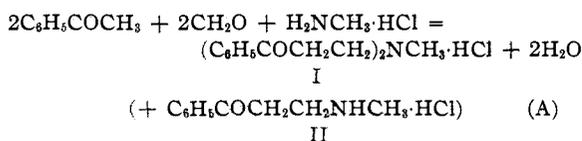
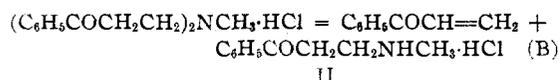


and an undetermined amount of methyl- β -benzoylethylamine hydrochloride (II).⁴

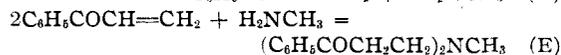
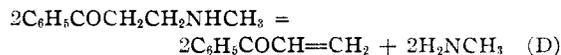
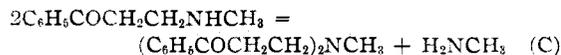


We repeated the experiment with the use of equimolecular amounts of the ketone and aldehyde, quantities which naturally would favor the formation of the secondary amine, and obtained compounds I and II in yields of 34 and 29%, respectively. In spite of the fact that the tertiary amine is produced in such a relatively large amount, equation A indicates a fairly satisfactory preparation of this secondary amine salt, since Mannich and Heilner⁵ showed that the tertiary amine hydrochloride is transformed quite readily by steam distillation into phenyl vinyl ketone and methyl- β -benzoylethylamine hydrochloride. U11-



fortunately, the extent to which the change takes place was not mentioned by these investigators. In one experiment we found the yield of compound II (eq. B) to be 78%.

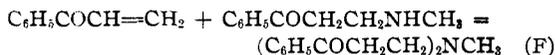
It was observed that when compound II is treated with alkali at ordinary temperature, the liberated base loses methylamine and is converted spontaneously into the base of compound I (eq. C). This is caused undoubtedly, by the intermediate formation of phenyl vinyl ketone⁵ and methylamine (eq. D); the unsaturated ketone can react with methylamine (eq. E)⁶ or with unchanged methyl- β -benzoylethylamine (eq. F) to form methyldi-(β -benzoylethyl)-amine.



(4) Compound II seems to be the only monoalkylamino ketone salt of this type which has been prepared hitherto by the Mannich reaction. The conversion of this product into a pyrazoline and into a ketotetrahydropyrimidine offer support for its structure (Mannich and Heilner, *Ber.*, **55**, 365 (1922)).

(5) Others have observed that certain basic ketones obtained by the Mannich reaction, for example β -dimethylaminoethyl 2-nitrophenyl ketone, are stable only in the form of a salt (Mannich and Dannehl, *Arch. Pharm.*, **276**, 206 (1938)).

(6) Bodendorf and Koralewski (*ibid.*, **271**, 115 (1933)) found that phenyl vinyl ketone and 50% aqueous dimethylamine react at ordinary temperature to give β -dimethylaminoethyl phenyl ketone in 72% yield.



In a separate experiment equimolecular amounts of phenyl vinyl ketone and methylamine were mixed, in alcoholic solution, at ordinary temperature; the reaction product was not methyl- β -benzoylethylamine but methyldi-(β -benzoylethyl)-amine.

When equimolecular quantities of α -acetylthiophene,⁷ paraformaldehyde and methylamine hydrochloride, amounts which should favor the formation of the secondary amine, methyl-2-(α -thenoyl)-ethylamine, were allowed to react, we were able to isolate only the tertiary amine, methyldi-[2-(α -thenoyl)-ethyl]-amine, in 61% yield. The latter was subjected to steam distillation under the same conditions as the phenyl analog, but in this case no evidence could be obtained that the secondary amine was formed, although in several experiments small quantities of α -thienyl vinyl ketone were obtained.

It seemed that if the hydrochloride of methylacetamide were employed in place of methylamine hydrochloride, it might be possible to obtain a secondary amine in the form of its acetyl derivative. We studied the interaction of acetophenone, $\text{RCOCH}_3 + \text{CH}_2\text{O} + \text{HN}(\text{COCH}_3)_2\text{CH}_3\cdot\text{HCl}$ ⁸ = $\text{RCOCH}_2\text{CH}_2\text{N}(\text{COCH}_3)_2\text{CH}_3\cdot\text{HCl} + \text{H}_2\text{O}$

paraformaldehyde and methylacetamide hydrochloride, but the only product we were able to isolate from this reaction was methyldi-(β -benzoylethyl)-amine hydrochloride.

Contrary to the statement in the literature⁹ that the typical condensation does not take place between acetophenone, formaldehyde and diethylamine hydrochloride, we found that these compounds do react to yield diethyl- β -benzoyl-ethylamine hydrochloride. When α -acetylthiophene was substituted for acetophenone, diethyl-2-(α -thenoyl)-ethylamine hydrochloride was obtained.

α -Propionylthiophene,¹⁰ formaldehyde and dimethylamine hydrochloride react to form the salt of dimethyl-2-(α -thenoyl)-propylamine, $(\text{CH}_3)_2\text{N}-\text{CH}_2\text{CH}(\text{COC}_4\text{H}_9\text{S})\text{CH}_3\cdot\text{HCl}$.

When submitted to steam distillation, this product yielded an oil which undoubtedly was 2-(α -

(7) "Organic Syntheses," **18**, 1 (1938).

(8) Actually the half hydrochloride $(\text{HN}(\text{COCH}_3)_2\text{CH}_3)_2\cdot\text{HCl}$ was employed.

(9) Levvy and Nisbet, *J. Chem. Soc.*, 1053 (1938).

(10) Scheibler and Schmidt, *Ber.*, **54**, 149 (1921). We prepared the ketone in 79% yield according to the method described in "Organic Syntheses" for α -acetylthiophene.

thenoyl)-propene. The latter reacted rapidly with phenylhydrazine to form a crystalline material; in all probability this was 1-phenyl-3-(α -thienyl)-4-methylpyrazoline.

It seems that dicyclohexylamine hydrochloride¹¹ is unsuitable for use in the Mannich reaction since condensation could not be effected between this salt, formaldehyde and acetophenone.

Experimental

General Procedures: (a) (Compounds 1, 2, 5, 6 and 8).—A mixture of 0.10 mole of the ketone, 0.10 mole of the amine hydrochloride, 0.12 mole of paraformaldehyde and about 20 cc. of absolute alcohol was heated on a steam-bath for two to three hours. The mixture was cooled, the precipitated material filtered and the filtrate concentrated to recover more of the desired compound.

(b) (Compounds 3, 4 and 7).—The reaction mixture was cooled and any precipitated product removed by filtration. To obtain the dissolved product, the solvent was

Conversion of Methyl-di-(β -benzoylethyl)-amine Hydrochloride into Methyl- β -benzoylethylamine Hydrochloride.

—Steam was passed into 15 g. of the tertiary amine hydrochloride until no more oily phenyl vinyl ketone distilled. The distillation flask was heated with a Bunsen burner in order to keep the volume of water as low as possible. When the aqueous solution in the distillation flask was evaporated to dryness 7 g. (78%) of the secondary amine hydrochloride was obtained.

Spontaneous Decomposition of Methyl- β -benzoylethylamine into Methyl-di-(β -benzoylethyl)-amine.—A solution of 2 g. of sodium hydroxide in 10 cc. of water was dropped slowly into 3.0 g. of methyl- β -benzoylethylamine hydrochloride, dissolved in 10 cc. of water, while the temperature of the amine solution was maintained at about 30°. The oily precipitate, which soon crystallized, weighed 2.15 g. (97%) and melted at 139–142°; m. p. 141–142°, after recrystallization from alcohol; mixed m. p. 141–142°.

A portion of the methylamine produced was removed from the reaction mixture by a stream of air and passed into hydrochloric acid; the methylamine hydrochloride obtained melted at 224–226°.

β -KETO AMINES

Compounds 1 and 4 were recrystallized from a mixture of acetone and alcohol; compounds 2 and 5, as well as the base of 5, from alcohol; compounds 3 and 7 from a mixture of acetone and ether; compound 6 from acetone; and compound 8 from water.

	Hydrochloride	Yield, %	M. p., °C.	Formula	Chlorine, %	
					Calcd.	Found
1	C ₉ H ₉ SCOCH ₂ CH ₂ N(CH ₃) ₂	47	178–179 ^a	C ₉ H ₁₄ ONSCI	16.14	16.25
2	C ₈ H ₉ SCOCH ₂ CH ₂ NC ₆ H ₁₀	74	201–202 ^a	C ₁₂ H ₁₈ ONSCI	13.65	13.63
3	C ₄ H ₉ SCOCH ₂ CH ₂ N(C ₂ H ₅) ₂	39	116–117	C ₁₁ H ₁₈ ONSCI	14.31	14.36
4	C ₄ H ₉ SCOCH(CH ₃)CH ₂ N(CH ₃) ₂	60	154–156	C ₁₀ H ₁₆ ONSCI	15.17	15.16
5	(C ₄ H ₉ SCOCH ₂ CH ₂) ₂ NCH ₃	61	185–186	C ₁₆ H ₁₈ O ₂ NS ₂ Cl	10.31	10.35
	Base		146–148	C ₁₆ H ₁₇ O ₂ NS ₂	N, 4.56	4.36
6	C ₈ H ₉ COCH ₂ CH ₂ NHCH ₃	29	140–142 ^b	C ₁₀ H ₁₄ ONCl	17.76	17.65
7	C ₆ H ₅ COCH ₂ CH ₂ N(C ₂ H ₅) ₂	45	108–110	C ₁₃ H ₂₀ ONCl	14.67	14.67
8	(C ₆ H ₅ COCH ₂ CH ₂) ₂ NCH ₃	34	161–162 ^c			

^a Levvy and Nisbet (*J. Chem. Soc.*, 1053 (1938)) stated that compound 1 melted at 172° and compound 2 at 199°; the yield was not reported in either instance. ^b Mannich and Heilner (*Ber.*, 55, 363 (1922)) report m. p. 139–141°. ^c *Ibid.*, m. p. 162°.

removed from the filtrate under reduced pressure, about 50 cc. of water added to the residue, and the mixture extracted three times with 50-cc. portions of ether. Any unchanged ketone can be recovered from the ether extracts. The aqueous layer was made alkaline, the precipitated base extracted with ether, the ether solution dried and treated with hydrogen chloride, whereupon the hydrochloride precipitated.

In the preparation of the hydrochlorides of methyl-di-(β -benzoylethyl)-amine and methyl- β -benzoylethylamine, a mixture of the two compounds is obtained as a precipitate. Since the latter is soluble in cold chloroform, it can be separated from the former with the aid of this solvent. Upon evaporation of the alcohol from the alcoholic filtrate, a mixture of methylamine hydrochloride and methyl- β -benzoylethylamine hydrochloride is obtained. Upon extraction with cold chloroform, the methylamine hydrochloride remains undissolved.

(11) Burger and Bryant (*THIS JOURNAL*, 63, 1055 (1941)) observed that dicyclohexylamine hydrochloride does not react with formaldehyde and 2- or 4-acetyldibenzothiophene.

Notes: Compound 1.—Nine grams of this substance was submitted to steam distillation. The oil in the distillate was extracted with ether, the extract dried with magnesium sulfate, the ether removed and the residue distilled. There was obtained 2.5 g. (44%) of α -thienyl vinyl ketone; b. p. 108–110° (12 mm.). *Anal.* Calcd. for C₇H₈OS: S, 23.20. Found: S, 23.40. The material rapidly became very viscous. When the unsaturated ketone was heated with phenylhydrazine on a steam-bath for a short time it was converted into 1-phenyl-3-(α -thienyl)-pyrazoline which melted at 102–103° (Harradence and Lions, *J. Proc. Roy. Soc. N. S. Wales.*, 72, 247 (1939), found 103°).

Compound 3.—Upon steam distillation α -thienyl vinyl ketone was obtained.

Compound 4.—When 8.7 g. of the product was subjected to steam distillation, 4.0 g. (71%) of an oily material was obtained which boiled at 118–120° (19 mm.). Undoubtedly this substance was 2-(α -thenoyl)-propene. *Anal.* Calcd. for C₈H₈OS: S, 21.06. Found: S, 21.15. One gram of the propene and 0.4 g. of phenylhydrazine were heated on a steam-bath for a few minutes. The oily

material crystallized when it was cooled and melted at 81–83° after recrystallization from alcohol. In all probability the product was 1-phenyl-3-(α -thienyl)-4-methylpyrazoline. *Anal.* Calcd. for $C_{14}H_{14}N_2S$: S, 13.23. Found: S, 13.34.

Compound 7.—Phenyl vinyl ketone was obtained when this compound was submitted to steam distillation and also when an attempt was made to distill the base under 18 mm. pressure; in the latter instance the yield of the unsaturated ketone was 80%. Phenyl vinyl ketone was identified by its boiling point (114–116° (18 mm.)) and by its reaction with phenylhydrazine to yield 1,3-diphenylpyrazoline (m. p. 151–152°) (Kohler, *Am. Chem. J.*, **42**, 386 (1909)); Jacob and Madinaveitia, *J. Chem. Soc.*, 1931 (1937). The picrate was formed when 3 g. of the base and 3 g. of picric acid, dissolved in 6 cc. of alcohol, were heated on a steam-bath. The product melted at 115–116° after recrystallization from alcohol which contained a small amount of acetone. *Anal.* Calcd. for $C_{19}H_{19}O_2N_4$: N, 12.90. Found: N, 12.75. Mannich (*Arch. Pharm.*, **273**, 284 (1935)) mentioned that this picrate melted at 114–115°, but he failed to describe the base.

Formation of Methyl-di-(β -benzoyl-ethyl)-amine from Phenyl Vinyl Ketone and Methylamine.—When 7.9 g. (0.06 mole) of phenyl vinyl ketone was added to 9.3 cc. (0.06 mole) of alcoholic methylamine the mixture became warm. After two hours the latter was cooled with ice whereupon 3.1 g. of the tertiary amine precipitated; m. p. 140–141°. After twelve hours at ordinary temperature, an additional 1.7 g. had separated and 0.64 g.

more was obtained after four days; total yield 61%.

Formation of Methyl-di-(β -benzoyl-ethyl)-amine Hydrochloride from Acetophenone, Paraformaldehyde and the Half Hydrochloride of Methylacetamide.—Methylacetamide,¹² dissolved in absolute ether, was treated with hydrogen chloride and the precipitated half hydrochloride¹³ recrystallized from acetone; m. p. 87–89°.

Anal. Calcd. for $C_6H_{12}O_2N_2Cl$: Cl, 19.41. Found: Cl, 19.55.

A mixture of 8.8 g. (0.073 mole) of acetophenone, 3.0 g. (0.100 mole) of paraformaldehyde, 8.0 g. (0.044 mole) of methylacetamide half hydrochloride and 10 cc. of absolute alcohol was heated on a steam-bath for forty-five minutes. The mixture was cooled and the precipitated material (4.7 g.) recrystallized from alcohol. The product melted at 160–162°, the melting point of methyl-di-(β -benzoyl-ethyl)-amine hydrochloride; mixed m. p. 160–162°. After conversion of the salt into the free base, the latter melted at 140–142°.

Summary

A study has been made of the interaction of several amine hydrochlorides with formaldehyde and acetophenone, α -acetylthiophene or α -propionylthiophene.

(12) Verley, *Bull. soc. chim.*, [3] **9**, 691 (1893).

(13) This product was postulated but not described by D'Alelio and Reid, *THIS JOURNAL*, **59**, 110 (1937).

ANN ARBOR, MICHIGAN

RECEIVED OCTOBER 7, 1941

[CONTRIBUTION OF THE DEPARTMENT FOR INORGANIC AND ANALYTICAL CHEMISTRY OF THE HEBREW UNIVERSITY]

Anomalies in Conductivity Measurements in Presence of Hydrogen Peroxide

By M. BOBTELSKY AND A. E. SIMCHEN

1. Introduction.—For some years we have studied with collaborators the problem of the catalytic decomposition of hydrogen peroxide in the presence of electrolytes,¹ including the phenomena appearing in the presence of hydrogen peroxide by conductometric measurements (*e. g.*, during the catalytic action of cobalt citrate complexes). In presence of increasing quantities of hydrogen peroxide, conductometric curves were obtained with pronounced maxima and minima of conductivity that could not be accounted for by simple chemical reactions. Therefore the only explanation possible was to suppose that these "anomalous" curves were due to specific conductivity phenomena in electrolytic solutions in presence of increasing quantities of hydrogen perox-

ide; we felt quite sure that there were no chemical compounds formed between hydrogen peroxide and the simple electrolytes.

A series of conductometric titrations of pure electrolytic solutions with increasing quantities of hydrogen peroxide were carried out. The measurements were made by the visual method by means of a "lyograph" (see below) at 50 cycles/sec. Comparison experiments were carried out with a Wheatstone bridge, at 1000 cycles/sec. The experimental results reported here have largely justified our previous assumption.

Neither the aim we had put before us in this work, nor the apparatus used, admitted of a further extension of the problem in the physical direction, *i. e.*, a study of alternating current polarization. In this respect we may mention the work of Jones and Christian,² who investigated this question with great thoroughness and suit-

(1) M. Bobtelsky and B. Kirson, *Compt. rend.*, **199**, 573 (1934); **208**, 1577 (1939); M. Bobtelsky and L. Bobtelsky-Chajkin, *ibid.*, **201**, 604 (1935); **203**, 872 (1936); **203**, 1158 (1936); M. Bobtelsky and M. Rappoport, *ibid.*, **205**, 234 (1937); M. Bobtelsky and A. E. Simchen, *ibid.*, **208**, 1646 (1939).

(2) G. Jones and S. M. Christian, *THIS JOURNAL*, **57**, 272 (1935).