18	**1e**	**2b**	O	CO_2Et	C	**3c**:**4c** (30:70, 70)
19	**1f**	**2a**	X = CN, Y = OAc	H	A	**3b**:**4b** (0:100, 40)[d]
20	**1f**	**2a**	X = CN, Y = OAc	H	B	**3b**:**4b** (20:80, 50)[d]
21	**1f**	**2a**	X = CN, Y = OAc	H	C	**3b**:**4b** (20:80, 70)[d]
22	**1f**	**2b**	X = CN, Y = OAc	CO_2Et	A	**3d**:**4d** (30:70, 45)[e]
23	**1f**	**2b**	X = CN, Y = OAc	CO_2Et	B	**3d**:**4d** (20:80, 50)[e]
24	**1f**	**2b**	X = CN, Y = OAc	CO_2Et	C	**3d**:**4d** (45:55, 75)[e]
25	**1g**	**2a**	OCH_2CH_2O	H	C	**3e**:**4e** (20:80, 65)[e]
26	**1g**	**2b**	OCH_2CH_2O	CO_2Et	C	**3f**:**4f** (0:100, 70)
28	**1h**	**2a**	X = H, Y = OH	H	C	**3g**:**4g** (20:80, 75)[e]
29	**1h**	**2b**	X = H, Y = OH	CO_2Et	C	**3h**:**4h** (0:100, 70)
30	**1i**	**2a**	O	H	C	**3a**:**4a** (100: 0, 75)[d]
31	**1i**	**2b**	O	CO_2Et	C	**3c**:**4c** (100: 0, 70)

[a] Method A: Toluene, reflux. Method B: Acetonitrile, reflux. Method C: CH_2Cl_2, NMO, rt. [b] Determined by integration of the ^1H NMR spectra of the crude reaction products. [c] Combined isolated yields. [d] Separated by chromatography on silica gel (hexane/AcOEt, 3:2). [e] Separated by crystallization.

The inspection of these data puts forward that the Pauson−Khand reaction of compounds **1a** (X, Y = O) and **1b** (X = CN, Y = OAc) with alkynes **2a** (R = H) and **2b** (R = CO_2Et) took place with a moderate-to-good regioselectivity (Table 1, entries 1−12). The formation of cyclopentenones **3a**−**d** was always favored, irrespective of the C-2, substituent, alkyne, or experimental conditions (methods A−C). Best yields were obtained when the reaction was carried out in CH_2Cl_2 (method C). However, the reaction of compounds **1c** (X, Y = OCH_2CH_2O) and **1d** (X = H, Y =OH) with either **2a** or **2b** was rather unselective from the regiochemical standpoint (Table 1, entries 13−16).

The observed behavior of compounds **1a**−**d** in the Pauson−Khand reaction is in contrast with the opposite regioselectivities reported for compounds **1a** and **1b**−**d** in their electrophilic additions to the C=C double bond, and in parallel with the results obtained in their 1,3-dipolar cycloaddition reactions.[4−6] No significant influence on the outcome of these reactions was exerted by the presence of the oxygen bridge in position 7, as similar regioselectivities have been reported[10] for the Pauson-Khand reactions of the 7-methylene analogues of compounds **1a** and **1d**.

On the other hand, 7-oxanorbornenic derivatives bearing substituents at the double bond have been shown to produce enhanced regioselectivities in 1,3-dipolar cycloadditions in comparison with the unsubstitued substrates.[6] However, halogenated alkenes are sensed to be reluctant to the Pauson−Khand reaction conditions.[11] Notwithstanding, the reactions of the 5-bromo derivatives **1e**−**h** and the 6-bromo derivative **1i** with alkynes **2a** (R = H) and **2b** (R = CO_2Et) allowed for the synthesis of cyclopentenones **3** and **4** in a combination of Pauson-Khand reaction and reductive dehalogenation (Scheme 1). The results are gathered in Table 1 (entries 17−31).

In the Pauson−Khand reactions of the 5-bromo derivatives **1e**−**h** (Table 1, entries 1−29), the regiochemistry of the cycloaddition was inverted as compared with that exhibited by the nonhalogenated compounds **1a**−**d** (Table 1, entries 1−16). The formation of cyclopentenones **4** was favored in all cases. As exemplified for **1f**, best yields were obtained when the reaction was carried out in CH_2Cl_2 at room temperature (method C), although better regiochemistries were consecuted in toluene (method A) or acetonitrile (method B) solutions at reflux temperature (compare Table 1 entries 19 with 21 and 23 with 24).[12] It is worth mentioning that, in contrast to the reactions of compounds **1c** and **1d**, where no regioselectivity was observed (Table 1, entries 13−16), the reaction of the corresponding 5-bromo derivatives **1g** and **1h** were highly or totally regioselective (Table 1, entries 25−29), since cyclopentenones **4f** and **4h** were obtained as the only products in their reactions with **2b**.

When the halogen atom was introduced into carbon C-6, the regiochemistry of the cycloaddition was the opposite of that observed with the 5-bromo derivatives. Thus, the reaction of compound **1i** with alkynes **2a** and **2b** gave rise to the regioselective formation of cyclopentenones **3a** and **3c** (Table 1, entries 30 and 31). This result should be compared with those obtained for compounds **1e** (Table 1, entries 17 and 18) and **1a** (Table 1, entries 3 and 9).

The regiochemistry of the Pauson−Khand reaction has been interpreted on the basis of a combination of electronic and steric factors during the first step of the reaction, i.e., the insertion of the alkene component into a formal C−Co bond of the alkyne−$Co(CO)_3$ complex.[1] The results obtained in the reactions of the 7-oxanorborne derivatives **1** put forward that the electronic nature of the endocyclic C=C double bond, tuned by the substituent on carbon C-2, plays a minor role in the regiochemical outcome of the reaction. The results obtained in the reactions of the bromo derivatives **1e**−**i** showed that the regiochemistry can be directed toward cyclopentenones **3** or **4** as a function of the emplacement of the halogen. These results indicate that the initial attack of the complexed alkyne is directed by the halogen toward the α-carbon atom, and the reductive dehalogenation step should take place later on the reaction sequence,[13]

(10) For the Pauson−Khand reactions of norborn-5-en-2-one and *endo*-norborn-5-en-2-ol with alkynes **2a** and propyne, see: MacWhorter, S. E.; Sampath, V.; Olmstead, M. M.; Schore, N. *J. Org. Chem.* **1988,** *53***,** 203.

(11) The Pauson−Khand reaction of bromoethylene with **2a** has been previously reported: Khand, I. U.; Pauson, P. L. *J. Chem. Res. (M)* **1977**, 165. No regiochemical considerations are possible in this case. To the best of our knowledge, no further Pauson−Khand reactions of halogenated alkenes have been considered in the literature.

(12) The enhancement of the regioselectivity in connection with a disminution in the chemical yield of the reaction may be attributed to unstability of adducts **3** under the thermal reaction conditions.

(13) Otherwise the same product distribution (**3:4** ratio) should have been obtained either starting from compounds **1** or the bromo derivatives **5** and **6**.

(14) For the intermediacy of hydridocobalt complexes in other Pauson−Khand related processes, see: (a) Montaña, A. M.; Moyano, A.; Pericàs, M. A.; Serratosa, F. *Tetrahedron* **1985**, *41*, 5995. (b) Billington, D. C.; Kerr, W. K.; Pauson, P. L.; Farnocchi, C. F. *J. Organomet. Chem.* **1988**, *356*, 213.

probably through the intermediacy of hydridocobalt complexes.[14]

Conclusions

The study carried out in this paper for the 7-oxanorbornenes **1a**−**d** and their bromo-substituted derivatives **1e**−**i** puts forward a new aspect of the Pauson−Khand reaction, i.e., the change in the regiochemistry in the presence of halogens directly bonded to the C=C double bond. Further applications of these findings as well as new synthetic transformations of the cyclopentenones herein obtained are now under development in our laboratory.

Experimental Section

All starting materials were commercially available research-grade chemicals and used without further purification. Toluene was distilled after refluxing over Na/benzophenone. Acetonitrile and CH_2Cl_2 were distilled after refluxing over CaH_2. Silica gel 60 F_{254} was used for TLC, and the spots were detected with UV. Flash column chromatography was carried out on silica gel 60. IR spectra have been recorded as $CHCl_3$ solutions. Melting points are uncorrected. ^1H and ^{13}C NMR spectra were recorded at 200 or 300 MHz and 50.5 or 75.5 MHz, respectively, in $CDCl_3$ solution with TMS as internal reference. Compounds **1**, **5**, and **6** were prepared as previously described.[5,6]

Pauson−Khand Reactions in Toluene (Method A). General Procedure. To a stirred solution of **2a**,**b** (0.51 mmol) in anhydrous toluene (3 mL) was added $Co_2(CO)_8$ (191 mg, 0.56 mmol) in one portion, and the solution was stirred for 1 h. A solution of **1a**−**d** or **5** (0.56 mmol) in toluene (1 mL) was added dropwise, and the reaction mixture was stirred at reflux temperature for 3−6 h for compounds **1a**−**d** (until complete disappearance of the olefin, monitored by TLC, hexane−EtOAc 3:7) and 48 h for compound **5**. The resulting suspension was filtered through Celite, the solvent was evaporated, and the residue was purified by column chromatography (silica gel, hexanes−EtOAc). Isomers **3** and **4** were separated by crystallization or by silica gel chromatography using hexane−ethyl acetate (3:2) as eluent (see Table 1).

Pauson−Khand Reactions in Acetonitrile (Method B). General Procedure. To solid $Co_2(CO)_8$ (191 mg, 0.56 mmol) was added a solution of **2a** and **2b** (0.51 mmol) in anhydrous acetonitrile (3 mL), and the solution was stirred for 1 h. A solution of **1a**−**d** or **5a**−**d** (0.56 mmol) in acetonitrile (1 mL) was added dropwise, and the reaction mixture was stirred at reflux temperature for 2−4 h for compound **1** (until complete disappearance of the olefin, monitored by TLC, hexane−EtOAc 3:7) and 24 h for compound **5**. All operations were continued as in method A.

Pauson−Khand Reactions in CH_2Cl_2 (Method C). General Procedure. To a stirred solution of **2a** and **2b** (0.83 mmol) in anhydrous CH_2Cl_2 (4 mL) was added $Co_2(CO)_8$ (311 mg, 0.91 mmol) in one portion, and the solution was stirred for 1 h. A solution of **1a**−**d**, **5a**−**d**, or **6** (0.91 mmol) in anhydrous CH_2Cl_2 (2 mL) was added, and the mixture was cooled at 0 °C. *N*-Methylmorpholine *N*-oxide monohydrate (NMO) (246 mg, 1.82 mmol) was added in one portion, and the temperature was raised to room temperature. The extent of the reaction was monitored by TLC (hexane−ethyl acetate 3:7). The treatment with NMO was repeated until complete disappearance of the starting materials (8−10 equiv). The reaction mixture was stirred for 2 h for compound **1** and 24 h for compounds **5** and **6**. All operations were continued as in method A.

4-Phenyl-10-oxatricycle[5,2,1,$0^{2,6}$]dec-4-ene-3,9-dione (3a): white solid, mp 228−230 °C, dec (EtOAc); IR (KBr) ν 1710; ^1H NMR (300 MHz, $CDCl_3$) δ 2.20 (d, J = 17.5 Hz, 1H), 2.60 (dd, J = 17.5 Hz, J = 5.8 Hz, 1H), 2.85 (d, J = 5.5 Hz, 1H), 3.30 (dd, J = 5.5 Hz, J = 3.0 Hz, 1H), 4.60 (s, 1H), 4.80 (d, J = 5.8 Hz, 1H), 7.40 (m, 3H), 7.70 (m, 2H), 7.75 (d, J = 3.0 Hz, 1H); ^{13}C NMR (75.5 MHz, $CDCl_3$) δ 208.1, 203.2, 156.2, 146.8, 132.0, 129.1, 128.5, 127.2, 81.5, 77.3, 48.8, 47.5, 42.0. Anal. Calcd for $C_{15}H_{12}O_3$: C, 74.99; H, 5.03. Found: C, 75.17; H, 5.25.

***endo*-9-Acetoxy-*exo*-9-cyano-4-phenyl-10-oxatricycle-[5,2,1,$0^{2,6}$]dec-4-ene-3-one (3b):** white solid; mp 201−203 °C (MeOH); IR (KBr) ν 1750, 1700; ^1H NMR (300 MHz, $CDCl_3$) δ 1.90 (d, J = 14 Hz, 1H), 2.10 (s, 3H), 2.90 (dd, J = 14 Hz, J = 5.5 Hz, 1H), 3.10 (m, 2H), 4.65 (d, J = 5.5 Hz, 1H), 5.18 (s, 1H), 7.28 (m, 3H), 7.65 (m, 2H), 7.70 (d, J = 3 Hz, 1H); ^{13}C NMR (75.5 MHz, $CDCl_3$) δ 204.1, 168.7, 156.0, 147.2, 130.4, 129.1, 128.5, 127.2, 117.9, 83.5, 77.4, 73.5, 48.5, 47.1, 43.8, 20.5. Anal. Calcd for $C_{18}H_{15}NO_4$: C, 69.89; H, 4.88; N, 4.52. Found: C, 70.01; H, 4.99; N, 4.68.

5-(Ethoxycarbonyl)-4-phenyl-10-oxatricycle[5,2,1,$0^{2,6}$]-dec-4-ene-3,9-dione (3c): colorless oil; IR ($CHCl_3$) ν 1760, 1710; ^1H NMR (200 MHz, $CDCl_3$) δ 1.15 (t, J = 7 Hz, 3H), 2.25 (d, J = 13 Hz, 1H), 2.65 (dd, J = 13 Hz, J = 6 Hz, 1H), 2.90 (d, J = 5.5 Hz, 1H), 3.55 (d, J = 5.5 Hz, 1H), 4.20 (q, J = 7 Hz, 2H), 4.60 (s, 1H), 5.06 (d, J = 6 Hz, 1H), 7.30 (m, 2H), 7.40 (m, 3H); ^{13}C NMR (50.5 MHz, $CDCl_3$) δ 207.9, 203.9, 164.9, 154.4, 150.1, 129.5, 129.3, 129.0, 127.9, 81.5, 77.8, 61.8, 48.6, 48.2, 42.1, 13.7. Anal. Calcd for $C_{18}H_{16}O_5$: C, 69.22; H, 5.16. Found: C, 69.40; H, 5.22.

***endo*-9-Acetoxy-*exo*-9-cyano-5-(ethoxycarbonyl)-4-phenyl-10-oxatricycle[5,2,1,$0^{2,6}$]dec-4-ene-3-one (3d):** colorless oil; IR ($CHCl_3$) ν 1760, 1710; ^1H NMR (200 MHz, $CDCl_3$) δ 1.10 (t, J = 7 Hz, 3H), 1.95 (d, J = 14 Hz, 1H), 2.10 (s, 3H), 2.85 (dd, J = 14 Hz, J = 6 Hz, 1H), 3.05 (d, J = 6 Hz, 1H), 3.30 (d, J = 6 Hz, 1H), 4.15 (q, J = 7 Hz, 2H), 4.85 (d, J = 6 Hz, 1H), 5.10 (s, 1H), 7.25−7.40 (m, 5H); ^{13}C NMR (50.5 MHz, $CDCl_3$) δ 204.6, 168.6, 164.8, 154.4, 150.8, 129.4, 129.3, 128.9, 127.8, 117.7, 83.7, 78.1, 73.5, 61.8, 48.2, 47.8, 43.8, 20.4, 13.7. Anal. Calcd for $C_{21}H_{19}NO_6$: C, 66.14; H, 5.02; N, 3.67. Found: C, 66.25; H, 5.24; N, 3.78.

9,9-Ethylenedioxy-4-phenyl-10-oxatricycle[5,2,1,$0^{2,6}$]-dec-4-ene-3-one (3e): white solid; mp 192−194 °C (EtOAc); IR (KBr) ν 1710; ^1H NMR (200 MHz, $CDCl_3$) δ 1.85 (d, J = 13 Hz, 1H), 2.28 (dd, J = 13 Hz, J = 5.5 Hz, 1H), 3.14 (m, 2H), 3.80−4.10 (m, 4H), 4.30 (s, 1H), 4.46 (d, J = 5.5 Hz, 1H), 7.35 (m, 3H), 7.65 (m, 2H), 7.70 (d, J = 3 Hz, 1H); ^{13}C NMR (50.5 MHz,$CDCl_3$) δ 206.3, 157.2, 146.2, 131.0, 128.7, 128.4, 127.1, 114.8, 82.1, 77.3, 65.3, 64.7, 49.4, 47.8, 42.4. Anal. Calcd for $C_{17}H_{16}O_4$: C, 71.82; H, 5.67. Found: C, 72.01; H, 5.92.

5-(Ethoxycarbonyl)-9,9-ethylenedioxy-4-phenyl-10-oxatricycle[5,2,1,$0^{2,6}$]dec-4-ene-3-one (3f): colorless oil, 50:50 mixture with **4f**; IR ($CHCl_3$) ν 1770, 1725; ^1H NMR (300 MHz, $CDCl_3$) δ 1.15 (t, J = 7 Hz, 3H), 1.90 (d, J = 13 Hz, 1H), 2.35 (dd, J = 13 Hz, J = 6 Hz, 1H), 3.25 (d, J = 6 Hz, 1H), 3.40 (d, J = 6 Hz, 1H), 3.90−4.20 (m, 4H), 4.25 (q, J = 7 Hz, 2H), 4.35 (s, 1H), 4.75 (d, J = 6 Hz, 1H), 7.25−7.40 (m, 5H); ^{13}C NMR (75.5 MHz,$CDCl_3$) δ 207.1, 165.3, 155.3, 149.8, 130.1, 129.1, 128.9, 127.8, 113.9, 82.3, 77.7, 65.3, 64.6, 61.5, 48.9, 48.7, 42.5, 13.7. Anal. Calcd for $C_{20}H_{20}O_6$: C, 67.41; H, 5.65. Found: C, 67.55; H, 5.90.

9-*endo*-Hydroxy-4-phenyl-10-oxatricycle[5,2,1,$0^{2,6}$]dec-4-ene-3-one (3g): white solid; mp 223−225 °C (hexane−EtOAc); IR (KBr) ν 3460, 1700; ^1H NMR (200 MHz, $CDCl_3$) δ 1.35 (dd, J = 13 Hz, J = 3 Hz, 1H), 1.95 (bs, 1H), 2.30 (m, 1H), 3.10 (dd, J = 5.5 Hz, J = 3 Hz, 1H), 3.45 (d, J = 5.5 Hz, 1H), 4.40 (d, J = 5.5 Hz, 1H), 4.50 (m, 1H), 4.60 (d, J = 5 Hz, 1H), 7.40 (m, 3H), 7.70 (m, 2H), 7.75 (d, J = 3 Hz, 1H); ^{13}C NMR (50.5 MHz,$CDCl_3$) δ 206.2, 157.7, 146.7, 130.4, 129.1, 128.4, 127.1, 81.7, 78.3, 70.5, 48.5, 48.4, 38.8. Anal. Calcd for $C_{15}H_{14}O_3$: C, 74.36; H, 5.82. Found: C, 74.18; H, 5.45.

5-(Ethoxycarbonyl)-9-*endo*-hydroxy-4-phenyl-10-oxatricycle[5,2,1,$0^{2,6}$]dec-4-ene-3-one (3h): colorless oil, 50:50 mixture with **4h**; IR ($CHCl_3$) ν 3450, 1720; ^1H NMR (200 MHz, $CDCl_3$) δ 1.15 (t, J = 7 Hz, 3H), 1.40 (dd, J = 13 Hz, J = 3 Hz, 1H), 2.10 (bs, 1H), 2.35 (m, 1H), 3.35 (d, J = 6 Hz, 1H), 3.45 (d, J = 6 Hz, 1H), 4.20 (q, J = 7 Hz, 2H), 4.35 (m, 1H), 4.60 (d, J = 5 Hz, 1H), 4.65 (d, J = 6 Hz, 1H), 7.30−7.40 (m, 5H); ^{13}C NMR (50.5 MHz,$CDCl_3$) δ 208.9, 165.7, 156.4, 150.0, 130.3, 129.0, 128.9, 127.8, 82.0, 77.7, 70.5, 61.6, 49.6,

47.7, 38.7, 17.7. Anal. Calcd for $C_{18}H_{18}O_5$: C, 68.78; H, 5.77. Found: C, 68.99; H, 5.55.

4-Phenyl-10-oxatricycle[5,2,1,0^{2,6}]dec-4-ene-3,8-dione (4a): white solid; mp 172−174 °C (EtOH); IR (KBr) ν 1790, 1720; ^{1}H NMR (300 MHz, $CDCl_3$) δ 2.15 (d, J = 17 Hz, 1H), 2.55 (dd, J = 17 Hz, J = 5.5 Hz, 1H), 2.80 (d, J = 5.5 Hz, 1H), 3.25 (dd, J = 5.5 Hz, J = 3 Hz, 1H), 4.30 (s, 1H), 5.10 (d, J = 5.5 Hz, 1H), 7.40 (m, 3H), 7.65 (d, J = 3 Hz, 1H), 7.70 (m, 2H); ^{13}C NMR (75.5 MHz, $CDCl_3$): δ 209.7, 204.4, 154.2, 146.8, 130.4, 129.1, 128.5, 127.2, 80.2, 78.9, 54.0, 43.2, 41.6. Anal. Calcd for $C_{15}H_{12}O_3$: C, 74.99; H, 5.03. Found: C, 75.14; H, 5.20.

***endo*-8-Acetoxy-*exo*-8-cyano-4-phenyl-10-oxatricycle-[5,2,1,0^{2,6}]dec-4-ene-3-one (4b):** colorless oil; IR ($CHCl_3$) ν 1750, 1705; ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.95 (d, J = 14 Hz, 1H), 2.15 (s, 3H), 2.65 (d, J = 5.5 Hz, 1H), 2.80 (dd, J = 14 Hz, J = 5.5 Hz, 1H), 3.35 (dd, J = 5.5 Hz, J = 3 Hz, 1H), 4.82 (d, J = 5.5 Hz, 1H), 5.05 (s, 1H), 7.40 (m, 3H), 7.62 (d, J = 3 Hz, 1H), 7.70 (m, 2H); ^{13}C NMR (75.5 MHz, $CDCl_3$) δ 204.6, 169.1, 155.2, 147.5, 130.4, 129.2, 128.5, 127.2, 117.9, 82.0, 79.1, 74.5, 53.6, 43.1, 41.5, 20.6. Anal. Calcd for $C_{18}H_{15}NO_4$: C, 69.89; H, 4.88; N, 4.52. Found: C, 70.02; H, 4.68; N, 4.45.

5-(Ethoxycarbonyl)-4-phenyl-10-oxatricycle[5,2,1,0^{2,6}]-dec-4-ene-3,8-dione (4c): colorless oil; IR ($CHCl_3$) ν 1760, 1710; ^{1}H NMR (200 MHz, $CDCl_3$) δ 1.15 (t, J = 7 Hz, 3H), 2.15 (d, J = 13 Hz, 1H), 2.55 (dd, J = 13 Hz, J = 6 Hz, 1H), 2.90 (d, J = 5.5 Hz, 1H), 3.55 (d, J = 5.5 Hz, 1H), 4.20 (q, J = 7 Hz, 2H), 4.75 (s, 1H), 5.09 (d, J = 6 Hz, 1H), 7.30 (m, 2H), 7.40 (m, 3H); ^{13}C NMR (50.5 MHz, $CDCl_3$) δ 209.0, 204.2, 164.1, 154.4, 150.1, 129.5, 129.3, 129.0, 127.9, 80.4, 79.1, 61.8, 53.2, 44.4, 41.6, 13.7. Anal. Calcd for $C_{18}H_{16}O_5$: C, 69.22; H, 5.16. Found: C, 69.11; H, 5.04.

***endo*-8-Acetoxy-*exo*-8-cyano-5-(ethoxycarbonyl)-4-phenyl-10-oxatricycle[5,2,1,0^{2,6}]dec-4-ene-3-one (4d):** white solid; mp 145−147 °C (hexane−EtOAc); IR ($CHCl_3$) ν 1770, 1710; ^{1}H NMR (200 MHz, $CDCl_3$) δ 1.20 (t, J = 7 Hz, 3H), 2.02 (d, J = 14 Hz, 1H), 2.25 (s, 3H), 2.80 (d, J = 6 Hz, 1H), 2.85 (dd, J = 14 Hz, J = 6 Hz, 1H), 3.65 (d, J = 6 Hz, 1H), 4.25 (q, J = 7 Hz, 2H), 4.75 (d, J = 6 Hz, 1H), 5.25 (s, 1H), 7.25−7.40 (m, 5H); ^{13}C NMR (50.5 MHz, $CDCl_3$) δ 205.0, 168.7, 164.2, 153.6, 150.8, 129.4, 129.3, 129.0, 127.9, 117.8, 82.4, 79.3, 74.2, 61.9, 52.8, 42.9, 42.7, 20.5, 13.7. Anal. Calcd for $C_{18}H_{16}O_5$: C, 69.22; H, 5.16. Found: C, 69.38; H, 5.27.

8,8-Ethylenedioxy-4-phenyl-10-oxatricycle[5,2,1,0^{2,6}]-dec-4-ene-3-one (4e): white solid; mp 145−147 °C (EtOH); IR (KBr) ν 1715; ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.70 (d, J = 13 Hz, 1H), 2.15 (dd, J = 13 Hz, J = 6 Hz, 1H), 2.67 (d, J = 5.5 Hz, 1H), 3.50 (dd, J = 5.5 Hz, J = 3 Hz, 1H), 3.80−4.10 (m, 4H), 3.95 (s, 1H), 4.70 (d, J = 6 Hz, 1H), 7.30 (m, 3H), 7.60 (d, J = 3 Hz, 1H), 7.65 (m, 2H); ^{13}C NMR (75.5 MHz,$CDCl_3$) δ 206.7, 157.3, 146.7, 131.1, 128.7, 128.6, 127.2, 114.1, 80.4, 79.2, 65.4, 64.6, 54.5, 42.4, 42.1. Anal. Calcd for $C_{17}H_{16}O_4$: C, 71.82; H, 5.67. Found: C, 71.91; H, 5.56.

5-(Ethoxycarbonyl)-8,8-ethylenedioxy-4-phenyl-10-oxatricycle[5,2,1,0^{2,6}]dec-4-ene-3-one (4f): colorless oil; IR ($CHCl_3$) ν 1770, 1710; ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.10 (t, J = 7 Hz, 3H), 1.85 (d, J = 13 Hz, 1H), 2.30 (dd, J = 13 Hz, J = 6 Hz, 1H), 2.80 (d, J = 6 Hz, 1H), 3.85 (d, J = 6 Hz, 1H), 3.90−4.20 (m, 4H), 4.25 (q, J = 7 Hz, 2H), 4.40 (s, 1H), 4.80 (d, J = 6 Hz, 1H), 7.25−7.40 (m, 5H); ^{13}C NMR (75.5 MHz, $CDCl_3$) δ 206.6, 165.2, 155.0, 149.5, 130.0, 129.1, 128.9, 127.7, 114.7, 80.6, 79.3, 64.7, 64.5, 61.4, 53.6, 43.7, 41.6, 13.7. Anal. Calcd for $C_{20}H_{20}O_6$: C, 67.41; H, 5.65. Found: C, 67.30; H, 5.49.

8-*endo*-Hydroxy-4-phenyl-10-oxatricycle[5,2,1,0^{2,6}]dec-4-ene-3-one (4g): colorless oil, mixture 80:20 with **3g**; IR ($CHCl_3$) ν 3450, 1710; ^{1}H NMR (200 MHz, $CDCl_3$) δ 1.25 (dd, J = 13 Hz, J = 3 Hz, 1H), 2.00 (bs, 1H), 2.30 (m, 1H), 2.70 (d, J = 5.5 Hz, 1H), 3.70 (dd, J = 5.5 Hz, J = 3 Hz, 1H), 4.35 (d, J = 5 Hz, 1H), 4.55 (m, 1H), 4.65 (d, J = 5.5 Hz, 1H), 7.35 (m, 3H), 7.60 (d, J = 3 Hz, 1H). 7.70 (m, 2H); ^{13}C NMR (50.5 MHz, $CDCl_3$) δ 206.2, 158.4, 146.7, 129.4, 128.2, 127.1, 126.9, 80.4, 79.0, 71.1, 55.2, 40.8, 38.2. Anal. Calcd for $C_{15}H_{14}O_3$: C, 74.36; H, 5.82. Found: C, 74.18; H, 5.59.

5-(Ethoxycarbonyl)-8-*endo*-hydroxy-4-phenyl-10-oxatricycle[5,2,1,0^{2,6}]dec-4-ene-3-one (4h): colorless oil; IR ($CHCl_3$) ν 3450, 1710; ^{1}H NMR (200 MHz, $CDCl_3$) δ 1.15 (t, J = 7 Hz, 3H), 1.35 (dd, J = 13 Hz, J = 3 Hz, 1H), 1.70 (bs, 1H), 2.30 (m, 1H), 2.80 (d, J = 5.5 Hz, 1H), 4.02 (d, J = 5.5 Hz, 1H), 4.20 (q, J = 7 Hz, 2H), 4.45 (m, 1H), 4.62 (bs, 1H), 4.72 (d, J = 5.5 Hz, 1H), 7.30−7.40 (m, 5H); ^{13}C NMR (50.5 MHz, $CDCl_3$) δ 207.3, 165.4, 155.9, 149.7, 130.1, 128.9, 128.8, 127.8, 80.6, 79.7, 71.2, 61.5, 54.4, 42.2, 38.1, 13.7. Anal. Calcd for $C_{18}H_{18}O_5$: C, 68.78; H, 5.77. Found: C, 68.69; H, 5.59.

Acknowledgment. DGCYT (Project PB-960641) is gratefully acknowledged for finantial support. One of us (M.C.M.) thanks Ministerio de Educación y Cultura (Spain) for a predoctoral grant.

Supporting Information Available: Experimental procedures for the transformation of **3b**−**f** and **4b**−**f** into **3a**,**c** and **4a**,**c**, and ^{1}H NMR spectra copies for compounds **3** and **4**. This material is available free of charge via the Internet at http://pubs.acs.org.

JO9903095