NOTES

Thiocarbonyls. III. The Willgerodt Reaction with Thioacetophenone[1]

By E. Campaigne and Phyllis V. Rutan

To account for the reaction of ketones in the Willgerodt reaction, King and McMillan[2] proposed the following sequence of steps: ketone → thioketone → mercaptan → olefin → mercaptan → etc. To show that these substances could act as intermediates in the reaction, mercaptans and olefins were successfully converted to the corresponding amides by the Willgerodt procedure. However, no thioketone has been shown to undergo a Willgerodt reaction. King and McMillan[2] found that "duplodithioacetone" was converted to propionamide when heated with ammonium polysulfide, but "duplodithioacetone" is neither dithioacetone nor trithioacetone.[3]

Trithioacetophenone has been found to yield phenylthioacetomorpholide by the Kindler procedure in better yield than that obtained from acetophenone in a parallel experiment. Since the refluxing temperature was well above the melting point of trithioacetophenone (122°) it was assumed to act through the monomeric form. The Kindler modification of the Willgerodt reaction was used to eliminate the possibility of hydrolysis of thioacetophenone to acetophenone as one step in the reaction.

In one experiment, acetophenone (12 g., 0.1 mole), morpholine (8.7 g., 0.1 mole), and sulfur (3.2 g., 0.1 mole) were mixed, refluxed for eight hours, and the mixture poured into 50 ml. of hot ethyl alcohol. The crystals of phenylthioacetomorpholide which formed on cooling melted at 78–79.5°, and weighed 15.9 g., which is equivalent to 72% of the theoretical yield.

In a second experiment, morpholine (4.4 g., 0.05 mole), sulfur (1.6 g., 0.05 mole) and trithioacetophenone (6.8 g., 0.017 mole) were mixed and refluxed for seven and one-half hours at a temperature of 145–150°. A copious evolution of hydrogen sulfide occurred in this case. Worked up in an identical manner, the yield of phenylthioacetomorpholide, m.p. 77–79°, was 9.2 g. or 83%. A mixed melting point determination of the two products showed no depression.

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[1] For the second paper of this series, see This Journal, **68**, 769 (1946).

[2] King and McMillan, *ibid.*, **68**, 1369 (1946).

[3] Campaigne, *Chem. Rev.*, **39**, 22 (1946).

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The Conversion of Certain Mercaptans into Acetates and Sulfides[1]

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In connection with certain research projects in these Laboratories, 2-hydroxyethylmercaptan and *t*-butylmercaptan were converted into 2-chloroethylthiol acetate, *t*-butyl chlorothiol acetate, *t*-butyl 2-hydroxyethyl sulfide and *t*-butyl 2-chloroethyl sulfide. They were isolated in a state of purity and several density, freezing point and vapor pressure determinations made.

Experimental

The intermediates, 2-hydroxyethyl and 2-chloroethyl mercaptan, were prepared according to the method of Bennett.[3] Yields were considerably lower than reported by Bennett, particularly for the 2-chloroethyl mercaptan. The 90% yield reported for the chloro compound was obtained for the crude product, but on distillation extensive polymerization could not be prevented. Yields of 33 to 44% for the purified material were obtained.

2-Chloroethylthiol Acetate.[4]—2-Chloroethyl mercaptan (50 g., 0.52 mole) was added dropwise with stirring to 0.9 mole of acetyl chloride at a reaction temperature of 50°. After the addition was complete, about fifty minutes, the reaction mixture was stirred at 50° for an additional two hours to complete the reaction. The large excess of acetyl chloride was unnecessary if its loss through volatilization was prevented by a carbon dioxide–acetone cooled scrubber. The reaction mixture was then fractionated in vacuum and the fraction of b. p. 74–76° at 17 mm. collected. For material of 99% purity see Table I.

***t*-Butyl Chlorothiol Acetate.**—*t*-Butyl mercaptan (50 g., 0.56 mole) was heated gently with 69 g., 0.62 mole, of chloroacetyl chloride for two hours at 60–90°. The mixture ceased refluxing at 90°, which indicated that the reaction was complete. The reaction mixture was then fractionated under vacuum and the fraction of b. p. 82–84° at 15–19 mm. collected. For material of purity of 99% see Table I.

***t*-Butyl 2-Hydroxyethyl Sulfide.**—This intermediate was prepared by condensing the sodium salt of *t*-butyl mercaptan with aqueous ethylene chlorohydrin at 60–70° with good stirring. The crude hydroxy sulfide which separated as an insoluble oil was drawn off, dried over silica gel and fractionated in vacuum. Yield of the once distilled product of b. p. 89–93° at 17 mm. was 80–85%. *Anal.* Calcd. for $C_6H_{14}OS$: S, 23.88. Found: S, 22.89.

***t*-Butyl 2-Chloroethyl Sulfide.**—*t*-Butyl 2-hydroxyethyl sulfide (116.5 g., 0.87 mole) was diluted with 30 ml. of ether and the mixture added beneath the surface of an ether–thionyl chloride mixture containing 114 g., 0.96 mole of thionyl chloride and 30 ml. of ether. The reaction was conducted in a 3-necked flask of the proper ca-

Table I

Analyses and Properties of Certain Acetates and Sulfides

Compound			2-Chloroethyl thiolacetate	*t*-Butyl chlorothioacetate	*t*-Butyl-2-chloroethyl sulfide
Formula			C_4H_7OClS	$C_6H_{11}OClS$	$C_6H_{13}ClS$
B. p.	°C.		76–76.5	89	81–82
	Mm.		17	21	30
Yield, %, once distd.			90	80	80
F. p., °C.			...	Below −70	−49 ± 1
Density	g./ml.		1.2010	1.1023	1.0001
	at °C.		20	25	25
Vapor. p.	Mm.		1.68	0.549	1.46
	°C.		30	25	25
Analyses, %	Cl	Calcd.	25.59	21.27	23.22
		Found	25.36	21.08	23.24
	S	Calcd.	23.14	19.24	21.00
		Found	22.81	18.83	20.85

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[1] Published with the permission of the Chief, Chemical Corps.

[2] Chemical Corps Technical Command, Edgewood Arsenal, Md.

[3] Bennett, *J. Chem. Soc.*, **121**, 2139 (1922).

[4] Alderman, U. S. Patent 2,212,141 (1941); prepared by author in 1938, E. A. T. R. 279.

pacity and with the necessary operating equipment. The reaction temperature during addition was 30–40° and 50–60° for half an hour after completing the addition. Total reaction period one and quarter hours. The excess thionyl chloride, solvent and volatile gases were immediately removed and the crude chlorinated product distilled under vacuum in an atmosphere of carbon dioxide. The yield of once-distilled product obtained under the above conditions was 80%. Employing ether as a solvent, and distillation of the product in an atmosphere of carbon dioxide, but without eliminating vapor phase reaction, the yield was 53%. Eliminating both the solvent and distillation of the product in an atmosphere of carbon dioxide the yield was 41%. The significant condition appears to be the elimination of vapor phase chlorination by introducing the hydroxy compound beneath the surface of the thionyl chloride–ether mixture. For material of purity of 99% see Table I.

Acknowledgment.—The author wishes to express thanks for the density, freezing point and vapor pressure determinations which were made by the Physical Department, Chemical Division, Edgewood Arsenal.

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The Vapor Phase Rearrangement of Pinacols

BY WILLIAM S. EMERSON

Our success in converting styrene glycol to phenylacetaldehyde[1] in the vapor phase suggested the possibility of applying this technique to the pinacol rearrangement. We have found that pinacol is converted to pinacolone in 94% yield by passing its vapors together with steam over silica gel impregnated with phosphoric acid. This compares favorably with the 65–72% yield obtained in the liquid phase with sulfuric acid.[2] Under similar conditions, using a catalyst of silica gel impregnated with sodium bisulfate, 2,3-diphenyl-2,3-butanediol yielded 98% of material boiling in the proper range for 3,3-diphenylbutanone, from which 63% of crude product was isolated.

Experimental

Pinacolone.—A quartz tube[1] was packed with silica gel impregnated with phosphoric acid (10 cc. of 85% acid poured on 90 cc. of silica). While steam (about five volumes) was continuously passed over the catalyst, a solution of 50 g. of pinacol in 50 cc. of dioxane was introduced over a one-hour period. The tube was held at 275–300° and evacuated to 170 mm. After the pinacol was added, the tube was steamed out for an additional fifteen minutes before cooling. The layers in the receiver were separated and the aqueous portion twice extracted with ether. The combined extracts and organic layer were dried over Drierite. Distillation yielded 35 g. of pinacolone, b. p. 95–105° (103–106°),[3] $n^{25}\mathrm{D}$ 1.4019. By redistilling the ether an additional 4.5 g. was obtained, b. p. 98–105°, $n^{25}\mathrm{D}$ 1.4020 to give a total yield of 39.5 g. (94%).

The 2,4-dinitrophenylhydrazone of the main fraction melted at 122–124° (125°).[3]

3,3-Diphenylbutanone.—The tube was packed with silica gel impregnated with sodium bisulfate (5 g. in 15 cc. of water poured on 110 cc. of silica) and held at 275–300° and 80–100 mm. While steam was continuously passed over the catalyst, a solution of 32.5 g. of 2,3-diphenyl-2,3-butanediol in 50 cc. of dioxane and 65 cc. of toluene was introduced over an eighty-minute period. Some difficulty was encountered in keeping the tube from clogging. The steam introduction was continued for fifteen minutes more before cooling the tube. The layers in the receiver were separated and the aqueous phase was twice extracted with benzene. Distillation yielded 23 g. of crude 3,3-diphenylbutanone, b. p. 175–185° (15 mm.) (180° (18 mm.)),[4] $n^{25}\mathrm{D}$ 1.5870. The tube was washed out with 25 cc. of dioxane and then with 50 cc. of benzene. These washings were similarly worked up to obtain an additional 6.5 g., b. p. 178–188° (15 mm.), $n^{25}\mathrm{D}$ 1.5890. The total yield of crude ketone was 29.5 g. (98%). By cooling and recrystallizing from hexane there was isolated from the combined fractions 10 g. of product, m. p. 36–38° (41.0–41.5°),[5] 2 g., m. p. 31–33°; and 7 g., m. p. $> 26° < 35°$ (oily). The total yield of solid material was 19 g. (63%).

The oxime of the first fraction melted at 147–149° (151°)[6] after two crystallizations from alcohol. The residual oil after the isolation of all the solid ketone fractions yielded 49% of very impure oxime, m. p. 104–109° after one crystallization from alcohol.

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(1) Emerson and Agnew, THIS JOURNAL, **67**, 518 (1945).

(2) Hill and Flosdorf, "Organic Syntheses," Coll. Vol. I, p. 462.

(3) Heilbron, "Dictionary of Organic Compounds," Oxford University Press, New York, N. Y., 1938, Vol. III, p. 493.

(4) Parry, *J. Chem. Soc.*, **107**, 108 (1915).

(5) Thorner and Zincke, *Ber.*, **11**, 1988 (1878).

(6) Tiffeneau and Levy, *Bull. soc. chim.*, [4] **41**, 1351 (1927).

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Further Evidence for the Configuration of Methionine

BY GUNTHER S. FONKEN AND RALPH MOZINGO

Hydrogenolysis of *d*(+)-methionine[1] (non-proteogenous) by Raney nickel catalyst has been found to give *d*(−)-α-aminobutyric acid. This is further evidence[2] that the levorotatory methionine found in proteins belongs to the same absolute configurational series as the other "*l*" α-amino acids.

It has been shown[3] that benzoyl-*l*(−)-cystine is converted into benzoyl-*l*(+)-alanine by Raney nickel catalyst. Using this procedure, *l*(−)-cystine has now been converted into *l*(+)-alanine, with no apparent racemization. Treatment of dextrorotatory methionine with excess Raney nickel catalyst gave an α-aminobutyric acid whose hydrochloride was levorotatory. Since the α-aminobutyric acids and their hydrochlorides have the same sign of rotation,[4] the amino acid is also levorotatory. Benzoylation of the α-aminobutyric acid gave levorotatory benzoyl-α-aminobutyric acid. From correlation of α-aminobutyric acid with alanine and the other amino acids,[5] it follows that levorotatory α-aminobutyric acid belongs to the "*d*" series. Dextrorotatory methionine then must belong also to the "*d*" series.

On the basis of the results reported here, levorotatory methionine and dextrorotatory α-aminobu-

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(1) Kindly supplied by Drs. William C. Rose and Madelyn Womack, University of Illinois; $[\alpha]^{28}\mathrm{D}$ +8.12°. *Anal.* Calcd. for $C_5H_{11}O_2SN$: N, 9.39. Found: N, 9.37.

(2) Windus and Marvel, THIS JOURNAL, **53**, 3490 (1931).

(3) Mozingo, Wolf, Harris and Folkers, *ibid.*, **65**, 1013 (1943).

(4) Fischer and Mouneyrat, *Ber.*, **33**, 2390 (1900).

(5) Clough, *J. Chem. Soc.*, **113**, 526 (1918).