Tetrahedron Vol. 45, No. 10, pp. 3107 to 3114, 1989
Printed in Great Britain.

0040-4020/89 $3.00+.00

A SIMPLE AND EFFICIENT ROUTE TOWARDS USEFULLY FUNCTIONALISED SIX AND SEVEN-MEMBERED RING SYSTEMS VIA α-HYDROXYCYCLOBUTANE REARRANGEMENT FOLLOWED BY RETROALDOL CLEAVAGE[1]

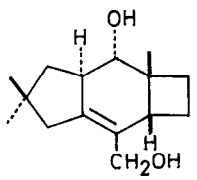
Brindaban C. Ranu,* Dipak C. Sarkar and Manas K. Basu

Department of Organic Chemistry, Indian Association for the Cultivation of Science, Jadavpur, Calcutta - 700 032, INDIA

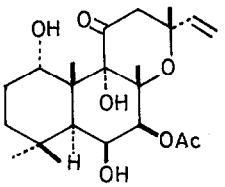
(*Received in Belgium* 22 *July* 1988)

Abstract - Acid-catalysed rearrangement of α-hydroxycyclobutane derivative 10 followed by retroaldol cleavage and oxidation in an one-pot operation furnishes 1β-methyl-1α,4α-cycloheptane dicarboxylic acid 12 in excellent yield. With proper selection of starting α-hydroxycyclobutane derivative this methodology leads to highly functionalised /5-7/ and /5-6/ fused ring systems 17 and 20 respectively.

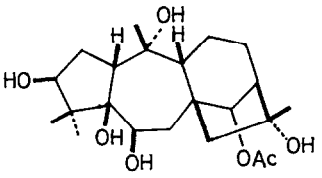
During the last two decades a wide variety of natural products bearing six and seven-membered ring as the core of their polycarbocyclic frameworks have been isolated[2] from marine, plant, insect and microbial sources and many of them have been shown to possess promising biological activities. Some typical examples of current interest are sterpurene sesquiterpenes[3] 1, forskolin[4] 2, grayanotoxins[5] 3, sipholenones[6] 4, and dolastane type diterpenoids[7] 5.



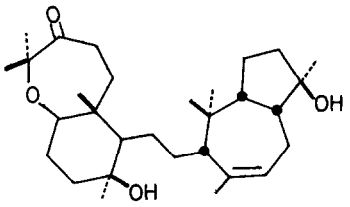
7,12-Dihydroxysterpurene 1



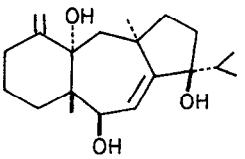
Forskolin 2



Grayanotoxin-1 3



Sipholenone-A 4



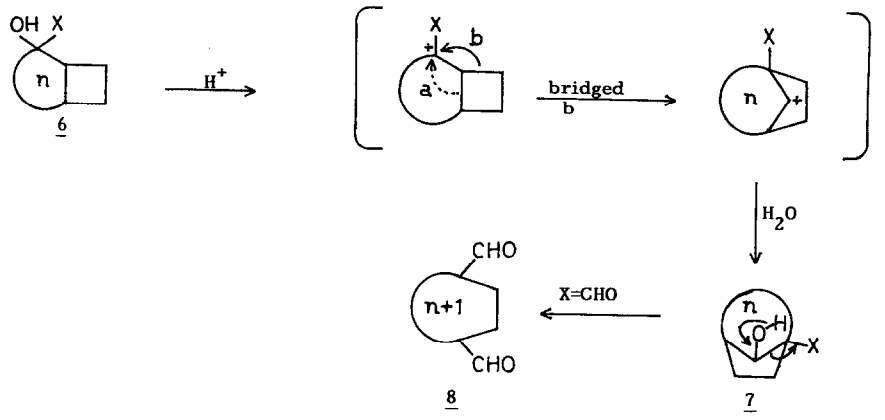
Dolatriol 5

The complexity in chemical structures of these compounds combined with associated biological activities have attracted intense attention[3-7] of the chemical community for synthetic studies. An important step towards synthesis of a polycarbocyclic molecule is the basic skeletal construction with appropriate functionalisation which often governs the step economy and the total yield. Thus,

numerous elegant methodologies have been developed during recent times for the construction of six[8] and seven-membered[9] carbocyclic systems, but there still remain several problems especially on the generality or efficacy of the procedures. In this paper, we describe a simple and efficient methodology for the construction of usefully functionalised six and seven-membered carbocycles.

The key concept in our synthetic approach is the solvolytic rearrangement of a suitably substituted α-hydroxycyclobutane derivative 6 in an aqueous acidic medium as delineated in Scheme 1. In cyclobutyl cation rearrangement[10] there are two alkyl shifts available which possess the driving force of relief of the cyclobutane strain. One would anticipate that the principle of maximum continuous orbital overlap would predict the favoured pathway. Thus, 'bridged' migration (path b) allowing perfect overlap of the migrating bond with the p-orbital at the carbinyl centre should be the preferred one, while 'fused' migration (path a) would seem to be constrained to occur in the nodal plane of the orbital.[10a,10h,10n] The bicyclic bridged unit 7 arising from the path b,[10b,10i] if substituted with formyl or acetyl group (X = CHO or COR) at the bridgehead, can undergo retroaldol cleavage[11] to give the rearranged carbocycle 8.

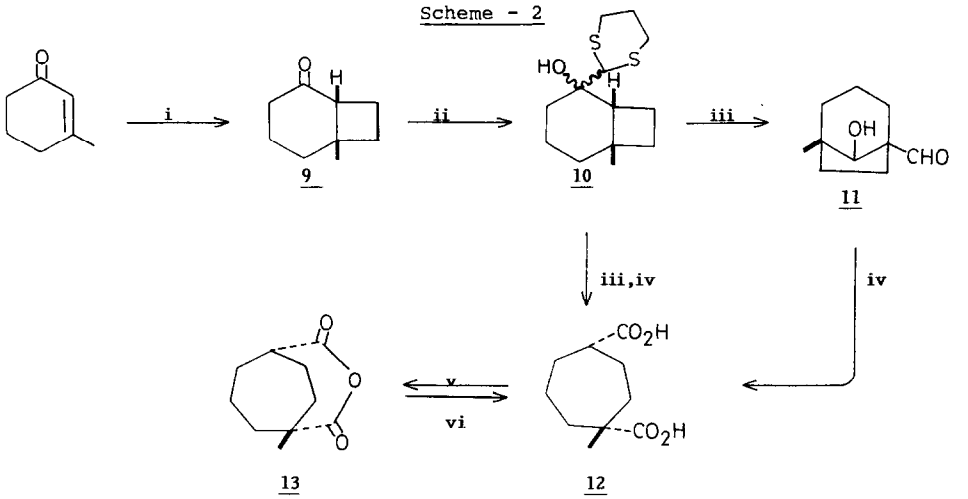
Scheme - 1



In order to explore the practical feasibility of the synthetic strategy delineated in Scheme 1, the α-hydroxycyclobutane derivative 10 was prepared in 90% yield by the reaction of 2-lithio derivative of 1,3-dithiane[12] with 6-methylbicyclo[4.2.0]octan-2-one 9 [13] (Scheme 2). This alcohol 10 when treated with HBF_4 and mercuric oxide (red) in aqueous tetrahydrofuran[12] underwent rearrangement to give a relatively unstable hydroxyaldehyde 11. As the aldehyde 11 started decomposing to a mixture of unidentified products on keeping even in a refregerator, the experiment was redesigned in which as soon as the starting alcohol 10 disappeared from the reaction mixture as indicated by TLC, the reaction mixture was titrated with Jones reagent[14] at 0-5°C in the same operation to afford the crystalline dicarboxylic acid 12, m.p. 113°C, in 70% yield. Obviously, the alcohol 10 undergoes a cyclobutyl cation rearrangement as depicted in Scheme 1 and simultaneous deprotection to give the hydroxyaldehyde 11 which then suffers a retroaldol cleavage and oxidation with Jones reagent to furnish the dicarboxylic acid 12. The intermediacy of the hydroxyaldehyde 11 in the rearrangement of alcohol 10 to dicarboxylic acid 12 under this one-pot operation is established by the treatment of the hydroxyaldehyde 11, just after isolation, with Jones reagent to give the diacid 12. The isolated yield of the acid 12 in the two-step procedure is lower than that in the one-pot operation, possibly due to decomposition of the hydroxyaldehyde 11. The homogeneity of the dicarboxylic acid 12 was indicated by GLC, TLC and ^1H NMR data of its methyl ester (CH_2N_2) (3 Me singlets at δ 1.20, 3.62 and 3.64). The relative stereochemistry of the two CO_2H groups in 12

was assigned as cis on the basis of the quantitative formation of an anhydride 13, IR 1810, 1740 cm^{-1} and its regeneration to the same acid 12. Thus this rearrangement is found to be stereospecific as most of the rearrangements of bridged compounds to fused-ring systems are.[15]

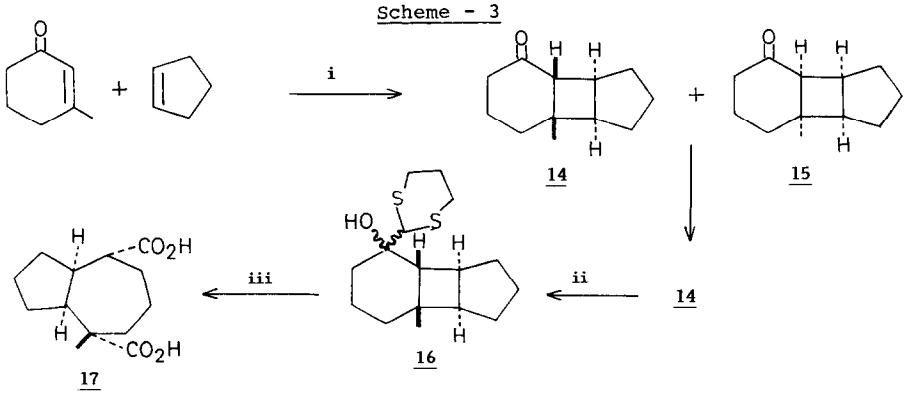
Scheme - 2



Reagents : i) $CH_2{=}CH_2$, hν, CH_2Cl_2 ; ii) 1,3 - dithiane, n-BuLi, THF; iii) HgO(red), HBF_4(48%), THF(15%); iv) Jones reagent; v) Ac_2O; vi) H_2O, warm, 100%

We next focussed our attention to expand the scope of this synthetic strategy for the construction of fused seven-membered ring system, the basic skeleton of a large number of natural products. Irradiation of 3-methyl-2-cyclohexenone with cyclopentene followed by treatment with alumina[16,10b] produced cis-transoid-cis tricycloundecanone 14 and corresponding cis-cisoid-cis isomer 15 in ca 2:1 mixture. During efforts of separation of this mixture we have observed that only the cis-transoid-cis isomer 14 forms a semicarbazone whereas the isomer 15 remains unaffected.[17] Pure 14[16] was obtained by regeneration of the semicarbazone following our methodology[18] with Dowex-50. Reaction of 14 with 2-lithio derivative of 1,3-dithiane then produced the alcohol 16 (Scheme 3) in 87% yield which was treated with HgO, HBF_4 followed by Jones reagent in an one-pot operation as above to afford a dicarboxylic acid 17,[19] m.p. 184°C, in 77% yield. The acid 17 clearly arises by retroaldol cleavage followed by oxidation of the analogous bicyclo[3.2.1]octane derivative as 11 in Scheme 2, generated by the 'bridged' migration[20] (Scheme 1) of the cyclobutyl alcohol derivative 16 .

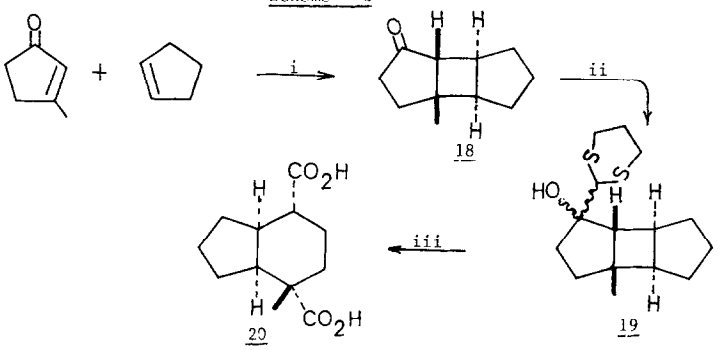
Scheme - 3



Reagents : i) hν , cyclohexane; ii) 1,3 - dithiane, n-BuLi, THF; iii) HgO(red), HBF_4 (48%), THF (15%)

To test the general applicability of this methodology for the construction of fused six-membered carbocycles, an appropriate tricyclo[5.3.0.0^{2,6}]decane derivative 18 was obtained as a single stereoisomer (cis-transoid-cis) by the photocycloaddition of 3-methylcyclopentenone and cyclopentene[21] in 87% yield (Scheme 4). Reaction of 2-lithio derivative of 1,3-dithiane with this ketone 18 afforded the corresponding alcohol 19 in 84% yield which was then treated under identical conditions with HBF_4, HgO and Jones reagent to give the cyclohexane dicarboxylic acid 20, m.p. 161°C (Scheme 4) in 75% yield.

Scheme - 4



Reagents: i) hν, cyclohexane; ii) 1,3-dithiane, n-BuLi, THF; (iii) HBF_4. HgO(red), THF (15%), Jones reagent.

Our converging synthetic strategy described herein, thus demonstrates an efficient and convenient methodology for the stereospecific synthesis of usefully functionalised derivatives of six and seven-membered ring systems in three steps and in good overall yield from readily available cycloalkenones and cycloalkenes. We believe, this new versatile synthetic approach for construction of functionalised carbocyclic skeleta will prove to be a useful addition to the armory of methods available to synthetic chemists and is endowed with great potential for elaboration to a wide variety of natural products.

EXPERIMENTAL

General : Melting points were determined with an electrical bath (Gallenhamp, England) in open capillary tubes and are uncorrected. IR spectra were recorded on a Perkin-Elmer Model 298 spectrometer and ^{1}H NMR spectra were obtained at 60 MHz on Varian EM 360, at 100 MHz on Jeol FX-100 and at 200 MHz on Varian XL-200 spectrometers in CCl_4 or $CDCl_3$ solutions, using tetramethylsilane as an internal standard. Thin layer chromatography was done on precoated silica gel plates (Eastman Kodak Co). Column chromatography was carried out with silica gel (B.D.H. India). Tetrahydrofuran (THF) was distilled from benzophenone-potassium under nitrogen, immediately prior to use. Elemental analyses were performed on Perkin Elmer 240C autoanalyser and by Mr. P.P. Bhattacharya of this laboratory. GLC was done on a Shimadzu GC-9A instrument using column OV-17 (2 m) and nitrogen as carrier gas. A medium pressure 450 W Hanovia lamp is used for irradiation during photolysis.

6-Methylbicyclo[4.2.0]octan-2-one (9). Ethylene gas was uniformly passed through a solution of 3-methyl-2-cyclohexenone (10 g, 0.09 mol) in methylene chloride (100 ml), cooled at -40°C (cooling bath), while being irradiated. The reaction was monitored by IR and ^{1}H NMR. After complete conversion (12 h) the reaction mixture was allowed to come to room temperature and dried over Na_2SO_4. Evaporation of solvent left a pale yellow oil which was distilled (b.p. 62-65°/3.5 mm) to give pure product 9[13] (7.5 g, 60%).

1β-Methyl-7β,2α,6α-tricyclo[5.4.0.0^{2,6}]undecan-8-one (14). 3-Methyl-2-cyclohexenone (6.0 g, 0.05 mol) and cyclopentene (18 g, 0.264 mol) in cyclohexane (100 ml) were irradiated at 0 to -10°C (ice-salt bath) under nitrogen. After completion of the reaction (monitored by IR and ^{1}H NMR, 10 h) the reaction mixture was dried over Na_2SO_4 and evaporated to leave a pale yellow oil. This oil was now passed through a column of basic alumina to provide a colourless oil (8.92 g, 92%) which is found to be a mixture of cis-transoid-cis isomer 14 and cis-cisoid-cis isomer 15 in the percentage composition of 62:38 as determined by ^{1}H NMR (Me-singlets at δ 0.94 and 1.30 characteristic of 14 and 15 respectively).[16]

The mixture of 14 and 15 (1 g, 5.6 mmol) was shaken well with a solution of sodium acetate (10 g) and semicarbazide hydrochloride (3 g) in water (15 ml) and kept in the refregerator for 5 h. A semisolid mass separated out and was extracted with ethyl acetate (3 x 40 ml). The ethyl acetate

extract was washed with water, dried over Na_2SO_4 and evaporated to leave a highly viscous mass which was washed with petroleum ether (60-80°) several times. The residual mass then solidified and was recrystallized from methanol to provide needle shaped crystal (600 mg), m.p. 184°C. This semicarbazone (424 mg, 1.8 mmol) was then refluxed in an aqueous (30 ml) suspension of Dowex-50 (1 g) for 5 h and filtered. The filtrate was extracted with petroleum ether (60-80°) (3 x 30 ml). The petroleum ether extract was dried over Na_2SO_4 and evaporated to furnish pure 14 (230 mg, 72%), IR (neat) 1690 cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$) δ 0.94 (s, 3H), 1.30-2.72 (m, 15 H).

1β-Methyl-7β,2α,6α-tricyclo[5.3.0.0^{2,6}]decan-8-one (18). 3-Methyl-2-cyclopentenone (1.3 g, 13.5 mmol) and cyclopentene (3.0 g, 44 mmol) in cyclohexane (100 ml) were irradiated under identical conditions as above for 12 h. The reaction mixture was dried (Na_2SO_4) and evaporated to leave a yellow oil which was sublimed at 0.2 mm of Hg (bath temperature 100-120°C) to afford 18 (1.94 g, 87%) as colourless oil, IR (neat) 1735 cm^{-1}; ^1H NMR (60 MHz, CCl_4) δ 1.0 (s, 3H), 1.48-2.60 (m, 13H). Anal. calcd for $C_{11}H_{16}O$: C, 80.46; H, 9.82. Found : C, 80.16; H, 9.82.

2-(2β-Hydroxy-6β-methyl-1β-bicyclo[4.2.0]octyl)1,3-dithiane (10). To a stirred solution of 1,3-dithiane (1.2 g, 10 mmol) in dry THF (40 ml) at -10°C (ice-salt bath) was added n-butyl lithium (12.5 ml of 1 M solution in hexane, 800 mg, 12.5 mmol) dropwise under nitrogen. Stirring was continued at -10°C for 2 h and the ketone 9 (1.2 g, 9 mmol) in THF (5 ml) was added dropwise. The mixture was stirred for another half an hour and stored at 0°C (refregerator) overnight (18 h). The reaction mixture was poured into water, saturated with NaCl and extracted with ether (4 x 30 ml). The ether extract was dried (Na_2SO_4) and evaporated to leave a yellow viscous liquid which was sublimed (bath temperature 180°C) at 0.1 mm of Hg to give 10 (some unreacted 1,3-dithiane and ketone 9 were recovered as low boiling fractions) as a pale yellow viscous liquid (1.5 g, 90%), IR (neat) 3600-3200 (broad), 920 cm^{-1}; ^1H NMR (60 MHz, CCl_4) δ 1.06 (s, 3H), 1.27-2.39 (m, 14H), 2.66-3.0 (m, 4H), 4.03 (s, 1H). Anal. calcd for $C_{12}H_{22}OS_2$: C, 60.44; H, 8.59. Found : C, 60.66; H, 8.84.

2-(8β-Hydroxy-1β-methyl-7β,2α,6α-tricyclo[5.4.0.0^{2,6}]undecyl)1,3-dithiane (16). The alcohol 16 was prepared in 87% yield from the ketone 14 (200 mg, 1.1 mmol) by treatment with 2-lithio derivative of 1,3-dithiane [made from 1,3-dithiane (150 mg, 1.2 mmol) and n-butyl lithium (80 mg, 1.25 mmol)] under identical procedure as above; IR (neat) 3540-3360 (broad), 910 cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$) δ 0.84 (s, 3H), 1.40-2.24 (m, 18H), 2.87 (m, 4H), 4.08 (s, 1H). Anal. calcd for $C_{16}H_{26}OS_2$: C, 64.40; H, 8.78. Found : C, 64.49; H, 9.06.

2-(8β-Hydroxy-1β-methyl-7β,2α,6α-tricyclo[5.3.0.0^{2,6}]decyl)1,3-dithiane (19). The ketone 18 (410 mg, 2.5 mmol) was treated with lithio derivative of 1,3-dithiane, prepared from 1,3-dithiane (320 mg, 2.6 mmol) and n-BuLi (167 mg, 2.6 mmol) under identical conditions as stated before for 10 to furnish 19 as a heavy viscous liquid (600 mg, 84.5%), IR (neat) 3580-3400 (b), 910 cm^{-1}; ^1H NMR (60 MHz, CCl_4) δ 0.91 (s, 3H), 1.24-2.21 (m, 16 H), 2.66-3.00 (m, 4H), 3.88 (s, 1H). Anal. calcd for $C_{15}H_{24}OS_2$: C, 63.36; H, 8.51. Found : C, 63.61; H, 8.57.

1-Methyl-5-formyl-8-hydroxybicyclo[3.2.1]octane (11). The alcohol 10 (200 mg, 0.78 mmol) in THF (5 ml) was added dropwise to a stirring suspension of mercuric oxide (red) (340 mg, 1.5 mmol) and fluoboric acid (48%) (135 mg, 1.5 mmol) in THF (15% aqueous, 15 ml), heated at 50-60°C (oil bath) under nitrogen. The reaction mixture was stirred at that temperature for 3 h (with the progress of the reaction, red mercuric oxide gradually dissolved and white precipitate appeared) for complete conversion (monitored by TLC), cooled, diluted with ether (50 ml) and filtered. The filtrate was washed with water, 5% sodium bicarbonate solution, brine, dried (Na_2SO_4) and evaporated to leave the hydroxyaldehyde 11 as a yellow oil (110 mg, 85%), IR (neat)[22] 3600-3100 (broad), 2715 (w), 1720 (s) cm^{-1}; ^1H NMR (60 MHz, CCl_4)[22] δ 1.06 (s, 3H), 1.58 (m, 10H), 4.27 (broad, 1H), 4.70 (broad, 1H), 7.00 (s, <1H). This compound is unstable and decomposes to mixture of unidentified products on keeping even in refregerator. Any attempt to purification by chromatography (silica gel or alumina) leads to rapid decomposition.

1β-Methyl-1α,4α-cycloheptanedicarboxylic acid (12). (a) The alcohol 10 (500 mg, 1.9 mmol) in THF (5 ml) was added dropwise to a stirring suspension of HgO (red) (850 mg, 3.9 mmol) and fluoboric acid (48%) (350 mg, 4 mmol) in THF (15% aqueous, 25 ml) heated at 50-60°C, under nitrogen. The reaction mixture was monitored by TLC for complete conversion (disappearance of alcohol 10 in TLC) and after it was achieved (3 h) the reaction mixture was cooled to 0°C and titrated with Jones reagent till the colour of Jones reagent persisted for 5 mins. After being stirred for another 10 mins, the reaction mixture was diluted with water (100 ml), saturated with NaCl and extracted with ether (3 x 30 ml). The ether phase was washed with water until acid-free and then extracted with 5% sodium bicarbonate solution. The bicarbonate washings were then acidified with dilute (1:1) HCl and extracted with ether (3 x 25 ml). The ether extract was washed with water, dried (Na_2SO_4) and evaporated to furnish a solid dicarboxylic acid 12 (271 mg, 70%), m.p. 112-113°C (ethyl acetate-petroleum ether (60-80°) as 1:4 mixture), IR (KBr) 3500 (b), 1708 cm^{-1}; ^1H NMR (100 MHz, $CDCl_3$) δ 1.24 (s, 3H), 1.64-2.48 (m, 10H), 2.88 (t, J = 8 Hz, 1H), 9.1 (broad, 2H). Anal. calcd for $C_{10}H_{16}O_4$: C, 59.98; H, 8.05. Found: C, 59.82; H, 8.06. A methyl ester of 12 was prepared using standard procedure with CH_2N_2, IR (neat) 1740 cm^{-1}, ^1H NMR (100 MHz, $CDCl_3$) δ 1.20 (s, 3H), 1.64-2.36 (m, 10H), 2.88 (t, J = 8 Hz, 1H), 3.62 (s, 3H), 3.64 (s, 3H).

(b) The crude hydroxy aldehyde 11 (110 mg, 0.65 mmol) in THF (10 ml) was titrated with Jones reagent at 0°C until the colour of Jones reagent persisted for 5 mins. Stirring was continued for another 10 mins. The reaction mixture was diluted with water (100 ml) and extracted with ether (3 x 30 ml). The ether phase was washed with water until acid-free and then extracted with 5% sodium bicarbonate solution. The bicarbonate washings were then acidified with dilute (1:1) hydrochloric and extracted with ether (4 x 20 ml). The ether extract was washed with water, dried (Na_2SO_4) and evaporated to leave a solid (50 mg, 38%) which was recrystallised from ethylacetate-petroleum ether (60-80°C) (1:4) to give pure 12, identical (m.p., IR, ^1H NMR) with the sample obtained by method a.

1β-Methyl-1α,4α-cycloheptane anhydride (13). The dicarboxylic acid (12) (50 mg, 0.25 mmol) was refluxed with freshly distilled acetic anhydride (1 ml) under anhydrous condition for 2 h. The reaction mixture was then evaporated under vacuum to give 13 as a viscous oil (44 mg, 97%), IR (neat) 1810, 1740 cm^{-1}; ^1H NMR (60 MHz, CCl_4) δ 1.27 (s, 3H), 1.6-2.94 (m, 11H). Anhydride 13 is very sensitive to moisture and is converted to acid 12 by warming with water.

6β-Methyl-1α,7α-bicyclo[5.3.0]decane-2α,-6α-dicarboxylic acid (17). The alcohol 16 (130 mg, 0.4 mmol) was treated with HgO (red)(200 mg, 0.9 mmol), fluoboric acid (100 mg, 1.1 mmol) in THF (15% aqueous, 15 ml) followed by Jones reagent under identical conditions as stated for 12 in a to furnish 17 (80 mg, 77%) as white crystals, m.p. 184°C (ethyl acetate-petroleum ether (60-80°C) as 1:3 mixture), IR (KBr) 3660-3450 (b), 1705 cm^{-1}; ^1H NMR (100 MHz, d_6-DMSO) δ 0.88 (s, 3H), 1.36-3.00 (m, 15H), 12.0 (broad, 2H). Anal. calcd for $C_{13}H_{20}O_4$: C, 64.98; H, 8.39. Found : C, 64.51; H, 8.17. A methyl ester of 17 was prepared with CH_2N_2, IR (neat) 1730 cm^{-1}; ^1H NMR (100 MHz, $CDCl_3$) δ 0.92 (s, 3H), 1.40-2.40 (m, 14H), 2.92-3.24 (m, 1H), 3.64 (s, 6H).

5β-Methyl-1α,6α-bicyclo[4.3.0]nonane-2α,5α-dicarboxylic acid (20). The acid 20 was obtained from the alcohol 19 (420 mg, 1.5 mmol) by treatment with HgO (red) (750 mg, 3.4 mmol) and HBF_4 (300 mg, 3.4 mmol) followed by titration with Jones reagent under identical conditions as mentioned for 12 in a as a white solid (250 mg, 75%), m.p. 161°C (ethyl acetate-petroleum ether (60-80°C) as 1:3 mixture), IR (KBr) 3500-3100 (b), 1710 cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$) δ 1.22 (s, 3H), 1.40-3.10 (m, 13H), 6.30-6.90 (broad, 2H). Anal. calcd for $C_{12}H_{18}O_4$: C, 63.70; H, 8.02. Found : C, 63.42; H, 8.29. A methyl ester of 20 was prepared with CH_2N_2, IR ($CHCl_3$) 1725 cm^{-1}; ^1H NMR (60 MHz, CCl_4) δ 1.06 (s, 3H), 1.50-3.10 (m, 13H), 3.57 (s, 6H).

Acknowledgements

We are grateful to Dr. R.V. Venkateswaran of this Department for his generous gift of some chemicals and helpful discussions. M.K.B. thanks CSIR, New Delhi, for awarding him a Junior Research Fellowship.

REFERENCES AND NOTES

1. For a preliminary report of part of this work, see : Ranu, B.C.; Sarkar, D.C. J. Chem. Soc. Chem. Commun. 1988, 245.

2. (a) Devon, T.K.; Scott, A. Handbook of Naturally Occurring Compounds; Academic Press, New York, 1972, Vol.2. (b) Glasby, J.S. Encyclopedia of the Terpenoids; Wiley Interscience, New York, 1982.

3. (a) Ayer, W.A.; Saeedi-Chomi, M.H.; Van Eggan, D.; Tagle, B.; Clardy, J. Tetrahedron 1981, 37, Suppl. No.1, 379. (b) Abell, C.; Leech, A.P. Tetrahedron Lett. 1987, 28, 4887. (c) Paquette, L.A.; Lin, H.S.; Coghlan, M.J. Tetrahedron Lett. 1987, 28, 5017. (d) Abell, C.; Leech, A.P. Tetrahedron Lett. 1988, 29, 1985.

4. (a) Ziegler, F.E., Jaynes, H.B.; Saindane, M.T. J. Am. Chem. Soc. 1987, 109, 8115. (b) Oplinger J.A.; Paquette, L.A. Tetrahedron Lett. 1987, 28, 5441. (c) Hashimoto, S.; Sakata, S.; Sonegawa, M.; Ikegami, S. J. Am. Chem. Soc. 1988, 110, 3670. (d) Corey, E.J.; Jardine, P.D.S.; Rohloff, J.C. J. Am. Chem. Soc. 1988, 110, 3672.

5. Kametani, T.; Matsumoto, H.; Honda, T.; Fukumoto, K. Tetrahedron 1981, 37, 3813.

6. Carmely, S.; Kashman, Y. J. Org. Chem. 1983, 48, 3517.

7. (a) Paquette, L.A.; Lin, H.S.; Belmont, D.T.; Springer, J.P. J. Org. Chem. 1986, 51, 4807. (b) Pattenden, G.; Robertson, G.M. Tetrahedron Lett. 1986, 27, 399. (c) Piers, E.; Friesen, R.W. J. Org. Chem. 1986, 51, 3405. (d) Mehta, G.; Krishnamurthy, N. Tetrahedron Lett. 1987, 28, 5945.

8. For some recent cyclohexannulation procedures, see : (a) Danheiser, R.L.; Martinez-Davila, C.; Sard, H. Tetrahedron 1981, 37, 3943. (b) Pietrusiewicz, K.M.; Monkeiwicz, J.; Bodalski, R. J. Org. Chem. 1983, 48, 788. (c) Pariza, R.J.; Fuchs, P.L. J. Org. Chem. 1983, 48, 2304. (d) Tang, P.C.; Wulff, W.D. J. Am. Chem. Soc. 1984, 106, 1132, (e) Meyer, W.L.; Brannon, M.J.; Burgos, C.G.; Goodwin, T.E.; Howard, R.W. J. Org. Chem. 1985, 50, 438.(f) Byers, J.H.; Spencer, T.A. Tetrahedron Lett. 1985, 26, 713. (g) Danheiser, R.; Fink, D.M. Tetrahedron Lett. 1985, 26, 2513. (h) Posner, G.H.; Lu, S.B.; Asirvatham, E.; Silversmith, E.F.; Shulman, E.M. J. Am. Chem. Soc. 1986, 108, 511. (i) Edstrom, E.D.; Livinghouse, T. J. Am. Chem. Soc. 1986, 108, 1334 (j) Adams, J.; Frenette, R.; Belley, M.; Chibante, F.; Springer, J.P. J. Am. Chem. Soc. 1987, 109, 5432.

9. For some recent methodologies of seven-membered ring formation, see : (a) Hudlicky T.; Govindan, S.V.; Frazier, J.O. J. Org. Chem. 1985, 50, 4166 and references cited therein. (b) Hosomi, A.; Otaka, K.; Sakurai, H. Tetrahedron Lett. 1986, 27, 2881 and references cited therein. (c) Wender, P.A.; Fisher, K. Tetrahedron Lett. 1986, 27, 1857. (d) Cavazza, M.; Pietra, F. J. Chem. Soc. Chem. Commun. 1986, 1480. (e) Abraham, W.D.; Bhupathy, M.; Cohen, T.

Tetrahedron Lett. 1987, 28, 2203. (f) Crimmins, M.T.; Gould, L.D. J. Am. Chem. Soc. 1987, 109, 6199. (g) Chou, T.; Lee, S.J.; Tso, H.H.; Yu, C.F. J. Org. Chem. 1987, 52, 5082. (h) Sampath, V.; Lund, E.C.; Knudsen, M.J.; Olmstead, M.M.; Schore, N.E. J. Org. Chem. 1987, 52, 3595. (i) Molander, G.A.; Shubert, D.C. J. Am. Chem. Soc. 1987, 109, 6877. (j) Davies, H.M.L.; Smith, H.D.; Korkor, O. Tetrahedron Lett. 1987, 28, 1853. (k) Trost, B.M.; MacPherson, D.T. J. Am. Chem. Soc. 1987, 109, 3483. (l) Trost, B.M.; Mikhail, G.K. J. Am. Chem. Soc. 1987, 109, 4124. (m) Sworin, M.; Lin, K.C. J. Org. Chem. 1987, 52, 5640. (n) Koft, E.R. Tetrahedron 1987, 43, 5775. (o) Mehta, G.; Pathak, V.P. J. Chem. Soc. Chem. Commun. 1987, 876. (p) Majetich, G.; Dafauw, J.; Ringold, C. J. Org. Chem. 1988, 53, 50 and references cited therein. (q) Mehta, G.; Rao, K.S. J. Org. Chem. 1988, 53, 425. (r) Welch, M.C.; Bryson, T.A. Tetrahedron Lett. 1988, 29, 521. (s) Paquette, L.A.; Poupart, M.A. Tetrahedron Lett. 1988, 29, 273. (t) Paquette, L.A.; Okazaki, M.E.; Caille, J.C. J. Org. Chem. 1988, 53, 477. (u) Broka, C.A. J. Org. Chem. 1988, 53, 575 and references cited therein. (v) Lee, T.V.; Boucher, R.J.; Rockell, C.J.M. Tetrahedron Lett. 1988, 29, 689. (w) Nakamura, E.; Isaka, M.; Matsuzawa, S. J. Am. Chem. Soc. 1988, 110, 1297. (x) Davies, H.M.L.; Oldenburg, C.E.M.; McAffe, M.J.; Nordahl, J.G.; Henretta, J.P.; Romines, K.R. Tetrahedron Lett. 1988, 29, 975. (y) Rigby, J.H.; Senanayake, C. J. Org. Chem. 1988, 53, 440. (z) Kotoh, T.; Tanino, K.; Kuwajima, I. Tetrahedron Lett. 1988, 29, 1819.

10. (a) Cargill, R.; Jackson, T.; Peet, N.; Pond, D. Acc. Chem. Res. 1974, 7, 106. (b) Corey, E.J.; Nozoe, S. J. Am. Chem. Soc. 1964, 86, 1652. (c) Duc, D.; Fetizon, M.; Lazare, S. J. Chem. Soc. Chem. Commun. 1975, 282. (d) Duc, K.; Fetizon, M.; Kone, M. Tetrahedron 1978, 34, 3513. (e) Yanagiya, M.; Kaneko, K.; Takashi, K.; Matsumoto, T. Tetrahedron Lett. 1979, 1761. (f) Tobe, Y.; Hayauchi, Y.; Sakai, Y.; Odaira, Y. J. Org. Chem. 1980, 45, 637. (g) Eaton, P.E.; Jobe, P.G.; Nyi, K. J. Am. Chem. Soc. 1980, 102, 6636. (h) Pirrung, M.C. J. Am. Chem. Soc. 1981, 103, 82. (i) Do Khac Manh, D.; Fetizon, M.; Flament, J.P. Tetrahedron 1975, 31, 1897. (j) Tobe, Y.; Ueda, Y.; Nishikawa, H.; Odaira, Y. J. Org. Chem. 1981, 46, 5009. (k) Smith, A.B. III; Jerris, P.J. J. Am. Chem.Soc. 1981, 103, 194. (l) Smith, A.B. III; Wexler, B.A. Tetrahedron Lett. 1984, 2317. (m) Sengupta, D.; Venkateswaran, R.V. J. Chem. Soc. Chem. Commun. 1986, 1638. (n) Bernassau, J.M.; Bouillot, A.; Fetizon, M.; Hanna, I.; Maia, E.R.; Prange, T. J. Org. Chem. 1987, 52, 1993.

11. (a) Challand, B.D.; Hikino, H.; Kornis, G.; Lange, G.; DeMayo, P. J. Org. Chem. 1969, 34, 794. (b) Begley, M.J.; Mellor, M.; Pattenden, G. J. Chem. Soc. Chem. Commun. 1979, 235. (c) Seto, H.; Fujimoto, Y.; Tatsuno, T.; Yoshioka, H. Synth. Commun. 1985, 15, 1217. (d) Benchick-le-Hocine, M.; Do Khac, D.; Fetizon, M.; Hanna, I.; Zeghdoudi, R. Synth. Commun. 1987, 17, 913. (e) Swindell, C.S.; Patel, B.P.; Desolms, S.J. J. Org. Chem. 1987, 52, 2346. (f) Disanayaka, B.W.; Weedon, A.C. J. Org. Chem. 1987, 52, 2905.

12. Ranu, B.C.; Sarkar, D.C. Synth. Commun. 1987. 17, 155.

13. 6-Methylbicyclo[4.2.0]octan-2-one 9 was prepared by the photocycloaddition of 3-methylcyclohexenone with ethylene gas by slight modification of the reported procedure : Cargill, R.L.; Darlton, J.R.; Morton, G.H.; Caldwell, W.E. Org. Synth. 1984, 62, 118.

14. Jones reagent was chosen as a suitable reagent for effecting anticipated rearrangement and subsequent oxidation to relatively stable carboxylic acid.

15. Uyehara, T.; Yamada, J.; Furuta, T.; Kato, T.; Yamamoto, Y. Tetrahedron Symposia-in-Print, Tetrahedron 1987, 43, 5605.

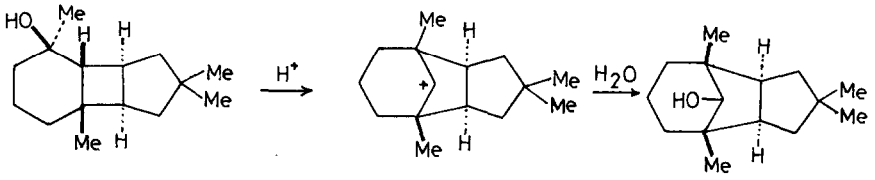
16. Bowman, R.M.; Calvo, C.; McCullough, J.J.; Rasmussen, P.W.; Snyder, F.F. J. Org. Chem. 1972, 37, 2084.

17. We have also observed some interesting anomolous behaviour of the cis-cisoid-cis isomer 15 which is being investigated and will be reported in due course.

18. Ranu, B.C.; Sarkar, D.C. J. Org. Chem. 1988, 53, 878.

19. The homogeneity of 17 as single isomer was established by GLC and ^1H NMR of its methyl ester (CH_2N_2) and the stereochemistry was assigned on the basis of its origin from the cis-transoid-cis ketone 14 and by analogy with the dicarboxylic acid 12.

20. Similar 'bridged' migration in the cis-transoid-cis tricyclo[5.4.0.$0^{2,6}$]undecane alcohol is also reported by Corey as in reference 10b.



21. Irradiation of 2-cyclopentenone and cyclopentene has been reported to give only cis-transoid-cis photoadduct : Eaton, P. E. J. Am. Chem. Soc. 1962, 84, 2454.

22. IR and ^{1}H NMR of 11 was recorded just after isolation and do not represent 100% pure compound.