2-Perhydrogeranyl-3-methyl-2-cyclohexen-1-one (XII).—The above ester XI (15.7 g.) was refluxed for eight hours with a solution of potassium hydroxide (5 g.) in ethanol (50 cc.). The alcohol was removed by distillation and the residue was diluted with water and extracted with ether. Removal of the ether and fractionation of the residue gave the ketone XII (6.6 g., 54%) boiling at 153–155° (3 mm.). The semicarbazone, after three crystallizations from aqueous alcohol (long standing in the refrigerator), melted at 93–95°.

Anal. Calcd. for $C_{18}H_{33}ON_3$: C, 70.31; H, 10.82. Found: C, 70.19; H, 10.57.

3,5-Dimethyl-2-cyclohexen-1-one (XIV).—Piperidine (13 g.) was added to a mixture of acetoacetic ester (520 g.) and acetaldehyde (88 g.). After the reaction (slow refluxing) had subsided (four hours), water (2 l.) and sulfuric acid (500 cc.) were added, and the mixture was refluxed for twenty-two hours. The cooled mixture was extracted with three 600-cc. portions of ether, the solvent was removed from the combined extracts, and the residue was fractionated. The products were the ketone XIV (47 g., 19%) boiling at 81° (9 mm.), 3,5-dimethyl-4-carbethoxy-2-cyclohexen-1-one (XIII, 23 g., 6%) boiling at 146° (12 mm.), and a little 3,5-dimethyl-4,6-dicarbethoxy-2-cyclohexen-1-one boiling at 205° (11 mm.). The semicarbazone of the ketone XIV, after crystallization from dilute alcohol, melted at 177–180.5°.[22]

2,3-Dimethylphenol (XV).—2,3-Dimethyl-2-cyclohexen-1-one (VIII, 2.0 g.) was heated at 200° with palladium-charcoal catalyst "d"[10] (0.22 g.) for seventy-two hours. The cooled mixture was diluted with petroleum ether (70 cc., b. p., 30–60°), filtered, and the filtrate was extracted with three 10-cc. portions of sodium hydroxide solution (17%). The combined extracts were acidified with hydrochloric acid and the phenol XV (1.04 g., 53%) was removed and crystallized from petroleum ether (b. p. 30–60°). The phenol melted at 71.5–72.5°, alone or when mixed with an authentic specimen.[23]

Summary

1. Hagemann's ester, 3-methyl-4-carbethoxy-2-cyclohexen-1-one (IV) has been alkylated in the 2-position with methyl, ethyl and perhydrogeranyl halides and the resulting substances have been converted into 2-alkyl-3-methyl-2-cyclohexen-1-ones.

2. Dehydrogenation of 2,3-dimethyl-2-cyclohexen-1-one (VIII) by action of a palladium catalyst gave 2,3-dimethylphenol in 53% yield; the dehydrogenation was attempted by other methods, but none of these attempts was successful.

3. By substitution of acetaldehyde for formaldehyde in the initial condensation, 3,5-dimethyl-2-cyclohexen-1-one has been prepared and it appears that this synthesis of cyclohexenones is general and may be varied widely by suitable choice of starting materials.

MINNEAPOLIS, MINNESOTA RECEIVED DECEMBER 5, 1942

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[22] The melting points given in the literature range from 178° to 180°; (a) Knoevenagel, *Ann.*, **297**, 165 (1897); (b) Mazurewitsch, *Chem. Zentr.*, **85**, I, 1653 (1914); (c) Baeyer and Piccard, *Ann.*, **407**, 342 (1915).

[23] Smith and Opie, *J. Org. Chem.*, **6**, 431 (1941).

[CONTRIBUTION FROM THE AVERY LABORATORY OF CHEMISTRY OF THE UNIVERSITY OF NEBRASKA]

Arsenicals Derived from Acetophenone

BY ROBERT L. CLARK[1] AND CLIFF S. HAMILTON

In an effort to obtain compounds of value in the treatment of spirochaetal and trypanosomal diseases, the synthesis of omega-hydroxy and omega-amino derivatives of 4-arsonoacetophenone was undertaken.

4-Arsonoacetophenone was converted to ω-chloro-4-arsonoacetophenone by the method of Sergeev and Kudryashev.[2] The product obtained in this investigation melted at 208–209°, whereas they reported a melting point of 189°. When ω-chloro-4-arsonoacetophenone was refluxed with potassium formate in a medium of methyl alcohol, ω-hydroxy-4-arsonoacetophenone resulted. In the same manner, secondary amines treated with ω-chloro-4-arsonoacetophenone to yield omega-amino derivatives.

When phenylhydrazine was treated with ω-chloro-4-arsonoacetophenone a product was obtained which contained no halogen. Hoogeveen[3] reported that similar reactions formed derivatives of 1,2-diazacyclobutene-2. The arsenic analysis indicated that such a type of compound was prepared in this investigation. Other derivatives involving the carbonyl group of ω-hydroxy- and ω-chloro-4-arsonoacetophenone were prepared by familiar procedures.

ω-Hydroxy-4-arsonoacetophenone was reduced with sulfur dioxide to give the corresponding arsine oxide.

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[2] Sergeev and Kudryashev, *J. Gen. Chem.*, (U. S. S. R.) **7**, 1488 (1937).

[3] Hoogeveen, *Rec. trav. chim.*, **50**, 669 (1931).

Experimental

4-Arsonoacetophenone was prepared by the method of Gibson and Levin.[4]

4-Acetylphenyldichloroarsine was obtained by a modification of the procedure used by Elson and Gibson.[5]

ω-Chloro-4-arsonoacetophenone (I).—4-Acetylphenyldichloroarsine (48 g., 0.18 mole) was dissolved in warm absolute alcohol (85 ml.). While the temperature was maintained at approximately 40°, chlorine was bubbled into the solution until there was a gain in weight of 12.2 g. (0.172 mole). After evaporation of the alcohol, hydrogen peroxide was added until all the trivalent arsenic was oxidized to the pentavalent state. The ω-chloro-4-arsonoacetophenone thus obtained was partially purified by dissolving in a saturated sodium bicarbonate solution, filtering through a charcoal mat, and reprecipitating by adding 1 *N* hydrochloric acid; m. p. 204–205°; yield 38 g. (76%). Although this product was used in subsequent reactions, further impurities could be removed by dissolving them in boiling dilute acetic acid. Purification by the use of sodium bicarbonate resulted in crystals of the arsonic acid. The product is insoluble in hot water, but quite soluble in hot methyl alcohol.

Anal. Calcd. for $C_8H_8O_4ClAs$: As, 26.90; Cl, 12.73. Found: As,[6] 26.81, 26.93; Cl, 12.71, 12.90.

ω-Chloro-4-arsonoacetophenone Semicarbazone (II).—To (I) (5 g., 0.018 mole), dissolved in a solution of sodium bicarbonate and diluted to about 50 ml., was added 50 ml. of a solution of semicarbazine hydrochloride (2.5 g., 0.022 mole). After warming on a water-bath for fifteen minutes the resulting precipitate was filtered off, washed with water and ethyl alcohol, dissolved in a sodium bicarbonate solution, filtered through a charcoal mat and reprecipitated with 1 *N* hydrochloric acid. The semicarbazone of (I) was obtained as a white solid; darkened at 215°; yield, 37%.

Anal. Calcd. for $C_9H_{11}O_4ClN_3As$: As, 22.32. Found: As, 22.15, 22.17.

ω-Chloro-4-arsonoacetophenone oxime (III) was prepared in a manner similar to the semicarbazone; m. p. 173–173.5°; yield, 38%.

Anal. Calcd. for $C_8H_9O_4ClNAs$: As, 25.47. Found: As, 25.50, 25.55.

3-*p*-Arsonophenyl-1-phenyl-(1,2-diazacyclobutene-2) (IV).—The reaction of (I) with phenylhydrazine hydrochloride was carried out in an analogous manner to the reaction with semicarbazine hydrochloride, except that no heat was necessary. 3-*p*-Arsonophenyl-1-phenyl-(1,2-diazacyclobutene-2) was isolated as a yellow powder; darkened at 210–215°; yield, 35%.

Anal. Calcd. for $C_{14}H_{13}O_3N_2As$: As, 22.55. Found: As, 22.37, 22.38.

ω-Hydroxy-4-arsonoacetophenone (V).—To 15 g. (0.054 mole) of (I) was added potassium formate (15 g., 0.183 mole), methyl alcohol (60 ml.) and water (1.5 ml.). This mixture was refluxed for one and a half hours and then filtered hot. The precipitate (14 g.) was recrystallized from 1 *N* hydrochloric acid (16 ml.), and the resulting product recrystallized once more from water (10 ml.) to yield yellow crystals of ω-hydroxy-4-arsonoacetophenone (2.3 g.); yield, 16%.

Anal. Calcd. for $C_8H_9O_5As$: As, 28.81. Found: As, 28.91, 28.81.

ω-Hydroxy-4-arsonoacetophenone Semicarbazone (VI).—To (V) (0.9 g., 0.0034 mole), anhydrous sodium acetate (0.45 g., 0.0055 mole), and water (6 ml.) was added semicarbazine hydrochloride (0.7 g., 0.0064 mole) dissolved in water (3 ml.). After standing at room temperature for four hours, the precipitated product was purified by dissolving in sodium bicarbonate solution, filtering through a charcoal mat and acidifying with 1 *N* hydrochloric acid. ω-Hydroxy-4-arsonoacetophenone semicarbazone was obtained in a white, crystalline form; yield, 65%.

Anal. Calcd for $C_9H_{12}O_5N_3As$: As, 23.63. Found: As, 23.43, 23.46.

ω-Hydroxy-4-arsonoacetophenone phenylhydrazone (VII) was obtained by a procedure nearly identical with that given for the preparation of the semicarbazone. It was isolated in the form of yellow-orange crystals; yield, 40%.

Anal. Calcd. for $C_{14}H_{15}O_4N_2As$: As, 21.39. Found: As, 21.19, 21.47.

ω-Hydroxy-4-arsenosoacetophenone (VIII).—To (V) (8.5 g.) dissolved in warm 1 *N* hydrochloric acid (85 ml.), was added potassium iodide (0.1 g.), and the solution saturated with sulfur dioxide. The yellow precipitate was washed thoroughly with water while on the filter paper. After drying in a vacuum desiccator for several hours, ω-hydroxy-4-arsenosoacetophenone was obtained as a yellow powder; yield 65%.

Anal. Calcd. for $C_8H_7O_3As$: As, 33.14. Found: As, 33.30, 33.25.

ω-Diethylamino-4-arsonoacetophenone Hydrochloride (IX).—Three grams (0.011 mole) of (I), methyl alcohol (15 ml.), and diethylamine (4.5 ml., 0.045 mole) were refluxed for forty-five minutes, filtered and evaporated to about 40% of its volume. Enough concentrated hydrochloric acid was added to make the solution slightly acid to congo red paper. After cooling three hours in the refrigerator the crystalline product was filtered (1 g.) and recrystallized from a medium of ethyl alcohol (5 ml.) and water (2 ml.). The white, crystalline, ω-diethylamino-4-arsonoacetophenone hydrochloride melted at 186–187°; yield, 33%.

Anal. Calcd. for $C_{12}H_{19}O_4NClAs$: As, 21.30. Found: As, 21.40, 21.27.

ω-Morpholino-4-arsonoacetophenone hydrochloride (X) was obtained by use of a procedure similar to that employed in the preparation of (IX). The white crystals of ω-morpholino-4-arsonoacetophenone melted at 172–173°; yield, 63%.

Anal. Calcd. for $C_{12}H_{17}O_5NClAs$: As, 20.49. Found: As, 20.40, 20.67.

ω-Piperidonyl-4-arsonoacetophenone hydrochloride (XI) was prepared in a manner similar to that used to produce (IX). It was obtained in the form of white crystals which melted at 186–187°; yield, 61%.

Anal. Calcd. for $C_{18}H_{19}O_4NClAs$: As, 20.60. Found: As, 20.80, 20.66.

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(4) Gibson and Levin, *J. Chem. Soc.*, 2392 (1931).

(5) Elson and Gibson, *ibid.*, 2388 (1931).

(6) See Cislak and Hamilton, THIS JOURNAL, **52**, 638 (1930).

Summary

Omega substituted derivatives of 4-arsonoacetophenone were prepared and identified.

LINCOLN, NEBRASKA RECEIVED JUNE 11, 1942

[CONTRIBUTION FROM THE CHEMICAL LABORATORY OF THE OHIO STATE UNIVERSITY]

Temperature–Concentration Equilibria in the System Dimethylaniline–Sulfur Dioxide[1]

BY J. RUSSELL BRIGHT[2] AND W. CONARD FERNELIUS[3]

Hill and Fitzgerald[4] studied pressure–composition equilibria in the system: sulfur dioxide–dimethylaniline. Although they obtained no solid phase even by cooling to $-10°$ and seeding with crystals of the sulfur dioxide-*o*-toluidine compound, the marked heat of absorption, the red color, and the positive deviation from Henry's law indicated that compound formation was probable. Gleason and Loonan[5] claim that dimethylaniline and sulfur dioxide give no solid products at 0°. The present study of temperature–concentration equilibria in the system sulfur dioxide–dimethylaniline shows the existence of the compound $C_6H_5(CH_3)_2N:SO_2$.

Experimental

The System $C_6H_5(CH_3)_2N:SO_2$.—The apparatus and technique were essentially that used by Booth and Germann[6] with the following modifications: purification of commercial sulfur dioxide was effected by drying (P_4O_{10}) and careful fractional distillation[7]; dimethylaniline, dried over sodium, was added directly to the melting point tube; pressures were measured by means of an absolute manometer[8,9]; and temperatures were measured by means of a carefully calibrated, two-junction copper–constantan thermocouple. Cooling curves were obtained directly by using a Leeds and Northrup Micromax recording potentiometer, Model S-4000. The probable accuracy of the temperature readings is ±0.4°. The temperature-concentration data are summarized in Table I.

Preparation of $C_6H_5(CH_3)_2N:SO_2$.—When dry sulfur dioxide gas was passed into a petroleum ether solution of dimethylaniline, a red oil settled out. The oil was separated from the solution by means of a separatory funnel: $d^{27}{}_4$ 1.08, m. p. 12.0°.

TABLE I

TEMPERATURE–COMPOSITION DATA OF THE SYSTEM $C_6H_5(CH_3)_2N$–SO_2

Concentration mole fraction $NC_6H_5(CH_3)_2$	Temp., °C.	Curve (Fig. 1)
0.000	-75.0^a	A. (Solid SO_2, liq., vapor)
.091	-77.5	
.133	-81.1	AB. (Solid SO_2, satd. soln., vapor)
.161	-85.1	
.178	-90.1	B. (Eutectic: solid SO_2, solid $C_6H_5(CH_3)_2N:SO_2$, satd. soln., vapor)
.198	-72.5	
.221	-59.1	
.248	-44.6	
.251	-41.3	
.274	-30.1	
.288	-24.4	
.314	-17.1	
.334	-10.5	
.349	-8.5	
.376	-1.1	
.424	$+7.1$	
.435	$+10.7$	
.474	$+12.1$	
.504	$+12.4$	BCD. (Solid $C_6H_5(CH_3)_2N:SO_2$, satd. soln., vapor)
.587	$+12.6$	
.649	$+11.5$	
.651	$+11.9$	
.669	$+10.9$	
.695	$+9.2$	
.749	$+5.3$	
.781	$+2.3$	
.838	-4.5	
.857	-6.8	D. (Eutectic: solid $C_6H_5(CH_3)_2N:SO_2$, solid $NC_6H_5(CH_3)_2$, satd. soln., vapor)
.885	-3.8	
.918	-0.5	
.934	-0.8	
1.000	$+2.0$	DE. (Solid $NC_6H_5(CH_3)_2$, satd. soln., vapor)
		E. (Solid $NC_6H_5(CH_3)_2$, liq., vapor)

[a] W. F. Giauque and C. C. Stephenson (THIS JOURNAL, **60**, 1389 (1938)) give the value $-75.46°$.

The System $C_6H_5(CH_3)_2N:SO_2$–$NC_6H_5(CH_3)_2$.—Both liquids were added to the melting point tube from microburets and temperatures recorded as noted above. The data are summarized in Table II.

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(1) Abstracted from a portion of a thesis presented by J. Russell Bright to the Graduate School of The Ohio State University, June 1940, in partial fulfillment of the requirements for the degree of Doctor of Philosophy.

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(4) A. E. Hill and T. B. Fitzgerald, THIS JOURNAL, **57**, 250–254 (1935).

(5) G. H. Gleason and A. C. Loonan, U. S. Patent 2,186,453, Jan. 9, 1940.

(6) H. S. Booth and A. F. O. Germann, *J. Phys. Chem.*, **30**, 369 (1926).

(7) For method see H. S. Booth and A. R. Bozarth, *Ind. Eng. Chem.*, **29**, 470 (1937).

(8) A. F. O. Germann, THIS JOURNAL, **36**, 2456 (1914).

(9) A. F. O. Germann, and H. S. Booth, *J. Phys. Chem.*, **21**, 8 (1917).