84. Synthesis of Tricyclo[6.2.1.0^{1,5}]undecadiones *via* Intramolecular Photoaddition of 5-(1-Cyclopentenylmethyl)-3-alkoxy-2-cyclopentenones

by **Wolfgang Oppolzer** and **Sidney C. Burford**

Département de Chimie Organique, Université de Genève, CH-1211 Genève, Switzerland

(10.III.80)

Summary

Irradiation of the dienone methyl ether **3a** furnished the unstable regioisomeric photoadducts **4a** and **5a** which on *Lewis* acid-catalyzed fragmentation afforded the tricyclic diketones **6**, **7** and **8**. The same mixture was obtained from the isobutyl ether **3b** *(Scheme 2).*

Introduction. - The tricyclo[6.2.1.0^{1,5}]undecane skeleton **A** *(Scheme 1)* is a basic structural feature of several natural products such as the zizaane type sesquiterpenes **B**[1]) and the gibberellins[2]). The development of short and selective approaches to specificially functionalized ring systems of this type remains a fascinating challenge despite a number of previous successful syntheses[1,2]).

Scheme 1

A **B**

Continuing our studies of intramolecular *de Mayo* reactions [3][3]) and their applications to the synthesis of natural products[4]) we envisaged the assembly of the system **A** by formation of the two C,C-bonds C(5),C(6) and C(1),C(10) in a single operation. Independently, *Pattenden et al.* have described a related construction of the bicyclo[3.2.1]octane system by subjecting 3-acetoxy-5-allyl-4-methyl-2-cyclopenten-1-ones to a photoaddition-retroaldol sequence [7]. However, we were unable to obtain 3-acyloxycyclopentenones **3c** regioselectively.

Preparation and irradiation of 5-(1-cyclopentenylmethyl)-3-methoxy-2-cyclopent-1-one (3a) *(Scheme 2).* - Kinetically controlled deprotonation [8] of the readily available enol ether **1a** with lithium diisopropylamide followed by alkylation of the resulting enolate with the bromide **2** furnished cleanly the dienone **3a** in 68%

---

[1]) For literature regarding the isolation and structural elucidation of zizaane type sesquiterpenes and for previous synthetic work in this area see [1].

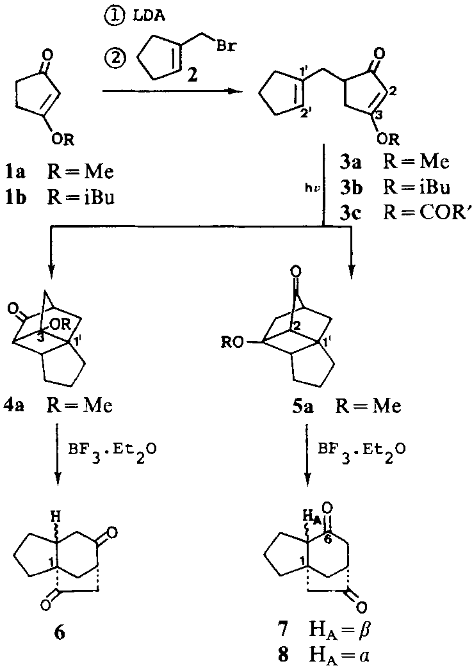
[2]) For references concerning previous structural and synthetic work on gibberellins see [2].

[3]) For a review on intermolecular *de Mayo* reactions see [4].

[4]) *e.g.* the syntheses of longifolene [5] and β-bulnesene [6].

0018-019X/80/4/0788-05$01.00/0

Scheme 2



yield. Irradiation of **3a** led to a mixture of unstable products from which the two major adducts **4a** and **5a** could be isolated. Their constitutions, tentatively assigned on the basis of IR., ^{1}H-NMR. and mass spectra, were ultimately confirmed by their fragmentation with boron trifluoride etherate[5]).

Fragmentation of the photoproducts 4a and 5a. - *Tamura et al.* have demonstrated the photoaddition of dimedone-*O*-butenyl ether and the cleavage of the resulting tricyclic β-alkoxyketone with a *Lewis* acid to give a bicyclic dihydrofuran [9]. Accordingly it might be expected that the photoproducts **4a** and **5a** would readily undergo a retro-aldol-like fragmentation under similar conditions. Indeed, treatment of **4a** with boron trifluoride etherate furnished smoothly the crystalline tricyclo[6.2.1.0^{1,5}]undecadione **6**. Under identical conditions **5a** gave a mixture of the stereoisomers **7** and **8** which was separated by HPLC. For practical reasons it was preferable to treat the crude mixture of photoproducts directly with boron trifluoride etherate. Subsequent chromatography yielded the crystalline dione **6** in 24% and the isomers **7** and **8** in 31% overall yield from **3a**.

Structure of the products 6, 7 and 8. - On the basis of the ^{1}H-NMR. (360 MHz) and ^{13}C-NMR. (25.2 MHz) spectra the constitution of the diketones was readily assigned. In the ^{1}H-NMR. spectrum the least polar crystalline diketone **6** shows between $\delta = 1.9$ and 2.6 ppm the signals of three methylene groups, each one coupled to one vicinal proton; in contrast, the diones **7** and **8** exhibit the signals

---

[5]) The configurations of **4a** and **5a** were not investigated.

of one isolated methylene group. The configuration of **6** was not determined. However, the deshielding of H_A in **8** giving rise to a triplet at $\delta = 2.63$ ppm indicates its *peri-syn*-planar position relative to the C(6)-carbonyl-*O*-atom. Since the dione **7** shows no signal downfield from $\delta = 2.15$ ppm which couples with protons appearing upfield from $\delta = 2.0$ ppm, the configurations of **7** and **8** were tentatively assigned as in *Scheme 2*. The ^{13}C-NMR. spectra are in agreement with these deductions. Thus, **6** shows a singlet at low field (58.6 ppm) corresponding to the quaternary C(1) (adjacent to a carbonyl group) whereas in the spectra of the diones **7** and **8** the C(1) singlet appears at 48.6 and 50.6 ppm, respectively. Further confirmation of these assignments follows from the interconversion of **7** and **8** by treatment of the isolated stereoisomers with boron trifluoride etherate.

Discussion. - The lack of regioselectively observed in the intramolecular photoaddition of **3a** does not violate the 'rule of five' [10](6); both processes, **3a**→**4a** and **3a**→**5a** allow initial formation of a diradical intermediate possessing a five membered ring. In order to study the possible influence of steric effects the isobutyl enol ether **3b** was subjected to the same photoaddition-fragmentation sequence giving a mixture of **6, 7** and **8** identical to that obtained from the methyl enol ether **3a**. It thus appears that the comparable rate of C(2),C(1')- and C(3),C(1')-bond formation is of electronic rather than of steric origin.

Financial support of this work by the *Swiss National Science Foundation, Sandoz Ltd.*, Basel and *Givaudan SA*, Vernier is gratefully acknowledged. We thank Mr. *J.P. Saulnier* for careful NMR. measurements and Mrs. *F. Klöti* for carrying out the mass spectra. Thanks are especially due to Dr. *U. Burger* for assistance in interpretation of NMR. spectra.

Experimental Part

General. All reactions were carried out under argon. The usual work-up procedure implies pouring the reaction mixture into a saturated aqueous solution of $NaHCO_3$, extraction with ether or CH_2Cl_2, washing the combined organic layers with saturated aqueous NaCl solution, drying (Na_2SO_4) and removal of the solvent *in vacuo*. Thin layer chromatography (TLC.) was carried out on *Merck* 0.25 mm (60F254) silica gel plates. Preparative chromatography was carried out on silica gel (*Merck* 0.05-0.20 mm) unless otherwise specified. High pressure liquid chromatography (HPLC.) was performed on a *Waters* Associates apparatus M-6000 using μ-Porasil (μ10, 4 mm ID×30 cm) columns and a R 401 refractometer detector. Gas chromatograms (GC.): 1 atm N_2; glass columns (3 mm ID×3 m), stationary phases on chromosorb W (acid washed, 80/100 mesh): column 1: 5% SE 30; column 2: 5% OV 17; column 3: 5% OV 225; retention time in min (area %). Melting points (m.p.) are not corrected. IR. spectra: CCl_4 unless otherwise specified, ν_{max} in cm^{-1}. UV. spectra: methanol, λ_{max} in nm (logε). NMR. spectra: in $CDCl_3$, internal standard tetramethylsilane ($\delta = 0$ ppm); abbreviations: *s* singlet, *d* doublet, *t* triplet, *qa* quartet, *m* multiplet, br. broad, *J* spin-spin coupling constant (Hz), ^{1}H-NMR. at 100 MHz, unless otherwise specified, ^{13}C-NMR. at 25.2 MHz. Mass spectra (MS.): signals are given in *m/z* (rel. %).

5-(1-Cyclopentenylmethyl)-3-methoxy-2-cyclopenten-1-one (3a) *(Scheme 2)*. - To a solution of dry diisopropylamine (0.45 g, 4.5 mmol) in dry THF (10 ml) were added with stirring first a 1.55 N solution of butyllithium in hexane (2.9 ml, 4.4 mmol) at −45°, then after 30 min HMPA (0.82 g, 4.6 mmol), and finally, dropwise at −70° a solution of 3-methoxy-2-cyclopenten-1-one(7) (**1a**, 0.45 g, 4 mmol) in THF (3 ml). Stirring of the mixture for 15 min at −70°, subsequent addition of 1-bromo-

---

(6) For a pertinent example see [9b].

(7) The known enones **1a** [11] and **1b** [12] were obtained following a procedure for the preparation of 3-ethoxy-2-cyclopenten-1-one [13].

methyl-1-cyclopentene (**2**) [14] (0.66 g, 4.1 mmol), further stirring at −70° for 15 min, pouring of the reaction mixture into a saturated aqueous solution of NH_4Cl followed by the usual work-up, chromatography (hexane/ethyl acetate 8:1) and distillation (140-145° (bath)/0.04 Torr) furnished the dienone **3a** (oil, 0.52 g, 68%). - UV.: 240 (4.21). - IR. (film): 1699, 1600, 1360, 1290, 1245, 1170, 995. - ^{1}H-NMR.: 1.8-2.5 (8 H); 2.5-2.9 (3 H); 3.85 (*s*, 3 H); 5.30 (br. *s*, 1 H); 5.40 (*m*, 1 H). - MS.: 192 (43, $C_{12}H_{16}O_2^+$), 111 (100), 112 (100).

Irradiation of 5-(1-cyclopentenylmethyl)-3-methoxy-2-cyclopentenone (3a). Irradiation of a solution of the dienone **3a** (1.18 g, 6.15 mmol) in cyclohexane (150 ml) through Pyrex at 15° using a 125 W medium pressure Hg-lamp *(Philips)* for 7 h, followed by evaporation of the solution *in vacuo* gave a colourless oil (1.25 g). TLC. (toluene/ethyl acetate 7:3): 3 spots, Rf 0.65, 0.35 and 0.25. Chromatography of the unstable crude mixture (64 mg) on Al_2O_3 (*Merck*, neutral, activity III, hexane/ether 8:2) furnished an unidentified compound (15 mg), followed by the more polar photoproduct **4a** (oil, 20 mg). - IR.: 1745, 1290. - ^{1}H-NMR.: 1.2-2.4 (11 H); 2.55 (*d*, J = 1.5, 1 H); 2.66 (*m*, 1 H); 3.35 (*s*, 3 H). - MS.: 192 (26, $C_{12}H_{16}O_2^+$), 178 (5), 164 (13), 152 (8), 149 (11), 112 (100), 111 (69), 109 (35).

Further elution afforded the most polar photoproduct **5a** (oil, 7 mg). - IR.: 1760 br., 1080. - ^{1}H-NMR.: 1.2-2.6 (13 H); 3.15 (*s*, 3 H). - MS.: 192 (31, $C_{12}H_{16}O_2^+$), 178 (59), 164 (18), 152 (18), 151 (16), 149 (48), 135 (57), 112 (100), 111 (80), 109 (61).

Tricyclo[6.2.1.0^{1,5}]undecan-7,10-dione (6) and tricyclo[6.2.1.0^{1,5}]undecan-6,9-diones (7 and 8). - a) *Fragmentation of the crude photoproduct mixture.* Boron trifluoride etherate (0.8 ml, 6.5 mmol) was added dropwise to a stirred solution of the crude photoproduct mixture (1.2 g) in dry benzene (200 ml) at +15°. After stirring for 30 min the mixture was poured into a saturated aqueous solution of NH_4Cl and subjected to the usual work-up. Distillation of a sample of the crude residue (108 mg) at 110-140° (bath)/0.01 Torr furnished a colourless oil (65 mg) which on GC. analysis (column 1, 150°) showed 4 major peaks: 11.0 (16.5), 12.1 (30), 14.2 (12), 17.0 (40); analogous results were obtained using the columns 2 and 3. HPLC. analysis showed 3 major peaks with 6.6, 9.0 and 10.2 min retention time in a ratio of *ca.* 2:1:1. Chromatography of the crude residue (hexane/ethyl acetate 2:1) gave the least polar diketone **6** (0.26 g, 24% yield from **3a**), m.p. 54-56° (ether/pentane); GC. (column 1, 150°): 12.1. - IR.: 1743, 1725. - ^{1}H-NMR. (360 MHz): 1.35 (*m*, 1 H); 1.52 (*m*, 1 H); 1.7-1.9 (2 H); 1.95 (*m*, 1 H); 2.0-2.15 (3 H); 2.23 (*t*, J = 15, 1 H); 2.30 ($d \times d$, J = 4 and 19, 1 H; irradiation at 2.05 → d, J = 19); 2.35 ($d \times d$, J = 5 and 13, 1 H; irradiation at 3.02 → d, J = 13); 2.47 ($d \times d$, J = 7 and 19, 1 H; irradiation at 3.02 → d, J = 19); 2.60 ($d \times d$, J = 5 and 15, 1 H; irradiation at 2.05 → d, J = 15); 3.02 ($d \times d$, J = 5 and 7, 1 H; irradiation at 2.35 → d, J = 7). - ^{13}C-NMR.: 216.3*s*, 209.9*s*, 58.6*s*, 49.5*d*, 46.8*d*, 42.4*t*, 41.5*t*, 39.7*t*, 29.5*t*, 27.4*t*, 23.9*t*. - MS.: 178 (90, $C_{11}H_{14}O_2^+$), 160 (20), 135 (79), 95 (31), 81 (100), 79 (42).

Further elution gave fractions containing the diketones **6**, **7** and **8** (50 mg) followed by a fraction containing the stereoisomers **7** and **8** (0.34 g, 31% yield from **3a**; GC., column 1, 150°: 16.4) and, finally, unchanged dienone **3a** (50 mg). Part of the fractions containing the isomers **7** and **8** (100 mg) was separated by preparative HPLC. using 2 μ-Porasil columns in series (hexane/ethyl acetate 6:1, flow rate 4.0 ml, min^{-1}, 2400 psi) to give the less polar isomer **7** (oil), retention time 9.2 min. GC. (column 1, 150°): 16.2. - IR.: 1753, 1713. - ^{1}H-NMR. (360 MHz): 1.7-2.05 (7 H); 2.12 (*m*, 1 H); 2.34 (*d*, J = 18, 1 H; irradiation at 2.46 → br. *s*); 2.46 (*m*, 1 H); 2.48 (*d*, J = 18, 1 H); 2.55-2.70 (2 H); 2.71 (*m*, 1 H). - ^{13}C-NMR.: 218.8*s*, 210.4*s*, 61.0*d*, 51.3*t*, 48.6*s*, 46.2*d*, 44.8*t*, 38.1*t*, 36.3*t*, 29.1*t*, 23.6*t*. - MS.: 178 (97, $C_{11}H_{14}O_2^+$), 135 (27), 81 (100).

Further elution (HPLC.) afforded the more polar isomer **8** (oil), retention time 10.3 min. GC. (column 1, 150°): 17.05. - IR.: 1757, 1724. - ^{1}H-NMR. (360 MHz): 1.55-1.95 (6 H); 1.90 (br. *d*, J = 19, 1 H; irradiation at 2.17 → br. *s*); 2.07 ($d \times d$, J = 4 and 12, 1 H; irradiation at 2.34 → d, J = 4); 2.17 ($d \times d$, J = 4 and 19, 1 H; irradiation at 1.90 → t, J = 4); 2.34 ($d \times d \times d$, J = 2 and 5 and 12, 1 H; irradiation at 2.07 → m; irradiation at 2.83 → $d \times d$, J = 2 and 12); 2.42 ($d \times d \times d$, J = 2, 4 and 15, 1 H; irradiation at 2.83 → $d \times d$, J = 2 and 15); 2.54 ($d \times d$, J = 4 and 15, 1 H; irradiation at 2.83 → d, J = 15); 2.63 (*t*, J = 9, 1 H; irradiation at 1.83 → br. *s*); 2.83 (*qa*, J = 4, 1 H). - ^{13}C-NMR.[8]: 214.9*s*, 207.1*s*, 61.4*d*, 50.6*s*, 50.1*d*, 45.5*t*, 44.8*t*, 40.3*t*, 36.4*t*, 21.4*t*, 20.8*t*. - MS.: 178 (100, $C_{11}H_{14}O_2^+$), 135 (90), 108 (53), 93 (35), 81 (80), 79 (48), 67 (28), 55 (29).

---

8) The ^{13}C-NMR. signals of **8** were assigned by subtracting the spectrum of **7** from that of a mixture of **7** and **8**.

b) *Fragmentation of the isolated photoproducts.* Boron trifluoride etherate (1 drop) was added to a solution of the isolated photoproduct **4a** (7 mg) in dry benzene (3 ml). The mixture was stirred at 20° for 20 min to give, after the usual work-up and bulb-to-bulb distillation, the diketone **6**, identified by TLC. (toluene/ethyl acetate 7:3) and GC. (column 1). An identical experiment with **5a** furnished a mixture of the diketones 7 and **8**.

Acid-catalyzed interconversion of the diketones 7 and 8. - a) *By silica gel.* A solution of 7 (4.6 mg, isolated by HPLC.) was stirred with silica gel (0.2 g) in ethyl acetate (3 ml) at 20° for 15 h. Filtration and evaporation of the solution gave an oil (4.4 mg) which was unchanged 7 (HPLC.: 2 μ-Porasil columns in series, hexane/ethyl acetate 4:1, flow rate 4 ml, min^{-1}, 2200 psi). An identical experiment with **8** (4.2 mg) gave a 1:9 mixture (4.2 mg, analyzed by HPLC. as above) of 7 and **8**.

b) *By boron trifluoride etherate.* Boron trifluoride etherate (2 drops) was added to a solution of 7 (4.4 mg) in dry benzene (0.5 ml). The solution was stirred at 20° for 30 min to give after the usual work-up a 9:1-mixture (4.2 mg, analyzed by HPLC. as described above) of 7 and **8**. An identical experiment with **8** (4.2 mg) gave a 1:4 mixture (4.0 mg, analyzed by HPLC. as above) of 7 and **8**.

Preparation of the isobutoxydienone 3b and its conversion to the diketones 7 and 8. - *5-(1-Cyclopentenylmethyl)-3-isobutoxy-2-cyclopenten-1-one* (**3b**). 3-Isobutoxy-2-cyclopenten-1-one[7] **1b** (0.30 g, 2.0 mmol) was successively treated with lithium diisopropylamide and 1-bromomethyl-1-cyclopentene (**2**) as described above for the transformation **1a**→**3a** to give after bulb-to-bulb distillation (bath 140-150°/0.22 Torr) the dienone **3b** as a colourless oil (0.31 g, 67%). - IR. (film): 1700, 1600, 1355, 1175, 1000. - ^{1}H-NMR.: 1.00 (*d*, $J=7$, 1 H); 1.75-2.45 (9 H); 2.5-2.85 (3 H); 3.75 (*d*, $J=6$, 2 H); 5.25 (*s*, 1 H); 5.40 (br. *s*, 1 H).

b) *Conversion of the dienone* **3b** *into the diketones* **6**, **7** *and* **8**. Irradiation of a solution of **3b** (191 mg, 0.81 mmol) in cyclohexane (150 ml) through Pyrex at 15° using a 125 W medium pressure Hg-lamp *(Philips)* for 9 h followed by evaporation of the solution gave a colourless oil (196 mg), TLC. (toluene/ethyl acetate 9:1): 3 spots, Rf 0.75, 0.50 and 0.45. Boron trifluoride etherate (2 drops) was added to stirred solution of the crude mixture (136 mg) in dry benzene (50 ml) at + 10°. The solution was stirred for 30 min then poured into a saturated aqueous solution of NH_4Cl and subjected to the usual work-up to give an oil (107 mg). GC. (column 1, 140°) of this oil showed 4 peaks: 15.2 (19), 16.7 (33), 20.8 (9) and 24.9 (38) which correspond to the crude products obtained from **3a**. Chromatography (hexane/ethyl acetate 9:1) of the crude mixture (100 mg) gave the dione **6** (14 mg), fractions containing **6**, 7 and **8**, followed by a mixture of 7 and **8** (39 mg) identified by TLC. (hexane/ethyl acetate 3:7) and GC. (column 1) comparison.

REFERENCES

[1] *E. Piers & J. Banville,* J. chem. Soc. Chem. Commun. *1979,* 1138.

[2] *E.J. Corey, R.L. Danheiser, S. Chandrasekaran, P. Siret, G.E. Keck & J.L. Gras,* J. Amer. chem. Soc. *100,* 8031 (1978); *E.J. Corey & J.G. Smith,* ibid. *101,* 1038 (1979); *A. Alexakis, M.J. Chapdelaine & G.H. Posner,* Tetrahedron Letters *1978,* 4209.

[3] *W. Oppolzer & T.G.C. Bird,* Helv. *62,* 1199 (1979).

[4] *P. de Mayo,* Accounts chem. Res. *4,* 41 (1971).

[5] *W. Oppolzer & T. Godel,* J. Amer. chem. Soc. *100,* 2583 (1978).

[6] *W. Oppolzer & R.D. Wylie,* reported at The Chemical Society, Second East Midlands Regional Symposium, December 1979.

[7] *M. Mellor, D.A. Otieno & G. Pattenden,* J. chem. Soc. Chem. Commun. *1978,* 138.

[8] *G. Stork & R.L. Danheiser,* J. org. Chemistry *38,* 1775 (1973).

[9] a) *Y. Tamura, Y. Kita, H. Ishibashi & M. Ikeda,* J. chem. Soc. Chem. Commun. *1971,* 1167; b) *Y. Tamura, H. Ishibashi, Y. Kita & M. Ikeda,* ibid. *1973,* 101; c) *Y. Tamura, Y. Kita, H. Ishibashi & M. Ikeda,* Tetrahedron Letters *1972,* 1977.

[10] *N.J. Turro,* 'Modern Molecular Photochemistry', Benjamin/Cummings, Menlo Park 1978, p. 429 and 458 and references cited therein.

[11] *J.M. McIntosh & P.M. Beaumier,* Canad. J. Chemistry *51,* 843 (1973).

[12] *H.N.A. Al-Jallo & E.S. Waight,* J. chem. Soc. B *1966,* 73.

[13] *C. Ruangsiyanand, H.J. Rimek & F. Zymalkowski,* Chem. Ber. *103,* 2403 (1970).

[14] *P.R. Pal, C.G. Skinner, R.L. Dennis & W. Shive,* J. Amer. chem. Soc. *78,* 5116 (1956).