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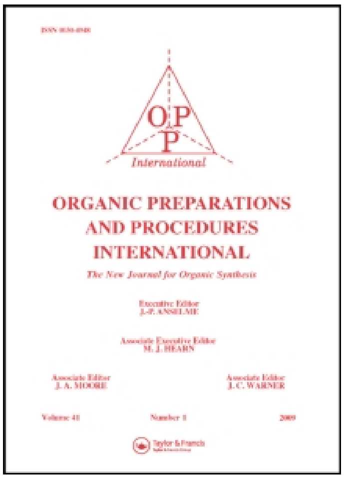

Organic Preparations and Procedures International

Publication details, including instructions for authors and subscription information:
http://www.informaworld.com/smpp/title~content=t902189982

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To cite this Article Reuvers, A. J. M. , Jongejan, J. A. , Klomp, J. and van Bekkum, H.(1971) '1,1,2,2-TETRAMETHYLCYCLOHEXANE', Organic Preparations and Procedures International, 3: 2, 83 — 86

To link to this Article: DOI: 10.1080/00304947109356040

URL: http://dx.doi.org/10.1080/00304947109356040

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ORGANIN PREPARATIONS AND PROCEDURES INT. 3(2), 83-86 (1971)

1,1,2,2-TETRAMETHYLCYCLOHEXANE

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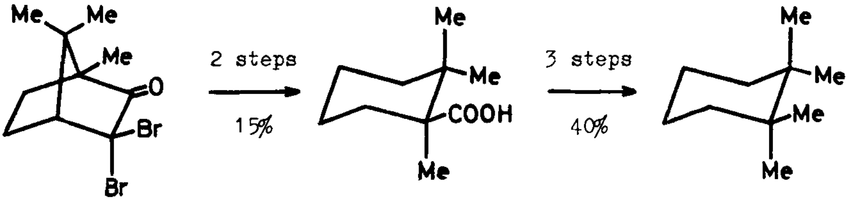

I IV VII

For studies on ring inversion in cyclohexane derivatives, we required 1,1,2,2-tetramethylcyclohexane. 1,2,2-Trimethylcyclohexanecarboxylic acid was chosen as the starting material of the synthesis. This acid has been prepared[1] in four steps from α,α-dibromocamphor (3,3-dibromo-2-oxo-1,7,7-trimethylbicyclo[2,2,1]heptane. The poor yield (5%) of this synthesis induced us to develop a more satisfying method.

α,α-Dibromocamphor was converted to bromocamphorenic acid by means of silver nitrate in boiling glacial acetic acid.[2] PMR analysis showed that two acids were formed in a 3:1 ratio, 3-bromo- and 4-bromocamphorenic acid (3- and 4-bromo-1,2,2-trimethylcyclohex-3-enecarboxylic acid). Attempted separation of these acids was unsuccesful, but proved to be unnecessary because both acids yielded 1,2,2-trimethylcyclohexanecarboxylic acid upon hydrogenation over 10% Pd/C. The overall yield of the acid was thus raised to 15%.

Lithium aluminum hydride reduction of 1,2,2-trimethylcyclohexanecarboxylic acid yielded 1,2,2-trimethylcyclohexanemethanol. Treatment with p-toluenesulfonyl chloride in pyridine gave the p-toluenesulfonate. This compound was chromatographed over silica and then reduced with lithium aluminum hydride in THF[3] to yield 1,1,2,2-tetramethylcyclohexane.

EXPERIMENTAL[4]

α,α-Dibromocamphor (I).—Camphor (500.0 g.) was brominated according to the literature.[1] The work-up procedure was modified as follows: the crude reaction mixture was poured on crushed ice and extracted with benzene (1 l.). The benzene sol'n was washed with a $NaHSO_3$ sol'n and then water. After drying over $MgSO_4$, the benzene was evaporated in vacuo and the resulting oil was left to crystallize. The crystals were filtered and washed twice with ice-cold pentane to give 749.2 g. (73.7%) pure I, mp. 59.5-60°.

3-Bromo- (II) and 4-bromocamphorenic acid (III)*.—Silver nitrate (59.0 g.) was added in small portions to a sol'n of I (100.0 g.) in boiling AcOH (325 ml.). When the addition was complete, the mixture was refluxed for 1 hr. The AgBr was filtered and washed with AcOH (50 ml.). The filtrate was cooled to 5° and ice water (400 ml.) was added. The ppte was filtered and taken up in ether (250 ml.). The ethereal sol'n was extracted twice with 2N KOH (100 ml.). The alkaline extracts were washed with ether and acidified with conc. HCl. The product was filtered, washed with water, dried, and sublimed in vacuo, yielding 12.6 g. (15.9%) of a mixture of 70% II and 30% III, mp. 160.5-161°. The estimation of the composition was based upon PMR analysis of the vinylic proton signal: 3-bromo-, triplet, J = 1.5 Hz, δ = 5.68 ppm; 4-bromo-, multiplet, $W_{\frac{1}{2}}$ = 8.8 Hz, δ = 5.8-6.0 ppm. The mixture was used as such in the next step.

1,2,2-Trimethylcyclohexanecarboxylic acid (IV).—The mixture of II and III (95.6 g.) in 96% EtOH was hydrogenated at 1 atm. H_2 over 10% Pd/C (2 g.). After the theoretical amount of H_2 had been taken up, the catalyst was filtered and the solvent removed in vacuo. The residue was recrystallized once from 50% EtOH yielding 61.7 g. (93.9%) IV, mp. 179-180° (lit.[1] mp. 179-180°). This acid was identical with an acid prepared from 3-t-butylcyclopentanol by means of a Koch synthesis.[5]

PMR (CCl_4): δ = 12.7 ppm (s, COO<u>H</u>); 2.4-1.3 (m, ring protons); 1.28 (s,

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* Next to the two bromocamphorenic acids 21 neutral products are formed in this reaction. These compounds are under investigation at the moment. No unconverted α,α-dibromocamphor could be detected by GLC analysis (1 m. SE-30, 200°).

1 Me-group); 1.06 (s, 2 Me groups).

1,2,2-Trimethylcyclohexanemethanol (V).—IV (61.7 g.) was reduced with $LiAlH_4$ (20.0 g.) in ether (500 ml.). The crude carbinol was recrystallized from hexane to give 55.7 g. (98.4 %), mp. 145-146°.

Anal. Calcd for $C_{10}H_{20}O$: C, 76.86; H, 12.90%. Found: C, 76.9; H, 12.8%. PMR (CCl_4): δ = 3.48 ppm (s, $C\underline{H}_2OH$); 3.39 (s, $O\underline{H}$); 1.42 (broad band, $W_{\frac{1}{2}}$ = 4.5 Hz,ring protons); 0.88 (s, 2 Me groups); 0.87 (s, 1 Me group).

p-Toluenesulfonate of 1,2,2-trimethylcyclohexanemethanol (VI).—V (55.7 g.) was mixed with TsCl (76.2 g.) and dry pyridine (300 ml.). The mixture was refluxed for 1 hr. and then poured on crushed ice. The p-toluenesulfonate was extracted with hexane. The extract was washed with water, 2N HCl, and again with water. It was dried over $MgSO_4$ and the solvent was removed in vacuo. The crude VI was chromatographed over silica (Merck kieselgel 0.05-0.2 mm.) using 5% EtOAc in benzene as eluent. The solvents were removed at 0.01 mm. Hg. There remained 84.8 g. (76.6%) of a colorless liquid, n_D^{25} 1.5173.

Anal. Calcd for $C_{17}H_{26}O_3S$: C, 65.77; H, 8.44%. Found: C, 65.9; H, 8.5%. PMR (CCl_4): δ = 7.78, 7.39 ppm (AB-pattern, J = 8 Hz, arom. $\underline{H}$); 3.38 (s, $C\underline{H}_2OTs$); 2.44 (s, arom. Me group); 1.35 (broad band, $W_{\frac{1}{2}}$ = 3.5 Hz, ring protons); 0.87 (s, 2 Me groups); 0.82 (s, 1 Me group).

1,1,2,2-Tetramethylcyclohexane (VII).—VI (52.2 g.) in THF (35 ml.) was added to $LiAlH_4$ (5.0 g.) in THF (70 ml.). The reaction mixture was refluxed for 30 hr. and then hydrolyzed with ice water, followed by 4N H_2SO_4. The THF sol'n was washed with 2N Na_2CO_3 sol'n and poured into water. The hydrocarbon was extracted with pentane. The pentane extract was washed 6 times with cold conc. H_2SO_4 and then with water. It was dried over K_2CO_3 and the solvent was distilled. The residue was distilled from Na to yield 12.5 g. (53.2%) VII, bp. 161-162°, n_D^{25} 1.4445.

Anal. Calcd for $C_{10}H_{20}$: C, 85.62; H, 14.38%. Found: C, 85.5; H, 14.3%. PMR (CCl_4): δ = 2.0-1.0 ppm (m, ring protons); 0.88 (s, 4 Me groups).

Dibromocampholide (γ-lactone of 3,4-dibromo-3-hydroxy-1,2,2-trimethylcyclohexanecarboxylic acid) (VIII).—I (220.0 g.) was treated with fuming HNO_3 as has been described[1] to yield 18.7 g. (8.1%) VIII, mp. 155-156° (lit.[1]

mp. 138-139°; lit.[6] mp. 152°.
PMR (DMSO-d_6): $\delta = 4.50$ ppm (d, J = 2 Hz, H on C_4); 3.3-1.4 (m, ring protons); 1.22, 1.05 and 1.03 (s, Me groups).

3-Bromocamphorenic acid (II).—VIII (93.4 g.) yielded 37.7 g. (53.2%) II in the way as has been described[1], mp. 161-161.5° (lit.[1,7] mp. 181°; lit.[6] mp. 159°).

Anal. Calcd for $C_{10}H_{15}BrO_2$: C, 48.58; H, 6.12%. Found: C, 48.4; H, 6.1%.
PMR (CCl_4): $\delta = 11.9$ ppm (s, COOH); 5.68 (t, J = 1.5 Hz, vinylic H); 2.7-1.4 (m, ring protons); 1.28, 1.19 and 1.11 (s, Me groups).

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(Received December 10, 1970)