The writer also reached the conclusion that Sample A was the purer one from the distillation characteristics of A and B.

Pure diallyl does not have a sharp odor, as sometimes claimed. It has a very penetrating, highly "unsaturated," nauseating odor, inducing anesthesia easily. It has a sweet taste when highly diluted with water. It must be kept in a sealed bottle as it is very volatile. Ordinary samples develop a sharp odor and deposit a yellow oil on standing; purified material in sealed tubes evidently keeps indefinitely. It can be conveniently identified by the preparation of the cyclic, crystalline, neutral, monosulfuric acid ester of hexane-2,5-diol, which melts at 90° corr.[2]

Summary

1. Detailed directions are given for the preparation of Δ-1,5-hexadiene from allyl halides and magnesium in ether.
2. The boiling point, dt/dp, melting point, density and refractive index of Δ-1,5-hexadiene have been accurately determined.

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[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY, YALE UNIVERSITY, AND FROM THE RESEARCH LABORATORY, ELI LILLY AND COMPANY, INDIANAPOLIS, INDIANA]

SYNTHESIS OF EPHEDRINE AND STRUCTURALLY SIMILAR COMPOUNDS. III. A NEW SYNTHESIS OF ORTHO-DIKETONES

BY HAROLD W. COLES, RICHARD H. F. MANSKE AND TREAT B. JOHNSON

RECEIVED APRIL 12, 1929 PUBLISHED JULY 5, 1929

The synthesis of ephedrine described in Papers I and II[1,2] necessitated the preparation of considerable quantities of 1-phenylpropane-1,2-dione. This substance has been prepared by the decomposition of isonitrosoethylphenyl ketone by means of dilute sulfuric acid[3] or by means of amyl nitrite.[4] In the first case decomposition is slow and in the second case by-products are formed in large amount so that the yield of diketone in either case is small. In view of the great stability of this oxime it is not surprising that the carbonyl group with which the hydroxylamine is associated displays sufficient affinity to combine readily with primary amines—a reaction upon which the synthesis of ephedrine depends.[5] The formation of a crystalline hydrate of benzoylformaldehyde is another

[1] Manske and Johnson, THIS JOURNAL, **51**, 580 (1929).

[2] Manske and Johnson, *ibid.*, **51**, 1906 (1929).

[3] Pechmann and Müller, *Ber.*, **21**, 2119 (1888); *ibid.*, **22**, 2128 (1889).

[4] Manasse, *ibid.*, **21**, 2176 (1888).

[5] The authors desire to call attention to two errors which occur in the first paper; *ethylbenzyl* (line 18, p. 581) should read *ethylphenyl*, and *specially* (line 2, p. 582) should read *spatially*.

illustration of this reactivity. The dialkyl isonitroso ketones are readily convertible to diketones by means of formaldehyde, but thus far the authors are not aware of a case in which alkylaryl isonitroso ketones can be similarly decomposed. The ease of oxidation of dialkylmalonates to the corresponding mesoxalates by interaction with oxides of nitrogen is well known.[6] Gilman and Johnson[7] have recently developed further the utility of this change and have shown that nitrogen tetroxide serves as the most practical reagent for accomplishing this oxidation. The success of this work suggested the possibility of using this oxide for the oxidation of the methylene group of ethylphenyl ketone. Fortunately the reactivity conferred on the methylene carbon atom by the phenyl and carbonyl groups is sufficient not only to provide a point of attack for the nitrogen tetroxide but also to lend sufficient stability to the resulting diketone to prevent complete disintegration by the further action of the oxidant, although it has not been possible to prevent the formation of benzoic acid in considerable quantities. The yield of pure diketone, though leaving much to be desired, is still greater than that by any other feasible method, and in point of time and attention required, the authors greatly prefer this method.

Ketonic aldehydes are oxidized with great facility and their preparation by this method has not been accomplished. Obviously hydroxy ketones do not lend themselves to the reaction. The authors are inclined to believe from present evidence that isonitroso ketones are intermediate products in the reaction, although a thorough search in the case of ethylphenyl ketone yielded no oxime. It would appear that the oxime presents less stability to nitrogen tetroxide than does the ketone. In one instance, α-hydrindone, the isonitroso ketone is more resistant to the action of the oxide than the unchanged ketone, so that the former is conveniently prepared by the action of nitrogen tetroxide on the latter. In fact, isonitroso-α-hydrindone exhibits considerable stability toward nitrogen tetroxide and when reaction does ensue deep-seated changes result and no diketo-hydrindone could be isolated from the reaction product. Thus far no synthesis of this interesting diketone has been accomplished. Hot dilute acids resinify the oxime, whereas sodium bisulfite[8] forms a resinous mixture as final product. The action of aqueous formaldehyde is unusual in that the oxime is readily soluble in the commercial 35% solution; on cooling the unchanged compound crystallizes out.

A second case of abnormality in cyclic ketones is that of α-ketotetrahydronaphthalene. Here the action of a small amount of nitrogen tetroxide induces rapid and complete decomposition. The product of the

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[6] Bouveault and Wahl, *Compt. rend.*, **137**, 196 (1903).

[7] Gilman and Johnson, This Journal, **50**, 3341 (1928).

[8] Müller and Pechmann, *Ber.*, **22**, 2557 (1898).

reaction consisted of comparatively insoluble resins from which neither unchanged ketone, diketone nor isonitrosoketone could be isolated.

The examples given in the experimental section suffice to show that the reaction here discussed is sufficiently general to serve as a useful method of preparing alkylaryl diketones.

Experimental Part

1-Phenyl-1,2-propanedione.—A mixture of ethylphenyl ketone (134 g.), finely powdered anhydrous calcium chloride (35 g.) and alcoholic hydrogen chloride (1 cc.), contained in a flask provided with an efficient mechanical stirrer, an inlet tube for the entry of the nitrogen tetroxide and an exit tube to accommodate the evolved gases, is treated with a stream of nitrogen tetroxide, the temperature being maintained at 60°. It is advisable to stir vigorously and introduce about 60 g. of the gas from a weighed tube in the course of three to four hours. Although there is considerable unchanged ketone in the reaction mixture at this stage, it is advisable to interrupt the reaction, since a point is reached where the rate of decomposition of diketone is nearly equal to the rate of its formation.

The reaction mixture is cooled somewhat and taken up in ether. The ethereal solution is washed with water, then exhaustively with aqueous sodium bicarbonate and finally with water. The ether is distilled from the solution and the residue distilled under reduced pressure. Distillation is continued until the residue begins to decompose. The distillate is treated with an equal volume of alcohol and vigorously shaken with 60 cc. of a saturated aqueous solution of sodium bisulfite. In the course of a few minutes, a colorless crystalline solid separates and the mixture gradually becomes pasty, the yellow color fading almost completely. The mixture is then cooled, filtered with suction and the solid washed with alcohol and finally with a little ether.

The bisulfite compound is conveniently decomposed by treatment with a warm solution of sodium carbonate. After cooling the diketone is extracted with ether, the solvent distilled and the diketone distilled in a rapid current of steam. The diketone is recovered from the steam distillate by extraction with ether and after drying and removal of solvent is distilled under reduced pressure. The yield of pure product boiling at 126–128° at 20 mm. is 26 to 28 g.

The filtrate from the bisulfite compound may be worked up for the recovery of unchanged ethylphenyl ketone by addition of water and extraction with ether. The amount recovered varies from 60 to 70 g.

Other Diketones.—Without further modification the above procedure was applied to the synthesis of a number of other diketones. Those listed below were used in the synthesis of substituted ephedrines, and the authors regard the successful isolation of the expected ephedrines as sufficient evidence of identity of the diketones: 1-phenyl-1,2-butanedione, b. p. 130–132° at 20 mm.; 1-*p*-ethylphenyl-1,2-propanedione, b. p. 138–140° at 20 mm.; 1-(2,5-dimethylphenyl)-1,2-propanedione, b. p. 140–144° at 20 mm. The yields in all cases varied between 30 and 40%. The corresponding substituted benzoic acid was isolated in considerable quantities. It is interesting to note that the *p*-ethyl derivative is devoid of the piercing unpleasant odor characteristic of the other diketones. Its odor is strongly reminiscent of anisaldehyde, although slightly more aromatic.

Isonitroso-α-hydrindone.—A solution of 52.8 g. of α-hydrindone in 50 g. of dry benzene containing a few drops of alcoholic hydrogen chloride was cooled in ice and treated with a stream of nitrogen tetroxide until the green color persisted for about one minute after stopping the entry of the gas. An equal volume of petroleum ether was cautiously added, the cooled mixture filtered and the oxime washed first with a mixture of benzene and petroleum ether and then with the latter. The yield was 25 g. After one recrystallization it melted at 210° (corr.) alone or admixed with an authentic specimen.[9] The mother liquor yielded 25 g. of unchanged α-hydrindone when it was washed with dilute alkali, dried and distilled under reduced pressure.

This is the fifth communication submitted during the tenure by one of us of the Eli Lilly and Company Fellowship.[10] The authors desire to express their appreciation not only to the executive staff of this company for the privilege thus enjoyed, but also to the members of the technical staff for their generous coöperation.

Summary

1. A new synthesis of alkylaryl diketones which promises to be quite general is described.

2. The synthesis of a cyclic *o*-diketone was not accomplished.

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[CONTRIBUTION FROM THE COLLEGE OF PHARMACY, UNIVERSITY OF MICHIGAN]

TETRA-ARYLDIARSYLS. I[1]

BY F. F. BLICKE AND F. D. SMITH[2]

RECEIVED APRIL 26, 1929 PUBLISHED JULY 5, 1929

In view of the fact that tetra-arylhydrazines[3] and hexa-arylethanes[4] dissociate spontaneously into diarylnitrogen radicals and triarylmethyls, respectively, it seemed possible that tetra-aryldiarsyls might behave in a similar manner

$$R_2As{-}AsR_2 \rightleftharpoons 2R_2As{-}$$
$$R_2N{-}NR_2 \rightleftharpoons 2R_2N{-}$$
$$R_3C{-}CR_3 \rightleftharpoons 2R_3C{-}$$

Several investigators have studied tetraphenyldiarsyl with regard to its tendency to dissociate into diphenylarsyl. Schlenk[5] determined the molecular weight of the substance in boiling benzene but found no evidence of dissociation. According to Porter and Borgstrom,[6] as well as Borgstrom and Dewar,[7] molecular weight determinations in naphthalene by the cryo-

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[9] Gabriel and Stelzner, *Ber.*, **29**, 2604 (1896).

[10] Richard H. F. Manske.

[1] This paper represents the third part of a dissertation submitted to the Graduate School by Mr. Smith in partial fulfilment of the requirements for the degree of Doctor of Philosophy in the University of Michigan.

[2] Parke, Davis and Company Fellow, 1927–1929.

[3] Wieland, "Die Hydrazine," Ferdinand Enke, Stuttgart, **1913**.

[4] References to the literature on hexa-arylethanes is to be found in "Organic Radicals," Gomberg, *Chemical Reviews*, 1, 141 (1924); also in Walden, "Chemie der frieien Radikale," S. Hirzel, Leipzig, **1924**.

[5] Schlenk, *Ann.*, **394**, 220 (1912).

[6] Porter and Borgstrom, THIS JOURNAL, **41**, 2051 (1919).

[7] Borgstrom and Dewar, *ibid.*, **44**, 2919 (1922).