1-Methyl-4-phenyl-4-(formamidomethyl)-piperidine.—Chloral (4.5 g.) was added slowly to 6.1 g. of the 4-aminomethyl compound with occasional cooling. After 12 hours at room temperature, the solid product was recrystallized from benzene; m.p. 108.5–110°; yield 4.4 g. (63.8%).

The dihydrochloride was recrystallized from ethanol; m.p. 276–277° (dec.).

Anal. Calcd. for $C_{14}H_{22}ON_2Cl_2$: N, 9.18; Cl, 23.23. Found: N, 9.22; Cl, 23.50.

1-Methyl-4-phenyl-4-(methylaminomethyl)-piperidine.—The formyl derivative (5.0 g.) was added in small portions to a stirred solution of 1.0 g. of lithium aluminum hydride in 50 cc. of ether. After the mixture had been stirred and refluxed for 4 hours, it was cooled, 2 cc. of water was added, dropwise, and the mixture filtered. The product obtained from the filtrate boiled at 117–119° (1.5 mm.); yield 3.8 g. (81%).

The dihydrochloride was recrystallized from ethanol; m.p. 256–257° (dec.).

Anal. Calcd. for $C_{14}H_{24}N_2Cl_2$: N, 9.62; Cl, 24.35. Found: N, 9.37; Cl, 24.68.

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Preparation of Cycloöctanone

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It was found that cycloöctanone can be obtained quite readily, in relatively large amounts, from the dimethyl ester of azelaic acid. This method is especially advantageous since azelaic acid has become a cheap commercial chemical.

The cyclization of the ester was attempted by Dieckmann[1] but he obtained only a resinous mass. By the use of sodium hydride[2] and high dilution technique, we converted dimethyl azelate into 2-carbomethoxycycloöctanone in 47.5% yield. Simultaneous hydrolysis and decarboxylation of the β-keto ester yielded cycloöctanone.[3]

Cycloöctanone was prepared also by a second procedure in which cycloheptanone cyanohydrin[4] was reduced with lithium aluminum hydride to 1-(aminomethyl)-cycloheptanol and the latter compound was then treated with nitrous acid.

Experimental

Dimethyl Azelate.—A practical grade of azelaic acid[5] was recrystallized from benzene with the use of Norite. After a second recrystallization from benzene, the acid melted at 94–97° and was sufficiently pure for the preparation of the ester.

A mixture of 752.8 g. of azelaic acid, 3.2 liters of methanol and 128 g. of concd. sulfuric acid was refluxed for 48 hours and then most of the solvent was removed under reduced pressure, the residue was poured into ice-water, the product extracted with ether, the ether solution shaken first with a saturated bicarbonate solution and then with water. The solution was dried with magnesium sulfate, the solvent removed and the ester distilled, yield 695.0 g. (80%), b.p. 145–153° (12 mm.).

2-Carbomethoxycycloöctanone.—To the middle neck of a 3-necked, 5-liter flask there was attached a jacketed 4″ condenser. The upper end of the condenser was fitted with a ball joint lubricated with glycerol to which a short tube was attached. A Hershberg stirrer passed through the joint and the condenser into the flask. A piece of rubber tubing connected to the top of the short tube made a seal between the tube and the shaft of the stirrer. To the other necks of the flasks a nitrogen inlet tube and a dilution apparatus[6] were attached.

After the whole apparatus had been filled with dry nitrogen, 60.0 g. (2.5 moles) of sodium hydride, 60 g. of 5-mm. glass beads and 2.5 liters of xylene[7] were placed in the flask. A very slow stream of nitrogen was passed through the apparatus throughout the experiment. The suspension was stirred rapidly and 2 cc. of absolute methanol was added. The flask was heated and as soon as the mixture refluxed vigorously, the addition of 216.0 g. (1 mole) of dimethyl azelate, dissolved in 1.8 liters of xylene, was begun. The addition was made at the rate of about nine drops per minute and required about nine days. After the addition had been completed, the mixture was refluxed for one hour, and then allowed to cool to room temperature. The nitrogen inlet tube was replaced by a dropping funnel, and 150.0 g. (2.5 moles) of acetic acid was added to the stirred solution at such a rate that the reaction mixture did not become warm. After the mixture had been stirred for one hour, 142 cc. of water was added slowly. A few crystals of sodium acetate were added to induce the precipitation of the sodium acetate in the mixture. The precipitate was filtered and washed with xylene. The xylene solution was washed with concd. sodium bicarbonate solution, dried over anhydrous magnesium sulfate and then fractionated through a 15-cm. Vigreux column. The product which boiled at 129–135° (17 mm.) weighed 87.0 g. (47.5%); about 90% of this material boiled at 130–133° (17 mm.).[8]

Cycloheptanone Cyanohydrin.—Cycloheptanone[9] (224.0 g., 2 moles) and 98.0 g. (2 moles) of sodium cyanide were placed in a 2-liter, 3-necked flask equipped with a thermometer, stirrer and a dropping funnel. The mixture was stirred, cooled to 0° and a mixture of 115 cc. of concd. sulfuric acid and 460 cc. of water was added dropwise, at such a rate that the temperature of the mixture could be maintained below 5° by the use of an ice–salt-bath. After the addition was completed, water was added to dissolve the inorganic salts, the product was extracted with ether, the extract was washed free from acid and then dried with anhydrous magnesium sulfate. The dried extract was used for the next experiment.[10]

1-(Aminomethyl)-cycloheptanol.—The ether solution of the cyanohydrin was added, dropwise, to a stirred mixture of 100 g. of lithium aluminum hydride and 1 liter of ether. After the mixture had been stirred and refluxed for 36 hours, 120 cc. of water was added dropwise. The mixture was stirred for one-half hour, filtered and the inorganic salts washed with ether. From the ether solution there was obtained 124 g. (44% based on cycloheptanone) of product; b.p. 125–129° (17 mm.).[11] The hydrochloride melted at 217–218° after recrystallization from isopropyl alcohol–ether.

Cycloöctanone. (A).—A mixture of 174.0 g. (0.95 mole) of 2-carbomethoxycycloöctanone and 120.0 g. (3 moles) of sodium hydroxide, dissolved in 2.28 liters of water, was

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(1) W. Dieckmann, *Ann.*, **317**, 49 (1901).

(2) Used previously in the Dieckmann cyclization by N. Green and L. B. LaForge, THIS JOURNAL, **70**, 2287 (1948).

(3) The procedure used successfully for the preparation of suberone (cycloheptanone) (F. F. Blicke, N. J. Doorenbos and R. H. Cox, *ibid.*, **74**, 2924 (1952)) could not be utilized for cycloöctanone since suberone condensed with nitromethane to form 1-(nitromethyl)-cycloheptanol in only 3% yield.

(4) Cyclohexanone cyanohydrin has been reduced with lithium aluminum hydride by H. R. Nace and B. B. Smith, *ibid.*, **74**, 1861 (1952).

(5) Purchased from The Matheson Company.

(6) For a description see N. J. Leonard and R. C. Sentz, *ibid.*, **74**, 1708 (1952). To neck D of this apparatus we connected a drip-tip condenser to which a calcium chloride tube was attached and a 1-liter Hershberg dropping funnel was inserted into neck E.

(7) All of the xylene used had been distilled from sodium.

(8) V. Prelog, L. Ruzicka, P. Barman and L. Frenkiel, *Helv. Chim. Acta*, **31**, 92 (1948), found 120° (12 mm.).

(9) F. F. Blicke, N. J. Doorenbos and R. H. Cox, THIS JOURNAL, **74**, 2924 (1952).

(10) B. Tchoubar (*Compt. rend.*, **215**, 224 (1942)), reported that the cyanohydrin boils at 138–139° (15 mm.). We found that upon distillation, under these conditions, about one-half of the cyanohydrin decomposed into cycloheptanone.

(11) B. Tchoubar (*Bull. soc. chim. France*, 160 (1949)), obtained this product in 50% yield by reduction of the cyanohydrin with hydrogen in the presence of platinum oxide; b.p. 124° (15 mm.); hydrochloride, m.p. 223°. Previously, B. Tchoubar (ref. 10) reported the melting point of the hydrochloride to be 185°.

stirred at room temperature until a clear solution had been obtained. The solution was stirred for 2 hours and then 400 g. (4 moles) of concd. hydrochloric acid was added slowly to the stirred mixture. After the latter had been stirred for 30 minutes, it was heated on a steam-bath for 3 hours. The mixture was extracted thoroughly with ether, the extract washed with concd. sodium bicarbonate solution, the ether removed and the residue treated with concd. sodium bisulfite solution. The latter converted the lower ketones into their bisulfite addition products but did not affect the cyclooctanone. The mixture was triturated thoroughly with ether to extract the cyclooctanone, filtered, the ether layer separated and the aqueous layer extracted with ether. The combined ethereal solutions were washed with concd. sodium bicarbonate solution and dried over anhydrous magnesium sulfate. Upon distillation, 92.0 g. of product, b.p. 115–120° (65 mm.), m.p. 26–29°, was obtained. This material was shaken for several hours with a saturated sodium bisulfite solution, the mixture filtered and the solid material washed with sufficient ether to dissolve all of the ketone in the filtrate. From the ether solution there was obtained 13.0 g. of ketone, b.p. 115–118° (64 mm.), m.p. 23° and 72.5 g. (61%) of ketone, b.p. 118–120° (64 mm.),[12] m.p. 38–39°.[10]

(B).—1-(Aminomethyl)-cycloheptanol (124.0 g.) dissolved in 400 cc. of 10% hydrochloric acid was stirred, cooled to 0–5° and maintained at this temperature while 69.0 g. of sodium nitrite, dissolved in 300 cc. of water, was added dropwise. During a period of 2 hours, the mixture was stirred and allowed to warm to room temperature. The mixture was heated on a steam-bath for 1 hour, cooled, the oily layer was separated and the aqueous layer extracted with ether. The combined oil and extract were dried and distilled, b.p. 85–87° (17 mm.), m.p. 32–34°, yield 67.1 g. (26.4% based on cycloheptanone).

Five grams of 1-(hydroxymethyl)-cycloheptanol was isolated from the high boiling fraction; b.p. 142–147° (22 mm.), m.p. 50–51° after recrystallization from heptane.[13]

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[12] E. P. Kohler, M. Tishler, H. Potter and H. T. Thompson (THIS JOURNAL, **61**, 1057 (1939)), obtained the pure ketone by hydrolysis of the semicarbazone, b.p. 115–115.5° (60 mm.), m.p. 43.8°.

[13] O. Wallach, *Ann.*, **345**, 148 (1906), found b.p. 135–140° (16 mm.), m.p. 50–51°.

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3-Trichloromethanesulfenyloxazolidine- and Thiazolidine-2,4-diones

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Because of the appearance of 3-trichloromethane sulfenyloxazolidine- and thiazolidine-2,4-diones in the recent literature,[1] we wish to report our independent work on compounds of this and related types.

Our method of preparation was essentially the same as that of Kittleson,[1] namely, the reaction of trichloromethanesulfenyl chloride (perchloromethylmercaptan) with the sodium or potassium salts of the appropriate oxazolidine- or thiazolidine-2,4-diones. By this method, we have prepared four 3-trichloromethanesulfenyl-5-alkyl- and/or 5,5-dialkyloxazolidine-2,4-diones (Table I); three 3-trichloromethanesulfenyl-5-alkyl- and/or 5,5-dialkylthiazolidine-2,4-diones (Table I) and twelve 3-trichloromethanesulfenyl-5-alkylidene- and/or 5-aralkylidenethiazolidine-2,4-diones (Table II).

Incidental to this work, the preparations of 5-alkylidenethiazolidine-2,4-diones were investigated. Condensation of aromatic and related aldehydes such as furfural and cinnamaldehyde, with thiazolidine-2,4-dione in acetic acid containing sodium acetate, in general, gave 5-aralkylidene-2,4-diones in good yields.[2] However, when this method was applied to certain aliphatic aldehydes, the desired 5-alkylidene derivatives were obtained in much lower yields (see Experimental section). Attempts to condense aliphatic ketones with thiazolidine-2,4-dione have been unsuccessful. Since Brown, Bradsher, McCallum and Potter[3] have reported the successful condensation of ketones with rhodanine to give 5-alkylidenerhodanines and we have found that rhodanine can be transformed into thiazolidine-2,4-dione by the treatment of chloroacetic acid,[4] three of the 5-alkylidene- (namely, isopropylidene-, *s*-butylidene- and cyclohexylidene-) rhodanines reported by Brown and co-workers were thus converted to the corresponding 5-alkylidenethiazolidine-2,4-diones. The product thus obtained apparently contained some unchanged rhodanines as evidenced by their melting points and sulfur analyses. The separation of the two materials by recrystallization was found to be difficult. However, the crude products were satisfactory for subsequent reaction with trichloromethanesulfenyl chloride.

Experimental[9]

Materials.—The sodium salts of the oxazolidine-2,4-diones were prepared according to the method of Stoughton.[10] They were not isolated but used directly in the reaction with trichloromethanesulfenyl chloride (see below).

Thiazolidine-2,4-dione,[11] 5-methyl-[12] and 5,5-dimethyl-[13] thiazolidine-2,4-diones were prepared by known methods.

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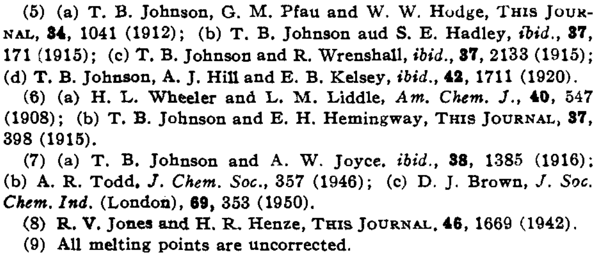
[1] (a) R. S. Heanley, A. R. Kittleson and P. V. Smith, U. S. Patent, 2,553,775 (1951)· (b) A. R. Kittleson, *Science*, **115**, 84 (1952).

[2] (a) F. Kucera, *Monatsh.*, **35**, 137 (1914); (b) D. Libermann, J. Hienberl and L. Hengl, *Bull. soc. chim., France*, 1120 (1948); (c) C. P. Lo, E. Y. Shropshire and W. J. Croxall, THIS JOURNAL, **75**, 4845 (1953).

[3] F. C. Brown, C. K. Bradsher, S. G. McCallum and M. Potter, *J. Org. Chem.*, **15**, 174 (1950).

[4] Many examples of "desulfurization" of heterocyclic compounds containing mercapto group by means of chloroacetic acid are known in the literature. For example, this method has been successfully applied to thiohydantoins,[5] thiouracils,[6] thiopyrimidines[7] and mercaptoquinolines.[8] The transformation of rhodanine to thiazolidine-2,4-dione by chloroacetic acid is believed to involve the sequence of reactions



[5] (a) T. B. Johnson, G. M. Pfau and W. W. Hodge, THIS JOURNAL, **34**, 1041 (1912); (b) T. B. Johnson and S. E. Hadley, *ibid.*, **37**, 171 (1915); (c) T. B. Johnson and R. Wrenshall, *ibid.*, **37**, 2133 (1915); (d) T. B. Johnson, A. J. Hill and E. B. Kelsey, *ibid.*, **42**, 1711 (1920).

[6] (a) H. L. Wheeler and L. M. Liddle, *Am. Chem. J.*, **40**, 547 (1908); (b) T. B. Johnson and E. H. Hemingway, THIS JOURNAL, **37**, 398 (1915).

[7] (a) T. B. Johnson and A. W. Joyce, *ibid.*, **38**, 1385 (1916); (b) A. R. Todd, *J. Chem. Soc.*, 357 (1946); (c) D. J. Brown, *J. Soc. Chem. Ind.* (London), **69**, 353 (1950).

[8] R. V. Jones and H. R. Henze, THIS JOURNAL, **46**, 1669 (1942).

[9] All melting points are uncorrected.

[10] R. W. Stoughton, THIS JOURNAL, **63**, 2376 (1941).

[11] J. Volhard, *J. prakt. Chem.*, [2] **9**, 9 (1874).

[12] H. L. Wheeler and B. Barnes, *Am. Chem. J.*, **24**, 78 (1900).

[13] H. Erlenmeyer and H. von Meyenburg, *Helv. Chim. Acta*, **20**, 1390 (1937).