Products of the Hydrogenation of 1,1,3-Trimethyl-5-carboxy-3-(*p*-carboxyphenyl)indan

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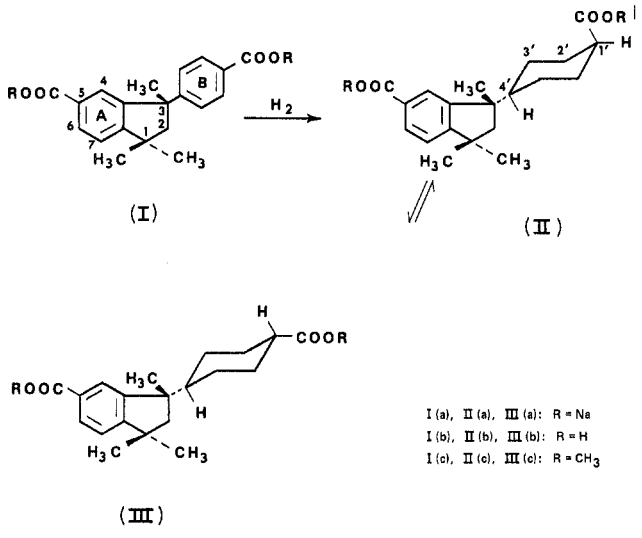
This investigation pertains to the stereochemistry of the catalytic hydrogenation of an aqueous solution of the sodium salt of 1,1,3-trimethyl-5-carboxy-3-(*p*-carboxyphenyl)indan (Ia), using ruthenium on carbon as catalyst.



1,1,3-Trimethyl-5-carboxy-3-(*p*-carboxyphenyl)indan has been known since 1933,[1] but it has only recently assumed commercial significance[2] under the acronym PIDA (phenylindandicarboxylic acid). The catalytic hydrogenation of this trimethylphenylindandicarboxylic acid or its derivatives has not been reported previously. The hydrogenation of the parent hydrocarbon, 1,1,3-trimethyl-3-phenylindan, with a nickel on diatomaceous earth catalyst has been reported in the patent literature[3] to result in saturation of the pendant ring, but no evidence was presented.

Selective Hydrogenation.—While aromatic acids can be hydrogenated directly in aqueous slurry by use of rhodium[4,5] or palladium[6] catalysts, better selectivity is obtained by hydrogenation of the solution of the sodium salt using ruthenium catalysis.[7] The conditions described in the Experimental Section afforded exclusively the *cis* and the *trans* isomers of 4′-[3-(1,3,3-trimethyl-5-carboxyindanoyl)]cyclohexanecarboxylic acid (II and III). These two isomers were produced in a 47:53 proportion as determined by gas chromatographic analysis of the dimethyl esters. No isomerization occurred during the esterification or chromatographic procedures.[8]

The dimethyl esters of the two stereoisomers were also separated by liquid chromatography. By working with 60:40 mixtures of the two cyclohexane derivatives, it was established that the order of elution was the same in both gas chromatography and liquid chromatography. The mass spectra of the separated dimethyl esters indicated reduction of only one aromatic ring (*m/e* 358).

Evidence that the indan ring remained intact was provided by the fact that the most intense mass-spectral peak of the dimethyl ester of the product corresponded to the trimethylindancarboxylic acid ester ion (*m/e* 217). Nmr spectra of the product had the aromatic region simplified by removal of the $A'_2B'_2$ pattern of ring B, leaving the AB pattern of ring A with a superimposed singlet owing to absorption by the third proton of ring A.

The lack of reduction at ring A is attributable to the severe steric effects of the methyl branching on the alicyclic portion of the indan ring and the asymmetric carbon in the 3 position, which contains methyl and carboxy phenyl groups, preventing adsorption of ring A on the carbon surface.

Stereochemistry of Products.—Absolute identification of the products of the hydrogenation of the trimethylphenylindandicarboxylic acid (I) as the *cis* and *trans* isomers (II and III) and evidence that the first isomer to be eluted from chromatography columns was *cis*-4-[3-(1,3,3-trimethyl-5-carboxyindanoyl]cyclohexanecarboxylic acid (II) were provided by nmr analyses. Two significant differences in the nmr spectrum were noted, which are due to the conformational differences of the proton and carbomethoxy group about C-1 of the cyclohexane ring.

The spectra of the first component eluted contained a proton peak at 2.60 ppm which did not occur in the spectra for the second component. We may assume that this is due to a proton equatorial to the carbomethoxy group on the cyclohexyl ring. It is known that for a wide variety of six-membered-ring systems the equatorial ring proton absorbs at lower field than does the axial proton.[9] The axial proton of the second component eluted (*trans* isomer) is probably masked by the cyclohexyl methylene group absorption at 1.9–2.2 ppm.

There also occurs a very slightly greater shielding of the carbomethoxy group in the axial position than in the equatorial position. This was detected by placing the samples of the two isomers in separate capillary tubes and rotating the combined tubes in the nmr field, producing a composite spectrum.[10] The absorption peak due to the carbomethoxy protons on the cyclohexane ring (δ 3.66) showed a shoulder peak which was not present in the spectra of the separate isomers. That the upfield peak was indeed due to the first compound was shown by varying the quantities of sample in the separate tubes.

Elution of the *trans* diequatorial conformer (IIIc) after the *cis* axial–equatorial conformer (IIc) is consistent with previous observations and has been attributed to the fact that the equatorial groups are

(1) N. Puranen, *Ann. Acad. Sci. Fennicae*, **37A**, No. 10, 1 (1933).
(2) A. Steitz, Jr., and J. O. Knobloch, *J. Paint Technol.*, **40**, No. 524, 384 (1968).
(3) G. C. Wiggins, U. S. Patent 2,629,751 (1953).
(4) F. F. Rosenblatt, U. S. Patent 2,675,390 (1954).
(5) M. Freifelder, D. A. Dunnigan, and E. J. Baker, *J. Org. Chem.*, **31**, 3438 (1966).
(6) H. C. Dehm and L. F. Maury, U. S. Patent 2,888,484 (1959).
(7) L. L. Ferstandig and W. A. Pryor, U. S. Patent 2,828,335 (1958).
(8) A. Steitz, Jr., *J. Org. Chem.*, **33**, 2978 (1968).
(9) N. S. Bhacca and D. H. Williams, "Applications of NMR Spectroscopy in Organic Chemistry," Holden-Day, Inc., San Francisco, Calif., 1964, p 47.
(10) E. M. Banas, *Appl. Spectrosc.*, **23**, No. 3 (1969).

more available and thus show larger attractive forces to other molecules.[11]

Equilibrium of Products.—The relative thermodynamic stability of two cyclohexanecarboxylic acids can be determined by keeping the mixture above its melting point for *ca.* 24 hr to achieve thermal equilibrium and then rapidly cooling the mixture below the freezing point.[8] The conformational equilibrium of the *cis* and *trans* isomers of 4-[3-(1,3,3-trimethyl-5-carboxyindanoyl)]cyclohexanecarboxylic acid (IIb and IIIb) should be analogous to that of 4-*t*-butylcyclohexanecarboxylic acid.[12] The conformational equilibrium at C-1 should be that predicted from the conformational free-energy differences of the carboxy group ($-\Delta G^\circ_{COOH} = RT \ln K = 1.2$ kcal/mol), favoring the equatorial carboxy conformation.[13] The comparison of the thermodynamic isomer equilibrium composition experimentally found with that theoretically expected is shown in Table I.

TABLE I

EQUILIBRIUM DATA FOR THE REACTION IIb ⇄ IIIb

Temp, °K	493	513	533	553	573
% *trans*, found[a]	81.7	78.4	77.1	75.8	75.8
% *trans*, calcd	77.4	76.5	75.7	75.0	74.2

[a] Based on the ratio of the two isomers; does not include the sample impurities.

The agreement between the theoretical and experimental values is reasonably good. Although 3–16% decarboxylation occurred during the equilibration, apparently it is not stereospecific. In these equilibrated samples the second peak in chromatography predominates. Since the *trans* isomer was expected to occur in excess owing to the stability of 1,4-diequatorial isomers, this constitutes confirmatory evidence that the original structural assignment to the second peak based on nmr data was correct.

Hydrogenation of Ia must be kinetically controlled, since the product mixture contains relatively large quantities of the *cis* isomers (47:53 ratio, *cis* isomer eluting first in chromatography) as compared with the equilibrated mixture above.[14] Hydrogenation mechanistically occurs by *cis* addition of hydrogen atoms from the catalyst surface.

For preparative purposes it was found convenient to extract the *cis* isomer IIb from a thermally equilibrated isomeric mixture of free acids containing 78% *trans* isomer with chloroform;[15] this yielded *trans* isomer of 95% purity. When the mixture of *cis* and *trans* acids was crystallized from alcohol containing finely divided carbon (Norit), the *cis* acid preferentially crystallized on the carbon. Removal of the carbon from the neutralized acid and acidification yielded the *cis* isomer in 88% purity. It is interesting that the *cis* isomer, which is kinetically favored during hydrogenation on carbon support, also selectively crystallizes in the presence of carbon, suggesting a common adsorption complex.

(11) N. L. Allinger and R. J. Curby, Jr., *J. Org. Chem.*, **26**, 933 (1961).

(12) Heating either isomer of 4-*t*-butylcyclohexanecarboxylic acid at 230° (503°K) gives a mixture containing 76% *trans* isomer corresponding to $-\Delta G^\circ = 1.15$ kcal/mol: E. L. Eliel, N. L. Allinger, S. J. Angyal, and G. A. Morrison, "Conformational Analysis," John Wiley & Sons, Inc., New York, N. Y., 1965, p 43.

(13) Reference 12, p 44.

(14) It should be emphasized that the equilibrium data were obtained on the free acid product, whereas the hydrogenation was on the sodium salt of the acid. However, the equilibrium for a cyclohexyl carboxylate ion favors the equatorial conformation (*trans* isomer in this case) even more than for the free acids, since the conformational free-energy difference of a carboxylate ion is greater (2.3 kcal/mol).

(15) R. Malachowski and J. Jankiewiczowna, *Chem. Ber.*, **67B**, 1783 (1934).

Experimental Section

Starting Materials.—1,1,3-Trimethyl-5-carboxy-3-(*p*-carboxyphenyl)indan is produced as a developmental product by Amoco Chemicals Corp. in over 99.5% purity, neut equiv 345 ± 1 (theory 345.7). The nmr spectra and assignments are: δ 1.12 (3 H, CH_3-1), 1.40 (3 H, CH_3-1), 1.80 (3 H, CH_3-3), 2.25 (q, 2 H, J = 13 cps, diastereometric protons, CH_2), 7.60 (m, 3H, aromatic protons), 8.20 (m, 4H, aromatic protons), and 11.0 (2H, carboxy proton).

Hydrogenation of 1,1,3-Trimethyl-5-carboxy-3-(*p*-carboxyphenyl)indan.—To an aqueous solution containing 20 wt % disodium 1,1,3-trimethyl-5-carboxy-3-(*p*-carboxyphenyl)indan was added 5 wt %, based on free dicarboxylic acid, ruthenium on carbon (5% Ru), and the mixture was hydrogenated at 150° (100 atm). Hydrogen absorption stopped after 6 hr when a 200-g sample was reduced in a 1-gal. autoclave. The product was filtered successively through coarse and fine paper to remove catalyst, acidified with 6 *N* sulfuric acid to pH 2–4, filtered, and washed with hot water. The dried acid amounted to 98 mol%, neut equiv 339 (theory 340), mp 220–230°. The acids were esterified with diazomethane[10] and analyzed by gas chromatography on a 3 ft × 0.125 in. column of 5% SE-30 silicone grease–0.5% Carbowax 6000 on Chromosorb W, with the temperature programmed from 150 to 250° at 10°/min. It contained 52.2% *trans* isomer, 46.6% *cis* isomer, and 1.2% monobasic acid. The aromatic portion of the nmr spectrum displays an AB quartet centered at δ 7.54. The chemical shift of H-7 is at δ 7.25 (J = 9.0 cps) and that of H-6 is at δ 7.84 (J = 9.0 cps); H-4 absorbs as a singlet at δ 7.69.

Anal. Calcd for $C_{20}H_{26}O_4$: C, 72.8; H, 7.88. Found: C, 72.6; H, 8.10.

Liquid Chromatography of Dimethyl Ester of 4′-[3-(1,3,3-Trimethyl-5-carboxyindanoyl]cyclohexanecarboxylic Acid.—The dimethyl esters were also separated on a silica gel column with 1:1 chloroform–benzene as eluent. The first cut was 99.5% pure by gas chromatography, and the second cut was 96% pure and contained 4% of the component of cut 1. The mass spectra for the two components were nearly identical, the most intense peak occurred at m/e 217, corresponding to bond rupture between the indan and cyclohexane rings. Nmr inspections were made on the two components separately and conjointly in a novel multicloistered cell. A peak at δ 2.60 in the first component is attributed to the equatorial hydrogen of the *cis* isomer. The conjoint spectrum shows a doublet at δ 3.66 not present in either component, indicating that a slight shift upfield occurred for this methoxy proton of the *cis* conformation.

Thermal Equilibration.—Two-gram samples of the hydrogenation product were heated in test tubes in a thermostatically controlled aluminum block at the designated temperatures for 24 hr. The molten samples were rapidly chilled to their solidification point, pulverized, and analyzed by esterification and gas chromatography (Table II).

TABLE II

Temp, °K	Feed	493	513	533	553	573
cis isomer	48.0	17.8	21.0	21.8	22.3	20.3
trans isomer	49.1	79.4	76.0	73.2	69.8	63.7
Monobasic acids	2.9	2.8	2.9	4.9	7.9	16.0

Chemical Separation.—A sample of hydrogenation product was heated at 220° (493°K) for 24 hr, pulverized, and extracted with five parts of chloroform for 4 hr. Chilling the extract gave 36 wt % of crystals analyzing as 94.8% *trans* isomer and 5.2% *cis* isomer by esterification and gas chromatography.

A sample of hydrogenated product was crystallized from 80% ethyl alcohol–water three successive times. The composition of the crystals remained at 40% *cis* and 60% *trans* isomer. However, when carbon was added for decolorization, the crystals adhering to carbon during filtration of carbon (20% of sample) were 88.3% *cis* and 11.7% *trans* isomer, as determined after sep-

aration from the carbon by dissolving in sodium hydroxide, filtration, and regeneration.

Registry No.—IIb, 22946-47-0; IIc, 22946-48-1; IIIb, 22966-73-0; IIIc, 22966-74-1.

Acknowledgment.—The author is indebted to the Research and Development Department of American Oil Co. for aid, particularly to E. M. Banas for nmr determinations, T. L. Hunter and G. W. Powers for chromatographic separations, and S. Meyerson for mass spectral determinations.

Vapor Phase Thermolyses of 3-Hydroxy-1,5-hexadienes. V. The Preparation of Allyl Vinyl Ketone[1]

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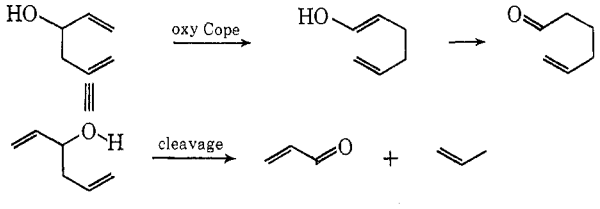
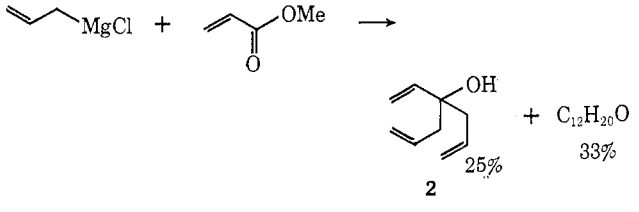
The synthetic utility of the oxy-Cope reaction[2] thus far has consisted of a potential route to Δ^5-unsaturated carbonyl compounds or secondary products derived therefrom.[2-4] The oxy-Cope reaction, however, is almost invariably accompanied by a competing β-hydroxyolefin cleavage[5] which, in this system, may provide a facile route to α,β-unsaturated carbonyls.

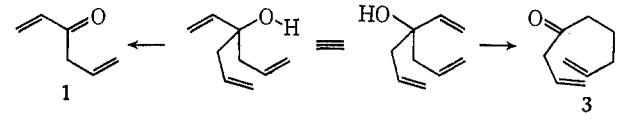


We have utilized this approach for the preparation of vinyl allyl ketone (1,5-hexadien-3-one) (**1**) in the following manner. The reaction of methyl acrylate with excess allylmagnesium chloride gave the expected 4-vinyl-1,6-heptadien-4-ol (**2**), albeit not as the major constituent of the product mixture.[6]



2

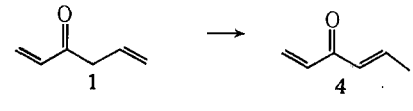
The structure of the previously reported[7] carbinol **2** was verified by its infrared spectrum and by quantitative hydrogenation to 4-ethyl-4-heptanol. The vapor phase thermolysis of **2** afforded the expected oxy-Cope product, 1,8-nonadien-4-one (**3**) and the desired cleavage product **1**.



1 **3**

Under these conditions, there is no apparent tendency for double bond migrations. Thus, the structure of **3** was established by spectral data, by quantitative hydrogenation to 4-nonanone, and by oxidation which gave glutaric and succinic acids by cleavage of C_3–C_4 and C_4–C_5 bonds, respectively. The absence of any Δ^1 double bond rearrangement was established by the ultraviolet spectrum, which showed only end absorption above 220 mμ, except for the small n $\rightarrow$ π^* band at 292 mμ, and by the nmr spectrum, which contains a two-proton doublet, with long range splitting, at δ 3.17, in agreement with a methylene group flanked by a carbonyl and a vinyl group.[8] Furthermore, the integrated areas of the nmr peaks clearly indicate the presence of six vinyl protons.

The structure assignment of **1** is based on spectral data and quantitative hydrogenation to 3-hexanone. Here again, the absence of any double bond migration is firmly established by the nmr spectrum, whose integrated peak areas indicate a 3:1 ratio of vinyl to aliphatic protons. The aliphatic doublet at δ 3.34 shows long range splitting and is in the region appropriate for its carbonyl and vinyl environment.[8] With prolonged standing, a small doublet gradually appeared at δ 2.1, indicative of the formation of a methyl group as in crotonaldehyde,[9] in accord with double bond migration to form vinyl propenyl ketone **4**.



1 **4**

The characteristics of **1** prepared by this method are not in accord with those reported previously. The preparation of Nazarov and Zareteskaya,[10] consisting of hydration of divinylacetylene in strong acid media, is reported to polymerize rapidly, and the only structure proof appears to be acidcatalyzed cyclohydration to 2-methyltetrahydro-4-pyrone. These properties, as well as the physical constants given, appear more in accord with the vinyl propenyl ketone structure **4**, and

(1) (a) Part IV: A. Viola and J. H. MacMillan, submitted for publication; (b) abstracted from part of the Ph.D. dissertation of E. J. I., Northeastern University, June 1968.

(2) J. A. Berson and M. Jones, Jr., *J. Amer. Chem. Soc.*, **86**, 5017, 5019 (1964); A. Viola and L. Levasseur, *ibid.*, **87**, 1150 (1965).

(3) A. Viola, E. J. Iorio, K. K. Chen, G. M. Glover, U. Nayak, and P. J. Kocienski, *ibid.*, **89**, 3462 (1967).

(4) J. Chuche and J. Wiemann, *Bull. Soc. Chim. Fr.*, 1491 (1968); J. W. Wilson and S. A. Sherrod, *Chem. Commun.*, 143 (1968); J. Chuche and N. Manisse, *C. R. Acad. Sci. Paris, Ser. C*, **267**, 78 (1968); A. Viola and J. H. MacMillan, *J. Amer. Chem. Soc.*, **90**, 6141 (1968).

(5) R. T. Arnold and G. Smolinsky, *ibid.*, **81**, 6443 (1959); *J. Org. Chem.*, **25**, 129 (1960); G. G. Smith and B. L. Yates, *J. Chem. Soc.*, 7242 (1965).

(6) The major $C_{12}H_{20}O$ component was shown to be 4-vinyl-1,9-decadien-4-ol, probably resulting from addition of the allyl Grignard reagent to one of the terminal allylic positions of **2**. The structure proof of this compound has been described (R. Proverb, Annual Student Symposium of the Northeastern Section of the American Chemical Society, M.I.T., Cambridge, Mass., May 1968), and the reaction, of which the above constitutes one example, will be further discussed in a subsequent paper.

(7) I. N. Nazarov and A. I. Kakhniashvili, *Sb. Statei Obshch. Khim.*, **2**, 919 (1954); *Chem. Abstr.*, **49**, 6848 (1955).

(8) R. M. Silverstein and G. C. Bassler, "Spectrometric Identification of Organic Compounds," 2nd ed, John Wiley & Sons, Inc., New York, N. Y., 1967.

(9) N. S. Bhacca, L. F. Johnson, and J. N. Shoolery, "High Resolution Nmr Spectra Catalog," Varian Associates, Palo Alto, Calif., 1962.

(10) I. N. Nazarov and I. I. Zareteskaya, *Bull. Acad. Sci. USSR, Div. Chem. Sci.*, 200 (1942); *Chem. Abstr.*, **39**, 1619 (1945).