[Contribution from the Department of Chemistry, The University of Wisconsin]

The Synthesis of 2-Carboethoxy-Δ^2-cyclohexenone[1]

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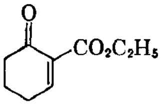
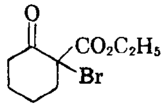
The literature concerning the synthesis and properties of 2-carboethoxy-Δ^2-cyclohexenone and some related compounds is corrected, and an unequivocal synthesis from acyclic starting materials is described.

The purpose of this paper is to correct the long-standing inaccuracies in the literature concerning the preparation and properties of 2-carboethoxy-Δ^2-cyclohexenone (I) and some related compounds and to record an unequivocal synthesis of this interesting dihydrobenzene system.

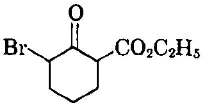
The synthesis of I was reported by Kötz,[3,4] by Ruhkopf[5] in 1939, and most recently by Mousseron[6] in 1954. These workers claim to have prepared the compound by aniline or thermal dehydrobromination of 2-bromo-2-carboethoxycyclohexanone (II). The following observations, obtained in this laboratory, strongly suggest that these claims are incorrect: 1) The bromo-2-carboethoxycyclohexanone the above authors had in hand was almost certainly the 6-bromo isomer (III); 2) authentic 2-bromo-2-carboethoxycyclohexanone, first characterized adequately in the course of this work, cannot be dehydrobrominated by the listed methods or several others; 3) the properties of authentic I, prepared by an unequivocal route, are at variance with the few available in the literature for material prepared as above.



I

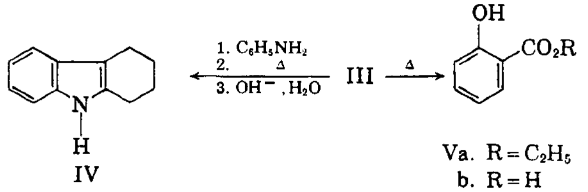


II



III

Kötz[3] reported that bromination of 2-carboethoxycyclohexanone at ice salt bath temperatures with passage of an inert gas through the reaction mixture gave II. Sheehan,[7] using essentially the same conditions but then treating the reaction mixture with anhydrous hydrogen bromide, obtained what he designated as III on the basis of analogy with the bromination of acetoacetic ester.[8] We have found that bromination of I using Kötz's conditions leads to material of the *same refractive index* as that of Sheehan. More important, the bromination product displays a conjugate-chelate type of infrared spectrum (bands at 5.80, 6.08 and 6.20 μ) and possesses a strong maximum in the ultraviolet, λ_{max} 269 mμ, ϵ_{max} 10,200. Further, on treatment of III with aniline in ether, following the procedure of Kötz, no volatile material was obtained on steam distillation; however, ether extraction yielded a high-boiling, viscous liquid which possessed a characteristic indole spectrum in the ultraviolet and infrared regions. A band at 5.82 μ in the latter was indicative of a carboxylic ester; and basic treatment resulted in hydrolysis and decarboxylation to tetrahydrocarbazole (IV), readily identified by its spectral characteristics, as well as by its melting point and mixed melting point with authentic material.



Alternatively, distillation of III at atmospheric pressure[3] followed by rectification in vacuum gave, in low yield, a liquid which from its infrared and ultraviolet spectra appeared to be ethyl salicylate (Va). This product gave a purple color with ferric chloride solution and on alkaline hydrolysis in an inert atmosphere it yielded the readily identifiable salicylic acid, m.p. 155°. Kötz reported a melting point of 128° for the acid secured in this manner which he considered to be the *dihydro* compound. It is likely, rather, that he had in hand an impure sample of Vb, his reported conversion of the acid to cyclohexenone notwithstanding.[9]

Mazza and Crapetta[10] reported a melting point

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(1) Abstracted from the doctoral thesis of Joseph E. Brenner, University of Wisconsin, 1958.

(2) Allied Chemical and Dye Corp. Fellow, 1957–1958. Present address: Department of Chemistry, Massachusetts Institute of Technology.

(3) A. Kötz, *Ann.*, **358**, 183 (1908).

(4) A. Kötz, *J. prakt. Chem.*, (2), **80**, 473 (1909).

(5) H. Ruhkopf, *Ber.*, **72**, 1978 (1939).

(6) M. Mousseron, R. Jacquier, A. Fontaine, and R. Zagdoun, *Bull. Soc. Chim.*, 1246 (1954).

(7) J. C. Sheehan and C. E. Mumaw, *J. Am. Chem. Soc.*, **72**, 2127 (1950).

(8) The α-bromoacetoacetic ester initially produced in the bromination is rapidly rearranged by the hydrogen bromide formed to the γ-isomer. This change appears to be markedly inhibited by water (H. Gault and L. Klees, *Bull. Soc. Chim.*, [4], **39**, 883 (1926).

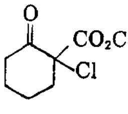
(9) P. D. Bartlett and G. F. Woods, *J. Am. Chem. Soc.*, **62**, 2933 (1940) have presented data which indicate that some of Kötz's thermometers read from 10–12° low; this circumstance is probably not involved here, since in the same paper,[3] Kötz gives the correct melting point for salicylic acid, obtained in another experiment.

(10) F. P. Mazza and C. Crapetta, *Gaz. Chim. Ital.*, **57**, 292 (1927).

of 125° for the acid they obtained by a complex sequence of manipulations of ethyl anthranilate, beginning with sodium in amyl alcohol reduction. This agreement is surprising unless the thermometer used by Mazza and Crapetta also read low or their sample was as impure. In fact, hydrolysis of authentic 2-carboethoxycyclohexenone (I), in complete disagreement with the above result, produces no "dihydrosalicylic acid," but affords cyclohexenone itself, isolated as its 2,4-dinitrophenylhydrazone.

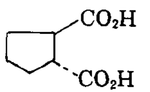
If 2-carboethoxycyclohexanone is brominated in a cold, vigorously stirred emulsion of carbon tetrachloride, ether, and a large excess of saturated potassium bicarbonate solution, 2-bromo-2-carboethoxycyclohexanone (II) can be obtained. Presumably, the aqueous base neutralizes the hydrogen bromide formed, preventing its isomerizing activity. The low refractive index of our product, the lack of evidence of enol in the infrared, faint, or absent color with ferric chloride, and lack of selective absorption in the ultraviolet (λ_{inf} 260 mμ, ϵ_{inf} 310), support the structural assignment. Unfortunately, treatment of II with aniline, dimethylaniline, or collidine yielded no characterizable product, and thermal treatment, *sicut ante*, gave salicylic ester in low yield, contaminated with some other phenolic material.[11]

2-Chloro-2-carboethoxycyclohexanone (VI) was prepared from 2-carboethoxycyclohexanone by sulfuryl chloride chlorination[12] in the presence of potassium carbonate. VI likewise could not be dehydrochlorinated by sodium acetate in acetic acid (reported by Kötz[4]), lithium chloride in dimethylformamide, or the organic bases aniline, dimethylaniline, or collidine.



VI

III $\xrightarrow[C_2H_5OH]{OH^-, H_2O}$



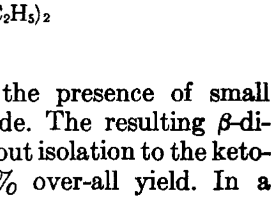
VII

An interesting reaction takes place when 6-bromo-2-carboethoxycyclohexanone (III) is boiled with aqueous ethanolic sodium hydroxide. *trans*-Cyclopentane-1,2-dicarboxylic acid is produced in 91% yield. It was characterized by its carbon-hydrogen analysis, melting point, and mixed melting point with authentic material,[13] and conversion *via* the crystalline *cis* anhydride to *cis* diacid. Similar basic treatment of II and VI gave intractable mixtures from which no crystalline acid could be isolated.

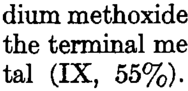
The successful synthesis of 2-carboethoxy-Δ²-cyclohexenone (I) was carried out as follows: the anion of acetylacetone, prepared with sodium hydride in a 1:1 mixture of benzene and dimethylformamide, was alkylated with β-chloropropionaldehyde diethylacetal in the presence of small amounts of potassium iodide. The resulting β-diketone was hydrolyzed without isolation to the keto-acetal, VIII, in about 45% over-all yield. In a large excess of diethyl carbonate, the action of sodium methoxide introduced a carboethoxy group on the terminal methyl,[14] yielding the β-ketoester acetal (IX, 55%). This structural assignment is in accord with the observations of Wallingford, *et al.*,[14] and it was confirmed by the alkylation of acetoacetic ester with chloropropionaldehyde diethylacetal to give, in 81% yield, the isomer X. The infrared spectra of IX and X were similar, but differed in significant detail. Further, on treatment with 2,4-dinitrophenylhydrazine reagent, IX yielded the derivative of 2-carboethoxycyclohexenone (I) (*vide infra*), while X afforded a bis-2,4-dinitrophenylhydrazone in high yield, presumably XI.

$(C_2H_5O)_2CHCH_2CH_2CH_2COCH_3$

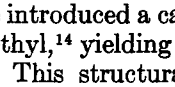
VIII



XI



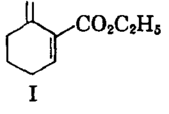
IX



X

Solution of the β-ketoester acetal (IX) in acetone containing a catalytic amount of *p*-toluenesulfonic acid and stirring for twelve hours under nitrogen

IX $\xrightarrow[\text{acetone}]{TsOH \cdot H_2O}$



I

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(11) The successful bromination and dehydrobromination with quinoline of 2-methyl-2-carboethoxycyclopentanone to the corresponding cyclopentenone has been reported (P. C. Dutta, *J. Ind. Chem. Soc.*, **26**, 109 (1949). However, the starting material is not an enolizable β-ketoester, nor can aromatization take place; thus the analogy is strained. M. Yanagita, S. Inayama, and R. Kitagawa, *J. Org. Chem.*, **21**, 612 (1956) were able to obtain 2-methyl-2-carboethoxy-Δ⁶-cyclohexenone in a similar manner. The only additional points of interest are that during the dehydrobromination, the carboethoxyl group was in part lost, and partial migration of the double bond occurred as well to afford a mixture of 2-methyl- and 6-methylcyclohexenones. Incidentally, this result suggests a rationalization of the appearance of phenol itself in the thermal decomposition of II and III.

(12) *Cf.* E. A. Falco, P. B. Russell, and G. H. Hitchings, *J. Am. Chem. Soc.*, **73**, 3753 (1951). The preparation of VI was also reported by Kötz,[3] but the structure of his product is equivocal for the same reasons as above, as rearrangement of the product by the acid formed, while less likely than before, is not impossible.

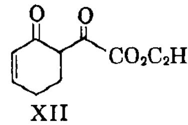
(13) Nitric acid oxidation of a sample of *trans*-1,2-bis-(hydroxymethyl)cyclopentane (A. T. Blomquist, J. Wolinsky, Y. C. Meinwald, and D. T. Longone, *J. Am. Chem. Soc.*, **78**, 6057 (1956), kindly furnished by Dr. Wolinsky, gave 78% yield of pure VII.

(14) V. H. Wallingford, A. H. Homeyer, and D. M. Jones, *J. Am. Chem. Soc.*, **63**, 2252 (1941).

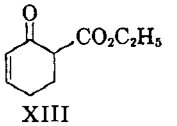
produced the desired 2-carboethoxycyclohexenone in 35–50% yield, the remainder being nonvolatile material. Apparently, *trans*-acetalization had occurred and the free aldehyde, under the influence of the acid catalyst, had undergone ring closure in this highly favorable case.

The unsaturated β-ketoester (I) was a highly enolic material with a characteristic odor resembling both ethyl salicylate and 2-carboethoxycyclohexanone; it dissolved readily in dilute base and produced a bright turquoise color with ferric chloride solution (Kötz[3,4] reported that his material gave a *brown* coloration with ferric chloride). In the infrared, I displayed bands at 5.75, 5.85, 6.10, 6.30, 13.38, and 14.42 μ among numerous others. However, it could be determined that only a trace, if any, of the fully aromatic salicylic ester could be present. 2-Carboethoxycyclohexenone had ultraviolet absorption maxima at 232 and 305 mμ, ε 7800 and 2700 respectively. Catalytic reduction with 30% palladium-on-charcoal in 95% ethanol resulted in the uptake of only about 0.15–0.20 equivalent of hydrogen; however, treatment of the reduction product with 2,4-dinitrophenylhydrazine reagent afforded a fair yield of the derivative of 2-carboethoxycyclohexanone. A probable explanation of the hydrogenation result is that I undergoes rapid disproportionation in the presence of the catalyst to yield ethyl salicylate and 2-carboethoxycyclohexanone. This supposition was confirmed by stirring a sample of I with palladium-on-charcoal in the absence of hydrogen. Hydrolysis of the reaction mixture permitted the isolation of 94% of the theoretical quantity of salicylic acid (*i.e.*, 0.47 mole per mole of I).

For purposes of comparison, we decided to prepare 6-carboethoxy-Δ^2-cyclohexenone (XIII). This was accomplished by reaction of cyclohexenone with diethyl oxalate in the presence of sodium methoxide[15] according to the published procedure.[4] The decarbonylation of the intermediate glyoxalate



XII



XIII

XII was not smooth, and the unsaturated β-ketoester obtained did not have a completely satisfactory carbon-hydrogen analysis. It gave a purple color with ferric chloride solution. Its infrared spectrum showed the expected bands at 5.73 and 5.94 μ but in the 6.0 μ–6.5 μ region, where 2-carboethoxycyclohexenone (I) and its saturated analog both absorb strongly, there was only a weak band at 6.18 μ. In this respect XIII resembles cyclohexenone itself (strong band at 5.95 μ, weak band at 6.20 μ). The ultraviolet, similarly, showed λ_{max} 225 mμ, ϵ_{max} 9700, almost identical with the spectrum of cyclohexenone.

Mousseron[6] reported a melting point of 155–156°, λ_{max} 365 mμ ϵ_{max} 26,900 for the 2,4-dinitrophenylhydrazone of XIII in poor agreement with our values for this compound. Mousseron further reported, for the 2,4-dinitrophenylhydrazone of I, a melting point of 228–230° and λ_{max} 356–357 mμ and 387–388 mμ, both ϵ_{max} 15,500 (a very low value for the 2,4-dinitrophenylhydrazone of an α,β-unsaturated ketone) in complete disagreement with our findings[16] (see Table I). In view of our inability to prepare I by Kötz's method, which Mousseron claims to have done, we are inclined to regard Mousseron's data as completely erroneous.

EXPERIMENTAL[17]

6-Bromo-2-carboethoxycyclohexanone (III). Bromine, 29.1 g., 0.182 mole, was added dropwise over a period of 1 hr. to a vigorously stirred solution of 2-carboethoxycyclohexanone,[18a] 31.0 g., 0.182 mole in 10 ml. of dry ether, cooled in an ice salt bath. The red color of the bromine was not discharged rapidly after about 75% had been added. The reaction mixture was diluted with ether and poured onto a mixture of 20 g. of sodium carbonate and ice. The product was worked up in the usual manner and gave a main fraction on distillation through a short column, 39.3 g., b.p. 104–106°/0.5 mm., n_D^{25} 1.5302, 86%. The product gave an intense purple color with ferric chloride solution. A sample was redistilled for analysis, b.p. 92–93°/0.3 mm., n_D^{25} 1.5280. Sheehan[7] reports b.p. 93–94°/0.4 mm., n_D^{25} 1.5260; infrared: 5.80 μ, 6.08 μ, 6.20 μ; ultraviolet: λ_{max} 268 mμ, ϵ_{max} 10,200.

Anal. Calcd. for $C_9H_{13}O_3Br$: C, 43.39; H, 5.26. Found: C, 43.54; H, 5.11.

An essentially identical result was obtained when the reaction mixture was flushed with nitrogen during the bromination.

Thermal decomposition of III. 6-Bromo-2-carboethoxycyclohexanone, 30.0 g., 0.12 mole, was heated at 220–240° in a current of dry nitrogen. The crude distillate, b.p. 165–190°, was collected and recycled. This distillate, *ca.* 15 g., was redistilled into two rough fractions, A, b.p. 40–60°/1 mm. and B, b.p. 80–110°/0.5 mm. The latter on saponification gave an acid, m.p. 160–161°, shown later to be *trans*-cyclopentane-1,2-dicarboxylic acid, and thus consisted largely of starting bromoketoester. The infrared spectrum of A was essentially that of ethyl salicylate (bands at 3.20 μ, 5.78 μ, 6.02 μ, 6.22 μ, 6.30 μ, 13.24 μ, 14.30 μ, and 15.07 μ); ultraviolet: λ_{max} 238 mμ, ϵ_{max} 7500; λ_{max} 306 mμ, ϵ_{max} 2800; (reported[19] for methyl salicylate λ_{max} 238 mμ, ϵ_{max} 9300;

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(15) This condensation, occurring on the side of the carbonyl remote from the double bond, has proved of great value in certain recent steroid syntheses, *e.g.*, the preparation of methyl 3-oxo-1,4,17(20)-pregnatriene-21-oate from 11-oxoprogesterone *via* 2,21-diethoxalyl-11-oxoprogesterone [J. Korman and J. A. Hogg, U. S. Patent 2,774,775; *Chem. Abstr.*, **51**, 6715 (1957)].

(16) S. N. Balasubrahmanyam, Indian Institute of Science, Bangalore, has reported (private communication) that he has obtained evidence for the production of XIII by the methods of Kötz for I (no experimental data).

(17) Infrared spectra of all liquids were taken on liquid films on Baird and "Infracord" spectrophotometers. Ultraviolet spectra were all measured on a Cary spectrophotometer on samples dissolved in 95% ethanol. Melting and boiling points are uncorrected.

(18) (a) M. R. Snyder, L. A. Brooks, and M. Shapiro, *Org. Syntheses*, Coll. Vol. II, 531 (1943); (b) E. J. Witzemannet, *et al.*, *Org. Syntheses*, Coll. Vol. II, 137 (1943).

(19) E. D. Bergmann, Y. Hirshberg, and S. Pinchas, *J. Chem. Soc.*, 2351 (1950).

TABLE I

ULTRAVIOLET SPECTRA OF 2,4-DINITROPHENYLHYDRAZONES

Compound	Melting Point	λ_{max}, mμ	ϵ_{max}	λ_{max}, mμ	ϵ_{max}
Cyclohexanone	162°	362	23,900	230	16,300
2-Carboethoxycyclohexanone	157–158°	358	23,500	230	14,800
Cyclohexenone	167–169°	373	29,100	251	16,900
2-Carboethoxycyclohexenone	164–165°	368	26,400	255	13,300
	228–230°[a]	356–357[a]	15,500[a]		
6-Carboethoxycyclohexenone	129–130°	367	28,600	253	14,400
	155–156°[a]	365[a]	26,900[a]		
Butylidene acetoacetic ester	131–133°	368	32,400	253	17,100

[a] Ref. 6. All other values were measured in this Laboratory and agreed satisfactorily with the literature values where available.

λ_{max} 306 mμ, ϵ_{max} 4400). Basic hydrolysis of A yielded salicylic acid in 87% yield, m.p. 155°, undepressed on admixture with an authentic sample. The hydrolysis was carried out under nitrogen.

Treatment of III *with aniline.* The bromoketoester, 30.0 g., 0.12 mole, was dissolved in 200 ml. dry ether and warmed for 10 min. on the steam bath with 45 g., 0.48 mole of freshly distilled aniline. When nearly all the ether had evaporated, a strongly exothermic reaction began. The mixture was allowed to stand overnight, then mixed with a solution of 45 g. of oxalic acid in 800 ml. of cold water. Steam distillation of this mixture[4] gave no steam volatile material. The mixture was then cooled and extracted thoroughly with ether. Removal of the ether, after drying with sodium sulfate, and distillation of the residue gave *ca.* 6 g. of a viscous liquid, b.p. *ca.* 175°/0.4 mm. The same result was obtained on omitting the steam distillation step, taking the reaction mixture up in ether, and washing with dilute hydrochloric acid. The ultraviolet spectrum of this distillate displayed bands at 225, 276, 284, and 292 mμ in a pattern indistinguishable from a normal indole. The infrared (chloroform) had a band at 5.82 μ (carboethoxyl carbonyl). Basic hydrolysis gave a good yield of material, m.p. 120–121° after recrystallization from ethanol-water, undepressed on admixture with an authentic sample of tetrahydrocarbazole.[20] The infrared spectra in chloroform were identical.

Favorski reaction of 6-bromo-2-carboethoxycyclohexanone. The bromoketoester (III), 3.0 g., 0.012 mole, was refluxed for 1 hr. with a solution of 3.0 g. of sodium hydroxide in 10 ml. water and 150 ml. of ethanol. Nitrogen was bubbled through the solution. Most of the alcohol was then evaporated and the solution acidified with concd. hydrochloric acid and saturated with ammonium chloride. Ether extraction and the usual workup gave 1.75 g. of crude acid, VII, 91% yield, m.p. 155–158°. A further recrystallization from benzene-methanol (clusters of small needles) and sublimation gave analytically pure material, m.p. 161–162° (reported[21] m.p. 160°).

Anal. Calcd. for $C_7H_{10}O_4$: C, 53.16; H, 6.33. Found: C, 53.09; H, 6.36. Neut. equiv.: Calcd.: 79.1. Found: 80.1, 80.3.

Oxidation of trans-1,2-bis(hydroxymethyl)cyclopentane.[13] The diol, 1.0 g., 0.0075 mole, was dissolved in 20 ml. of concd. nitric acid at room temperature in a flask fitted with an air condenser. After a few minutes of shaking, a *violent* reaction took place. The mixture was then warmed for 1 hr. at 60°, the excess nitric acid removed under reduced pressure, and the residual solid dissolved in 20 ml. of hot water from which deposited on cooling 920 mg. of crystals, m.p. 162–163°, 78% yield. This material did not depress the melting point of VII. The infrared spectra (Nujol mull and potassium bromide pellet) showed little resolution but were superimposable. Following the method of Perkin,[21] a sample of VII was heated with acetyl chloride to form the *cis* anhydride, m.p. 70–72°, which on alkaline treatment afforded *cis*-cyclopentane-1,2-dicarboxylic acid, m.p. 140–141°.

2-Bromo-2-carboethoxycyclohexanone (II). 2-Carboethoxycyclohexanone, 30.0 g., 0.176 mole, was added to 200 ml. of water, 150 g. of potassium bicarbonate, 50 ml. of ether, and 50 ml. of carbon tetrachloride. Bromine, 28.2 g., 0.176 mole was added dropwise over a period of 2 hr. to the cooled vigorously stirred emulsion. The red color which persisted on completion of the reaction was removed by shaking with a small amount of cold dilute sodium thiosulfate solution. The product was extracted with additional ether. The usual workup gave a main fraction, 30.0 g., b.p. 97–93°/0.3 mm., n_D^{25} 1.4937–1.4942, 69% yield. A sample was redistilled for analysis, b.p. 84–86°/0.1 mm., n_D^{25} 1.4932. The infrared had a strong broad band at 5.79 μ, weak traces at 6.05 and 6.20 μ; ultraviolet: λ_{inf} 260 mμ, ϵ_{inf} 310; λ 220 mμ, ϵ 810.

Anal. Calcd. for $C_9H_{13}O_3Br$: C, 43.39; H, 5.26. Found: C, 43.60; H, 5.33.

2-Chloro-2-carboethoxycyclohexanone (VI). Sulfuryl chloride, 14.8 g., 0.11 mole, in 10 ml. of carbon tetrachloride, was added to a stirred mixture of 17.1 g., 0.10 mole, of 2-carboethoxycyclohexanone and 16.7 g. of potassium carbonate in 50 ml. carbon tetrachloride with cooling in an ice salt bath. When the addition was complete, ice water and additional carbon tetrachloride were added. The organic layer was separated, dried, and distilled to yield 15.5 g. of material, b.p. 73–100°/0.4 mm. Redistillation gave 12.1 g., b.p. 85–91°/0.4 mm., n_D^{25} 1.4715–1.4728, 59%. The product gave a very faint coloration with ferric chloride. The infrared had one intense band centered at 5.77 μ and no absorption in the 6.0 μ–6.5 μ region; ultraviolet: λ_{max} *ca.* 257 mμ, ϵ_{max} 110, calculated as due to starting material.

6,6-Diethoxyhexane-2-one (VIII). Sodium hydride, 9.6 g., 0.40 mole, was placed in a thoroughly dried 1 l. round bottomed flask fitted with reflux condenser, mercury-seal stirrer, and dropping funnel and immediately covered with 50 ml. of 1:1 dry benzene–dimethylformamide under a blanket of dry nitrogen. The flask was placed in an ice bath and 40 g., 0.40 mole, acetylacetone (Eastman Kodak Co. Yellow Label, dried by azeotropic distillation with benzene using a water separator) in 50 ml. of the same solvent added dropwise with stirring over a period of 1 hr. The ice bath was replaced by a heating mantle and the flask was warmed until the sodium enolate had dissolved and the last traces of hydride had disappeared. Then 55 g., 0.32 mole, of chloropropionaldehyde diethylacetal[15b] in 50 ml. of 1:1 benzene-dimethylformamide were added rapidly, followed by 800 mg. of dry potassium iodide. The mixture was refluxed gently for 24 hr. The major portion of the solvent was removed under reduced pressure and then a solution of 20 g., 0.50

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(20) This was prepared in essentially quantitative yield from cyclohexanone phenylhydrazone and Amberlite IR-120 resin in hot water (S. Yamada, I. Chibata, and R. Tsurui, *Pharm. Bull. Jap.*, 1, 14 (1953); *Chem. Abstr.*, 48, 12078 (1954).

(21) W. H. Perkin, Jr., *J. Chem. Soc.*, 572 (1894).

mole, of sodium hydroxide in 800 ml. water added with stirring. After warming to 85° over a period of 0.5 hr., an oily layer separated. The mixture was then cooled, and extracted with ether. The usual workup gave, after a short forerun, 31 g. of material, b.p. 100–105°/8 mm., 51% yield. A sample, redistilled for analysis, had the following constants: b.p. 123°/18 mm., n_D^{25} 1.4231; infrared: single sharp band in carbonyl region, 5.80 μ.

Anal. Calcd. for $C_{10}H_{20}O_3$: C, 63.79; H, 10.71. Found: C, 63.99; H, 10.41.

Ethyl 3-keto-7,7-diethoxyheptanoate (IX). Sodium methoxide (Matheson Chemical Co.), 13.5 g., 0.25 mole, was placed in a dried three necked 500 ml. flask fitted with a mechanical stirrer, dropping funnel, and short Vigreux column with a fractional take-off head. The sodium methoxide was immediately covered with 200 ml. of diethyl carbonate (Eastman Kodak Co., White Label, dried by refluxing with and distillation from calcium hydride). The flask was evacuated and refilled with dry nitrogen several times through the take-off head. The ketoacetal (VIII), 38 g., 0.20 mole, in 50 ml. of diethyl carbonate was added in a few minutes. The mixture was then heated, with vigorous stirring, at a pressure of about 120 mm. at 100° for 2.5 hr., alcohol and diethyl carbonate being allowed to distill slowly. The pressure was then reduced further and most of the carbonate removed. After cooling, the thick dark red mixture was poured on a mixture of ice and water and washed from the flask with ice water, then acidified with 20 g. glacial acetic acid in 50 ml. ice water. Extraction with ether and the usual work-up gave 30 g. of material, b.p. 110–125°/0.3 mm. with some superheating, 58% yield; ultraviolet: λ_{max} 248 mμ, ϵ_{max} 850; infrared: bands at 5.75, 5.83, 6.08, and 6.14 mμ. A sample, redistilled for analysis twice, had the following characteristics: b.p. 114–125°/0.3 mm., n_D^{25} 1.4380.

Anal. Calcd. for $C_{13}H_{24}O_5$: C, 59.98; H, 9.29. Found: C, 60.17; H, 9.35.

Ethyl 2-acetyl-5,5-diethoxypentanoate (X). Sodium hydride, 2.4 g., 0.10 mole, was suspended in 100 ml. of 1:1 benzene-dimethylformamide under a blanket of nitrogen. Acetoacetic ester, 16 g., 0.125 mole, in 20 ml. of the same solvent was added dropwise with cooling and stirring. The mixture was then warmed to 80° and when all the hydride had dissolved, 0.5 g. potassium iodide was added, followed by chloropropionaldehyde diethylacetal, 17 g., 0.10 mole, in 20 ml. of benzene-dimethylformamide over a period of 1 hr. The bath temperature was raised to 120° and the mixture refluxed 22 hr., then cooled, and ice water containing 5 ml. of glacial acetic acid added. Ether extraction and the usual workup afforded 21.2 g. of product, b.p. 103–106°/0.15 mm., n_D^{25} 1.4328, yield 81%. An analytical sample had the following properties: b.p. 103–105°/0.1 mm., n_D^{25} 1.4352; ultraviolet λ_{max} 241 mμ, ϵ_{max} 1200; infrared: bands at 5.74, 5.81, 6.10 μ, shoulder 6.15 μ.

Anal. Calcd. for $C_{13}H_{24}O_5$: C, 59.98· H, 9.29. Found: C, 60.11; H, 9.29.

The bis-2,4-dinitrophenylhydrazone (XI) of X was prepared in the usual manner. It was a light yellow in color. A sample, recrystallized for analysis, separated as balls of microscopic needles from 95% ethanol-benzene, m.p. 154°.

Anal. Calcd. for $C_{21}H_{22}N_8O_{11}$: C, 46.15; H, 4.14. Found: C, 46.39; H, 4.00.

2-Carboethoxy-Δ^2-cyclohexenone (I). The β-ketoester acetal (IX), 20 g., 0.077 mole, was dissolved in 250 ml. acetone; *p*-toluenesulfonic acid monohydrate, 150 mg., was added with stirring. The air in the 500 ml. flask was replaced with nitrogen and the stirring (magnetic) continued for 12 hr. The acetone was then removed under reduced pressure at 65° after the addition of 150–200 mg. sodium bicarbonate, until a volume of about 40 ml. remained. The mixture was filtered through Celite and further concentrated on the steam bath in a stream of nitrogen. The residue was distilled under nitrogen to give 7.4 g. of a mobile liquid, b.p. 74–76°/0.5 mm., 57%. The pot residue weighed 4.2 g. A sample was redistilled for analysis, b.p. 59°/0.1 mm., n_D^{25} 1.5051; ultraviolet: λ_{max} 232 mμ, ϵ_{max} 7800; λ_{max} 305 mμ, ϵ_{max} 2700; infrared: 5.75, 5.85, 6.10, 6.30, 13.38, and 14.42 μ.

Anal. Calcd. for $C_9H_{12}O_3$: C, 64.27; H, 7.19. Found: C, 63.97; H, 6.98.

The 2,4-dinitrophenylhydrazone, prepared in the usual manner, separated as red-orange needles from ethanol–ethyl acetate, m.p. 164–165°.

Anal. Calcd. for $C_{15}H_{16}N_4O_6$: C, 51.72; H, 4.63. Found: C, 51.86; H, 4.65.

Acid hydrolysis of I. 2-Carboethoxycyclohexenone, 427 mg., 2.54 mmoles, was refluxed for 1 hr. with 20 ml. of 1*N* sulfuric acid. Steam distillation gave four 40-ml. fractions, each of which were treated with 50 ml. 0.1% 2,4-dinitrophenylhydrazine in 2*N* hydrochloric acid. After standing 3 hr., they were extracted with benzene to give 239 mg. of crude derivative, 47% on the basis of reagent taken, 1.85 mmoles. The relatively low yield is attributed to insufficient reagent for the first fractions of the distillate. After two recrystallizations from ethanol–ethyl acetate the derivative melted at 166–168°, mixed melting point with authentic cyclohexenone 2,4-dinitrophenylhydrazone (m.p. 167–169°) was 167–168°. The ultraviolet spectra were identical. Repetition of the hydrolysis of I and treatment of the steam distillate with excess 2,4-dinitrophenylhydrazine as above permitted the isolation of the derivative of cyclohexenone in 80% crude yield.

The catalytic reduction of I. 2-Carboethoxycyclohexenone, 465 mg., 2.77 mmoles, was hydrogenated in 20 ml. of 95% ethanol at room temperature and pressure in the presence of 250 mg. of 30% palladium-on-charcoal. Thirteen milliliters of hydrogen was absorbed in 5 min. (calculated 70 ml.) and uptake ceased. Butylidene acetoacetic ester, 306 mg., 1.66 mmoles, was then added and rapid uptake of the calculated amount of hydrogen (41 ml.) took place.

In another run, 432 mg., 2.57 mmoles of I was hydrogenated in the same manner. Ten of the calculated sixty-four milliliters were absorbed in 13 min. when the reaction ceased. The catalyst was removed by filtration and 2,4-dinitrophenylhydrazine reagent added. The crude derivative, 485 mg., 54% yield, separated. After three recrystallizations it melted at 148–151°, mixed melting point with the authentic 2,4-dinitrophenylhydrazone of 2-carboethoxycyclohexanone (m.p. 157–158°) was 151–153°. Purification was better effected by silica gel (Davison Chemical Co.) chromatography, which gave material, m.p. 158°, no depression on admixture with the authentic derivative. The ultraviolet spectra were identical.

The disproportionation of I *with palladium-on-charcoal.* 2-Carboethoxycyclohexenone, 2.0 g., 0.012 mole, was dissolved in 30 ml. of 95% ethanol and stirred overnight with 500 mg. of 30% palladium-on-charcoal. The catalyst was removed by filtration and the solution refluxed with 5 g. of potassium hydroxide in 5 ml. of water. The mixture was diluted with water, extracted with ether to remove neutral material, and acidified with concentrated hydrochloric acid. Reextraction with ether gave 0.77 g. of crude product, 94% of the calculated 0.006 mole of salicylic acid. After recrystallization from hot water and sublimation it melted at 158–159° and did not depress the melting point of an authentic specimen of salicylic acid.

6-Carboethoxy-Δ^2-cyclohexenone (XIII). Sodium, 3.7 g., 0.161 mole, was dissolved in 45 ml. of absolute ethanol and the cooled solution added under nitrogen to a cold (−12°) stirred mixture of cyclohexenone, 15 g., 0.156 mole, and ethyl oxalate, 24 g., 0.165 mole at such a rate that the temperature did not rise above −5°. After the addition was complete, the mixture was allowed to stand at 5° for 15 hr. Ice and 1 equivalent of sulfuric acid were added, and the mixture, diluted with ice water, was subjected to the usual workup. Distillation gave 22 g. of a bright yellow liquid, b.p. 147–160°/10 mm., presumably mainly the glyoxalate XII. Two redistillations of this with 1 g. of powdered soft glass containing a trace of iron powder[18a] gave 7.2 g. of a light yellow liquid, b.p. 67–76°/0.3 mm. as well as about 4 g. of unchanged glyoxalate and much tar. The former was distilled twice more for the preparation of a sample which had the following properties, b.p. 73–74°/0.3 mm., n_D^{25} 1.4806. This sample did not have a satisfactory carbon-hydrogen analysis, possibly because of contamination with unchanged glyoxalate XII. However, XIII formed a 2,4-dinitrophenylhydrazone (see below) which gave highly acceptable analytical data.

Anal. Calcd. for $C_9H_{12}O_3$: C, 64.27; H, 7.19. Found: C, 62.04; H, 7.19.

The 2,4-dinitrophenylhydrazone, prepared in the usual manner, separated as orange-yellow needles from ethanol-ethyl acetate, m.p. 129–130°.

Anal. Calcd. for $C_{15}H_{16}N_4O_6$: C, 51.72; H, 4.63. Found: C, 51.86; H, 4.66.

Butylidene acetoacetic ester. This compound was prepared in 76% yield by the method of Cope and Hoffman.[22] A carefully redistilled sample had the following characteristics: b.p. 56°/0.1 mm., n_D^{25} 1.4515. It gave no color with ferric chloride solution; ultraviolet: λ_{max} 220 mμ, ϵ_{max} 6800; infrared: bands at 5.80, 5.98, 6.11 μ, shoulder 6.20 μ. The compound formed a 2,4-dinitrophenylhydrazone, m.p. 131–133°, orange-yellow needles from ethanol.

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MADISON, WIS.

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[22] A. C. Cope and C. M. Hoffman, *J. Am. Chem. Soc.*, 63, 3456 (1941).

[CONTRIBUTION FROM THE CHEMISTRY DEPARTMENT OF THE UNIVERSITY OF MICHIGAN]

Some Exploratory Syntheses of Benzosuberans and Tetrahydrobenzazepinones and Some Related Diazoöxides

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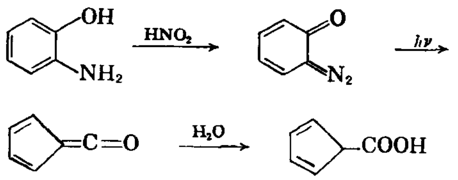
The following new diazoöxides have been investigated in exploration of the feasibility of their ring contraction as a general laboratory preparative method: benzosuberan-5-ol-2,3-diazoöxide, benzosuberan-3,2-diazoöxide, 4,5-dihydro-1-benzazepin-2(3H)-one-7,8-diazoöxide, acetophenone-3,4-diazoöxide, acetanilide-3,4-diazoöxide, benzophenone-3,4-diazoöxide, and diphenylmethane-3,4-diazoöxide. Irradiation with ultraviolet light of intensities available without unusual equipment led to mixtures of dyes presumably arising from coupling of ring-contraction products with the parent diazoöxides. Thermal rearrangement was successful for converting naphthalene-1,2-diazoöxide to indenecarboxylic acid derivatives, but similar treatment was not successful with diazoöxides derived from the benzene ring. Naphthalene-1,2-diazoöxide is reduced to β-naphthol in preparative yields by heating with benzyl alcohol or benzylamine. Several synthetic sequences leading to benzosuberan and 3,4-dihydrobenzazepinone derivatives are reported.

INTRODUCTION

In 1944 Süs reported[2] the first example of the extension to *o*-diazoöxides of the Wolff rearrangement[3] of α-diazo ketones. This process accomplishes the remarkable result of shrinking a benzene ring, as it exists in the *o*-aminophenols from which *o*-diazoöxides are prepared, to cyclopentadienecarboxylic acid derivatives. As reported by Süs and extended[4] by him and by De Jonge and Dijkstra,[5] the conversion is brought about by radiation in the near ultraviolet.



We were interested in exploring the compatibility of the benzene ring-shrinking process to compounds containing carbonyl and amide groups, particularly in cases where the benzene ring is fused to a seven-membered ring. At the same time, we were interested in adapting the reaction as a preparative procedure capable of being accomplished with ordinary equipment. As it has been reported, the reaction requires exceptionally intense ultraviolet radiation for success in synthetic applications; the lower intensities ordinarily available lead to appreciable quantities of dyes derived from coupling of yet unphotolyzed diazoöxide with the cyclopentadiene system. The work reported here consists of the synthesis and investigation of some derivatives of benzene *o*-diazoöxide, some investigations of experimental techniques for rearranging them and also naphthalene-1,2-diazoöxide, and some synthetic schemes leading to diazoöxides in the benzosuberan and 3,4-dihydrobenzazepinone series.

RESULTS AND DISCUSSION

Acetophenone-3,4-diazoöxide was prepared as a highly unstable, explosive solid by diazotizing 3-amino-4-hydroxyacetophenone and liberation of

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[1] From the doctoral thesis of W.L.B., Edgar C. Britton, Fellow in Organic Chemistry, 1953–1955. Present address: American Cyanamid Co., Bound Brook, N. J.

[2] O. Süs, *Ann.*, 556, 65 (1944).

[3] W. E. Bachmann and W. S. Struve, *Org. Reactions*, I, 38 (1942).

[4] O. Süs, *Ann.*, 593, 91 (1955).

[5] J. De Jonge and R. Dijkstra, *Rec. trav. chim.*, 67, 328 (1947).