10 cc. of 10% hydrochloric acid at 50° for 10 minutes and allowed to stand at room temperature for 30 minutes. The solution was distilled until no more ketone came over (100 cc. of distillate) and the product was extracted with petroleum ether. Concentration and evaporative distillation at 140–150° (10 mm.) yielded 2.35 g. (82%) of *trans*-10-methyl-2-decalone (X), $n^{24}D$ 1.4872. The 2,4-dinitrophenylhydrazone, which formed in good yield, was recrystallized from methyl acetate–methanol and melted at 178–179° alone and when mixed with this derivative of authentic *trans*-10-methyl-2-decalone.[3,4,13]

(13) We are grateful to Prof. R. B. Woodward for an authentic sample of *trans*-10-methyl-2-decalone which was used to prepare the 2,4-dinitrophenylhydrazone, m.p. 177–178°.

DETROIT, MICHIGAN

[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY, KRISHNAGAR COLLEGE]

Spiro Compounds. 1. Synthesis of 1,2,3,4-Tetrahydronaphthalene-2,2-spiro-(2′-*n*-propylcyclopentane) and Its Rearrangement on Catalytic Dehydrogenation

BY DHIRENDRA NATH CHATTERJEE

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The spirohydrocarbon 1,2,3,4-tetrahydronaphthalene-2,2-spiro-(2′-*n*-propylcyclopentane) (I) has been synthesized in order to study the rearrangement of the alkyl substituted spirocyclopentane ring during dehydrogenation. On dehydrogenation with platinum-on-charcoal at 300–330°, this spiran yielded 1-methylpyrene. The synthesis of the spiran has been effected starting from the anhydride of 2-*n*-propylcyclopentane-1-carboxy-1-acetic acid and benzene.

Dehydrogenation has been an important tool in elucidating the constitution of many natural products, and also has found fruitful application in other fields. The reaction, however, is complicated and attended by side reactions, for the understanding of which a study of the dehydrogenation of a wide range of polynuclear hydroaromatic compounds is desirable. With this end in view, the catalytic dehydrogenation of a particular spiran has been carried out. Selenium dehydrogenation of a large number of spirans had previously been studied by Clemo and Ormston,[1] Cook and Hewett,[2] Levitz and Bogert,[3] Sengupta[4] and others, who had noted ring transformation during dehydrogenation. Recently Sengupta and Chatterjee[5,6] have synthesized a large number of tetralin derivatives containing an alkyl substituted spirocyclopentane ring and studied their catalytic dehydrogenation. They have found that such spirans with a methyl substituent in the spirocyclopentane ring undergo ring transformation during dehydrogenation giving a methylphenanthrene or its derivative. The methyl group present in the spirocyclopentane ring is not eliminated.[5] On the other hand it has been noted by them[6] that the spiran with an ethyl substituent in the spirocyclopentane ring (I, C_2H_5 in place of C_3H_7) on catalytic dehydrogenation under similar conditions yields pyrene. A probable interpretation of this peculiar ring transformation, as occurring through the intermediate formation of a partially reduced 4-ethylphenanthrene and cyclodehydrogenation of the latter, has been given. In order to see whether similar ring transformation takes place with a spiran having a propyl substituent in the spirocyclopentane ring, the spiran 1,2,3,4 - tetrahydronaphthalene - 2,2 - spiro - (2′-*n*-propyl-cyclopentane) (I) has been synthesized by an extension of the method developed earlier.[5] The anhydride of 2-*n*-propylcyclopentane-1-carboxy-1-acetic acid was condensed with benzene in the presence of aluminum chloride to give a single keto acid which has been proved to be α,α-(2′-*n*-propylcyclopentane)-β-benzoylpropionic acid (II). The keto acid reacted with salicylaldehyde in the presence of hydrogen chloride giving a pyrylium salt. This shows the presence of a keto-methylene grouping[7] and as such excludes the alternative structure for the keto-acid. The keto acid II was readily reduced to α,α-(2′-*n*-propylcyclopentane)-γ-phenylbutyric acid (III) by the Clemmensen method. Cyclization of the butyric acid (III) by 85% sulfuric acid afforded 1-keto-1,2,3,4-tetrahydronaphthalene - 2,2 - spiro - (2′ - *n* - propylcyclopentane) (IV). Failure of this ketone to yield a semicarbazone or 2,4-dinitrophenylhydrazone, due to the hindered position of the keto group, lends additional support to the constitution of the keto acid II from which it was derived.[8] On reduction, which was somewhat sluggish, by the Clemmensen method, the spiro-ketone IV afforded the desired spiran I. This on dehydrogenation with 10% platinum-on-charcoal catalyst at 300–330° gave 1-methylpyrene. This is, therefore, in line with the observation made by Sengupta and Chatterjee[6] with respect to the dehydrogenation of the corresponding ethyl substituted spiran, and the same explanation seems probable. The cyclopentane ring undergoes fission near the heavy propyl group with the formation of an intermediate which by angular cyclization forms a partially reduced 4-*n*-propylphenanthrene. This then undergoes cyclodehydrogenation to 1-methylpyrene. Formation of new rings by cyclodehydrogenation under conditions of catalytic dehydrogenation, have been observed by a number of workers,[9,10]

(1) G. R. Clemo and J. Ormston, *J. Chem. Soc.*, 352 (1933).

(2) J. W. Cook and C. L. Hewett, *ibid.*, 365 (1934).

(3) M. Levitz and M. T. Bogert, *J. Org. Chem.*, **8**, 253 (1934).

(4) S. C. Sengupta, *J. Ind. Chem. Soc.*, **11**, 389 (1934); *ibid.*, **16**, 349 (1939); *ibid.*, **17**, 101 (1940).

(5) S. C. Sengupta and D. N. Chatterjee, *ibid.*, **29**, 438 (1952); *ibid.*, **30**, 27 (1953); *ibid.*, **31**, 11 (1954).

(6) S. C. Sengupta and D. N. Chatterjee, *ibid.*, **31**, 285 (1954); *Science and Culture*, **19**, 47 (1953).

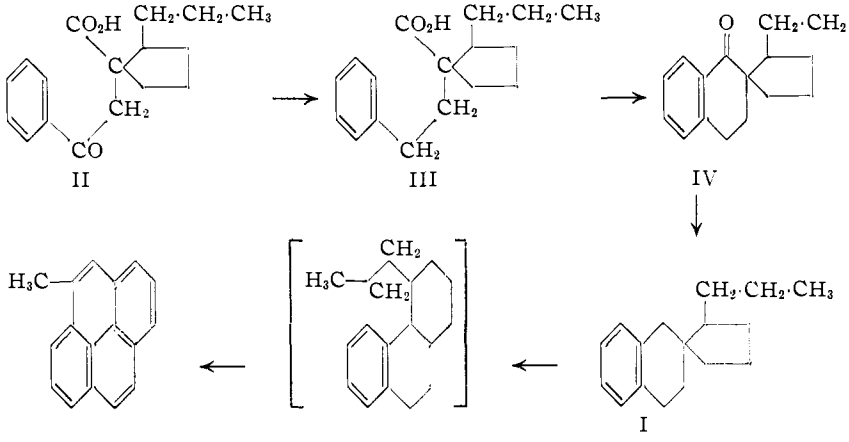
(7) (a) W. H. Perkin, Jr., R. Robinson and M. R. Turner, *J. Chem. Soc.*, **93**, 1085 (1908); (b) R. D. Desai and M. A. Wali, *Proc. Ind. Acad. Sci.*, **6A**, 135 (1937).

(8) W. Cocker, B. E. Cross, A. K. Fateen, C. Lipman, E. R. Stuart, W. H. Thompson and D. R. A. Whyte, *J. Chem. Soc.*, 1781 (1950).

(9) W. Baker, J. F. W. Mcomie and J. M. Norman, *ibid.*, 1114 (1951).

(10) B. A. Kazanski and A. F. Plate, *J. Gen. Chem. (U.S.S.R.)*, **9**, 496 (1939).

and from various examples known it can be concluded that six-membered rings can be involved in the formation of new rings by cyclodehydrogenation, but the same is not true of cyclopentane ring.



Experimental[11]

2-*n*-Propylcyclopentanone.—Sixty-two grams of 2-carbethoxycyclopentanone[12] was added dropwise from a dropping funnel to 16 g. of powdered potassium covered with 400 ml. of dry benzene, cooled in ice. It was kept at room temperature for 12 hours and then heated on the steam-bath for 24 hours after addition of *n*-propyl iodide (45 ml.). The product was treated with cold water and the separated benzene layer was washed with 15% aqueous sodium hydroxide, water in succession and dried. Removal of the solvent by fractionation and distillation of the residual oil furnished 60 g. (75%) of 2-*n*-propyl-2-carbethoxycyclopentanone as colorless liquid, b.p. 115–117° (10 mm.), $n^{31}D$ 1.4470.

Anal. Calcd. for $C_{11}H_{18}O_3$: C, 66.6; H, 9.1. Found: C, 66.41; H, 9.2.

It formed a **semicarbazone** which crystallized from aqueous ethanol in needles, m.p. 159–160°.

Anal. Calcd. for $C_{12}H_{21}O_3N_3$: C, 56.47; H, 8.23. Found: C, 56.28; H, 8.41.

The above propylated keto-ester was hydrolyzed by boiling under reflux with 300 ml. of 6 *N* hydrochloric acid for 12 hours. The separated oil was thoroughly extracted with 500 ml. of ether after saturating the product with ammonium sulfate. The ether extract was washed with 5% aqueous sodium carbonate, water and dried. The oil left after careful fractionation of ether distilled at 175–177° giving 30 g. (80%) of 2-*n*-propylcyclopentanone, $n^{30}D$ 1.4382. The **semicarbazone** crystallized from aqueous ethanol in fine needles, m.p. 205° dec.

Anal. Calcd. for $C_9H_{17}ON_3$: C, 59.0; H, 9.3. Found: C, 58.65; H, 9.42.

Ethyl 2-*n*-Propylcyclopentylidinecyanoacetate.—A solution of 27 g. of ethyl cyanoacetate, 30 g. of 2-*n*-propylcyclopentanone and 4 g. of ammonium acetate in 10 ml. of glacial acetic acid and 50 ml. of benzene was heated in an oil-bath at 130–140° for 6 hours and then at 140–150° for 12 hours, and the water that formed was removed continuously with a modified Dean and Stark separator.[13] The mixture was cooled, diluted with 500 ml. of ether, washed with four 50-ml. portions of water and dried over sodium sulfate and the solvent removed. The residual oil, on fractionation gave 50 g. (92%) of the unsaturated nitrile, b.p. 142–144° (6 mm.), $n^{31}D$ 1.4810.

Anal. Calcd. for $C_{13}H_{19}O_2N$: C, 70.6; H, 8.6. Found: C, 70.41; H, 8.45.

It absorbed bromine slowly in chloroform solution and gave 2-*n*-propylcyclopentanone on oxidation.

2-*n*-Propylcyclopentane-1-carboxy-1-acetic Acid.—A solution of 36 g. of potassium cyanide in 72 ml. of water was added to 50 g. of the foregoing unsaturated nitrile dissolved in 260 ml. of 95% ethanol. There was slight evolution of heat and the clear solution was allowed to stand for a week, when small amounts of the potassium salt of the condensation product separated. Ethanol was distilled off from water-bath and the dark semi-solid mass was boiled under reflux with 400 ml. of concd. hydrochloric acid for 48 hours. It was cooled in ice and the separated acid was dissolved in 500 ml. of 5% aqueous sodium carbonate. Treatment with norite and subsequent acidification of the cooled alkaline filtrate with hydrochloric acid yielded 35 g. (70% based on the propylated ketone) of the dicarboxylic acid. This was twice crystallized from aqueous acetic acid when stout cubes melting at 124° (28 g.) were obtained.

Anal. Calcd. for $C_{11}H_{18}O_4$: C, 61.68; H, 8.4. Found: C, 61.62; H, 8.44.

The **anhydride** of the above dicarboxylic acid, obtained by heating the acid with excess of acetic anhydride for 6 hours, was a colorless liquid, b.p. 168–170° (20 mm.), $n^{31}D$ 1.4730.

Anal. Calcd. for $C_{11}H_{16}O_3$: C, 67.3; H, 8.1. Found: C, 67.12; H, 8.25.

The **anilic acid**, prepared by heating the anhydride with aniline in benzene solution, crystallized from aqueous ethanol in plates, m.p. 164°.

Anal. Calcd. for $C_{17}H_{23}O_3N$: C, 70.6; H, 7.9. Found: C, 70.42; H, 8.17.

α,α-(2′-*n*-Propylcyclopentane)-β-benzoylpropionic Acid (II).—26.8 g. of powdered aluminum chloride (0.2 mole) was added portionwise during a quarter of an hour to a solution of 19.6 g. of the anhydride of 2-*n*-propylcyclopentane-1-carboxy-1-acetic acid (0.1 mole) in 60 ml. of dry benzene, cooled in ice, the bath temperature being kept in the range of 0–5°. The mixture was allowed to stand in ice-bath for 6 hours and then at the room temperature for 12 hours after which it was heated at 50–60° for 3 hours. The complex was decomposed with ice and hydrochloric acid and excess benzene removed by steam distillation. The light brown residue was extracted with aqueous sodium carbonate (charcoal). Acidification of the alkaline filtrate with hydrochloric acid yielded an oil which readily solidified on trituration with petroleum–ether. After crystallization from aqueous acetic acid and finally from hexane, 18 g. (65%) of the keto acid II was obtained as fine needles, m.p. 110–111°.

Anal. Calcd. for $C_{17}H_{22}O_3$: C, 74.4; H, 8.0. Found: C, 74.42; H, 8.06.

The **2,4-dinitrophenylhydrazone**, prepared in alcoholic sulfuric acid solution, crystallized from ethyl acetate as bright yellow needles, m.p. 216° dec.

Anal. Calcd. for $C_{23}H_{26}O_6N_4$: C, 60.79; H, 5.7. Found: C, 60.55; H, 6.01.

Pyrylium Salt of the Keto Acid II.—A mixture of the keto acid (0.1 g.) and salicylaldehyde (0.1 g.) in absolute ethanol (10 ml.) was saturated with dry hydrogen chloride at 0° and kept in an ice-chest for 3 days. The separated pyrylium salt was filtered, washed with alcohol and dried *in vacuo*. It was a crimson-red powder, soluble in aqueous alkali and did not melt up to 290°.

α,α-(2′-*n*-Propylcyclopentane)-γ-phenylbutyric Acid (III).—Fifty grams of granulated zinc was amalgamated by shaking with a solution of 2.5 g. of mercuric chloride in 50 ml. of water and 1 ml. of concentrated hydrochloric acid for 10 minutes. The liquid was then decanted and the zinc was covered with 20 ml. of water, 50 ml. of concd. hydrochloric acid and 30 ml. of toluene. To this 10 g. of the keto acid II was added followed by 15 ml. of acetic acid and the reaction mixture was gently refluxed for 24 hours and a total of 50 ml. of concd. hydrochloric acid being added at

(11) Melting points and boiling points are not corrected.

(12) P. S. Pinkney, "Organic Syntheses," Coll. Vol. II, 2nd Ed., John Wiley and Sons, Inc., New York, N. Y., 1943, p. 116.

(13) A. C. Cope, C. M. Hofmann, C. Wyckoff and E. Hardenbergh, THIS JOURNAL, **63**, 3452 (1941).

intervals in 60-ml. portions over that period. This was then diluted with water and extracted with ether. The solvent was removed under reduced pressure and the residual oil was extracted with hot aqueous sodium carbonate. The reduced acid III separated on acidification of the alkaline filtrate as oil which soon solidified. After crystallization from petroleum–ether (b.p. 40–60°), it afforded 7 g. (75%) of colorless needles, m.p. 114–115°. A mixed m.p. with the keto acid II was depressed.

Anal. Calcd. for $C_{17}H_{24}O_2$: C, 78.4; H, 9.2. Found: C, 78.52; H, 8.85.

1-Keto-1,2,3,4-tetrahydronaphthalene-2,2-spiro-(2′-*n*-propylcyclopentane (IV).—Five grams of the butyric acid (III) was heated on the steam-bath, with stirring, with a mixture of 15 ml. of sulfuric acid (sp. gr. 1.84) and 5 ml. of water for 1.5 hours. The dark brown reaction mixture was poured in a thin stream on crushed ice and the ketone extracted with ether. The ether solution was washed with aqueous ammonia and water and was dried (sodium sulfate). The neutral matter left after removal of ether, afforded, on distillation, 3.5 g. (78%) of the spiro-ketone IV as colorless oil having a characteristic sweet odor, b.p. 168–170° (6 mm.), $n^{30}D$ 1.5464.

Anal. Calcd. for $C_{17}H_{22}O$: C, 84.3; H, 9.1. Found: C, 84.12; H, 9.31.

The ketone did not form semicarbazone or 2,4-dinitrophenylhydrazone.

1,2,3,4-Tetrahydronaphthalene-2,2-spiro-(2′-*n*-propylcyclopentane) (I).—Three grams of the spiro-ketone IV was gently boiled under reflux with 15 g. of amalgamated zinc, covered with 15 ml. of concd. hydrochloric acid, 6 ml. of water, 9 ml. of toluene and 4.5 ml. of acetic acid for 48 hours, with addition of 10-ml. portions of concd. hydrochloric acid at 12-hour intervals. The reaction mixture was then cooled, diluted with water and extracted three times with 50-ml. fractions of ether. The ether solution was washed with water, dried and evaporated to a light brown oil which was separated into two fractions by distillation *in vacuo:* (a) b.p. 150–155° at 6 mm. (1.5 g.), (b) b.p. 165–172° at 6 mm. (1 g.). The first fraction on redistillation yielded 1.1 g. (40%) of the spiran as colorless oil, b.p. 150–152° (6 mm.), $n^{30}D$ 1.5358. The second fraction, on redistillation gave 0.8 g. of the unreduced spiro-ketone.

Anal. Calcd. for $C_{17}H_{24}$: C, 89.5; H, 10.5. Found: C, 88.92; H, 10.25.

Dehydrogenation of the Spirohydrocarbon (I) with Platinum-on-charcoal.—A mixture of 1.0 g. of the spirohydrocarbon (I) and 0.1 g. of 10% platinum-on-charcoal catalyst[14] was heated in a metal-bath in an atmosphere of carbon dioxide at 290–300° for 6 hours. The temperature was then raised to 330° in course of 6 hours when evolution of hydrogen ceased. The mass was cooled and extracted with 50 ml. of benzene. The extract, which exhibited violet fluorescence, was filtered and the light brown oil, left after removal of the solvent, was distilled over sodium under reduced pressure. The liquid distillate (0.5 g.) was warmed with an ethanolic solution of picric acid and the separated picrate after one crystallization from absolute ethanol was obtained as red needles, m.p. 227°.[15]

Anal. Calcd. for $C_{23}H_{15}N_3O_7$: C, 62.0; H, 3.4. Found: C, 61.9; H, 3.42.

The picrate was decomposed with aqueous ammonia and the liberated hydrocarbon was taken up in ether. The ether solution was washed with water. Removal of the solvent afforded 0.1 g. of the solid **hydrocarbon** which crystallized from methyl alcohol in colorless flakes, m.p. 147°.[15] The mixed m.p. of this sample with an authentic sample of pyrene was depressed.

Anal. Calcd. for $C_{17}H_{12}$: C, 94.44; H, 5.56. Found: C, 94.4; H, 5.6.

The *sym*-trinitrobenzene complex was prepared with the hydrocarbon in ethanolic solution. After crystallization from methanol–benzene mixture, it was obtained as orange needles, m.p. 246–247°.

Anal. Calcd. for $C_{23}H_{15}N_3O_6$: C, 64.3; H, 3.5. Found: C, 64.42; H, 3.47.

The hydrocarbon responded to the color reaction shown by Bachmann and Edgerton[15] in the case of 1-methylpyrene. It gave a golden yellow solution with concd. sulfuric acid having a green fluorescence. On gentle warming, the color became olive-green with intense violet fluorescence.

Acknowledgment.—The author expresses his indebtedness to Dr. S. C. Sengupta, Professor of Chemistry, Presidency College, Calcutta, for his valuable help and interest in this work. This investigation was aided by a grant sanctioned by the Government of West Bengal.

(14) R. P. Linstead and S. L. S. Thomas, *J. Chem. Soc.*, 1127 (1940).

(15) W. E. Bachmann and R. O. Edgerton, THIS JOURNAL, **62**, 2970 (1940), record m.p. of 1-methylpyrene as 147.5–148.5° and that of its picrate as 226–227°.

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[CONTRIBUTION FROM THE BIOCHEMICAL INSTITUTE AND THE DEPARTMENT OF CHEMISTRY, UNIVERSITY OF TEXAS, AND THE CLAYTON FOUNDATION FOR RESEARCH]

Syntheses of DL-α-Lipoic Acid

BY LESTER J. REED AND CHING-I NIU

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Crystalline DL-α-lipoic acid has been obtained in good yield from ethyl 6,8-dibromoöctanoate and from the corresponding dichloro ester. The former ester was treated with potassium thiolacetate in boiling ethanol, followed by alkaline hydrolysis and oxidation of the resulting 6,8-dimercaptoöctanoic acid (dihydro-α-lipoic acid) with iodine or with oxygen in the presence of ferric ion. Both the dibromo and the dichloro esters were converted in high yield to 6,8-dibenzylmercaptoöctanoic acid by treatment with sodium benzylmercaptide in boiling ethanol, followed by alkaline hydrolysis. 6,8-Dibenzylmercaptooctanoic acid was reduced in high yield to 6,8-dimercaptoöctanoic acid with sodium in liquid ammonia. Ethyl 6,8-dibromooctanoate was produced by addition of anhydrous hydrogen bromide to ethyl 6-oxo-7-octenoate, followed by reduction with sodium borohydride to give ethyl 8-bromo-6-hydroxyoctanoate, which was converted to the dibromo ester with phosphorus tribromide. The dichloro ester was obtained by addition of ethyl δ-chloroformylvalerate to ethylene in the presence of aluminum chloride, followed by reduction with sodium borohydride to produce ethyl 8-chloro-6-hydroxyoctanoate, and treatment of the latter with thionyl chloride.

DL-α-Lipoic acid (6-thioctic acid) was obtained in low yield[1,2] by treating 4-(α-tetrahydrofuryl)-butyric acid with hydrogen bromide or potassium iodide–phosphoric acid to produce a mixture of halogen-substituted lactones of octanoic acid, which were converted to dimercaptoöctanoic acids by treatment with thiourea and acid. The dimercaptoöctanoic acids were oxidized to a mixture of

(1) C. S. Hornberger, Jr., R. F. Heitmiller, I. C. Gunsalus, G. H. F. Schnakenberg and L. J. Reed, THIS JOURNAL, **75**, 1273 (1953).

(2) M. W. Bullock, J. A. Brockman, Jr., E. L. Patterson, J. V. Pierce, M. H. von Saltza, F. Sanders and E. L. R. Stokstad, *ibid.*, **76**, 1828 (1954).