Tetrahedron Vol 23, pp 4167 to 4176 Pergamon Press Ltd 1967 Printed in Great Britain

TRANSFORMATION REACTIONS OF α-PINENE—I

REACTIONS OF ETHYL (−)-2,2-DIMETHYL-3-KETOCYCLOBUTYL ACETATE

L. R. SUBRAMANIAN and G. S. KRISHNA RAO

Department of Organic Chemistry, Indian Institute of Science, Bangalore, India

(*Received* 14 *January* 1967; *accepted for publication* 30 *January* 1967)

Abstract- Some transformation reactions of α-pinene to give 4- and 3-membered ring compounds, not hitherto obtained from this source, are described. The study furnished a convenient method of preparation of the optically active cyclobutanone IVa, the title compound which served as the key substrate for all the transformations reported.

α-PINENE has long attracted the attention of terpene specialists and chemical technologists. Chemical manipulation[1] of this abundantly occurring terpene hydrocarbon to obtain diverse chemicals ranging from synthetic camphor to substituted cyclobutane compounds makes a fascinating study.

Pinonic acid, readily obtained from α-pinene is a reactive compound[2] which can undergo a variety of reactions typical of the cyclobutane, the ketomethyl and the carboxyl functions present in it. The object of this paper is to report our findings in the preparation, properties and reactions of the cyclobutanone IVa, and chiefly its conversion to cyclopropane compounds, e.g. *trans*-homocaronic acid and related compounds by a ring contraction sequence of the substituted cyclobutanone into which pinonic acid was converted *via* Baeyer–Villiger oxidation.[3,4]

(+)-α-Pinene, isolated from the turpentine oil derived from the oleoresin of *Pinus wallichiana*,[5] was used for the preparation of (+)-pinonic acid (Ia)[6] required in this

[1] B. D. Sully, *Chem & Ind.* 263 (1964); X. A. Dominguez and G. Leal, *J. Chem. Educ.* **40**, 347 (1963); P. Z. Bedoukian, *Am. Perf. & Cosm.* **79**(4), 27 (1964); K. Kulka, *Perf. & E. Oil Rec.* **53**, 147 (1952); R. T. Thampy, *Chem. Age of India* **12**, 145 (1961); D. V. Banthorpe and D. Whittaker, *Quart. Rev.* **20**, 373 (1966).

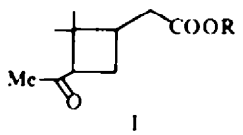
[2] C. L. Arcus and G. J. Bennett, *J. Chem. Soc.* 3180 (1958); G. W. Hedrick and R. V. Lawrence, *Ind. & Engg. Chem.* **52**, 853 (1960); J. D. Park, N. L. Allphin, S. K. Choi, R. L. Settine and G. W. Hedrick, *Ind. Engg. Chem.* **4**(3), 149 (1965).

[3] C. H. Hassal, *Organic reactions* (Edited by R. Adams) Vol 9, pp. 73–106. Wiley, New York (1957).

[4] In the extensive investigations of J. M. Conia on '*Small ring compounds*' [J. M. Conia *et al. Bull. Soc. Chim. Fr.* (Parts I to VIII) 726–778 (1963); *Ibid.* (Parts IX to XIII) 1957 1985 (1964)], the physical properties of a number of optically active cyclobutanones and the detailed mechanistic picture of the ring contraction of 2-bromocyclobutanones to cyclopropane carboxylic acids are given. In this study an entirely new procedure is reported to obtain the optically active cyclobutanones which are new and so are their various reactions.

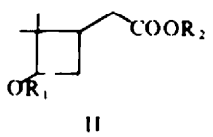
[5] The oleoresin, called *Kail resin*, was obtained from the Silvicultural Forest Research Division, Punjab (India). Investigations on this oleoresin and the turpentine oil derived from it have not been reported in literature. Our study (unpublished results) has shown this turpentine to be unusually rich in (+)-α-pinene (85–90%) unlike the currently exploited Indian turpentines from *Pinus longifolia roxb.* syn. *Pinus roxburghi* which contain 40–50% of α- and β-pinenes [V. S. Prabhakar, M. C. Nigam, K. L. Handa and G. D. Kelkar, *Indian Oil and Soap J.* **29**, 285 (1964)].

[6] M. Delepine, *Bull. Soc. Chim. Fr.* 1369 (1936).

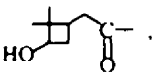
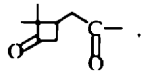


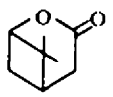
I

a. R = H
b. R = Et



II

a. R_1 = Ac, R_2 = Et
b. R_1 = R_2 = H
c. R_1 = R_2 = Ac
d. R_1 = H, R_2 = Et
e. R_1 = H, R_2 = Me
f. R_1 =  , R_2 = Me
g. R_1 =  , R_2 = Me



III

work. Ethyl (+)-pinonate[7] on Baeyer–Villiger cleavage[3] gave ethyl (−)-2,2-dimethyl-3-acetoxycyclobutyl acetate (IIa) in an excellent yield. Hydrolysis of IIa furnished the hydroxycyclobutylacetic acid IIb. Its esterification[7] gave ethyl (−)-2,2-dimethyl-3-hydroxycyclobutyl acetate (IId).[8]

The hydroxy acid IIb on refluxing with acetic anhydride followed by fractionation furnished the bridged δ-lactone III in poor yield along with a higher boiling fraction, probably the acetate mixed anhydride IIc as revealed in the IR spectrum [IR (neat): 1821, 1746 cm^{-1}]. These bands completely disappeared on exposure to moist air. The bridged δ-lactone III on ethanolysis[9] furnished ethyl 2,2-dimethyl-3-hydroxycyclobutyl acetate (IId), having an IR spectrum completely superimposable with that of the ethyl ester of IIb described above.

Oxidation of IId with Jones reagent,[10] $Na_2Cr_2O_7$ –H_2SO_4[11] and CrO_3 –HOAc[12] gave ethyl (−)-2,2-dimethyl-3-ketocyclobutyl acetate (IVa)[13] in about 50% yield together with a higher boiling byproduct *vide infra* in moderately good yield. However, IId could be conveniently oxidized to IVa in 75% yield by chromic acid in pyridine either (i) by Sarret's[14] procedure or (ii) according to Cornforth's recent modification[15] without the byproduct formation.

[7] B. A. Parkin and G. W. Hedrick, *J. Org. Chem.* **25**, 1417 (1960).

[8] During esterification of IIb (MeOH–$CHCl_3$–*p*TS) a higher boiling hydroxyester [B.p. 187°/2 mm, IR (neat): 3590 (O–H) and 1736 cm^{-1} (ester C=O)] was also formed invariably in amounts varying according to experimental conditions. On methanolysis it gave IIe with a completely superimposable IR spectrum with the authentic sample. Since pyridine-chromic acid oxidation of this fraction furnished a higher boiling cyclobutanone ester [B.T. 165–170°/1·5 mm, IR (neat): 1783 (cyclobutanone) and 1735 cm^{-1} (ester C=O)], the structures of the higher boiling esters which are under further investigation, are presumed to be IIf and IIg, the former arising from an intermolecular esterification.

[9] S. Neelakantan, T. R. Seshadri and S. S. Subramaniam, *Tetrahedron* **18**, 597 (1962).

[10] K. Bowden, I. M. Heilbron, E. R. H. Jones and B. C. L. Weedon, *J. Chem. Soc.* 39 (1946) and later papers.

[11] H. C. Brown and C. P. Garg, *J. Am. Chem. Soc.* **83**, 2952 (1961).

[12] Ch. R. Engel, K. F. Jennings and G. Just, *J. Am. Chem. Soc.* **78**, 6153 (1956); F. Sondheimer and D. Elad, *J. Am. Chem. Soc.* **80**, 1967 (1958).

[13] Studies in the optical rotatory dispersion of the laevo rotatory ketoester IVa derived from (+)-α-pinene, its dextro rotatory antipode derived from (−)-α-pinene by a similar sequence of reactions and related cyclobutanone systems will be communicated separately.

[14] G. I. Poos, G. E. Arth, R. E. Beyler and L. H. Sarett, *J. Am. Chem. Soc.* **75**, 422 (1953); G. I. Poss, W. F. Johns and L. H. Sarett, *Ibid.* **77**, 1026 (1955).

[15] R. H. Cornforth, J. W. Cornforth and G. Popjak, *Tetrahedron* **18**, 1351 (1962).

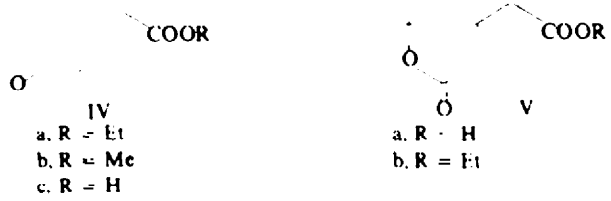
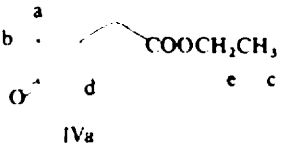
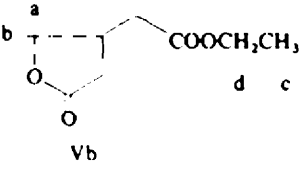
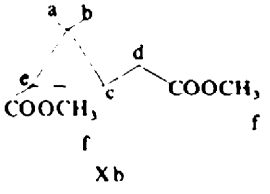
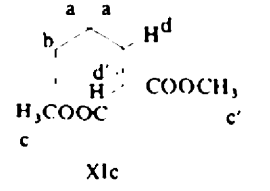


TABLE 1

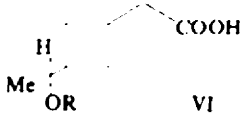
Sl. No.	Compound	Chemical Shift centred at (in τ values)	Assignment
1.	 IVa	8·98 } (3H, singlet) 8·80 } (3H, singlet) 8·77 (3H, triplet) $J = 7$ c/s 7·54 (3H, multiplet) 6·99 (2H, multiplet) 5·90 (2H, quartet)	a, b c d e
2.	 Vb	8·74 } 8·57 } (3H, singlet) 8·74 7·57 (5H, multiplet) 5·89 (2H, quartet)	a, b c d
3.	 Xb	8·86 } (3H, singlet) 8·78 } (3H, singlet) 8·28 (1H, multiplet) 7·66 (2H, multiplet) 7·33 (1H, doublet) $J = 7$ c/s* 6·37 } 6·33 } (6H)	a, b c d e f, f'
4	 XIc	8·80 (6H, singlet) 7·66 (2H, singlet) 6·38 } 6·32 } (6H) 4·35 } (1H, doublet) 3·10 } (1H, doublet) $J = 16$ c/s	a b c, c' d, d'

* K. B. Wiberg and B. J. Nist, *J. Am. Chem. Soc.* **85**, 2788 (1963). D. J. Patel, M. E. H. Howden and J. D. Roberts, *J. Am. Chem. Soc.* **85**, 3218 (1963)

The higher boiling byproduct obtained above from the hydroxyester IId on CrO_3 oxidation under acidic conditions analysed for one oxygen more ($C_{10}H_{16}O_4$) than the ketoester IVa ($C_{10}H_{16}O_3$), the expected normal oxidation product. Spectral data (Experimental and Table 1) indicated that it is a saturated ethyl ester with the

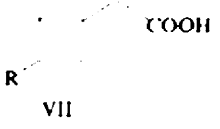
gem-dimethyl group attached to an oxygen bridge of a γ-lactone as in Vb. On acidic hydrolysis it furnished a solid acid which in presence of triethylamine[16] showed a band at 1760 cm $^{-1}$ (in Chf) confirming the presence of the γ-lactone. That indeed Vb was the structure of the byproduct was confirmed by Baeyer–Villiger oxidation of the ketoester IVa with perbenzoic acid, when the lactone ester Vb was obtained, the IR spectrum of which was superimposable in all respects with that of the by-product. Final confirmation came from the lactone acid which has the same m.p. (87–89°) reported for terpenylic acid Va.[17] Interestingly ethyl terpenylate (Vb) was found to be the product of oxidation of the keto ester IVa itself under these conditions. To our knowledge[18] this appears to be the first instance of a Baeyer–Villiger type of cleavage of a ketone to a lactone brought about by chromic acid under acidic conditions. Further experimental support will be necessary to check if this is characteristic of cyclobutanones.

The expected structure IVa for the cyclobutanone ester was confirmed by spectral data[19] (Experimental) and analysis. The NMR[20] signals (Table 1) also fully support the assignment IVa. The IR spectrum was completely superimposable with that of ethyl dl-2,2-dimethyl-3-ketocyclobutyl acetate obtained[21,22] by a different route *viz.*, the pyrolysis of *cis* dl-pinolic acid (VIa) or its acetate VIb and oxidative degradation of the resulting vinyl VIIa and ethylidene VIIb cyclobutylacetic acids and gas chromatographic separation of the ethyl esters of the corresponding oxidation products.



VI

a, R = H
b, R = Ac



VII

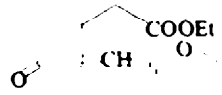
a, R = $-CH=CH_2$
b, R = $=CH-CH_3$

The cyclobutanone ester IVa furnished in satisfactory yield a solid furfurylidene derivative VIII. Conventional removal of the keto group[23] and conversion of the furfurylidene moiety into a 5-carbon chain[24] is expected to be useful in the synthesis of 1,2-disubstituted 3,3-dimethylcyclobutane compounds with the characteristic substitution pattern of a number of naturally occurring cyclobutane ring containing terpenoids.[25]

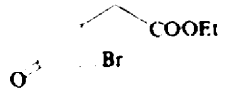
[16] K. Nakanishi, *Infrared Absorption Spectroscopy, Practical* p. 44. Holden-Day, San Francisco (1962).
[17] J. L. Simonsen, *J. Chem. Soc.* **91**, 184 (1907).
[18] cf. K. B. Wiberg in *Oxidation in Organic Chemistry* (Edited by K. B. Wiberg) pp. 69–184. Academic Press, New York (1965).
[19] cf. J. M. Conia, J. Gore, J. Salaun and L. Ripoll, *Bull. Soc. Chim. Fr.* 1976 (1964).
[20] cf. B. Braillon, J. Salaun, J. Gore and J. M. Conia, *Bull. Soc. Chim. Fr.* 1981 (1964).
[21] J. D. Park, R. L. Settine and G. W. Hedrick, *J. Org. Chem.* **27**, 902 (1962).
[22] We thank Dr. G. W. Hedrick for kindly sending us the IR spectrum.
[23] J. F. W. Keana in *Steroid Reactions* (Edited by Carl Djerassi) pp. 22–30. Holden-Day, San Francisco (1963).
[24] R. Robinson, *J. Chem. Soc.* 1390 (1938); A. Koebner and R. Robinson, *Ibid.* 1994 (1938).
[25] J. M. Mellor and S. Munavalli, *Quart. Rev.* **18**, 270 (1964); T. G. Halsall and D. W. Theobald *Ibid.* **16**, 101 (1962); F. J. Corey, R. B. Mitra and H. Uda, *J. Am. Chem. Soc.* **86**, 485 (1964); V. Jarolim, M. Streibl, I. Dolejs and F. Sorm, *Coll. Czech. Chem. Comm.* **22**, 1266 and 1277 (1957).

With one mole of bromine, the ketoester IVa gave ethyl (−)-2,2-dimethyl-3-keto-4-bromocyclobutyl acetate (IX).[26]

The bromoketoester IX on heating under reflux with water[27] furnished a mixture of products. The separated *trans*-homocaronic acid was repeatedly crystallized[28] and identified as its dimethyl ester (Xb, homogenious by TLC) by comparison of its IR

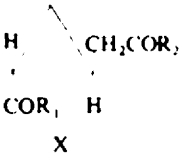


VIII



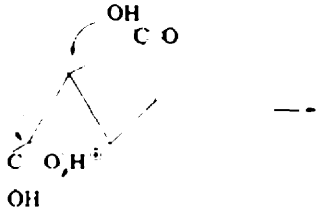
IX

spectrum with that of the authentic dimethyl (±)-*trans*-homocaronate.[29,30] The NMR spectral data (Table 1) also support this structure. The dimethyl ester Xb was hydrolysed successfully to *trans*-homocaronic acid by heating under reflux with dil HBr.[31] The crude acid from the filtrate (after removal of the *trans*-homocaronic acid which separated as a solid on cooling) on esterification (ethanol-chloroform-*p*-toluenesulfonic acid) followed by chromatographic separation furnished two esters, one identified as diethyl *trans*-homocaronate (Xc) and the other (more strongly held

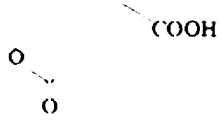


X

a. $R_1 = R_2 = OH$
b. $R_1 = R_2 = OMe$
c. $R_1 = R_2 = OEt$
d. $R_1 = OH, R_2 = OEt$
e. $R_1 = NH_2, R_2 = OEt$
f. $R_1 = Cl, R_2 = OEt$
g. $R_1 = R_2 = NH_2$



Xa



Va

on the column) as ethyl terpenylate Vb by comparison of IR spectra with authentic specimens. The formation of terpenylic acid could be rationalized on the basis of acid catalysed (resulting from the HBr liberated in the reaction) cleavage of the

[26] The spectral data for the cyclobutanone carbonyl before and after bromination are in good agreement with the values reported by Conia for similar cyclobutanones.

[27] cf J. M. Conia and J. L. Ripoll, *Bull. Soc. Chim. Fr.* 755 (1963).

[28] The m.ps and rotation data of the various samples of homocaronic acid obtained by different reactions on IX to be described presently are summarized in Table 2.

[29] L. Crombie, J. Crossley and D. A. Mitchard, *J. Chem. Soc.* 4957 (1963).

[30] We thank Prof. L. Crombie for sending us the infrared spectrum.

[31] cf T. Matsumoto, A. Nagai and Y. Takahashi, *Bull. Chem. Soc. Japan*, 36, 481 (1963).

cyclopropane ring followed by ring closure to the lactone acid as depicted.[32]

Action of sodium ethoxide on the bromocyclobutanone ester (IX) gave, besides the expected semi-benzilic rearrangement product,[27, 33] *viz.*, diethyl *trans*(−)-homocaronate, some amount of the diethyl 3,3-dimethyl-4-hexene-1,6-dioate (XIb), the retro-Michael product of the cyclopropane diester.[29, 32] The total mixture of the saturated ester Xc and the unsaturated ester XIb on complete hydrolysis with alcoholic sodium hydroxide furnished the solid 3,3-dimethyl-4-hexene-1,6-dioic acid (XIa). The *trans* geometry of the double bond for the unsaturated acid XIa was established by the coupling constant[34] (J = 16 c.s, Table 1) of the olefinic protons in the NMR spectrum of XIc. On hydrogenation XIa gave β,β-dimethyladipic acid (XII).[32] Use of slightly less than the required amount of sodium ethoxide gave on the other hand, diethyl *trans*(−)-homocaronate (Xc) and a small amount of the unchanged starting material IX, separated by TLC. The structure of the *trans*-homocaronic acid[28] obtained by the above method was confirmed by the IR and the NMR spectra (Table 1) of its dimethyl ester.

XI

a. R = H
b. R = Et
c. R = Me

XII

Treatment of bromocyclobutanone ester (IX) with aq silver nitrate[35] (15 hr) gave a mixture of a solid and a liquid product. The solid was readily separated and was identified as *trans*-homocaronic acid[28] (Xa). The liquid was shown to be ethyl *trans*(+)-2,2-dimethyl-3-carboxycyclopropyl acetate (Xd). Treatment of IX with aq silver nitrate for only 5 hr gave exclusively the half ester Xd in good yield. Hydrolysis of Xd (acidic as well as basic) furnished *trans*-homocaronic acid.[28]

The bromocyclobutanone ester (IX) on reaction with liquid ammonia[27] gave ethyl *trans*(−)-2,2-dimethyl-3-carboxamidocyclopropyl acetate (Xe). The acid chloride Xf of the half ester Xd on saturation with ammonia in benzene solution furnished the same solid amide ester Xe. The amide ester Xe has the interesting property of converting a variety of organic solvent media such as hydrocarbons, fatty oils, terpene rich essential oils, etc., into stable non-elastic gels when warmed with up to 1% by weight of the compound.[36] However, the crystalline diamide Xg obtained from the ester amide Xe does not exhibit this behaviour.

The action of dil sodium hydroxide on the bromocyclobutanone ester (IX) gave *trans*-homocaronic acid.[37]

In the above experiments of the bromocyclobutanone ester (IX) with various nucleophiles to give stereospecifically *trans*-cyclopropane compounds, the same

[32] cf. G. Widmark, *Arkiv for Kemi* **11**, 195 (1957)
[33] J. M. Conia and J. Salaun, *Bull. Soc. Chim. Fr.* 1957 (1964)
[34] R. H. Bible, *Interpretation of NMR Spectra* p. 38, Plenum Press, New York (1965)
[35] J. M. Conia and J. L. Ripoll, *Bull. Soc. Chim. Fr.* 773 (1963)
[36] The preparation of Xe and the method of producing the various gels have been covered by a patent
[37] cf. Refs 27 and 28.

stereospecific semi-benzilic ring contraction mechanism must be operative as demonstrated by Conia.[33]

Table 2 below gives the m.p. and optical rotation data[38] of the *trans*-homocaronic acid obtained by various reactions as indicated. It could be seen from the Table that the only reasonably reliable rotation values are those at 232 mμ (due to the carboxylic acid chromophore), where [α] is a maximum. Specimens 2,3,4 and 6 (Table 2) exhibit [α] of almost identical order within the limits of experimental

TABLE 2

Sl. No	Reaction by which *trans*-homocaronic acid was obtained	m.p.[39]	ORD data[38,40] [α] λ (λ in mμ) value at λ_{max} underlined
1	IX with water	180–182°	+6° 400, −34° 278, 0° 253, 160 231
2	IX with aq $AgNO_3$	169–170°	+2° 400, +22° 278, 0° 263, −330 232
3	IX with aq NaOH	169–170·5°	+6° 400, +38° 283, 0° 255, −290 231
4.	Xd with aq HBr	167–169°	+6° 400, +36° 278, 0 258, −310 231
5.	Xd with aq NaOH[41]	170–171°	-
6.	Xc with aq HBr	169–170°	0° 400, +24° 283, 0° 263, 320 232

error, while entry No. 1 indicates a specimen of greater extent of racemization. However, the IR spectra (mull) of all the specimens (1 to 6) were completely identical. The sample of the acid (entry 2 of Table 2), m.p. 169–170° could not be, however, converted to one of a higher m.p.[39] in an attempt to bring about complete racemization by refluxing with 10% HBr (5 hr). There was no change in its m.p. after three recrystallizations.

EXPERIMENTAL[42]

Ethyl (−)-2,2-dimethyl-3-acetoxycyclobutyl acetate (IIa)

Compound Ib(21·2 g) was mixed with 260 ml standardized, moist $CHCl_3$ soln containing perbenzoic acid (approx 0·12 mole) and the resulting cloudy soln was swirled at intervals and allowed to stand in the dark at room temp. After the theoretical amount of perbenzoic acid has been consumed (ca. 15 days), the $CHCl_3$ soln was shaken with 10% Na_2CO_3 aq until free of acid. Distillation after removal of solvent gave IIa (20 g), b.p. 103–105° 1 mm, n_D^{26} 1·4478, $[\alpha]_D$ −23·8° (c, 6·1); IR (neat): 1736 (ester C=O), 1238 cm^{-1} (acetate) (Found: C, 63·2; H, 8·9. $C_{12}H_{20}O_4$ requires: C, 63·1; H, 8·7%.)

2,2-Dimethyl-3-hydroxycyclobutylacetic acid (IIb)

The above IIa (21 g) was refluxed with alcoholic NaOH aq (16 g) for 18 hr. The residue after removal of alcohol was taken up in water and acidified under cooling with cold conc HCl. The liberated acid was

[38] We are grateful to Prof. W. Klyne for the ORD data and his comments.

[39] Crombie[29] reports m.p. 193–195° for *trans*-dl-homocaronic acid.

[40] The ORD curves were recorded at the same concentration in methanol.

[41] The pure specimen was obtained much later and could not be included in the samples sent for ORD determination.

[42] All m.ps and b.ps are uncorrected. Bt. refers to bath temp. Optical rotations were measured as neat liquids or in $CHCl_3$ at 25 ± 2°. UV spectra (cyclohexane) were determined on a Beckmann DU spectrophotometer, the IR spectra on a Perkin-Elmer 137 and the NMR spectra on Varian A-60 spectrometers (CCl_4) at 60 Mc with TMS as internal standard. Microanalyses were carried out by Messrs. B. R. Seetharamaiah and D. P. Bose of this department.

All organic extracts were washed neutral and dried (Na_2SO_4) prior to removal of the solvent unless otherwise stated. Pet. ether refers to the fraction 40–60°.

extracted with ether, washed with brine and the solvent evaporated to give the crude acid (14 g). An analytical sample was prepared by two short-path distillations, b.t. 130–145° 1 mm, n_D^{25} 1·4630; IR (neat): 3540–2500 (OH and COOH), 1712 cm^{-1} (acid C=O). (Found: C, 60·8; H, 8·8. $C_8H_{14}O_3$ requires: C, 60·74; H, 8·9%.)

Ethyl (−)-2,2-dimethyl-3-hydroxycyclobutyl acetate (IId)

The acid IIb (15·8 g) in $CHCl_3$ (100 ml) was gently refluxed with EtOH (25 ml) and *p*-toluenesulfonic acid (500 mg) using a universal azeotropic separator[43] until no more water separated. The reaction mixture was diluted with water and washed with dil Na_2CO_3 aq. Removal of solvent and distillation gave IId (12 g), b.p. 95–97° 0·8 mm, n_D^{27} 1·4510, α_D −2·2° (neat); IR (neat): 3580 (OH), 1736 cm^{-1} (ester C=O). (Found: C, 64·5; H, 10·0. $C_{10}H_{18}O_3$ requires: C, 64·5; H, 9·7%.)

The ester IIe prepared in an analogous manner using MeOH for esterification had b.p. 93–94° 2 mm, n_D^{26} 1·4520, $[\alpha]_D$ −0·52° (neat). (Found: C, 62·8; H, 9·4. $C_9H_{16}O_3$ requires: C, 62·79; H, 9·3%.) *3,5-Dinitrobenzoate* of IIe had m.p. 97–98° from n-hexane. (Found: N, 7·69. $C_{16}H_{18}O_8N_2$ requires: N, 7·65%.)

[3.1.1]-*Bicyclo-2-oxa-7,7-dimethylheptan-3-one* (III)

The acid IIb (1 g) was refluxed with Ac_2O (5 ml) for 3 hr. After removal of excess Ac_2O under suction, the residue was diluted with water and extracted with ether. The ether layer was then washed with dil $NaHCO_3$ aq and the solvent evaporated. IR spectrum of the crude material (800 mg) showed bands due to anhydride absorption (1821, 1746 cm^{-1}), which disappeared on exposure to moist air. Short path distillation of this crude material yielded small quantity of the lactone (200 mg) contaminated with acidic impurity as revealed in the IR spectrum, b.t. 120–125° 2 mm. This was taken up in ether and washed free of acid with dil $NaHCO_3$ aq. The residue after removal of ether was subjected to short-path distillation to give the δ-lactone (100 mg), b.t. 90–100° 3 mm; IR (neat): 1742 cm^{-1} (δ-lactone). (Found: C, 68·1; H, 8·67. $C_8H_{12}O_2$ requires: C, 68·58; H, 8·57%.)

Ethanolysis of the δ-lactone (III)

Sodium (80 mg) was added to the lactone III (100 mg) in abs EtOH (10 ml) and the mixture was refluxed (2 hr). The reaction mixture was poured into water and acidified with dil HCl and extracted with ether. Removal of solvent and distillation yielded IId (70 mg), b.t. 90–100° 1 mm. The IR spectrum of this ester was identical with that of IId prepared by the direct esterification of IIb.

Oxidation of IId: *Ethyl (−)-2,2-dimethyl-3-ketocyclobutyl acetate* (IVa)

(a) *Acidic conditions.** To a stirred soln of IId (18 g) in ether (50 ml) was added dropwise chromic acid soln prepared from $Na_2Cr_2O_7 \cdot 2H_2O$ (9·9 g) in 96% H_2SO_4 (7·5 ml), diluted with water to 50 ml in about 15 min at 20°. After stirring the soln for 2 hr, the ether layer was separated and the aq layer was extracted 3 times with ether. On removal of solvent and distillation, two fractions were obtained. Fraction 1: b.p. 80–82°/0·5 mm (10 g). Fraction 2: b.p. 120–122°/0·5 mm (4·5 g). Fraction 1 was redistilled to give the pure IVa (8 g), b.p. 80–82°/0·5 mm, n_D^{24} 1·4468, α_D −14·98° (neat); λ_{max} 274 (ε 22), 280 (ε 24), 294 mμ (ε 26). IR (neat): 1783 (cyclobutanone), 1738 cm^{-1} (ester C=O). (Found: C, 65·2; H, 8·7. $C_{10}H_{16}O_3$ requires: C, 65·22; H, 8·69%.) The IVb obtained from IIe by CrO_3 oxidation had b.p. 82–84° 1 mm, $[\alpha]_D$ −13° (neat). (Found: C, 63·57; H, 8·1. $C_9H_{14}O_3$ requires: C, 63·53; H, 8·2%.)

The *furfurylidene* derivative VIII, prepared by treating IVa (184 mg) with furfural (960 mg) in abs EtOH in presence of 33% NaOH aq (1·5 g) had m.p. 116–117° (pet ether); λ_{max} 317 (ε 31,200), 330 mμ (ε 31,440). IR (Nujol): 1732 (conj. cyclobutanone), 1631 cm^{-1} (conj. C=C). (Found: C, 68·6; H, 6·7. $C_{15}H_{18}O_4$ requires: C, 68·7; H, 6·87%.)

(b) *Basic conditions.*[13] The ester IId (10 g) in pyridine (25 ml) was added to chromic acid soln prepared from CrO_3 (16·2 g in 13 ml water) in pyridine (160 ml) and was left in a dark place for 3 days. The reaction mixture was diluted with water, filtered and the filtrate was thoroughly extracted with ether. The ether extract on washing free from pyridine by ice cold dil HCl and distillation furnished only IVa (7·5 g).

Sarret's procedure[14] also gave similarly IVa in 75% yield.

[43] S. N. Balasubrahmanyam, *J. Chem. Ed.* 37, 475 (1960).

* Though oxidation of IId with (i) Jones reagent[10], (ii) $Na_2Cr_2O_7$–H_2SO_4[11] and (iii) CrO_3–AcOH[12] gave both the ketoester (IVa) and the higher boiling fraction 2, only the last procedure is described here.

Ethyl (−) terpenylate (Vb)

(a) Fraction 2 obtained above under acidic conditions of oxidation was redistilled, b.p. 120–122° (0·5 mm) (3·5 g), n_D^{26} 1·4520, α_D −26·1° (neat); IR (neat): 1776 (γ-lactone), 1730 cm^{-1} (ester C=O). (Found: C, 59·7; H, 8·0. Calc for $C_{10}H_{16}O_4$: C, 60·0; H, 8·0%.) Hydrolysis of the above fraction with conc HCl gave *terpenylic acid*[17] (Va). An analytical sample was prepared by sublimation, b.t. 120–140°/0·5 mm, m.p. 87–89°, IR (Nujol): 3400 (broad, COOH), 1733 cm^{-1} (broad, γ-lactone and acid C=O). (Found: C, 55·79; H, 7·1. $C_8H_{12}O_4$ requires: C, 55·8; H, 6·97%.)

(b) *By Baeyer-Villiger oxidation of* IVa. The ketoester IVa (1·84 g) in $CHCl_3$ (10 ml) was treated with a soln of perbenzoic acid (1·5 equivs) in $CHCl_3$ and allowed to stand in a dark place for 15 days. The $CHCl_3$ soln was washed with dil $NaHCO_3$ aq and the solvent evaporated. Distillation gave Vb, b.p. 128°/1 mm, $[\alpha]_D$ −35·64°, n_D^{26} 1·4550. The IR spectrum was found to be identical in all respects with that of fraction 2 above.

(c) *By chromic acid oxidation of the ketoester* (IVa). (i) *With Jones reagent.* The ketoester IVa (300 mg) was stirred with 2 ml of Jones reagent containing 780 mg of CrO_3 for 3 hr. Usual workup gave the crude oxidation product whose IR spectrum was identical with that of ethyl (−)-terpenylate in all respects, b.t. 110–120°/2 mm (230 mg), $[\alpha]_D$ −20° (*c*, 38·6). (ii) *With* $Na_2Cr_2O_7$–H_2SO_4. The ketoester IVa (300 mg) was stirred (magnetic stirrer) with 2 ml of chromic acid soln containing $Na_2Cr_2O_7 \cdot 2H_2O$ (300 mg) and H_2SO_4 (0·225 ml diluted to 1·5 ml). Usual workup gave only the starting material without any apparent change. However, with very vigorous stirring (mechanical stirrer) and increased reaction time (10 hr), it gave ethyl terpenylate, identified from its IR spectrum. (iii) *With* CrO_3–HOAc. The ketoester IVa (368 mg) in AcOH (2 ml) was mixed with chromic acid soln (250 mg in 0·5 ml water). There was immediate evolution of heat and the reaction mixture was left overnight. Usual workup gave a crude product whose IR spectrum was completely identical with that of Vb.

Ethyl (−)-2,2-dimethyl-3-oxo-4-bromocyclobutyl acetate (IX)

To a stirred soln of IVa (7·4 g) in $CHCl_3$ (100 ml) maintained at 35°, dry Br_2 (6·4 g) in $CHCl_3$ (25 ml) was added dropwise. After the addition was over, stirring was continued for 5–10 min until it decolourized. The $CHCl_3$ soln was shaken once with ice cold water, cold $NaHCO_3$ aq, twice with ice cold water and dried over $CaCl_2$. Evaporation of solvent and distillation yielded IX (8·9 g), b.p. 114–116°/1 mm, n_D^{20} 1·4818, α_D −3·2° (neat); λ_{max} 318 mμ (ε 158), IR (neat): 1792 (cyclobutanone), 1733 cm^{-1} (ester C=O). (Found: C, 45·4; H, 5·2. $C_{10}H_{15}O_3Br$ requires: C, 45·6; H, 5·7%.)

Reactions of bromoketoester (IX)

(i) *Action of water.* The ketobromoester IX (3 g) was refluxed with water (25 ml) for 24 hr. The clear soln on keeping overnight deposited crystals of trans-*homocaronic acid* (Xa) which were filtered (650 mg) and recrystallized thrice from nitromethane, m.p. 180–182°, IR (Nujol): 1712, 1698 cm^{-1} (acid C=O). (Found: C, 56·2; H, 7·1. Calc for $C_9H_{12}O_4$: C, 55·8; H, 7·0%.)

Homocaronic acid Xa on treatment with diazomethane in ether gave Xb, b.t. 100–110°/10 mm, n_D^{22} 1·4452, α_D +2·36° (neat); IR (neat): 1745 (ester C=O), 1724 cm^{-1} (ester C=O in conjugation with cyclopropane). (Found: C, 60·0; H, 8·1. Calc for $C_{10}H_{16}O_4$: C, 59·98; H, 8·0%.) The ester Xb (200 mg) was refluxed with 20% HBr (10 ml) for 2 hr. The clear soln was concentrated under suction and the separated solid (150 mg) recrystallized from nitromethane, m.p. 180–182°. The IR spectrum (Nujol) was identical with that of Xa obtained by the action of water on IX.

The filtrate from the action of water on IX after removal of solid homocaronic acid was extracted with ether. The residue obtained (1 g) after evaporation of ether was esterified with EtOH (10 ml) in $CHCl_3$ soln using *p*-toluenesulfonic acid as catalyst. Usual workup gave crude mixture of esters. Chromatography (SiO_2) furnished Xc (1:1 pet ether–benzene) *vide infra* and *ethyl terpenylate* (Vb) (1:1 benzene–ether).

(ii) *Action of sodium ethoxide.* To a suspension of dry EtONa (850 mg, 1·25 mole equivs) in dry ether (50 ml) IX (2·63 g) in dry ether (50 ml) was added slowly with stirring during 10 min at room temp. After stirring for additional 2 hr, water was added to the reaction mixture and the organic layer extracted with ether. Evaporation of solvent gave 1·8 g of residue, α_D −1·64° (neat), IR (neat): 1656 cm^{-1} (C=C). Reducing the reaction time from 2 hr to 15 min did not affect the results.

Repetition of this experiment using EtONa (580 mg, 0·85 mole equivs) and with a reaction time of 10 min furnished a crude material showing the presence of unchanged cyclobutanone [IR (neat) 1783 cm^{-1}], but no unsaturation. Compound Xc was separated (1 g) from the unreacted product by TLC over silica gel. An analytical sample was obtained by short-path distillation, b.t. 105–110°/2 mm, α_D −8·0° (neat),

n_D^{23} 1·4428; IR (neat): 1742 (satd ester C=O), 1730 cm^{-1} (ester C=O in conj with cyclopropane) (Found: C, 62·9; H, 8·8. Calc. for $C_{12}H_{20}O_4$: C, 63·1; H, 8·7%.) Compound Xc was hydrolysed with aq HBr to homocaronic acid as described earlier, m.p. 169–170°, IR spectrum identical with *trans*-homocaronic acid

The crude product (1·8 g) of EtONa (1·25 mole equivs) treatment above was saponified with alcoholic NaOH to give XIa (700 mg), m.p. 112–113° (water), IR (Nujol): 3000 (broad COOH), 1709, 1695 (acid C=O) and 1647 cm^{-1} (C=C). The *dimethyl ester* XIc was prepared by the treatment of XIa in ether with diazomethane, b.t. 122–126°/15 mm; IR (neat): 1742 (satd ester C=O), 1727 (unsatd ester C=O), 1656 cm^{-1} (C=C)

The acid XIa (100 mg) was hydrogenated[32] using Pt black in AcOH as catalyst to give *β,β-dimethyladipic acid* (XII), m.p. 86–87° [$CHCl_3$–pet ether (60–80°)]. IR (Nujol): 3000 (OH of acid), 1700 cm^{-1} (acid C=O).

(iii) *Action of silver nitrate.* The ketobromoester IX (2 g) was stirred with $AgNO_3$ aq (1·5 g in 10 ml of water) for 15 hr. The precipitated AgBr was filtered off and the filtrate extracted with ether. The ether extract was re-extracted with $NaHCO_3$ aq which on acidification (dil HCl) followed by ether extraction gave 1·1 g of a semi-solid residue. It was dissolved in ether. Addition of pet ether precipitated from this soln 450 mg of a solid, m.p. 169–170° (crystallized thrice from nitromethane). Its IR spectrum was identical with that of *trans*-homocaronic acid *vide supra*. The filtrate on evaporation gave 580 mg of Xd (see below).

Treatment of IX (2·1 g) with $AgNO_3$ aq (1·58 g in 10 ml of H_2O) as above but only for 5 hr gave exclusively the viscous halfester Xd (1·3 g). An analytical sample was prepared by short path distillation, b.t. 150–155°/2 mm, $[\alpha]_D$ +1·64° (*c*, 22·7); IR (neat): 1730 (ester C=O), 1695 cm^{-1} (acid C=O). (Found: C, 60·1; H, 8·0. $C_{10}H_{16}O_4$ requires: C, 60·0; H, 8·0%.) The halfester Xd was hydrolysed separately by dil HBr and alcoholic NaOH to *trans*-homocaronic acid. After 3 crystallizations from nitromethane the samples had m.p. 167–169° and 170–171° respectively. The IR spectra of both the samples (Nujol mull) were identical with that of *trans*-homocaronic acid

(iv) *Action of liquid ammonia.* The ketobromoester IX (2·63 g) was stirred with liquid ammonia (600 ml) until all the ammonia was evaporated. The residue left in the flask was taken up in hot benzene (50 ml) and filtered. On cooling the soln a clear transparent gel was obtained. It was filtered and the solid purified by dissolving it in excess benzene and precipitating with pet ether. Filtration gave the *amide ester* Xe (1·1 g) as snow white fluffy powder, m.p. 105–106°, $[\alpha]_D$ −10·0° (*c*, 30·5); IR (Nujol): 3510, 3300 (NH of amide), 1730 (ester C=O), 1645 cm^{-1} (amide C=O). (Found: C, 59·8; H, 8·3; N, 7·1. $C_{10}H_{17}O_3N$ requires: C, 60·3; H, 8·54; N, 7·0%.)

The acid chloride Xf (100 mg) prepared from Xd by treatment with $SOCl_2$ was dissolved in benzene (10 ml) and saturated with dry ammonia gas. The benzene soln was filtered and the product was precipitated with pet ether. It was reprecipitated once again in the same manner to give the Xe, m.p. 105° with no depression on admixture with the amide ester obtained directly from IX

The trans-*homocarondiamide* Xg was prepared from Xe (500 mg) by refluxing it with alcoholic ammonia (10 ml) for 4 hr. After removing the solvent under suction, the solid was sublimed (b.t. 140–160°/0·2 mm) and the sublimate crystallized from alcohol, m.p. 195–196°, IR (Nujol): 3510, 3300 (NH of amide), 1661, 1626 cm^{-1} (amide C=O). (Found: N, 16·19. $C_8H_{14}O_2N_2$ requires: N, 16·46%.)

(v) *Action of aqueous sodium hydroxide.* The ketobromoester IX (500 mg) was refluxed with NaOH aq (1 g in 10 ml of water) for 3 hr. The sodium salt was acidified with dil HCl and concentrated to half the volume. The solid separated was recrystallized 3 times from nitromethane (130 mg), m.p. 169–170·5°. The IR spectrum in Nujol mull was identical with that of *trans*-homocaronic acid

Acknowledgement—We are indebted to Dr Sukh Dev, Assistant Director, National Chemical Laboratory, Poona (India) for the NMR spectra and Professor D. K. Banerjee of this department for his keen interest in this work and constant encouragement. One of us (L.R.S.) thanks the authorities of the Indian Institute of Science for the grant of a research scholarship