

Synthesis of 1-isopropyl-8,9-benzospiro [5,5] undecane-7-ol and its catalytic dehydrogenation

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Abstract. Catalytic dehydrogenation of 1-isopropyl-8,9-benzospiro [5,5] undecane-7-ol (**5**) has been carried out to study the effect of isopropyl group on the spirocyclohexane ring during the ring transformation of the spiro [5,5] system. The dehydrogenation of **5** gave 1-isopropylphenanthrene as the main product. For the synthesis of **5**, the anhydride of 1-carboxy-2-isopropylcyclohexane-1-acetic acid (**1**) was condensed with benzene to give the single ketoacid **2** which was reduced catalytically to **3**. Intramolecular acylation of the acid chloride of **3** gave the spiroketone **4** which was reduced to **5**.

Keywords. Spirocyclohexane ring; synthesis; dehydrogenation; catalysis; aromatic compounds.

1. Introduction

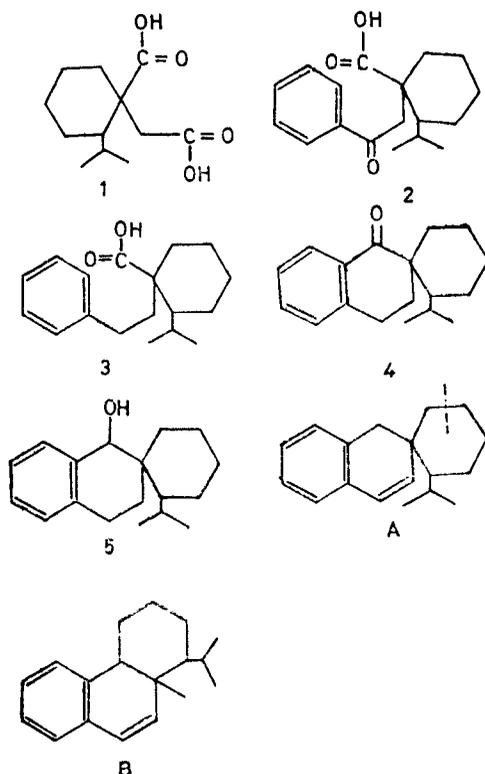
Dehydrogenation is an important step in the synthesis of aromatic compounds as well as an important tool for organic chemists to elucidate the structure of complex natural products. Mitra and Dutta Gupta (1976) noted the elimination of *n*-propyl group and loss of another carbon atom giving phenanthrene derivatives as the final dehydrogenation product during the catalytic dehydrogenation of spiro [5,5] undecanes having a 1-*n*-propyl substituent in the spirocyclohexane ring. They considered the fission of the spirocyclohexane ring between the spiro carbon atom and the carbon atom bearing the heavy *n*-propyl group to explain the formation of the isolated dehydrogenation products. To study the effect of the isopropyl group in 1-position of the spiro-ring of the spiro [5,5] undecane system on the ring transformation during its dehydrogenation, we have synthesised 1-isopropyl-8,9-benzospiro [5,5] undecane-7-ol (**5**).

2. Results and discussion

From the catalytic dehydrogenation product of **5**, the major product isolated is a hydrocarbon characterised as 1-isopropylphenanthrene on the basis of elemental analysis and comparison of the m.p. of the hydrocarbon and its picrate with litera-

ture report (Haworth *et al* 1934). In this case isopropyl group was not eliminated but the loss of one carbon atom was observed in the final product. Probably in this case, after dehydration ring fission took place away from the alkyl substituent as shown in structure B indicated by a broken line to give an intermediate which angularly cyclised to the intermediate (structure A) having an angular carbon atom which was knocked off during its aromatisation.

2.1. Synthesis of 1-isopropyl-8,9-benzospiro [5, 5] undecane-7-ol (5)



For the synthesis of 5, the anhydride of 1 was condensed with benzene under Friedel-Crafts condition to give a single ketoacid $\alpha\alpha$ -(2-isopropylcyclohexane)- β -benzoylpropionic acid (2). It showed IR absorptions at 770 and 710 cm^{-1} for five adjacent hydrogen atoms of the benzene ring and characteristic UV absorptions at 210 and 240 m μ . It formed pyrylium salt with salicylaldehyde and so its alternative structure was eliminated. The ketoacid (2) could not be successfully reduced by the Clemmensen method which only gave a mixture of high melting bimolecular reduction products. However, ketoacid (2) was readily reduced to $\alpha\alpha$ -(2-isopropylcyclohexane)- γ -phenylbutyric acid (3) in good yield by catalytic reduction in ethanol solution containing a few drops of HClO_4 at 50 lb pressure of H_2 . The IR spectrum of the first fraction (minor fraction) of the distillate showed an absorption also at 1745 cm^{-1} indicating the formation of some ester. The acid 3 which was collected as the second fraction (major portion) showed absorptions at 1700 cm^{-1} for acid carbonyl and at 742 and 700 cm^{-1} for five adjacent hydrogen atoms of

benzene ring. Intramolecular acylation of the acid chloride of 3 afforded 1-isopropyl-8,9-benzo-7-ketospiro [5,5] undecane (4). The spiroketone (4) was reduced to 1-isopropyl-8,9-benzospiro [5,5] undecane-7-ol (5). Absorption at 3350 cm^{-1} for its OH and at 750 cm^{-1} for the 1,2-disubstituted benzene ring was observed in its IR spectrum.

2.2. 1-Carboxy-2-isopropylcyclohexane-1-acetic acid (1)

For the synthesis of 2-isopropylcyclohexanone, potassio salt of cyclohexanone-2-carboxylate was alkylated with isopropyl iodide. It resisted hydrolysis with con. HCl but could be hydrolysed with hydrobromic acid under refluxing condition to give 2-isopropylcyclohexanone. It underwent Knoevenagel reaction (Cope *et al* 1941) to give ethyl 2-isopropylcyclohexylidene cyanoacetate. Potassium cyanide addition to the nitrile ester and subsequent hydrolysis with the mixture of HBr and acetic acid gave the acid (1).

3. Experimental

All the m.p.'s are uncorrected. IR spectra were recorded at the Central Drug Research Institute, Lucknow. Microanalyses were performed by A Bernhardt, Microanalytisches Laboratorium, West Germany.

3.1. Ethyl 2-isopropylcyclohexanone-2-carboxylate

2-Carboethoxycyclohexanone (400 g) was added dropwise to molecular potassium (92 g) covered with dry benzene (900 ml) cooled in ice. It was allowed to stand overnight when it formed a cake. Isopropyl iodide (400 g) was added in one lot to the potassio derivative and heated on a steam bath for 20 hr. The product was decomposed with ice-cold water and the benzene layer was collected, washed with KOH aq (15%), dried and then distilled. It collected at $134\text{--}138^\circ/16\text{ mm}$, yield 335 g. (Found: C, 67.81; H, 9.40. Calc. for $\text{C}_{12}\text{H}_{20}\text{O}$, C, 67.91; H, 9.43%). It formed semicarbazone which crystallised from methanol in colourless needles, m.p. $160\text{--}162^\circ$. (Found: C, 57.81; H, 8.49; N, 15.56. $\text{C}_{13}\text{H}_{23}\text{N}_3\text{O}_3$ requires C, 57.99; H, 8.55; N, 15.16%). Its oxime crystallised from methanol in colourless needles, m.p. $85\text{--}86^\circ$. (Found: C, 63.55; H, 9.08; N, 6.20. $\text{C}_{12}\text{H}_{21}\text{NO}_3$ requires C, 63.43; H, 9.25; N, 6.17%).

3.2. 2-Isopropylcyclohexanone

2-Isopropylcyclohexanone-2-carboxylate (330 g) was hydrolysed by refluxing with HBr (1200 ml, 48%) for 22 hr. After dilution with water, the solution was saturated with NaCl and extracted with ether. The ether extract was washed with water, Na_2CO_3 solution, and finally with water till neutral and dried (Na_2SO_4). Removal of solvent and distillation gave the ketone (170 g). b.p. $65\text{--}70^\circ/2.5\text{ mm}$. (Found: C, 77.23; H, 11.39. $\text{C}_9\text{H}_{16}\text{O}$ requires C, 77.14; H, 11.43%). Semicarbazone, colourless needles, m.p. $179\text{--}180^\circ$. (Found: C, 60.89; H, 9.79; N, 21.33. $\text{C}_{10}\text{H}_{16}\text{N}_3\text{O}$ requires C, 60.91; H, 9.64; N, 21.32%).

Vavon and Conia (1946) noted b.p. of the ketone as $83^\circ/17\text{ mm}$ and m.p. of its semicarbazone as 180° C .

3.3. *Ethyl 2-isopropylcyclohexylidencyanoacetate*

A mixture of 2-isopropylcyclohexanone (140 g), ethyl cyanoacetate (129 g), ammonium acetate (8 g), glacial acetic acid (12.2 ml) and benzene (700 ml) was heated under reflux in an oil bath at 160–165° for 20 hr with collection of water in a Dean-Stark separator. The benzene solution was washed with water, dried (Na_2SO_4) and the solvent removed. The residual oil distilled at 145–150°/1.5 mm, yield 200 g (Found: C, 71.29; H, 8.81; N, 5.71. $\text{C}_{14}\text{H}_{21}\text{NO}_2$ requires C, 71.49; H, 8.93; N, 5.95%).

3.4. *1-Carboxy-2-isopropylcyclohexane-1-acetic acid (1)*

A solution of potassium cyanide (66 g) in water (130 ml) was added to the foregoing nitrile ester (100 g) dissolved in rectified spirit (400 ml). It was allowed to stand for six days when a considerable amount of the potassium salt separated. The alcohol was distilled off and the dark residue was refluxed with a mixture of hydrobromic acid (450 ml; 48%), and glacial acetic acid for 30 hr. The separated solid acid was collected. The mother liquor on dilution with water gave further amount of the acid. The combined solids were dissolved in hot dilute sodium carbonate solution (charcoal) and filtered. Acidification of the solution afforded the acid (1) which crystallised from benzene-petroleum (40–60°) in colourless cubes, m.p. 145–147°, yield 52 g (Found: C, 62.91; H, 8.76. $\text{C}_{12}\text{H}_{20}\text{O}_4$ requires C, 63.15; H, 8.77%).

3.5. *Anhydride of the acid (1)*

The acid 1 (50 g) was refluxed with acetic anhydride (90 ml) for 6 hr. The anhydride was collected as a liquid (38 g), b.p. 155–160°/1.0 mm. (Found: C, 68.37; H, 8.45. $\text{C}_{12}\text{H}_{18}\text{O}_3$ requires C, 68.57; H, 8.57%).

3.6. *aa-(2-Isopropylcyclohexane)- β -benzoylpropionic acid (2)*

Anhydrous aluminium chloride (42 g) was gradually added to a well stirred solution of the anhydride (30 g) of the acid 1 in the dry benzene (60 ml) cooled in ice. The reaction mixture was allowed to stand at room temperature for 12 hr and warmed at 60–65° for 30 min. The product was decomposed with ice and hydrochloric acid and the unreacted benzene was removed by steam. The residual gum was collected, dissolved in hot dilute sodium carbonate solution (charcoal), filtered and the ketoacid 2 was precipitated with HCl. The crude acid melted at 120–124°. It (22 g) crystallised from a mixture of benzene and petroleum ether (60–80°) in colourless crystals, m.p. 127–129°. (Found: C, 75.11; H, 8.52. $\text{C}_{18}\text{H}_{24}\text{O}_3$ requires C, 75.0; H, 8.33%). The pyrylium salt of 2 separated from a solution of the ketoacid 2 (0.1 g), and salicylaldehyde (0.1 g) in absolute alcohol (10 ml) saturated with dry hydrogen chloride at 0° and kept in a refrigerator for three days. It was readily soluble in alkali and did not melt upto 290°.

3.7. *aa-(2-Isopropylcyclohexane)- γ -phenylbutyric acid (3)*

A mixture of the solution of the ketoacid (2; 18 g) in ethanol containing 1 ml of perchloric acid and Pd-C (1.8 g; 10%) was stirred at 50–55° C in an atmosphere of hydrogen of 55 Psi pressure. The required amount of hydrogen was absorbed

in 6 hr. Catalyst was filtered off and it was diluted with water. Its ether extract was washed with water, and dried (Na_2SO_4). Removal of the solvent gave an oil which distilled at $175\text{--}180^\circ/0.2$ mm as a thick colourless liquid. It solidified on cooling, m.p. $125\text{--}128^\circ$. It crystallised from petroleum ether ($40\text{--}60^\circ$) in colourless needles, m.p. $130\text{--}131^\circ$, yield 12 g (Found: C, 78.71; H, 9.43. $\text{C}_{18}\text{H}_{26}\text{O}_2$ requires C, 78.83; H, 9.49%); ν_{co} 1700 cm^{-1} .

3.8. 1-Isopropyl-8,9-benzo-7-ketospiro [5, 5] undecane (4)

The acid 3 (10 g) was converted into its acid chloride following the general procedure. The acid chloride was dissolved in petroleum ether ($60\text{--}80^\circ$) and anhydrous aluminium chloride (6 g) was added in portions with stirring. The mixture was kept at room temperature for 12 hr and warmed at $60\text{--}65^\circ$ for 1 hr. The product was decomposed with ice and hydrochloric acid. It was extracted with ether. The ether extract was washed with water, aqueous ammonia and finally with water to make it neutral. It was dried (Na_2SO_4) and the solvent was removed. The residual oil distilled at $145\text{--}150^\circ/0.3$ mm as a light straw coloured liquid (5 g) with a characteristic smell. (Found: C, 84.12; H, 9.34. $\text{C}_{18}\text{H}_{24}\text{O}$ requires C, 84.37; H, 9.37%).

3.9. 1-Isopropyl-8,9-benzospiro [5, 5] undecane-7-ol (5)

The foregoing spiroketone (4; 4 g) in dry tetrahydrofuran (50 ml) was gradually added to a slurry of lithium aluminium hydride (4.5 g) in dry THF (50 ml) cooled in ice water. It was then refluxed for 3 hr. It was decomposed with dil. acid and extracted with ether. After usual procedure, the residual oil was collected at $140\text{--}142^\circ/0.2$ mm, as a thick colourless liquid which soon solidified on cooling. It crystallised from petroleum ether ($60\text{--}80^\circ$) as colourless needles, m.p. $118\text{--}120^\circ$, yield 2.5 g (Found: C, 83.69; H, 10.16. $\text{C}_{18}\text{H}_{26}\text{O}$ requires C, 83.72; H, 10.08%). IR (Nujol) 3350, 1090 (secondary OH), 750 cm^{-1} (1, 2-disubstituted benzene ring).

3.10. Dehydrogenation of 5

The spiro-ol 5 (2 g) was heated with Pd-C (0.2 g; 10%) in a sealed tube at $360\text{--}380^\circ$ for 20 hr. The product was extracted with ether, dried (Na_2SO_4) and the solvent removed. The residual oil was chromatographed on alumina with petroleum ($60\text{--}80^\circ$). The first eluate gave a small amount of oil. The subsequent eluates gave low melting solid with blue fluorescence, which appeared identical in TLC. The solids were converted into trinitrobenzene complex in methanol. Repeated crystallisation gave orange needles, m.p. $161\text{--}163^\circ$ (Found C, 63.71; H, 4.54; N, 9.71. $\text{C}_{23}\text{H}_{19}\text{N}_3\text{O}_6$ requires C, 63.74; H, 4.39; N, 9.69%).

The regenerated hydrocarbon crystallised from methanol as colourless leaflets, m.p. $83\text{--}84^\circ$. (Found: C, 92.19; H, 7.10. $\text{C}_{17}\text{H}_{16}$ requires C, 92.72; H, 7.27%), λ_{max} (EtOH) 255, 272, and 310 nm (log 4.9, 4.2, 3.9). The picrate prepared from the purified hydrocarbon crystallised from ethanol in yellow needles, m.p. $123\text{--}124^\circ$ (Found: C, 61.21; H, 4.16; N, 9.49. $\text{C}_{23}\text{H}_{19}\text{N}_3\text{O}_7$ requires C, 61.47; H, 4.23; N, 9.35%).

Haworth *et al* (1934) recorded the m.p.'s of 1-isopropylphenanthrene and its picrate as $85\text{--}86^\circ$ and $125\text{--}126^\circ$ respectively.

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