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EXPERIMENTS IN THE 4-ARYLCYCLOALK-2-EN-1-ONE SERIES—IV[1]

4-PHENYLCYCLOHEPTA-1,3-DIONE

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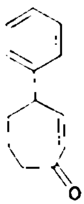
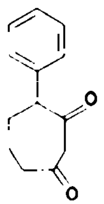
Abstract—4-Phenylcyclohepta-1,3-dione (II) and 2-acetyl-2-phenylcyclopentanone (IV) have been prepared and their properties studied.

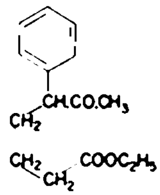
In continuation of previous attempts to synthetize 4-phenylcyclohept-2-en-1-one (I), the synthesis of 4-phenylcyclohepta-1,3-dione (II) was undertaken, in the hope that this might conveniently be transformed into I. The synthesis of II was modeled on that of the lower homolog 4-phenylcyclohexa-1,3-dione[2] and started from the same point of departure, *viz* phenylacetone. The four additional carbon atoms were introduced by means of ethyl γ-iodobutyrate. The use of sodium hydroxide,[3] sodium ethoxide[4] and sodium isopropoxide[5] was unsatisfactory, but with sodium hydride in a mixture of benzene and dimethylformamide,[6] the desired ethyl 6-oxo-5-phenylheptoate (III) was obtained in 60 per cent yield. In its cyclization, the ester group can *a priori* attack either side of the ketone carbonyl. In fact, both reactions took place, and a mixture of equal parts of 4-phenylcyclohepta-1,3-dione (II) and 2-acetyl-2-phenylcyclopentanone (IV) was obtained.



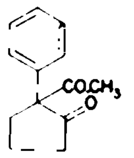
I



II



III



IV

Surprisingly, neither II nor IV reacted with the usual ketone reagents. Their structures, however, are supported by their behaviour and their spectra. The former gives a vivid colour reaction with ferric chloride and is strongly acidic, the latter is refractory in both respects. Compound II forms a very stable hydrate and in the infra-red spectrum, exhibits a very intense hydroxyl band; its width (2800–3200 cm^{-1}) recalls

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[1] Part III: E. D. Bergmann and S. Yaroslavsky, *J. Amer. Chem. Soc.* **81**, 2772 (1959).

[2] E. D. Bergmann and J. Szmuszkovicz, *J. Amer. Chem. Soc.* **75**, 3226 (1953).

[3] E. M. Schultz, J. B. Bicking, S. Mickey and F. S. Crossley, *J. Amer. Chem. Soc.* **75**, 1072 (1953).

[4] M. Tiffeneau and L. Levy, *Bull. Soc. Chim.* [4], **33**, 759 (1923).

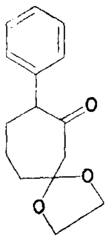
[5] C. M. Suter and A. W. Weston, *J. Amer. Chem. Soc.* **64**, 533 (1942).

[6] F. J. Marshall and W. N. Cannon, *J. Org. Chem.* **21**, 245 (1956).

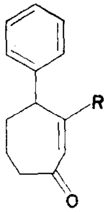
the absorption of a carboxylic hydroxyl group; indeed, the enol form of II is a vinylogous carboxylic acid. For II, the ultra-violet spectrum in ethyl alcohol shows two maxima 251 mμ (3·43); 289 mμ (3·12), which is indicative of alicyclic 1,3-diketones[7] and has been explained by Blout *et al.*[8]

For synthetic experiments, e.g. the Stobbe reaction, the monoketal of II appeared to offer possibilities. The monoketalization was attempted in the manner which had proved successful for cyclohexa-1,3-dione[9] and in the expectation that the less hindered carbonyl would react preferentially, giving V. In fact, no ketalization took place; the product obtained was either the β-hydroxyethyl ether VI or VII, which are derived from the two enolic forms of II, the latter reacting like a carboxyl group yielding the ester, or a mixture of both. The analysis conformed with the formula (as monohydrate), and the infra-red spectrum revealed the presence of an alcoholic hydroxyl group (3450 cm^{-1}) in addition to the carbonyl band.

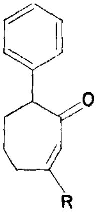
The diketone (II) was, therefore, converted into its enol monoethyl ether, probably the mixture of the two isomers VIII and IX. These enol ethers, too, give fairly stable monohydrates.[10] Their absorption spectrum showed a maximum at 250 mμ (3·43), exactly, as the corresponding cyclohexane derivatives.[2]



V



VI R=OCH$_2$CH$_2$CH
VIII R=OC$_2$H$_5$



VII R=OCH$_2$CH$_2$OH
IX R=OC$_2$H$_5$

The Stobbe reaction with the mixture of the enol ethers VIII and IX produced an oily acidic product, which could not be characterized as such, but gave upon treatment with polyphosphoric acid, in 20 per cent yield, a crystalline neutral material of the composition $C_{17}H_{14}O_3$. The compound showed two infra-red absorption bands in the carbonyl region, at 1687 and at 1823 cm^{-1}. The former represents a seven-membered ring carbonyl,[11] the latter indicates the presence of a β,γ-unsaturated γ-lactone.[12] Formula X is proposed for this compound. It would be formed from IX by the following route (see top of page 156). The Stobbe product (IX A) has the structure of a substituted 3-benzylidenepropionic acid and is thus capable of undergoing the classical α-naphthol synthesis of Fittig and Erdmann[13]; the product, as a derivative of the unstable *o*-hydroxyphenylacetic acid,

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[7] H. Bastron, R. E. Davis and L. W. Butz, *J. Org. Chem.* **8**, 522 (1943).

[8] E. R. Blout, V. W. Eager and D. C. Silverman, *J. Amer. Chem. Soc.* **68**, 566 (1946).

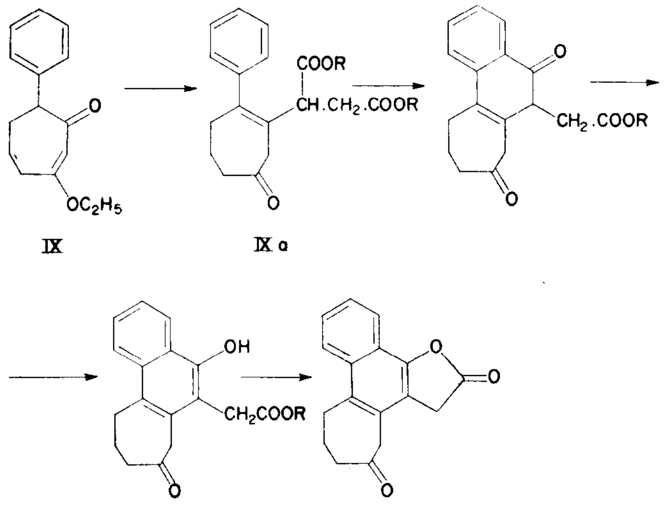
[9] M. W. Cronyn and J. E. Goodrich, *J. Amer. Chem. Soc.* **74**, 3331 (1952).

[10] The analytical figures given by Bergmann and Szmuszkovicz[2] for the analogous monoethyl ethers derived from 4-phenylcyclohexa-1,3-dione also point to the existence of monohydrates of these compounds.

[11] C. D. Gutsche, *J. Amer. Chem. Soc.* **71**, 3513 (1949) found the carbonyl peak for 2- and 3-phenylcycloheptanone at 1688 cm^{-1}, whilst 4-phenylcycloheptanone[1] absorbs at 1700 cm^{-1}.

[12] J. F. Grove and H. A. Willis, *J. Chem. Soc.* 877 (1951); R. S. Rasmussen and R. R. Brattain, *J. Amer. Chem. Soc.* **71**, 1073 (1949).

[13] R. Fittig and H. Erdmann, *Ber. Dtsch. Chem. Ges.* **16**, 43 (1883); *Liebigs Ann.* **227**, 242 (1885).



forms immediately a coumaran-2-one (X).[14] This mechanism is supported by a number of analogous observations made on products from Stobbe reactions with substituted benzyl ketones (IX also belongs to this class). These observations are reported in the following paper.

EXPERIMENTAL

Ethyl γ-bromobutyrate.[15] A mixture of 250 g γ-butyrolactone, saturated with gaseous hydrogen bromide, with benzene and absolute ethanol was subjected to azeotropic distillation. When no more water appeared in the trap, the benzene solution was cooled, washed with sodium carbonate and water, and dried over magnesium sulphate. Distillation yielded 500 g (90 %) of ethyl γ-bromobutyrate, b.p. 98–100°/20 mm.

Ethyl γ-iodobutyrate.[16] A mixture of 288 g sodium iodide, 280 g ethyl γ-bromobutyrate and 1200 ml acetone was shaken for 4 hr. After filtration, the acetone was distilled off and the residue taken up in benzene. The benzene layer was washed several times with sodium bisulphite solution and water, dried and distilled. Thus, 319 g (92 %) ethyl γ-iodobutyrate, b.p. 100–101°/20 mm, was obtained.

Ethyl 6-oxo-5-phenylheptoate (III). To a well-stirred mixture of 14·3 g (0·6 mole) sodium hydride, 222 ml dry benzene and 222 ml anhydrous dimethylformamide, 80 g (0·6 mole) phenylacetone was added dropwise during 20 min at 5–10°. The beginning of the reaction is indicated by foam formation. If this does not occur, the mixture is gently heated before continuing the addition of phenylacetone. After the addition, the stirring was continued for 20 min and 157 g (0·65 mole) ethyl γ-iodobutyrate added dropwise at 10°. The reaction mixture was allowed to reach room temp and then heated at 50–60° for 5 hr. After cooling, 20 ml ethanol, and then water, was added, and the benzene layer washed with sodium bisulphite and water. Distillation yielded 20 g (35 %) phenylacetone, b.p. 108°/20 mm, and 87 g (60 %) III, b.p. 135°/1 mm $\lambda_{\max}^{\mathrm{EtOH}}$ 220 (3·87), 260 (2·53), 284 mμ (2·47) $\tilde{\nu}_{\mathrm{C=O}\,\max}^{\mathrm{KBr}}$ 1711, 1733 cm^{-1}. (Found: C, 72·3; H, 7·6. $C_{15}H_{20}O_3$ requires: C, 72·6; H, 8·0 %). The ester (III) gave an orange-yellow 2,4-dinitrophenylhydrazone which was recrystallized from ethanol, m.p. 78°.

4-Phenylcyclohepta-1,3-dione (II). To a stirred solution of sodium ethoxide in boiling ethanol (from 8·54 g sodium and 200 ml absolute ethanol), 91 g III was added dropwise. The heating was

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[14] A. v. Baeyer and P. Fritsch, *Ber Dtsch Chem Ges.* **17**, 973 (1884).

[15] D. J. Cram and H. Steinberg, *J. Amer Chem. Soc.* **76**, 2753 (1954); G. D. Johnson, W. B. Lindsey and B. R. Jones, *J. Amer. Chem. Soc.* **78**, 461 (1956).

[16] R. C. Fuson, R. T. Arnold and H. G. Cooke, *J. Amer. Chem. Soc.* **60**, 2272 (1938); N. J. Leonard, R. C. Fox and M. Oki, *Ibid.* **76**, 5708 (1954).

continued for 2 hr and the mixture, after cooling, acidified by 30 ml acetic acid followed by water. The product was extracted with ether and the *acidic product* transferred into sodium carbonate solution (5%). Acidification with cold dil. sulphuric acid (5%) gave an oil which was extracted again with ether and washed with sodium chloride solution. Distillation yielded 36 g (50%) 4-phenylcyclohepta-1,3-dione (II), b.p. 180°/1 mm. The product gave a deep-violet colour reaction with ethanolic ferric chloride and did not react with 2,4-dinitrophenylhydrazine or semicarbazide. It holds tenaciously about one molecule of water; therefore, its analysis is not altogether satisfactory. λ_{max}^{EtOH} 251 (3·43); 289 mμ (3·12). ν_{max}^{liq} 1700 (shoulders at 1714 and 1724 cm^{-1}); 2800–3200 cm^{-1} (hydroxyl). (Found: C, 72·1; H, 7·3. $C_{13}H_{14}O_2$ requires: C, 77·2; H, 7·0. $C_{13}H_{14}O_2 \cdot H_2O$ requires: C, 71·0; H, 7·3%).

2-*Acetyl-2-phenylcyclopentanone* (IV). The ethereal solution of the *neutral* product obtained in the foregoing experiment was washed with water, dried and distilled. Thus, 34 g (50%) 2-acetyl-2-phenylcyclopentanone, b.p. 135°/1 mm, was obtained. It gave no colouration with ferric chloride and did not react with 2,4-dinitrophenylhydrazine. ν_{max}^{liq} 1717 cm^{-1} (broad). (Found: C, 77·3; H, 7·3. $C_{13}H_{14}O_2$ requires: C, 77·2; H, 7·0%).

Reaction of II *with ethyleneglycol.* A mixture of 22 g II, 6·2 g ethyleneglycol and 0·5 g *p*-toluenesulphonic acid in 80 ml dry benzene was distilled azeotropically. The benzene layer was washed with sodium carbonate and water, dried and distilled. Thus, 9 g (30%) of a mixture of the enol ethers VI and VII, b.p. 180–185°/1 mm, was obtained; the product formed a stable monohydrate. ν_{max}^{liq} 1700, 1723, 3450 cm^{-1}. (Found: C, 67·7; H, 7·6. $C_{15}H_{18}O_3$ requires: C, 73·1; H, 7·3. $C_{15}H_{18}O_3 \cdot H_2O$ requires: C, 68·1; H, 7·6%).

Reaction of II *with ethanol.* A solution of 34 g II, 35 ml ethanol and 0·9 g *p*-toluenesulphonic acid in 190 ml benzene was refluxed azeotropically for 8 hr. After addition of water, the benzene layer was separated, washed with sodium carbonate and water, and dried. Distillation afforded 35 g (quantitative yield) of the enol ethers VIII and IX, b.p. 140°/1 mm, λ_{max}^{EtOH} 250 mμ (3·43). (Found: C, 72·9; H, 8·2; OC_2H_5, 18·6. $C_{15}H_{18}O_2$ requires: C, 78·2; H, 7·8; OC_2H_5, 19·5. $C_{15}H_{18}O_2 \cdot H_2O$ requires: C, 72·7; H, 8·1; OC_2H_5, 18·1%).

Stobbe condensation of the enol ethers (VIII) *and* (IX). A mixture of 12 g (0·5 mole) sodium hydride, 87 g (0·5 mole) diethyl succinate, 82 g (0·33 mole) of the mixture of VIII and IX and 1 ml ethanol in 300 ml dry benzene was refluxed for 16 hr with vigorous agitation. To the cooled mixture, 32 g glacial acetic acid, then ether and water were added. The acidic product was extracted into sodium carbonate solution, acidified with dil. hydrochloric acid and extracted again with ether. Evaporation of the ether yielded 45 g (38%) of an oily acidic product which was used for the next step without further purification. From the neutral ethereal layer, 4·5 g diethyl succinylosuccinate, m.p. 126° (from ethanol), and 40 g (45%) of unchanged enol ethers, b.p. 140°/1 mm, were obtained.

Lactone of 4-hydroxy-1,2-(4′-oxocyclohepteno)-naphthalene-3-acetic acid (X). The oily acidic product from the foregoing experiment (10 g) and 100 g polyphosphoric acid were heated at 100° for 3 hr. After addition of ice-water the mixture was extracted with ether and the extract washed several times with sodium carbonate and water, and dried. Evaporation left an oily residue which crystallized slowly. On trituration with ethanol, it yielded 1·5 g (20%) of X which melted, after recrystallization from butanol, at 193–194°. $\lambda_{max}^{CHCl_3}$ 251 (4·21), 334 mμ (3·68). $\nu_{C=O\,max}^{KBr}$ 1687, 1823 cm^{-1}. (Found: C, 76·6; H, 5·6. $C_{17}H_{14}O_3$ requires: C, 76·7; H, 5·3%). The orange-yellow 2,4-dinitrophenylhydrazone was amorphous.