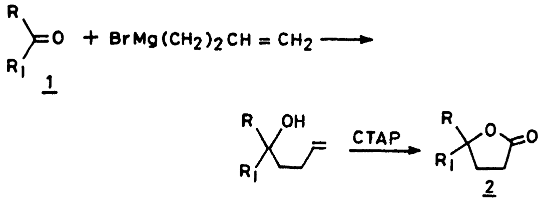
A Simple Iterative Approach to the Synthesis of *cis-cisoid-cis*-Tricyclo[6.3.0.0^{2,6}]undecane Carbon Skeleton

Padma S. Vankar and Srinivasan Chandrasekaran*
Department of Chemistry, Indian Institute of Technology, Kanpur 208016, India

(Received September 5, 1988)

Synopsis. In an iterative synthesis utilizing only four reagents, cyclopentanone has been converted into *cis-cisoid-cis*-tricyclo[6.3.0.0^{2,6}]undecane carbon skeleton in high yield.

There is much current interest in the synthesis of linearly fused tricyclopentanoids (triquinanes) which is mainly due to their wide occurance in nature with promising biological properties and their likely role as building blocks for the synthesis of the $C_{20}H_{20}$ regular (pentagonal) polycycle, dodecahedrane.[1] As a result, several novel approaches to this ring system have been developed in recent years.[2] In the course of our studies on oxidative transformations with hexadecyltrimethylammonium permanganate (CTAP)[3] we developed a general two step methodology for the synthesis of γ-lactones **2** from ketones **1** (Scheme 1) in very good yield.[4]

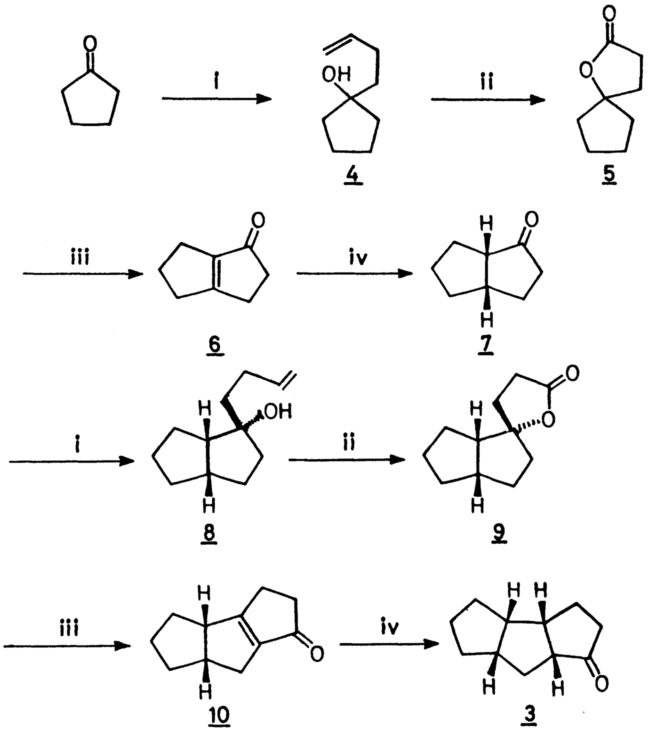


Scheme 1.

Herein, we report an efficient application of this oxidative cyclization strategy in an iterative approach to set up the *cis-cisoid-cis*-tricyclo[6.3.0.0^{2,6}]undecane carbon skeleton. It is anticipated that easy accessibility to **3** and its derivatives would open new possibilities for further synthetic exploitation.

Reaction of cyclopentanone with Grignard reagent derived from 4-bromo-1-butene[5] gave the alcohol **4**[6] (62%) which was then subjected to oxidative cyclization with hexadecyltrimethylammonium permanganate (CTAP) to yield the spirolactone **5**[4] (71%). Treatment of the lactone **5** with phosphorus pentaoxide in methanesulfonic acid[8] for 2 h at 50 °C led to the bicyclic enone **6**[8] (98%). Hydrogenation of **6** in ethyl acetate containing palladium on carbon produced the saturated cis-bicyclic ketone **7**[9] (99%).

To continue the synthesis the bicyclic ketone **7** was subjected to the same sequence of reactions. Thus, reaction with the Grignard reagent produced the adduct **8** (64%). Oxidative cyclization with CTAP afforded the spirolactone **9** (60%). On action of phosphorus pentaoxide in methanesulfonic acid the lactone **9** yielded the tricyclic enone **10** (92%). Catalytic hydrogenation of **10** with palladium on carbon resulted in the cis addition of hydrogen to the less hindered face of the olefin[10] to give the product **3** (95%) (Scheme 2).



Scheme 2. Reagents:
i, $BrMgCH_2CH_2CH=CH_2$; ii, CTAP, CH_2Cl_2; iii, P_2O_5–$MeSO_3H$; iv, Pd/C, H_2

Experimental

The NMR spectra were taken on a Varian EM-390 spectrometer and Brucker WP-80 spectrometer. IR spectra were measured using a Perkin Elmer 1320 spectrometer and mass spectra were obtained from a VG micromass 7070F mass spectrometer.

Oxidative Cyclization of 4 with CTAP. To a solution of **4**[6] (1.4 g, 10 mmol) in chloroform (30 ml) was added a solution of CTAP (8.08 g, 20 mmol) in chloroform (25 ml) at room temperature (28 °C) and the mixture was stirred for 6 h. Solvent was evaporated under reduced pressure and ether (200 ml) was added to the residue which was filtered through a pad of Celite. The filter cake was washed thoroughly with ether and the combined filtrate was evaporated. The residue was purfied by flash chromatography on silica gel (elution with 4 : 1 ether–petroleum ether) to get the spirolactone **5**[4] (0.980 g, 71%) as a colorless oil. IR(CCl_4) 1780 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ=1.5—2.35 (m, 10H) and 2.4—2.7 (m, 2H); MS *m/z* 140 (M^+).

Reaction of 5 with Methanesulfonic Acid–Phosphorous Pentaoxide. A solution of **5** (0.700 g, 5 mmol) in freshly distilled methanesulfonic acid (50 g) containing phsophorus pentaoxide (5 g) was stirred under nitrogen at 50 °C for 2 h. The mixture was cooled in an ice bath and water (150 ml) was carefully added. It was then extracted with ether (3×100 ml). The combined ether extract was washed with 10% potassium carbonate solution and water and then dried over anhydrous magnesium sulfate. After evaporation of solvent the product was purified by flash chromatography on silica gel (elution with 1 : 10 ether-petroleum ether) to afford **6**[8] (0.600 g, 98%) as a colorless oil. IR(CCl_4) 1645, 1710 cm^{-1}; ^1H NMR($CDCl_3$) δ=1.8—2.0 (m, 2H) and 2.3—2.7 (m, 8H): MS *m/z* 122 (M^+).

Catalytic Hydrogenation of 6. To a solution of **6** (0.610 g, 5 mmol) in ethyl acetate (20 ml) was added 5% palladium on charcoal (0.100 g) and treated with hydrogen at 40 psi for 1 h. The catalyst was filtered and the solvent was evaporated to yield the bicyclic ketone **7**[9] (0.605 g, 99%) as an oil. IR(CCl_4) 1735 cm^{-1}; ^1H NMR($CDCl_3$) δ=1.4—2.0 (m, 9H), 2.2—2.4 (m, 2H), and 2.5—2.7 (m, 1H); MS *m/z* 124 (M^+).

Grignard Reaction of 7 with 4-Bromo-1-butene. Grignard reagent derived from 4-bromo-1-butene[5] (1.35 g, 10 mmol) and magnesium powder (0.288 g, 12 mmol) in dry THF (25 ml) was treated with **7** (1.240 g, 10 mmol) in dry THF (10 ml) at 0 °C for 1 h. The product was purified by flash chromatography on silica gel (elution with 1 : 2 ether-petroleum ether) to yield the alcohol **8** (1.152 g, 64%) as a coloress oil. IR(CCl_4) 3480, 3080, 1640 cm^{-1}; ^1H NMR ($CDCl_3$) δ=1.2—2.0 (m, 15H), 2.1—2.3 (m, 2H), 4.8—5.1 (m, 2H), and 5.5—5.9 (m, 1H); MS *m/z* 180 (M^+). Found: *m/z* 180.1510. Calcd for $C_{12}H_{20}O$: M, 180.1515.

Oxidative Cyclization of 8 with CTAP. To a solution of **8** (0.360 g, 2 mmol) in dichloromethane (8 ml) was added CTAP (1.62 g, 4 mmol) in dichloromethane (10 ml) and the mixture was stirred at room temperature for 4 h. The product after purification by flash chromatography on silica gel (elution with 1 : 2 ether-petroleum ether) yielded the spiro lactone **9** (0.216 g, 60%) as an oil. IR(neat) 1770 cm^{-1}; ^1H NMR ($CDCl_3$) δ=1.3—1.8 (m, 14H) and 2.2—2.5 (t, 2H); MS *m/z* 180 (M^+).

Reaction of 9 with Methanesulfonic Acid-Phosphorus Pentaoxide. A solution of **9** (0.360 g, 2 mmol) in freshly distilled methanesulfonic acid (30 g) was added to phsophorus pentaoxide (3 g) and the mixture was heated under nitrogen at 50 °C for 2 h. The product was worked up as described in the synthesis of **6**. The tricyclic enone **10** (0.300 g, 92%) was isolated as an oil after chromatographic purification. IR(neat) 1700, 1640 cm^{-1}; ^1H NMR ($CDCl_3$) δ=1.3—1.8 (m, 7H) and 2.1—2.6 (m, 7H); MS *m/z* 162 (M^+). Found: *m/z* 162.1041. Calcd for $C_{11}H_{14}O$: M, 162.1045.

Catalytic Hydrogenation of 10. A solution of **10** (0.162 g, 1 mmol) in ethyl acetate (5 ml) was added to 5% Pd–C and treated with hydrogen at 40 psi for 2 h. The ctalyst was filtered and the solvent was removed to give the tricyclic ketone **3** (0.155 g, 95%) as an oil homogeneous to TLC. IR(neat) 1725 cm^{-1}; ^1H NMR ($CDCl_3$) δ=1.2—2.0 (m, 13H) and 2.2—2.6 (m, 3H); MS *m/z* 164 (M^+). Found: *m/z* 164.1198. Calcd for $C_{11}H_{16}$: M, 164.1201.

The authors are thankful to DST, New Delhi for financial support.

References

1) G. Mehta, *J. Sci. Ind. Res. (India)*, **37**, 256 (1978): L. A. Paquette, *Topics in Current Chemistry*, **79**, 43 (1979); P. E. Eaton, *Tetrahedron*, **35**, 2189 (1979).

2) L. A. Paquette, *Topics in Current Chemistry*, **119**, 1 (1984); L. A. Paquette, Y. Miyahara, and C. W. Doecke, *J. Am. Chem. Soc.*, **108**, 1716 (1986).

3) V. Bhushan, R. Rathore, and S. Chandrasekaran, *Synthesis*, **1984**, 431.

4) R. Rathore, P. S. Vankar, and S. Chandrasekaran, *Tetrahedron Lett.*, **27**, 4079 (1986).

5) G. A. Kraus and L. Langrebe, *Synthesis*, **1984**, 885.

6) G. E. Gream, A. K. Serelis and T. I. Stoneman, *Aust. J. Chem.*, **27**, 1711 (1974).

7) P. E. Eaton and R. H. Mueller, *J. Am. Chem. Soc.*, **94**, 1015 (1972).

8) S. Dev and C. Rai, *J. Ind. Chem. Soc.*, **34**, 266 (1957); F. Cooke, R. Moerck, J. Schwindeman, and P. Magnus, *J. Org. Chem.*, **45**, 1046 (1980); A. C. Cope and W. Schmitz, *J. Am. Chem. Soc.*, **72**, 3056 (1950); H. Jones and H. T. Taylor, *J. Chem. Soc.*, **1959**, 4017; G. Mehta and K. S. Rao, *Tetrahedron Lett.*, **25**, 1839 (1984).

9) B. M. Trost and M. J. Bogdanowicz, *J. Am. Chem. Soc.*, **95**, 5311 (1973); A. C. Cope, M. Brown, and H. E. Petree, *ibid.*, **80**, 2852 (1958); Y. Fujikura, N. Takaishi, and Y. Inamato, *Tetrahedron*, **37**, 4465 (1981).

10) P. E. Eaton, R. S. Sidhu, G. E. Langford, D. A. Cullison, and C. L. Pietruszewski, *Tetrahedron*, **37**, 4479 (1981).