Geometrical Isomers of 3,6-Dimethyl-7-phenyl-2,4,6-heptatrienoic Acid

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The 2-*cis* (I) and 2-*trans* (II) isomers of 3,6-dimethyl-7-phenyl-2,4,6-heptatrienoic acid and their methyl esters have been isolated and their structures established by their NMR characteristics. The 4-carboxy derivative (III) has been obtained in two isomeric forms: (1) m.p. 165–167°, the 2-*cis*-4-*cis* isomer (from the β-methylglutaconate condensation) and (2) m.p. 116°; 191° (from saponification of its ester). The latter is assigned a bimolecular structure on the basis of its molecular weight and absorption characteristics.

Previously described techniques[1-5] used in assigning configurations to isomers of the methylphenyl substituted pentadienoic[5] and heptatrienoic[4] acids have been applied to the heptatrienoic acids obtainable from α-methylcinnamaldehyde. The Reformatsky reaction with 5-methyl-6-phenyl-3,5-hexadien-2-one (IV), from acetone and α-methylcinnamaldehyde, gives a 72% yield of a mixture (*ca.* 60:40) of the 2-*cis* and 2-*trans* isomers of 3,6-dimethyl-7-phenyl-2,4,6-heptatrienoic acid esters. Saponification gives the 2-*trans* acid, m.p. 181–182°, which is readily separated as its insoluble potassium salt. The 2-*cis* acid, m.p. 170–171°, is obtained free of the *trans* isomer by recrystallization of the solid from the mother liquors. Both give methyl esters configurationally pure at the 2-bond as established by their n.m.r. characteristics (Table I). The τ values for the 3-methyl groups are 7.68 *cis* to carbomethoxy and 7.90 *trans* to carbomethoxy. The deshielding effect of the *cis* carbomethoxy (0.22 τ) on the 3-methyl group protons is somewhat less than that (0.31 τ) for the 3-methyl-7-phenylheptatrienoic isomers but nearly the same as that (0.23 τ) observed for the 3-methyl-5-phenyl-pentadienoic isomers. The assignment of the absorption band at 7.68 τ to the 3-methyl group cis to the carbomethoxy group is confirmed by its enhanced deshielding (0.25 τ) observed in measurements on the acid in pyridine. The magnitude of this shift is comparable to that (0.25 τ) observed with 3-methyl-5-phenyl-2,4-pentadienoic acid in pyridine.[4] The 2-*cis* configuration is further confirmed by the presence of the very low field (τ = 2.15) proton on C-4 deshielded by the methoxycarbonyl *cis* to it.

TABLE I

NUCLEAR MAGNETIC RESONANCE ABSORPTION DATA[a]

	I (2-*cis*)	II (2-*trans*)	III (diacid)	IV[c] (ketone)
H-2	4.50	4.32	4.18	
H(3-CH$_3$)	7.90	7.68	8.05	7.82
H-4	2.15 (J = 16 c.p.s.)	3.82 (J = 16 c.p.s.)	. . .	3.95 (J = 16 c.p.s.)
H-5	3.42 (J = 16 c.p.s.)	3.33 (J = 16 c.p.s.)	(Obscured)	2.93 (J = 16 c.p.s.)
H(6-CH$_3$)	7.95	7.98	8.00	8.02
H-7	3.53	3.48	3.36	3.30
H(3-CH$_3$[b])	7.87	7.43	7.83	

[a] For description of instrumentation, techniques, and conventions, see Experimental. All absorption maxima, except the aromatic proton absorption at a = 2.2–2.9 and the methoxyl proton absorption at τ = 6.4, of significant intensity are listed. [b] These values are for the acid in pyridine. [c] Values are given for comparable structural units. See formula IV.

The configuration at the 4–5 double bond is established as *trans* in both isomers by the characteristic J splitting values (16 c.p.s.) for the H-4–H-5 couplings in each isomer and also by the presence of a strong band in the infrared at 960 cm.$^{-1}$ (2-*trans* isomer) and 965 cm.$^{-1}$ (2-*cis* isomer) in the range characteristic for that of the C—H out of plane deformation in the *trans* CH═CH grouping. The infrared absorption in the 3-methyl analogs was in the same range but slightly higher (994, 988 cm.$^{-1}$). The J values for these 3,6-dimethyl compounds provide a more positive assignment for the protons in these configurations than was possible for the 3-methyl analogs in which the absence of the 6-methyl group introduced additional couplings and obscured the doublet at 3.42 τ for the H-5. The assignment of the doublet absorptions at 3.82 τ to the H-4 and 3.33 τ to the H-5 in II seems reasonable with reference to the H-5 value of τ = 3.42 in I and suggest a reversal of the assignments for these two protons in the corresponding monomethyl compounds. The starting ketone and the α-methylcinnamaldehyde both gave n.m.r. absorption maxima indicating that they were pure and *trans* at the bond adjacent to the ring. The protons of the methyl group in the propenylbenzene structure in other compounds under study in our laboratories, show an n.m.r. absorption in the range of 7.95–8.02 τ when *cis* to the benzene ring.

The condensation of α-methylcinnamaldehyde with β-methylglutaconic ester gives a dicarboxylic

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(1) L. M. Jackman and R. H. Wiley, *Proc. Chem. Soc.* (London), 196 (1958).

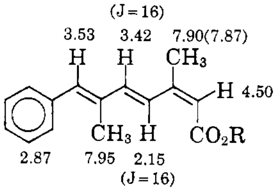
(2) L. M. Jackman and R. H. Wiley, *J. Chem. Soc.*, 2881 (1960).

(3) L. M. Jackman and R. H. Wiley, *ibid.*, 2886 (1960).

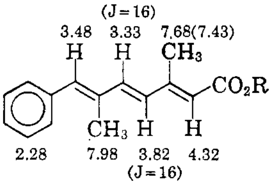
(4) R. H. Wiley, P. F. G. Nau, and T. H. Crawford, *J. Org. Chem.*, **26**, 4285 (1961).

(5) R. H. Wiley, T. H. Crawford, and C. E. Staples, *ibid.*, submitted.

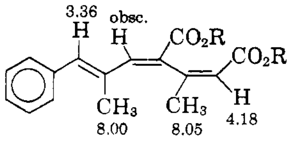
acid, m.p. 165–167°, to which the 2-*cis*-4-*cis* structure (III) is assigned by analogy with other reaction products obtained in this reaction. The low λ_{max} 302, ϵ 24,300 are in accord with the nonplanar structure associated with other compounds of this type. The position and intensity of this maximum are somewhat lower than those observed in the 3-methyl-7-phenylheptatrienoic acid series (λ_{max} 316.5, ϵ 36,000). The decarboxylation of this dicarboxylic acid gives the 2-*cis* acid, m.p. 170–171°, identical with the Reformatsky product.



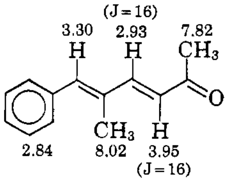
I



II



III



IV

An isomer of the dicarboxylic acid has been obtained by saponification of its methyl ester, m.p. 57°. This is of particular interest because previously no geometrical isomer of this type of 2-*cis*-4-*cis* structure has been obtained and unambiguously characterized.[6] This acid has a double melting point—116°; 191°— and is convertible to the material showing only the higher melting point on vacuum drying at 76°. Both materials, that with the double and that with the single melting point, have identical ultraviolet, n.m.r., and infrared spectral characteristics but are different from the acid, m.p. 165°. The ebullioscopic molecular weight in toluene for this acid is double that required of the heptatrienoic acid. The methyl ester also has the characteristics of a dimeric material. From this we conclude that the product is in fact a dimer, presumably formed *via* a diene addition which may be reversible and that a geometrical isomer of the 2-*cis*-4-*cis* diacid is still not in hand.

Experimental

5-Methyl-6-phenyl-3,5-hexadien-2-one.—This compound was obtained in 85% yield from the sodium hydroxide-catalyzed condensation of α-methylcinnamaldehyde (Distillation Products Industries) with acetone in water–methanol; b.p. 113–117°/0.2 mm.; m.p. 70–72° (ex. petroleum ether). The analytical sample melted at 72.5–73.5°; reported,[7] 62°; λ_{max} 311 mμ; ϵ 32,500.

Anal. Calcd. for $C_{13}H_{14}O$: C, 83.83; H, 7.58. Found: C, 83.68; H, 7.48.

The Reformatsky Reaction.—The above ketone, 24 g., and 24 g. of methyl bromoacetate in 250 ml. of dry benzene reacted vigorously when added (30 min.) to 10 g. of zinc under benzene. The mixture was decomposed with acetic acid, diluted with ether, and washed with water. The crude, dry product wax refluxed 30 min. with 1.5 g. of *p*-toluenesulfonic acid in 800 ml. of benzene to give the theoretical amount of water. The unsaturated ester, 48 g., 72%, b.p. 140–150°/0.3 mm. was collected. The n.m.r. absorption indicated this to be a mixture of 2-*cis* and 2-*trans* isomers.

The crude, unsaturated ester (45 g.) was saponified by warming to solution in a solution of 50 g. of potassium hydroxide in 200 ml. of water and 800 ml. of methanol, standing 1 day at room temperature, and cooling 8 hr. to precipitate 16.1 g. of the potassium salt of the 2-*trans* isomer. Acidification and recrystallization for ethanol gave 12.3 g. of yellow needles, m.p. 181–182°; λ_{max} 318 mμ; ϵ 45,000.

Anal. Calcd. for $C_{15}H_{16}O_2$: C, 78.92; H, 7.06; neut. equiv., 228.3. Found: C, 79.06; H, 7.15; neut. equiv., 227.8.

The methyl ester of the 2-*trans* acid was prepared using diazomethane in ether and recrystallized from methanol–water, m.p. 54°; λ_{max} 324 mμ; ϵ 46,300 (methanol).

Anal. Calcd. for $C_{18}H_{18}O_2$: C, 79.31; H, 7.49. Found: C, 79.54; H, 7.71.

The *p*-bromophenacyl ester of the 2-*trans* acid was prepared, m.p. 170.5–171° from ethanol–water.

Anal. Calcd. for $C_{23}H_{21}O_3Br$: C, 64.95; H, 4.98. Found: C, 64.88; H, 4.98.

The 2-*cis* acid was obtained from the methanol solutions from which the solid potassium salt had precipitated. Removal of methanol under reduced pressure, extraction of the residue with ether, and acidification of the residue precipitated the crude acid, m.p. 110–140°. After several recrystallizations from ethanol, there was obtained 5.3 g. of the 2-*cis* acid as yellow crystals, m.p. 170–171°; λ_{max} 321 mμ; ϵ 39,700 (methanol).

Anal. Calcd. for $C_{15}H_{16}O_2$: C, 78.92; H, 7.06; neut. equiv., 228.3. Found: C, 78.86; H, 7.15; neut. equiv., 228.8.

The methyl ester was prepared from the acid and diazomethane in ether; m.p. 33°; λ_{max} 328 mμ; ϵ 39,600 (methanol).

Anal. Calcd. for $C_{18}H_{18}O_2$: C, 79.31; H, 7.49. Found: C, 79.34; H, 7.57.

The *p*-bromophenacyl ester of the 2-*cis* acid, m.p. 130–131°, recrystallized from ethanol–water.

Anal. Calcd. for $C_{23}H_{21}O_3Br$: C, 64.95; H, 4.98. Found: C, 65.09; H, 5.00.

Condensation of α-Methylcinnamaldehyde with β-Methylglutaconic Ester.—A solution of 7.38 g. of ethyl methyl β-methylglutaconate (Distillation Prod. Industries) and 12.2 g. of α-methylcinnamaldehyde in 13 ml. of methanol was mixed with a solution of 21 g. of potassium hydroxide in 150 ml. of methanol with cooling. The precipitate which had formed after 1 week in a refrigerator was collected, washed with ether, and dried to give 7.7 g. of a crude solid product. Acidification of an aqueous solution of this precipitate with 20% hydrochloric acid gave an oil which solidified on trituration with benzene, m.p. 140–145°. Recrystallization from acetone–benzene gave 2.2 g. of 4-carboxy-3,6-dimethyl-7-phenyl-2-*cis*-4-*cis*-6-*trans*-heptatrienoic acid, m.p. 165–167°; λ_{max} 302 mμ; ϵ 24,300 (ethanol). Analytical data are for the unrecrystallized product, m.p. 146–148°. The melting points depend on the rate of heating and take place with evolution of gas.

Anal. Calcd. for $C_{16}H_{16}O_4$: C, 70.57; H, 5.92; neut. equiv., 136.1. Found: C, 70.63; H, 5.90; neut. equiv., 136, 138.

Decarboxylation of the acid with lutidine–cupric acetate gave the 2-*cis* acid, m.p. 168–169°. This material shows no depression of the melting point when mixed with an authen-

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[6] R. H. Wiley and H. Ellert, *J. Am. Chem. Soc.*, **79**, 2266 (1957).

[7] M. Scholtz, *Ber.*, **32**, 1936 (1899).

tic sample of the 2-*cis* acid prepared by the Reformatsky reaction.

The dimethyl ester of the 4-carboxy acid was obtained by action of diazomethane on the crude diacid from the condensation. The reaction mixture was added to water and the aqueous layer extracted with ether. Acidification of the aqueous layer precipitated an oil which partially solidified. This, with diazomethane, gave an oil (65%), b.p. 135°/0.05 mm., which solidified and was recrystallized from methanol-water, m.p. 57–57.5°; λ_{max} 288 mμ; ϵ 4220 (methanol).

Anal. Calcd. for $C_{18}H_{20}O_4$: C, 71.98; H, 6.71. Found: C, 72.03; H, 7.11.

Saponification of the diester with potassium hydroxide in ethanol under reflux gave a crude solid diacid which was recrystallized from benzene–petroleum ether. This product melts at 116–118°, solidifies, and remelts at 191–193°, λ_{max} 287.5 mμ, ϵ 4050 (methanol).

Anal. Calcd. for $C_{32}H_{32}O_8$: C, 70.57; 5.92; neut. equiv., 136.1, mol. wt., 554. Found: C, 70.44; H, 6.08; neut. equiv., 135; mol. wt. (ebull. toluene), 510 ± 5%.

Vacuum drying of the acid m.p. 116°; 191° at 76° for 10 hr. gave a product showing no melting at 116°; m.p. 191°. There are no differences in the ultraviolet, n.m.r., or infrared between these two compounds.

Anal. Calcd. for $C_{32}H_{32}O_8$: C, 70.57; H, 5.92; neut. equiv., 136.1; mol. wt. 554. Found: C, 70.44; H, 6.08; neut. equiv., 135.5; mol. wt. (ebull. toluene), 558. ± 5%.

The ultraviolet absorption measurements were made with a Beckman DK-2 recording spectrometer in the solvents (spectrograde) stated. The infrared absorption measurements were made with a Baird double beam recording spectrometer with sodium chloride optics and in chloroform (0.04 g./ml.) or as potassium bromide pellets. The n.m.r. measurements were made with a Varian high resolution (Model HR-4302) spectrometer with 60-Mc. oscillator with superstabilizer and field homogeneity control. The calibrations were made by the side band technique at several frequencies. Tetramethylsilane was used as an internal reference standard. Data for the acids were obtained in pyridine solutions; the esters in the carbon tetrachloride at about 15% concentration. Values are given in τ units.[8] Microanalyses by Micro Tech Laboratories, Skokie, Ill. Melting points are not corrected. The acids melt with gas evolution and are best used comparatively at controlled rates of heating.

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(8) G. V. D. Tiers, *J. Phys. Chem.*, **62**, 1151 (1958).

The Isomeric Dinitrocyclohexanes. I. Synthesis of Epimeric 1,3- and 1,4-Dinitrocyclohexanes[1]

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1,4-Dinitrocyclohexane (II) has been prepared by peroxytrifluoroacetic acid oxidation of 1,4-cyclohexanedione dioxime (I) and by sodium borohydride reduction of *cis-* or *trans*-1,4-dibromo-1,4-dinitrocyclohexane (VII). Oxidation of *trans*-1,4-dibromo-1,4-dinitrosocyclohexane (IIIa) by peroxytrifluoroacetic acid affords *trans*-VII. Incidental to the synthetic work the stereochemistry of the isomers of dibromo compounds IIIa and VII and the corresponding dichloro compounds has been established. 1,3-Dinitrocyclohexane has been prepared by peroxytrifluoroacetic acid oxidation of 1,3-cyclohexanedione dioxime and by reaction of 2,6-dinitrohexyl acetate with sodium methoxide. Both epimers of II and IX have been prepared.

Recent years have marked rapid progress in the development of synthetic methods for preparing nitroalkanes and conformational analysis of cyclohexane compounds. It was of interest to extend this knowledge to the preparation of the isomeric dinitrocyclohexanes and to establish the configurations of the six possible isomers. Two of these, of unknown configuration, have been described previously.[2-5]

1,2-Dinitrocyclohexane is prepared by adding dinitrogen tetroxide to cyclohexene.[2-4] The product, a liquid,[2] probably is a mixture of epimers; one (m.p. 46°) has been separated from the mixture.[3,4] One isomer of 1,4-dinitrocyclohexane is formed, in trace amounts, as a by-product of vapor-phase nitration of cyclohexane.[5] No synthesis of 1,3-dinitrocyclohexane has previously been re-

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(5) E. H. Schmorr, *J. Org. Chem.*, **24**, 868 (1959).