[Contribution from Converse Laboratory, Harvard University]

SPIRO[4.5]DECANONE-1

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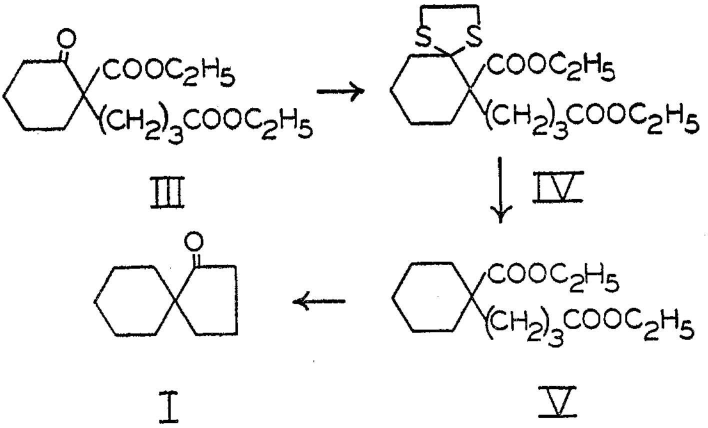
Relatively few of the simple spiroketones have been reported in the literature. Spiro[7.8]hexadecanone-8 (1), spiro[6.6]tridecanone-1 (2), and spiro[5.6]dodecanone-7 (3) and -dione-1,7 (4) appear to be the only known ketones of their respective types. Some spiro compounds related to dihydroresorcinol have been prepared (5, 6). Several compounds related to spiro[4.5]decanone-6 are known (3, 7–10), as are several related to spiro[4.5]decanone-1 (11–14). Spiro[4.4]nonanone-1 has been prepared (7, 11, 15–17). The report (18) of the synthesis of spiro[3.5]nonanone-1 is probably incorrect, since the last step, a Dieckmann reaction on a succinnic ester, tends not to form cyclobutanone derivatives. A number of these ketones were prepared by the pinacol rearrangement (1, 3, 7, 8, 10), or the related rearrangement of epoxides (4, 9). Similar spiroketones are formed (19) during the treatment of certain ethynyl diols with formic acid.



Spiro[4.5]decanone-1 has been prepared by the scheme shown in the diagram. From the reaction of butyrolactone with hydrogen bromide, followed by esterification, the methyl and ethyl esters (IIa, IIb) of 4-bromobutyric acid were obtained. The ethyl ester IIb reacted with the sodio derivative of 2-carbethoxycyclohexanone to form III, diethyl 4-(1′-carboxy-2′-oxocyclohexyl)butyrate, in good yield. Since this ketoester is sensitive to both acid and base, its reduction to V was carried out by the elegant method of Mozingo (20, 21), in fair yield. Diethyl 4-(1′-carboxycyclohexyl)butyrate (V) was converted to I by the action of sodium hydride, and subsequent hydrolysis. The infrared absorption spectrum is given in Figure 1; several derivatives are described in the experimental part.

When the spiroketone I was distilled through a column of alumina heated to 400°, a mixture was formed, consisting mostly of material of boiling point below room temperature. Azulene was formed in about 0.5% yield, and was identified by its ultraviolet absorption spectrum (22) and its distribution constant in phosphoric acid/ligroin (23).

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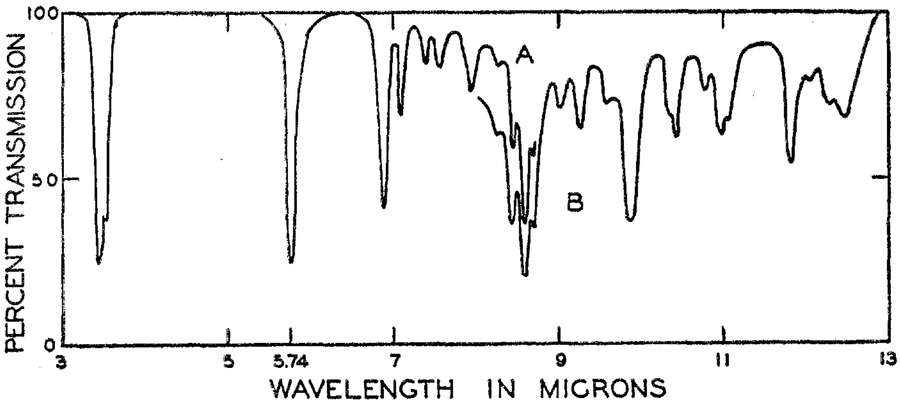

FIGURE 1. INFRARED ABSORPTION SPECTRUM OF SPIRO[4,5]DECANONE-1 DETERMINED ON a Baird spectrometer: A, 2% solution in carbon tetrachloride; B, 5% in carbon disulphide. No significant absorption was observed at $2\text{–}3\mu$ or $13\text{–}16\mu$.

EXPERIMENTAL[1]

Methyl 4-bromobutyrate, IIa, was prepared by saturating γ-butyrolactone[2] with anhydrous hydrogen bromide, and esterifying the crude product by the method of Clinton and Laskowski (24). The yield of ester b.p. 97–101° at 35 mm. was 85–90% from butyrolactone.

Ethyl 4-bromobutyrate, IIb, was prepared similarly, using the esterification procedure of van Rysselberge (25); b.p. 98–100° at 35 mm.; 68–70% from butyrolactone.

Diethyl 4-(1'-carboxy-2'-oxocyclohexyl)butyrate, III. In a 3-liter 3-necked flask, equipped with a heating jacket, a stirrer, a dropping-funnel, and a reflux condenser with a calcium chloride-filled drying tube, was placed 36 g. (1.5 gram-atoms) of metallic sodium. Commercial anhydrous ethanol (450 cc.) was added gradually, and the mixture stirred and warmed gently until the sodium had completely dissolved. With stirring but no heating, 170 g. (1.0 mole) of 2-carbethoxycyclohexanone (26) was added rapidly. The mixture was stirred for 5 minutes, then 300 g. (1.54 moles) of ethyl 4-bromobutyrate was added rapidly. The mixture was then stirred and refluxed for 3 hours, cooled, poured into 800 cc. of water, and extracted with three 200-cc. portions of chloroform. Upon distillation of the chloroform solution, there was obtained a small amount (8%) of ethyl cyclopropanecarboxylate (b.p. 130°, n_D^{21} 1.4210; lit. (27) b.p. 134°, n_D^{15} 1.4217) and III, b.p. 144–152° at 2 mm. (or 133–136° at 0.8 mm.); yield, 254 g. (75%, based on the carbethoxycyclohexanone used).

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[1] All melting points were determined with Anschütz thermometers in a Hershberg melting point apparatus. Analyses were performed by Mrs. Shirley Golden, Converse Laboratory. James C. Allen and Mitchell J. Rosenholz assisted with some of the preparations.

[2] The butyrolactone was kindly furnished by the Cliffs-Dow Chemical Company of Marquette, Michigan.

When the ratio of bromoester to carbethoxycyclohexanone was decreased to 1:1, the yield of product dropped to 70%. When the alkylation was run in dry benzene, using sodium hydride to prepare the salt, and refluxing 8 hours, more ethyl cyclopropanecarboxylate was formed, and much less of the desired compound was obtained.

Anal. Calc'd for $C_{15}H_{24}O_5$ (MW 284.34): C, 63.35; H, 8.51.

Found: C, 63.50; H, 8.59.

1,2-Ethanedithiol was prepared essentially according to *Organic Syntheses* (28).

6-(4'-Carbethoxybutyl)-6-carbethoxy-1,4-dithiaspiro[4,5]decane, IV. To 140 g. (0.72 mole) of the ketoester, 70 g. (0.75 mole) of ethylene mercaptan, and 300 cc. of benzene, was added 200 g. (1.47 moles) of zinc chloride which had been freshly fused and powdered. The mixture was refluxed for two hours, then cooled by adding ice to the hot mixture (gradual cooling results in the formation of a glassy layer). The mixture was transferred to a separatory-funnel with small portions of conc'd hydrochloric acid and acetone, cold water was added, and the mixture was extracted with ether and chloroform. Distillation of the organic mixture yielded IV, b.p. 190–195° at 0.10 mm., in 83% yield (146 g.). The thioketal was not obtained analytically pure.

Diethyl 4-(1'-carboxycyclohexyl)-butyrate, V. The mercaptal (171 g.) was treated with the Raney nickel [W-4 (29)] prepared from 6 kilograms of alloy, in several portions. Only that volume of alcohol was used which was required to efficiently rinse the mercaptal into the slurry, and to prevent evaporation of alcohol from exposing the catalyst to the air. The mixture was thoroughly stirred two or three times during the reduction. After two or three hours, the solution was sucked into 1-liter round-bottomed flasks, and the catalyst washed four or five times with 1- to 2-liter portions of 95% ethanol. The alcohol distilled from the solutions was used for subsequent washing, unless it contained chloroform. The solution was removed from the catalyst by drawing it through a 30 mm. diameter Pyrex sintered-glass filtering disk into a round-bottomed flask, the pressure in which was reduced to about 100 mm. by connection to the aspirator and an air-leak. When most of the solution had siphoned away, the disk was repeatedly pressed into the slurry until the volume below it became hard; in this fashion most of the solution could be removed without danger of igniting the nickel.

To each portion of the crude ester, from 25 g. of thioacetal, obtained by evaporating the ethanol and distilling chloroform from the residue until the water had been entirely removed, was added 5 cc. of anhydrous ethanol, 500 cc. of chloroform, and 1 cc. of concentrated sulfuric acid, and the mixture refluxed overnight. The cool solution was washed once with 3% aqueous sodium carbonate, and twice with water.

Distillation of the combined solutions yielded 81 g. of V, b.p. 110–125° at 0.7 mm. The yield of ester is 64% (on mercaptal) and 53% from the ketoester.

A sample was redistilled (b.p. 135–136° at 1.3 mm.) and analyzed.

Anal. Calc'd for $C_{15}H_{26}O_4$ (MW 270.36): C, 66.63; H, 9.69.

Found: C, 66.49; H, 9.83.

Spiro[4,5]decanone-1, I. In a 2-liter 3-necked flask, equipped with a Hershberg stirrer, a reflux condenser with drying tube, and a dropping-funnel, was placed 24 g. (1.0 mole) of sodium hydride and 250 cc. of reagent grade benzene. One-half cc. of methanol was added, the mixture stirred and warmed until gentle refluxing began, when 81 g. (0.30 mole) of V was added dropwise. The mixture was stirred and refluxed 8 to 10 hours; 10 cc. of di-*n*-butyl ether and 40 cc. of toluene were added, and the flask surrounded by a bath of ice and brine. The condenser and drying tube were removed, and replaced by a low-temperature thermometer. Methanol (40 ml.) was added slowly at 0-5° (this required 30 minutes); and, after the foaming had subsided, 1 liter of ice-water was added, slowly at first, then more rapidly, while maintaining the temperature of the mixture below 5°. The mixture and the cooling bath were allowed to warm slowly to room temperature overnight; the thermometer was replaced by a reflux condenser, and the mixture refluxed 1 hour. The warm mixture was acidified by careful addition of the solution prepared by adding 50 cc. of conc'd sulfuric acid to 100 g. of ice, and refluxed 1 hour longer. The cool mixture was separated, and the aqueous layer extracted with three 250-cc. portions of chloroform. The combined organic solution was extracted once with a 3% aqueous sodium carbonate solution, once with water, and distilled, first at atmospheric pressure until the low-boiling solvents had been removed, and finally at a water-pump vacuum. The yield of ketone ($C_{10}H_{16}O$, MW 152.23) of b.p. 107–114° at 22 mm., was 33.7 g. (74%) (d^{25} 0.978; n_D^{25} 1.4798; γ, 33.0 dynes/cm, M_D, 44.2, calc'd 44.0; parachor, 373, calc'd 356).

The 2,4-dinitrophenylhydrazone melted at 185–186°, after being recrystallized several times from ethanol.

Anal. Calc'd for $C_{16}H_{20}N_4O_4$ (MW 332.35): C, 57.82; H, 6.07; N, 16.86.
Found: C, 57.72; H, 5.91; N, 16.83.

The *oxime*, prepared in the usual way, melted at 95–96° (from ethanol).

Anal. Calc'd for $C_{10}H_{17}NO$ (MW 167.24): C, 71.81; H, 10.25; N, 8.38.
Found: C, 72.00; H, 10.12; N, 8.11.

The *semicarbazone* melted at 245–247° (dec.) in a sealed evacuated tube, inserted into the bath at 240°.

Anal. Calc'd for $C_{11}H_{19}N_3$ (MW 209.29): C, 63.12; H, 9.15; N, 20.08.
Found: C, 62.91; H, 8.95; N, 19.52.

SUMMARY

The preparation of spiro[4.5]decanone-1, and of some of its derivatives, is described.

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