A Convenient Synthesis of βγ-Unsaturated Carboxylic Acids and Esters. The Isomeric 5-t-Butylcyclohex-2-enecarboxylic Acids

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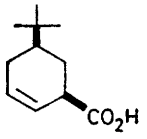
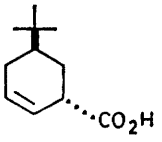
A procedure is described for the conversion of six-membered ring allylic bromides *via* the corresponding nitriles into βγ-unsaturated acids and esters. In this way *cis*- and *trans*-5-t-butylcyclohex-2-enecarboxylic acids have been prepared. Configurations of the latter are assigned on the basis of hydrogenation to the known saturated acids.

In the course of investigations on the effect of a neighbouring carboxy-group on the stereochemistry of epoxidation of olefins, we required the *cis*- and *trans*-5-t-butylcyclohex-2-enecarboxylic acids, (I) and (II). An attractively simple route to such βγ-unsaturated acids consists of the conversion of an allylic halide into the nitrile by displacement with cyanide ion, followed by hydrolysis. This procedure has been rarely used, however, largely because of ready isomerisation to the αβ-unsaturated isomers both at the nitrile stage and during the hydrolysis. A reported preparation of vinylacetic acid [1] based on this approach involves the reaction of copper(I) cyanide with allyl chloride. In our hands copper(I) cyanide proved a capricious reagent, giving very variable yields of nitrile (45% at best) with cyclohex-2-enyl bromide and consistently low yields of nitrile from 3-bromo-5-t-butylcyclohexenes.



(I)



(III)

We now find, at least in the case of cyclohex-2-enyl bromides, that substitution without isomerisation can be performed at room temperature in high yield by using sodium cyanide in dry *N*-methyl-2-pyrrolidone.[2] Attempts to carry out the displacement by using sodium cyanide in other dipolar aprotic solvents [2] or in aqueous acetone [3] gave, after work-up, predominantly cyclohex-2-enol (from cyclohex-2-enyl bromide). Methanolysis of the βγ-unsaturated nitrile to the corresponding ester was carried out with dry methanol–hydrogen chloride. Finally, acid-catalysed hydrolysis of the ester afforded the βγ-unsaturated acid.

In this way 3-bromocyclohexene was converted into cyclohex-2-enecarboxylic acid, and the epimeric 5-t-butylcyclohex-2-enecarboxylic acids were prepared from the 3-bromo-5-t-butylcyclohexenes. Samples of methyl *cis*- and *trans*-5-t-butylcyclohex-2-enecarboxylate were obtained by preparative g.l.c. of the ester mixture, which comprised 55% of the *cis*- and 40% of the *trans*-form together with a small amount of the conjugated unsaturated ester. The predominance of the *cis*-ester (CO_2Me pseudoequatorial) can be explained in terms of predominant axial bromination in the allylic substitution (by *N*-bromosuccinimide) used to form the 3-bromo-5-t-butylcyclohexenes, followed by inversion in the nitrile-forming step.

The stereochemistry of the two esters was assigned on the basis of hydrogenation followed by hydrolysis to the known *cis*- and *trans*-3-t-butylcyclohexanecarboxylic acids.[4]

^{13}C N.m.r. chemical shift data for compounds obtained in this investigation are available as Supplementary Publication No. SUP 21877 (2 pp.).†

† For details of Supplementary Publications see Notice to Authors No. 7 in *J.C.S. Perkin I*, 1975, Index issue.

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EXPERIMENTAL

N-Methyl-2-pyrrolidone was dried by azeotropic distillation with benzene to remove water, followed by conventional distillation.

Cyclohex-2-enecarbonitrile. 3-Bromocyclohexene (2 g, 12.5 mmol), dry sodium cyanide (1.25 g, 25 mmol), and anhydrous *N*-methyl-2-pyrrolidone (10 ml) were stirred at 20 °C for 90 min. The mixture was poured into water and the product isolated with ether. Distillation gave the nitrile (1.2 g, 90%), b.p. 89° at 23 mmHg (lit.,[3] 67.5—68° at 8 mmHg), τ (CCl_4) 4.1 and 4.4 (2 H, AB system CH=CH), 6.85 (1 H, m, C*H*·CN), and 7.8—8.4 (6 H).

Methyl Cyclohex-2-enecarboxylate.—Dry hydrogen chloride was bubbled vigorously into a refluxing solution of cyclohex-2-enecarbonitrile (12.8 g, 0.12 mol) in dry methanol (100 ml). After 6 h a considerable amount of precipitate had formed. The gas flow was stopped and the mixture was stirred at 20 °C for 14 h. Ether (100 ml) was added and the mixture was poured onto ice (400 g). Isolation with ether followed by distillation gave the *ester* (13.3 g, 79%), b.p. 64—65° at 12 mmHg (Found: C, 68.4; H, 8.5. $C_8H_{12}O_2$ requires C, 68.5; H, 8.6%), τ (CCl_4) 4.28 (2 H, s, CH=CH), 6.37 (3 H, s, Me), 7.0 (1 H, m, CH·CO_2), and 7.9—8.4 (6 H, m).

Cyclohex-2-enecarboxylic Acid.—The methyl ester (600 mg) and toluene-*p*-sulphonic acid (100 mg) in 1,4-dioxan–water (9 : 1; 20 ml) were heated under reflux for 3 h. The mixture was added to water and the product was extracted into ether. After washing with brine (× 3) the acid was extracted into aqueous sodium carbonate. Acidification of the aqueous washings followed by isolation with ether gave the acid (480 mg, 88%), b.p. 130° (bath) at 14 mmHg (lit.,[5] 120° at 10 mmHg) (Found: C, 66.85; H, 8.1. Calc. for $C_7H_{10}O_2$: C, 66.6; H, 8.0%), τ (CCl_4) −2.15 (1 H, s, CO_2H), 4.23 (2 H, s, CH=CH), 6.91 (1 H, m, CH·CO_2), and 7.9—8.5 (6 H, m).

Methyl cis- *and* trans-5-*t-Butylcyclohex-2-enecarboxylate.*—The crude product from allylic bromination [6] of 4-t-butylcyclohexene (78 g, 0.565 mol), dry sodium cyanide (49 g), and anhydrous *N*-methyl-2-pyrrolidone (500 ml) were stirred at 20 °C for 12 h. Work-up as before followed by distillation gave t-butylbenzene (14.2 g), b.p. 52° at 10 mmHg, and the isomeric 5-t-butylcyclohex-2-enecarbonitriles (63 g, 69%), b.p. 115—120° at 10 mmHg. The nitrile mixture in anhydrous methanol (500 ml) was heated under reflux for 6 h while dry hydrogen chloride gas was passed through. Isolation as before followed by spinning-band distillation gave a mixture of esters (45.5 g, 60%), b.p. 98—110° at 8 mmHg, shown by g.l.c. to comprise methyl 5-t-butylcyclohex-1-enecarboxylate and methyl *trans*- and *cis*-5-t-butylcyclohex-2-enecarboxylate in the ratio 5 : 40 : 55. Preparative g.l.c. (15% PEGA at 200 °C) gave *methyl* trans-5-*t-butylcyclohex-2-enecarboxylate* (Found: C, 73.2; H, 10.1. $C_{12}H_{20}O_2$ requires C, 73.4; H, 10.3%), τ (CCl_4) 4.28 (2 H, m, CH=CH), 6.40 (3 H, s, OMe), 6.95 (1 H, m, CH·CO_2), 7.2—9.0 (5 H, m), and 9.12 (9 H, s, Bu^t); *methyl* cis-5-*t-butylcyclohex-2-enecarboxylate* (Found: C, 73.6; H, 10.3%), τ (CCl_4) 4.31 (2 H, m, CH=CH), 6.39 (3 H, s, Me), 7.0br (1 H, m, CH·CO_2), 8.0 (3 H), 8.7 (2 H), and 9.11 (9 H, s, Bu^t); and *methyl* 5-*t-butylcyclohex-1-enecarboxylate* (Found: C, 73.7; H, 10.2%), τ (CCl_4) 3.15 (1 H, m, CH=), 6.38 (3 H, s, Me), 7.5—9.0 (7 H), and 9.10 (9 H, s, Bu^t).

cis- *and* trans-5-*t-Butylcyclohex-2-enecarboxylic Acids.*—The carboxylic acids were obtained as before by hydrolysis in aqueous 1,4-dioxan containing toluene-*p*-sulphonic acid. The trans-*isomer* had b.p. 110° (bath) at 0.05 mmHg and formed needles [from light petroleum (b.p. 40—60 °C)], m.p. 93—93.5° (Found: C, 72.3; H, 10.0. $C_{11}H_{18}O_2$ requires C, 72.5; H, 10.0%), τ (CCl_4) −2.12 (1 H, s, CO_2H), 4.21 (2 H, s, CH=CH), 6.89 (1 H, m, CH·CO_2), 7.6—8.9 (5 H), and 9.11 (9 H, s, Bu^t). The cis-*isomer* had b.p. 110° (bath) at 0.05 mmHg, m.p. 83.5—84.5° (Found: C, 72.7; H, 9.9%), τ (CCl_4) −2.17 (1 H, s, CO_2H), 4.25 (2 H, m, CH=CH), 6.9br (1 H, m, CH·CO_2), 7.7—8.3 (3 H), 8.4—8.9 (2 H), and 9.11 (9 H, s, Bu^t).

Methyl trans- *and* cis-3-*t-Butylcyclohexanecarboxylate.*—Methyl *trans*-5-t-butylcyclohex-2-enecarboxylate (260 mg) was hydrogenated in methanol (10 ml) over platinum oxide (*ca.* 50 mg) at 20 °C. Distillation gave *methyl* trans-3-*t-butylcyclohexanecarboxylate* (235 mg), b.p. 100° (bath) at 10 mmHg (Found: C, 72.4; H, 10.9. $C_{12}H_{22}O_2$ requires C, 72.7; H, 11.2%), τ (CCl_4) 6.34 (3 H, s, OMe), 7.3 (1 H, m, CH·CO_2), 7.7—8.0 (2 H), 8.2—9.0 (7 H), and 9.13 (9 H, s, Bu^t). In a similar way the cis-*isomer*, b.p. 100° (bath) at 10 mmHg (Found: C, 72.4; H, 11.0%), τ (CCl_4) 6.38 (3 H, s, OMe), 7.6—9.0 (10 H), and 9.12 (9 H, s, Bu^t), was prepared.

trans- *and* cis-3-*t-Butylcyclohexanecarboxylic Acids.*—The *trans*-ester (235 mg) and sodium hydroxide (2 equiv.) in aqueous 10% methanol (20 ml) were stirred at 20 °C for 14 h. Isolation of the acid fraction (190 mg) followed by crystallisation from light petroleum (b.p. 40—60 °C) gave *trans*-3-t-butylcyclohexanecarboxylic acid, m.p. 116—117° (lit.,[4a] 114—115.5°; lit.,[4b] 119—120°), τ (CCl_4) −2.1 (1 H, s, CO_2H), 7.20 (1 H, m, CH·CO_2), 7.6—9.1 (9 H), and 9.12 (9 H, s, Bu^t) (lit.,[4b] 7.19 and 7.5—9.1). Similarly, hydrolysis of the *cis*-ester gave the *cis*-acid, m.p. 94.5—95.5° (lit.,[4a] 94.5—95.0°; lit.,[4b] 94.5—95.5°), τ (CCl_4) 7.6—9.1 (10 H) and 9.12 (9 H, s, Bu^t) (lit.,[4b] 7.5—9.1°).

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