ing reaction of the phenoxazine type described above. The oily product was chromatographed over 60–100 mesh "Florisil." Elution with benzene brought off unchanged 10-(2-chloroethyl)phenothiazine and 95% benzene–5% acetone eluted the product, an oil weighing 5.95 g. (79%).

Anal. Calcd. for $C_{18}H_{22}N_2O_2S$: C, 65.42; H, 6.72; N, 8.47. Found: C, 65.52; H, 6.84; N, 8.42.

The *hydrochloride* melted at 143–144°.

Anal. Calcd. for $C_{18}H_{23}ClN_2O_2S$: C, 58.93; H, 6.05; N; 7.63. Found: C, 59.01, 58.85; H, 6.02, 5.87; N, 7.94, 7.72.

10-{2-[Bis(2-chloroethyl)amino]ethyl}phenothiazine. Prepared essentially in accordance with the procedure described above for the phenoxazine type, the product was a white crystalline solid (from petroleum ether, b.p. 65–75°), m.p. 54.5–55.5°. The yield was 55%.

Anal. Calcd. for $C_{18}H_{20}Cl_2N_2S$: C, 58.85; H, 5.50; N, 7.62. Found: C, 58.99, 58.74; H, 5.44, 5.38; N, 7.53, 7.58.

The *hydrochloride* melted with decomposition at 126–131° at atmospheric pressure but in an evacuated capillary tube at 132–133°.

Anal. Calcd. for $C_{18}H_{21}Cl_3N_2S$: C, 53.54; H, 5.24; N, 6.93 Found: C, 53.30, 53.30; H, 4.81, 4.99; N, 6.54, 6.59.

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The Preparation of 1,2-(α-Ketotetramethylene)ferrocene

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In connection with some other work we had need of a considerable quantity of 1,2-(α-ketotetramethylene)ferrocene. This compound has been previously reported by Rinehart,[2] who prepared it from ferrocene and succinic anhydride[3] by a modification of the normal α-tetralone synthesis. Although the initial Friedel-Crafts reaction of ferrocene and succinic anhydride proceeded smoothly in the manner reported, the hydrogenation of β-ferrocenoylpropionic acid to γ-ferrocenylbutyric acid failed repeatedly in our hands.[4] In an effort to circumvent the hydrogenation an attempt was made to reduce the keto acid by either the Clemmensen or Wolff-Kishner method. Both these reactions resulted in extensive decomposition of the material, and failed to yield any identifiable substances.

In order to resolve the difficulties cited, β-ferrocenoylpropionic acid was reduced with sodium borohydride to γ-ferrocenylbutyrolactone, which with no unusual purification was smoothly hydrogenated to γ-ferrocenylbutyric acid.

The overall yield for these two steps, based on crude β-ferrocenoylpropionic acid is 71%, which compares favorably with the 93% reported by Rinehart[3] for the direct reduction if one takes into account the loss of β-ferrocenoylpropionic acid in purification.

The cyclization of γ-ferrocenylbutyric acid to 1,2-(α-ketotetramethylene)ferrocene was carried out with polyphosphoric acid as mentioned by Rinehart.[2]

EXPERIMENTAL[5]

β-Ferrocenoylpropionic acid. This material was prepared from succinic anhydride and ferrocene, using essentially the procedure of Reinhart *et al.*[3]

From 20.0 g. of ferrocene and 7.08 g. of succinic anhydride, in the presence of 15.6 g. of aluminum chloride, 18.5 g. (91%) of crude product, m.p. 167–169° was obtained. The melting point was not increased significantly by recrystallization. Concentration of the nonacidic fraction of the reaction mixture to dryness afforded 8.70 g. of recovered ferrocene.

γ-Ferrocenylbutyrolactone. To a solution of 13.6 g. of β-ferrocenoylpropionic acid in 635 ml. of isopropyl alcohol was added 32.0 g. of sodium borohydride. The mixture was heated under reflux 2 hr., cooled, diluted with water, filtered through Celite, and cautiously acidified with dilute hydrochloric acid. The orange solution was extracted with chloroform, the extracts washed with water, 5% sodium carbonate, and dried over magnesium sulfate. Removal of the chloroform *in vacuo* gave 12.7 g. of crude lactone. Recrystallization from cyclohexane–ethyl acetate gave 9.3 g. (77%) of yellow crystals m.p. 130–132°. The analytical sample was crystallized from cyclohexane, m.p. 132–133°.

Anal. Calcd. for $C_{14}H_{14}FeO_2$: C, 62.26; H, 5.22. Found: C, 62.59; H, 5.47.

The infrared spectrum of this compound (Nujol) showed a single carbonyl band at 5.66 μ.

γ-Ferrocenylbutyric acid. A solution of 10.6 g. of γ-ferrocenylbutyrolactone in 218 ml. of acetic acid was hydrogenated 16 hr. at 50 p.s.i. and room temperature, using 2.0 g. of platinum oxide catalyst. After filtering the reaction mixture through Celite to remove the spent catalyst and dilution with water, sufficient ascorbic acid was added to discharge the green color caused by the presence of a small quantity of ferrocinium ion. The resulting pale orange solution was extracted with chloroform, washed thoroughly with water, and extracted with 10% sodium carbonate. Acidification of the basic extracts gave 9.8 g. (92%) of product, m.p. 115–117°. This material was sufficiently pure for conversion to α-ketotetramethyleneferrocene.

1,2-(α-Ketotetramethylene)ferrocene. A mixture of 9.8 g. of γ-ferrocenylbutyric acid and 150 g. of polyphosphoric acid was allowed to stand at room temperature, with occasional stirring for 2.5 hr. The reaction mixture was poured into water, allowed to stand several hours, and extracted with chloroform. The extracts were washed with water, 5% sodium carbonate, dried, and the solvent removed at reduced pressure affording 4.04 g. (44%) of ketotetramethylene

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(4) We were in one instance able to successfully carry out the hydrogenation on an exhaustively purified sample of the acid. However, this reduced drastically the overall yield for the sequence.

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ferrocene. Recrystallization from hexane gave red crystals m.p. 83–85°. Reported[2] 85°. Infrared maximum (carbonyl) 6.03 μ.

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Synthesis of Some Heterocyclic Ketols by Ion-Exchange Resin Catalysis

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A series of heterocyclic ketols and their dehydration products, which were of interest to us because of their cardiovascular and tranquilizing properties, were prepared from the isomeric pyridinecarboxaldehydes and several *o*-hydroxyacetophenones. The use of conventional catalysts[2] such as sodium hydroxide[3–5] or piperidine[6,7] which have been employed in the condensation of heterocyclic aldehydes and ketones generally gave rather poor yields of the pyridalacetophenones. Frequently, large amounts of intractable, oily by-products were formed and only occasionally could any of the corresponding ketols be isolated. It appeared probable that the use of a basic catalyst, such as an ion-exchange resin, in a heterogeneous reaction medium might provide a more selective control over the course of the reaction and permit isolation of the desired ketols with a minimum of side reactions. In recent years a wide variety of reactions has been catalyzed by both anionic and cationic exchange resins[8,9] and the absence of a large excess of strong alkali is sometimes advantageous when sensitive compounds are being prepared.

We have found the strongly basic ion-exchange resin Amberlite IRA-400 (OH^-) in ethanol to give primarily the heterocyclic ketols accompanied in some instances by lesser amounts of the corresponding 2′-hydroxy-*trans*-pyridalacetophenones. The ketols which lost the elements of water most readily could not be isolated and were obtained either as the ketol hydrochlorides or were converted directly to their dehydration products. The ketol hydrochlorides were dehydrated in good yields to the corresponding pyridalacetophenones by simply warming in aqueous solution or, in other instances, by refluxing briefly in concentrated hydrochloric acid. While this investigation[10] was under way Raut and Wender[11] described the α,β-unsaturated ketones derived from 2- and 3-pyridinecarboxaldehyde and *o*-hydroxyacetophenone in the presence of aqueous-ethanolic potassium hydroxide and Corvaisier and Tirouflet[6b] reported the formation of the corresponding 2- and 4-ketols in the presence of sodium methylate.

When 3-pyridinecarboxaldehyde and *o*-hydroxyacetophenone were condensed in the presence of Amberlite IRA-400 (OH^-) and ethanol both the easily dehydrated ketol hydrochloride (2′,3-dihydroxy-3-(3-pyridyl)propiophenone hydrochloride, I) and the α,β-unsaturated ketone (2-hydroxy-β-(3-pyridyl)acrylophenone, Ia) were obtained. Compound I was dehydrated to Ia upon recrystallization from warm water or upon conversion to the ketol base and recrystallization from methanol.

The condensation of 2-pyridinecarboxaldehyde with *o*-hydroxyacetophenone under the same conditions gave the stable ketol (2′,3-dihydroxy-3-(2-pyridyl)propiophenone, II) and none of the dehydration product (2-hydroxy-β-(2-pyridyl)acrylophenone, IIa) was isolated. Compound II, however, was dehydrated to IIa by refluxing for a few minutes in concentrated hydrochloric acid. 4-Pyridinecarboxaldehyde reacted like the 2-isomer and with *o*-hydroxyacetophenone gave only the ketol (2′,3-dihydroxy-3-(4-pyridyl)propiophenone, III). The latter was dehydrated to the α,β-unsaturated ketone (2-hydroxy-β-(4-pyridyl)acrylophenone, IIIa) by refluxing in concentrated hydrochloric acid or by heating with polyphosphoric acid. In the presence of Dowex-3 (OH^-), a weakly basic ion-exchange resin, 4-pyridinecarboxaldehyde and *o*-hydroxyacetophenone gave only a trace of the ketol (III). When aqueous-ethanolic sodium hydroxide was used as the condensation catalyst the three isomeric pyridinecarboxaldehydes and *o*-hydroxyacetophenone gave the corresponding pyridalacetophenones.

3 - Pyridinecarboxaldehyde and 2 - hydroxy - 3-methoxyacetophenone in the presence of Amber-

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