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The Rearrangement of Tropones to Dihydrobenzene Derivatives

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The positions of the double bonds in 1-phenylcyclohexadiene-1, 2-dicarboxylic acid, which had been obtained previously by the alkaline rearrangement of 2-phenyltropone-7-carboxylic acid, were elucidated from the spectral data. A similar rearrangement of tropone derivatives to dihydrobenzene derivatives was also observed. Tropone-2-carboxylic acid gave 2, 5-cyclohexadiene-1, 2-dicarboxylic acid, while 2-phenyltropone-5-carboxylic acid afforded 1-phenyl-2, 4-cyclohexadiene-1, 4-dicarboxylic acid. 2-Phenyltropone was also rearranged by alkali to 2-phenyl-2, 5-cyclohexadiene-1-carboxylic acid.

It is well known that tropones with halogen, alkoxyl or tosyloxyl groups on the 2-position easily undergo rearrangement with bases to give benzoic acid derivatives. On the other hand, relatively little is known concerning the rearrangement reaction of tropones with no such active substituents. Tropone is known to give only resinous materials when it is treated with alkali or ammonia.[1] 2-Phenyltropone and 2-*p*-methoxyphenyltropone are fairly stable on alkali and give biphenyl-2-carboxylic acid and 2-*p*-methoxyphenylbenzoic acid respectively.[2,3] Bartels-Keith *et al.* have also described that tropone-4-carboxylic acid gives terephthalic acid.[4] The rearrangement of the tropone derivative to the dihydrobenzene derivative was observed first when thiocolchicine (I) was treated with sodium methoxide to give dihydro γ-lactam (II).[5,6]

Previously it was reported that 2-phenyltropone-7-carboxylic acid gave an acid, $C_{14}H_{12}O_4$ (III), when it was treated with a dilute aqueous sodium hydroxide solution, and that III was assumed to be 1-phenylcyclohexadiene-1, 2-dicarboxylic acid from some chemical evidence, but the positions of the double bonds remained unsettled.[7] In this paper the positions of the double bonds of III, deduced from the spectral data, will be described;

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[1] T. Nozoe, T. Mukai and K. Takase, *Sci. Repts. Tohoku Univ., Ser. I*, **39**, 164 (1956).

[2] T. Nozoe, T. Mukai, J. Minegishi and T. Fujisawa, *ibid.*, **37**, 388 (1953).

[3] T. Nozoe, S. Seto, T. Ikemi, T. Sato and K. Watanabe, *ibid.*, **38**, 130 (1954).

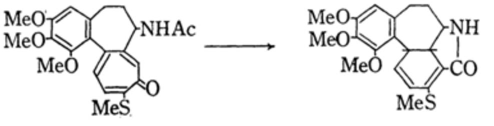
[4] J. R. Bartels-Keith, A. W. Johnson and A. Langemann, *J. Chem. Soc.*, **1952**, 4461.

[5] G. Muller, B. P. Vaterlaus and L. Velluz, *Bull. Soc. Chim. France*, **1957**, 434; B. P. Vaterlaus and G. Muller, *ibid.*, **1957**, 1329.

[6] In a private communication Professor Toshio Mukai noted that the reaction of 2-phenyltropone and liquid ammonia in the presence of ammonium chloride gave an amide of 2-phenylcyclohexadiene-1-carboxylic acid. *Cf.* Ref. 2.

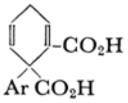
[7] K. Kikuchi, This Bulletin, **34**, 1610 (1961).

also a similar rearrangement of tropone-2-carboxylic acid, 2-phenyltropone-5-carboxylic acid, and 2-phenyltropone will be reported.

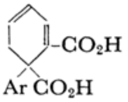


I II

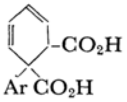
The infrared spectrum of the dimethyl ester (IV) of III shows strong absorption bands at 1740 and 1722 cm^{-1} (saturated and α, β-unsaturated ester). The NMR spectrum of IV exhibits signals at 3.00 (2H, methylene protons, a multiplet), 3.60 and 3.77 (6H, methoxyl protons), 5.91 (2H, olefinic protons, a slightly broadened singlet), and 7.1—7.6 ppm (6H, phenyl and one olefinic protons, a multiplet).⁸⁾ These data clearly exclude the IIIc structure among the three possible isomeric 1-phenylcyclohexadiene-1, 2-dicarboxylic acids (IIIa, IIIb and IIIc). The ultraviolet spectrum of IV fails to show an absorption maximum above 220 mμ. It is expected that, if the double bonds were conjugated in cyclohexadiene derivatives, the absorption maximum in ultraviolet spectrum would appear in the 260—290 mμ region.⁹⁾ These spectral data indicate, therefore, that III is 1-phenyl-2, 5-cyclo-hexadiene-1, 2-dicarboxylic acid (IIIa).



IIIa
Va



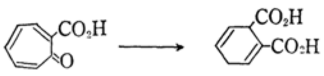
IIIb
Vb



IIIc Ar$=C_6H_5$
Vc Ar$=\alpha$-$C_{10}H_7$

Similarly, the acid obtained by the alkaline rearrangement of 2-α-naphthyltropone-7-carboxylic acid was assumed to be 1-α-naphthylcyclohexadiene-1, 2-dicarboxylic acid (V).⁷⁾ The infrared spectra of the acid (V) and its dimethyl ester (VI) show absorption bands at 1693 and 1723 cm^{-1} respectively. The NMR spectrum of VI exhibits signals at 3.07 (2H, methylene protons, a multiplet), 3.39 and 3.79 (6H, methoxyl protons), 5.97 (2H, olefinic protons, a multiplet), and 7.2—8.1 ppm (8H, naphthyl and one olefinic protons, a multiplet). From these data, the Vc structure can be excluded among the three isomers (Va, Vb and Vc), but Va and Vb could not be distinguished on the basis of the splitting patterns of the NMR signals and the ultraviolet spectrum.

The rearrangement reaction of tropone-2-carboxylic acid¹⁰⁾ was next examined. In this case an acid (VII) with a melting point of 220—222°C (decomp.) was obtained, though in a poor yield; it was identified as 2, 5-cyclohexadiene-1, 2-dicarboxylic acid.¹¹⁾



VII

Such a rearrangement was supposed to occur also with tropone-4-carboxylic acid derivatives. First, the rearrangement of tropone-4-carboxylic acid⁴⁾ with alkali was examined according to the Bartels-Keith's procedure, with only a slight modification; however, no dihydrotere-(or iso)-phthalic acid was isolated. 2-Phenyltropone-5-carboxylic acid was isolated. 2-Phenyltropone-5-carboxylic acid was then synthesized, and its behavior toward alkali was studied.

The reaction of 5-cyanotropolone¹²⁾ and phenylmagnesium bromide gave 5-cyano-2-phenyltropone (VIII), the acid hydrolysis of which afforded 2-phenyltropone-5-carboxylic acid (IX). Similarly, 2-chloro-5-cyanotropone (X), which was obtained by the reaction of 5-cyanotropolone with thionyl chloride, was treated with phenylmagnesium bromide to give 4-cyano-2-phenyltropone (XI).¹³⁾ The acid hydrolysis of XI, however, did not afford the expected 2-phenyltropone-4-carboxylic acid.

When the acid (IX) was heated with a dilute sodium hydroxide solution, a dicarboxylic acid, $C_{14}H_{12}O_4$ (XII), was obtained as colorless crystals. XII reduced an alkaline-ammoniacal silver nitrate solution. The prolonged heating of XII with a dilute sodium hydroxide solution gave biphenyl-4-carboxylic acid. When XII was treated with concentrated sulfuric acid, biphenyl-4-carboxylic acid was also formed, but no halochromic coloration was observed. In the reaction of III or 2-phenylcyclohexadiene-1-carboxylic acid (see below) and sulfuric acid, an intense halochromic coloration was observed as a result of the formation of fluorenone. These results indicate that XII is a 1-phenylcyclohexadiene-1, 4-dicarboxylic acid

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8) The NMR spectra were measured in deuteriochloroform, using tetramethylsilane as an internal standard, on a Varian A-60 spectrometer.

9) Methyl 1, 3-cyclohexadiene-1-carboxylate and methyl 1, 5-cyclohexadiene-1-carboxylate, for example, exhibit absorption maxima at 287—288 mμ (ε 12000) and 274—279 mμ (ε 2780) respectively (W. J. Bailey, R. Barclay, Jr., and R. A. Baylouny, *J. Org. Chem.*, **27**, 1851 (1962)).

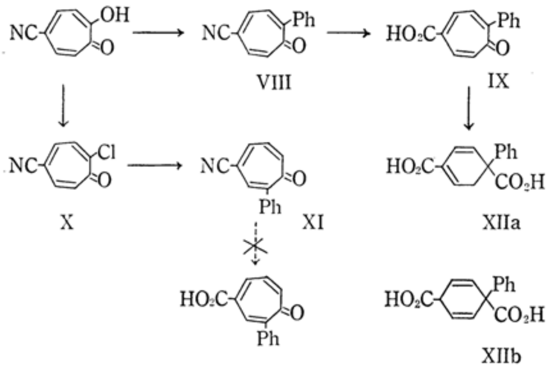
10) T. Nozoe, Y. Kitahara, K. Takase and I. Murata, This Bulletin, **37**, 1292 (1964).

11) M. J. Goldstein and G. L. Thayer, Jr., *J. Am. Chem. Soc.*, **87**, 1925 (1965). In the earlier literature this acid was described as 2, 6-cyclohexadiene-1, 2-dicarboxylic acid.

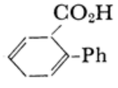
12) Y. Kitahara, *Sci. Repts. Tohoku Univ., Ser. I*, **40**, 74 (1956).

13) As it is well known that the reaction of tropolones with phenylmagnesium bromide or phenyl lithium gives 2-phenyltropone derivatives through the normal substitution of hydroxyl group, while the reaction of 2-chlorotropones with bases usually affords 7-substituted tropones, it is apparent that VIII and XI are actually 5- and 4-cyano-2-phenyltropones.

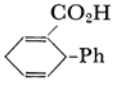
and not a 4-phenylcyclohexadiene-1, 3-dicarboxylic acid. Two double-bond isomers (XIIa and XIIb) are possible in the former. The infrared spectrum of XII exhibits a carbonyl absorption at 1690 cm^{-1}, and the ultraviolet spectrum shows an absorption maximum at 265—270 mμ (ε 3400). From these results it is clear that the acid (XII) is 1-phenyl-2,4-cyclohexadiene-1, 4-dicarboxylic acid (XIIa).



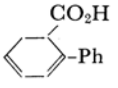
A similar rearrangement was expected to occur in 2-phenyltropone itself. As expected, when it was stirred at 60°C with a dilute sodium hydroxide solution for about 40 hr, colorless crystals with a melting point of 85—120°C were obtained in a 25% yield. The separation of pure components from this mixture was difficult, but repeated recrystallizations from aqueous methanol gave an acid (XIII) with a melting point of 133—136°C. The analytical value agreed with $C_{13}H_{12}O_2$. The treatment of XIII with concentrated sulfuric acid developed a deep bluish-purple color, and the mixture gave fluorenone. This indicates that XIII is 2-phenylcyclohexadiene-1-carboxylic acid. The NMR spectrum of XIII exhibits signals at 2.90 (2H, methylene protons), 4.31 (1H, methine proton), 6.00 (2H, olefinic protons), 6.22 (1H, olefinic proton), 7.1—7.4 (5H, phenyl protons), and 13.6 ppm (1H, carboxyl proton). From this result, among the nine double-bond isomers possible for XIII, five can be excluded; the following four (XIIIa—XIIId) remain to be considered. XIIIb is a known substance[14]; this also can be excluded from consideration. The infrared spectrum of XIII exhibits a strong absorption band at 1697 cm^{-1}, and in the ultraviolet region XIII shows an absorption maximum at 248 mμ (ε 8700), indicating the presence of styrene chromophore. From these spectral data, the acid is thought to be 2-phenyl-2, 5-cyclohexadiene-1-carboxylic acid (XIIIa).



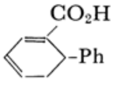
XIIIa



XIIIb



XIIIc



XIIId

Experimental

1-Phenyl-2, 5-cyclohexadiene-1, 2-dicarboxylic Acid (IIIa) and Its Dimethyl Ester (IV). Obtained by the procedure described before.[7]

1-α-Naphthyl-2,5(?)-cyclohexadiene-1,2-dicarboxylic Acid (V). Obtained by the procedure described before.[7]

The Dimethyl Ester (VI). Obtained by the action of diazomethane on V. Colorless crystals, mp 147—148°C.

Found: C, 74.46; H, 5.52%. Calcd for $C_{20}H_{18}O_4$: C, 74.52; H, 5.63%.

The Reaction of Tropone-2-carboxylic Acid and Alkali. A solution of 510 mg of tropone-2-carboxylic acid in 5.0 m*l* of a 1 N sodium hydroxide solution was heated at 90°C for 1 hr, and the resulting dark reddish-brown solution was acidified with dilute hydrochloric acid. The solution was extracted with ether, the solvent was evaporated, and the residue thus obtained was washed with ether and a small amount of alcohol; 46 mg of pale brown crystals, mp 214—222°C (decomp.), were thus obtained. Water was evaporated from the aqueous layer, the residue was extracted with alcohol, and the solvent was evaporated to give 6 mg of second crops as colorless crystals, mp 214—219°C (decomp.). Recrystallization from water gave colorless crystals, mp 220—222°C (decomp.). The melting point and the infrared spectrum were identical with those of 2, 5-cyclohexadiene-1, 2-dicarboxylic acid (VII).

5-Cyano-2-phenyltropone (VIII). Into a solution of phenylmagnesium bromide, prepared from 0.56 g of magnesium and 3.20 g of bromobenzene in 25 m*l* of absolute ether and diluted with 25 m*l* of dry tetrahydrofuran, there was stirred 1.00 g of powdered 5-cyanotropolone under ice cooling; the whole was then heated at 50—55°C for 3 hr. The reaction mixture was decomposed with dilute hydrochloric acid and ice and extracted with 50 m*l* of chloroform, and the organic layer was washed successively with 2 N sodium hydroxide and water. The solvent was evaporated, and the residue was washed with a mixture of ether and petroleum ether to give 510 mg of yellowish-orange crystals with a melting point of 134—137°C. The solvent was evaporated from the filtrate, and the residue was dissolved in a mixture of benzene and petroleum ether (1 : 1) and passed through 10 g of active alumina. From the benzene eluate, 46 mg of second crops, mp 134—137°C, was obtained. Recrystallization from alcohol gave VIII as yellow needles, mp 136—138°C.

Found: C, 81.24; H, 4.02; N, 6.46%. Calcd for $C_{14}H_9ON$: C, 81.14; H, 4.38; N, 6.76%.

2-Phenyltropone-5-carboxylic Acid (IX). A solution of 440 mg of 5-cyano-2-phenyltropone in 4.5 m*l* of 75% sulfuric acid was heated at 140°C for 1 hr; the mixture was then poured onto crushed ice. The precipitate was collected by filtration and washed with ethanol to give 400 mg of IX as yellow crystals, mp 237—239°C (decomp.). Recrystallization from dioxane gave yellow scales, mp 243—244°C (decomp.).

Found: C, 74.12; H, 4.68%. Calcd for $C_{14}H_{10}O_3$: C, 74.33; H, 4.46%.

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[14] J. S. Meek, B. T. Poon, R. T. Merrow and S. J. Cristol, *J. Am. Chem. Soc.*, **74**, 2669 (1952).

2-Chloro-5-cyanotropone (X). A solution of 170 mg of 5-cyanotropolone and 270 mg of thionyl chloride in 4.0 m*l* of benzene was refluxed for 7.5 hr. The evaporation of the solvent and the excess of thionyl chloride afforded a crystalline residue; this residue was then dissolved in chloroform, and the chloroform solution was washed with aqueous sodium carbonate and water. The evaporation of the solvent gave 130 mg of X as pale yellow crystals, mp 138—141°C. Recrystallization from a mixture of benzene and cyclohexane afforded pale yellow needles, mp 143—144°C.

Found: C, 58.74; H, 2.59; N, 8.21%. Calcd for C_8H_4ONCl: C, 58.03; H, 2.43; N, 8.46%.

4-Cyano-2-phenyltropone (XI). Into a solution of phenylmagnesium bromide, prepared from 2.00 g of bromobenzene and 0.37 g of magnesium in 15 m*l* of absolute ether, there was added, drop by drop, 1.00 g of 2-chloro-5-cyanotropone in 15 m*l* of dry tetrahydrofuran under ice cooling; the mixture was then stirred for a further 1.5 hr at 0°C. The mixture was decomposed with dilute sulfuric acid, benzene was added, and the organic layer was washed with water. The evaporation of the solvent left a dark brown oil, which was dissolved in a mixture of benzene and petroleum ether (1 : 1) and chromatographed on 15 g of alumina. The fraction eluted with benzene gave 305 mg of yellow crystals, mp 83—85°C. Recrystallization from a mixture of benzene and cyclohexane afforded XI as yellow needles, mp 84—85°C.

Found: C, 81.21; H, 4.26; N, 6.41%. Calcd for $C_{14}H_9ON$: C, 81.14; H, 4.38; N, 6.76%.

The Attempted Hydrolysis of 4-Cyano-2-phenyltropone (XI). The treatment of 320 mg of XI with 3.0 m*l* of 75% sulfuric acid much as in the case of IX gave yellow crystals, which, after recrystallization from dioxane, afforded 270 mg of yellow microcrystals, mp 216—217°C (decomp.). The analytical values, however, did not coincide with that for 2-phenyltropone-4-carboxylic acid.

The Reaction of 2-Phenyltropone-5-carboxylic Acid (IX) and Alkali. A 220-mg sample of IX was dissolved in 2.0 m*l* of 1 N sodium hydroxide; the solution was then heated on a water bath for 1.5 hr, during which time the solution turned brown. The mixture was neutralized with dilute hydrochloric acid, and the small amount of brown precipitate which separated was removed on filtration. The filtrate was further acidified, and the pale brown crystals were collected. Recrystallization from dilute ethanol gave 1-phenyl-2, 4-cyclohexadiene-1, 4-dicarboxylic acid (XIIa) as pale brown crystals, mp 254—256°C (decomp.). Yield, 108 mg. An analytical sample was recrystallized from aqueous ethanol to give colorless microprismatic crystals, mp 265°C (decomp.).

Found: C, 69.22; H, 4.78%. Calcd for $C_{14}H_{12}O_4$: C, 68.84; H, 4.95%.

XIIa immediately reduced an alkaline-ammoniacal silver nitrate solution, but from the solution no crystalline product was obtained.

The Reaction of XIIa and Concentrated Sulfuric Acid. The addition of 7 mg of XIIa to concentrated sulfuric acid and the heating of the mixture on a water bath gave a pale brown solution under effervescence; after the solution had stood for several minutes, fine needles separated out from it. The mixture was poured onto water, and the precipitate was collected and recrystallized from aqueous ethanol to give pale brown needles, mp 218—221°C; this substance was identical with biphenyl-4-carboxylic acid.

The Reaction of XIIa and Alkali. The heating of 50 mg of XIIa with 0.4 m*l* of 2 N sodium hydroxide on a water bath for about 20 hr gave a sparingly soluble sodium salt, from which biphenyl-4-carboxylic acid was obtained as pale brown needles, mp 218—220°C.

The Reaction of 2-Phenyltropone and Alkali. A 360-mg sample of 2-phenyltropone suspended in 6.0 m*l* of 1 N sodium hydroxide was stirred at 60°C for about 40 hr, during which time the solution turned dark red. The black solid (135 mg) was filtered off, and the filtrate was neutralized cautiously with dilute hydrochloric acid. An oily precipitate, which separated at pH 5—4, amounted to 98 mg. This oil gradually solidified to a colorless mass, mp 60—105°C, but it could not be purified. The second fraction, which precipitated at pH 3—1, amounted to 86 mg, mp 80—120°C. This was recrystallized from aqueous methanol to give 35 mg of colorless crystals, mp 131—137°C. Several recrystallization from the same solvent gave 2-phenyl-2, 5-cyclohexadiene-1-carboxylic acid (XIIIa) as colorless scales, mp 133—136°C.

Found: C, 77.70; H, 6.17%. Calcd for $C_{13}H_{12}O_2$: C, 77.98; H, 6.04%.

The acid in concentrated sulfuric acid developed a deep reddish-purple color. The dilution of the mixture with water gave fluorenone, mp 78—80°C.

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