of the racemization by strong acids warrants further investigation.

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## An Improved Procedure for the Preparation of Glycine

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By modifying the Orten and Hill synthesis of glycine,[1] it is possible to improve their yield of 60–64% of pure glycine to 75–77%.

**Method.**—Pour a solution of 0.5 mole (47.2 g.) of good-quality monochloroacetic acid in 100 cc. of water into a rapidly swirling four-pound bottle of ammonium hydroxide of sp. gr. 0.9 (1.8 kg. or 30 moles). After twenty-four hours (longer standing is not necessary), evaporate the solution to dryness on a water-bath, preferably under reduced pressure. Dissolve the crust in a minimum amount of warm water, and filter out traces of insoluble material. With the aid of vacuum, dry the material as thoroughly as possible in a 2-liter round-bottom flask on a water-bath. Dissolve out the ammonium chloride by refluxing with 1 liter of methanol on a water-bath for about four hours. After cooling to room temperature, filter with suction on a 7-cm. Büchner. Place the glycine (about 36 g. dry weight) in a 500-cc. flask fitted with a condenser, and add just enough water (about 50 cc.) to dissolve the solid completely upon boiling. Discontinue heating and place the flask and condenser under a hood. Slowly add four volumes of methanol (about 200 cc.), keeping the flask swirling. Cool to 30° or less, then suction-filter the material as dry as possible. Repeat the precipitation with the same amounts of water and methanol. Wash the cake with two 50-cc. portions of methanol, allowing it to soak in well before being suctioned off.

When dry, the glycine weighs 28–29 g., 75–77% yield. It contains no chloride and not more than a faint trace of ammonia. Analysis gave 18.54% N (Kjeldahl method), calcd. 18.67%; m. p. 233–236° with decomposition.

**Discussion.**—Methanol of 99% or more by weight is satisfactory. The yield would probably be slightly reduced if 95% methanol were used. The preliminary removal of ammonium chloride can be done by seven hours of Soxhlet extraction with 500 cc. of methanol on a water-bath at 85°, but 99.5–100% methanol must be used, since even a little water greatly increases the solubility of glycine in warm methanol. The yields are a little lower, about 27–28 g.

However, Soxhlet extraction with 99.5–100% methanol gives excellent results in purifying certain amino acids prepared from the corresponding bromo acids. This is probably due to the fact that ammonium bromide is more soluble in methanol than is ammonium chloride. By treating α-bromo-*n*-butyric acid for twenty-four hours with aqueous ammonia in a 1 to 50 ratio, we obtained a 65% yield of very pure α-amino-*n*-butyric acid by Soxhlet extraction alone, without the necessity of subsequent precipitation from aqueous solution with methanol. An additional 15% of pure amino acid was isolated from the methanol extract through the copper salt.

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(1) Orten and Hill, THIS JOURNAL, **53**, 2797 (1931).

# NEW COMPOUNDS

### 2-Methyl-1,4-naphthoquinone Derivatives

With a view to obtaining derivatives of 2-methyl-1,4-naphthohydroquinone and 2-methyl-1,4-naphthoquinone sufficiently soluble for therapeutic use, the following four compounds were made. The first was not tested for coagulation time, the solution being insufficiently stable. The other three compounds were ineffective at the 12 microgram level in the usual chick assay.

**2-Methyl-1,4-naphthohydroquinone Acetate Acid Succinate.**—0.5 g. of 2-methyl-1,4-naphthohydroquinone hydrogen succinate[1] was heated on the steam-bath with 3.0 cc. of acetic anhydride for two hours. The mixture was poured into water and left overnight and the product recrystallized twice from ether–pentane mixture. The compound forms white aggregates of tiny needles, melting at 129° and dissolving in dilute sodium hydroxide solution.

*Anal.* Calcd. for $C_{17}H_{16}O_6$: C, 64.54; H, 5.10. Found: C, 64.55; H, 5.32.

**2-Methyl-1,4-naphthoquinone-*p*-carboxyphenylhydrazone.**—A solution of 1.5 g. of 2-methyl-1,4-naphthoquinone, 100 cc. of 95% alcohol, 3.5 cc. of acetic acid and 1.6 g. of *p*-hydrazinobenzoic acid[2] was refluxed for two hours, allowing most of the alcohol to evaporate. The solid which separated was taken up in potassium carbonate solution, the solution extracted with ether and the aqueous layer

(1) Baltzly and Buck, THIS JOURNAL, **63**, 882 (1941).
(2) Anchel and Schoenheimer, *J. Biol. Chem.*, **114**, 539 (1936).

acidified. The resulting solid was filtered off (carbon dioxide atmosphere) and recrystallized from alcohol or acetic acid. The compound forms brick-red aggregates of jagged prisms melting at 265° (dec.) and dissolving in dilute sodium hydroxide solution.

*Anal.* Calcd. for $C_{18}H_{14}O_3N_2$: C, 70.56; H, 4.61. Found: C, 70.62; H, 4.77.

**2-Methyl-1,4-naphthoquinone Guanylhydrazone.**—To 3.0 g. of 2-methyl-1,4-naphthoquinone dissolved in 20 cc. of hot alcohol, was added a solution of 6.2 g. of aminoguanidine bicarbonate[3] in dilute nitric acid (3.2 cc. concentrated acid in 18 cc. of water). After refluxing for one hour, yellow crystals separated; 600 cc. of hot water was added to dissolve them, and excess ammonia then added. The solid which separated was recrystallized twice from water, as the nitrate, and then twice from alcohol as the base. The compound forms red, slender, felted needles and melts at 218° (dec.). It is soluble in dilute acetic, lactic and citric acids, but the mineral acid salts are very sparingly soluble.

*Anal.* Calcd. for $C_{12}H_{12}ON_4$: C, 63.12; H, 5.30. Found: C, 63.41; H, 5.56.

**2-Methyl-1,4-naphthoquinone Pyridinium Chloride Acethydrazone.**—A solution of 4.2 g. of 2-methyl-1,4-naphthoquinone, 50 cc. of alcohol, 5 cc. of acetic acid and 4.5 g. of Girard reagent P (acethydrazide pyridinium chloride)[4] was refluxed for one hour. The product crystallized out on cooling and was filtered off, extracted with a little hot alcohol, and then recrystallized twice from a larger volume of alcohol. The compound forms light yellow felted needles, melting at 241° (dec.). It gives a relatively stable solution in water. As it is hygroscopic and retains water obstinately, it was dried for two hours at 120° *in vacuo* for analysis.

*Anal.* Calcd. for $C_{18}H_{16}O_2N_3Cl$: N, 12.29; Cl, 10.38. Found: N, 12.35; Cl, 10.51.

(3) Thiele and Barlow, *Ann.*, **302**, 311 (1898).
(4) Girard and Sandulesco, *Helv. Chim. Acta*, **19**, 1095 (1936).

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## Substituted Amides of 2,4,6-Trimethylbenzoic Acid

A number of N-substituted 2,4,6-trimethylbenzamides have been prepared. The procedure of Shriner and Fuson[1] was employed, 1.5 g. of the appropriate amine dissolved in 20 cc. of dry benzene being added to 0.0025 mole of 2,4,6-trimethylbenzoyl chloride dissolved in 25 cc. of dry benzene. The 2,4,6-trimethylbenzoyl chloride was identical with that previously employed for dielectric constant measurements.[2]

(1) Shriner and Fuson, "Identification of Organic Compounds" 1st ed., John Wiley and Sons, New York, N. Y., 1935, p. 146.

The amides obtained, none of which have been described previously in the literature, are listed in the table together with their melting points, general physical appearance and nitrogen analyses. They were crystallized from ethanol or aqueous ethanol with the exception of the last two which were crystallized from ligroin.

The author is indebted to Dr. M. Z. Fineman who furnished a sample of *o-t*-butylaniline used in the preparation of one of the amides. This amine was prepared by Dr. Fineman by the nitration of *t*-butylbenzene and separation of the *o*-nitro derivative by fractionation[3] followed by reduction,[4] b. p. 108–109° (14 mm.), acetyl derivative, m. p. 162°.

2,4,6-TRIMETHYLBENZOYLAMINES

| Amine | Description | M. p., °C. (uncor.) | N analyses, % Calcd. | Found |
|---|---|---|---|---|
| Ethylamine | Colorless plates | 114.5–115.5 | 7.32 | 7.46 |
| *i*-Propylamine | Colorless transparent plates | 113.5–115 | 6.82 | 7.24 |
| Benzylamine | Colorless plates | 137.5–138.5 | 5.53 | 5.59 |
| *α*-Phenylethylamine | Colorless needles | 130 –131 | 5.24 | 5.51 |
| *o*-Toluidine | Colorless needles | 124 –125.5 | 5.53 | 5.76 |
| *m*-Toluidine | Colorless plates | 110 –111.5 | 5.53 | 5.45 |
| *p*-Toluidine | Flat transparent needles | 173 –174 | 5.53 | 5.65 |
| *p*-Anisidine | Thin colorless needles | 185 | 5.20 | 5.40 |
| *p*-Phenetidine | Needles | 171 –172 | 4.94 | 5.17 |
| *o-t*-Butylaniline | Colorless needles | 150.5–152 | 4.74 | 4.65 |
| *β*-Naphthylamine | Light tan | 165 –166.5 | 4.84 | 5.04 |
| Piperidine | Transparent prisms | 75.5– 77 | 6.06 | 5.63 |
| Morpholine | Colorless plates | 70 – 71.5 | 6.01 | 6.32 |

The nitrogen analyses were performed by an improved micro-Kjeldahl method of Ma and Zuazaga.[5]

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(2) Kadesch and Weller, THIS JOURNAL, **63**, 1310 (1941).
(3) Craig, *ibid.*, **57**, 195 (1935).
(4) Shoesmith and Mackie, *J. Chem. Soc.*, 2334 (1928).
(5) Ma and Zuazaga, *Ind. Eng. Chem., Anal. Ed.*, in press.