metal had reacted. Work-up and distillation of the nitrogeneous material gave the following fractions:

Fraction	B.P. (Mm.)	n_D^{20}	Amount, G.
1	75–84 (2.5)	1.4624	1.6
2	94–104 (2.5)	1.4832	1.9
3	108–110 (2.5)	1.5010	10.5
4	Residue		5.0

Fraction 3 did not give classification tests for a carbonyl compound or a tertiary nitrogen atom. Permanganate oxidation[11] of a 5.0-g. sample of fraction 3 yielded picolinic acid, 1.2 g. (40% based on sample alone, 28.1% based on phenyl hexanoate), m.p. 135°. Reported m.p. 133–134°.[11] Work-up of the neutral fraction gave phenol, 80.0 g.

LAFAYETTE, IND.

(11) G. R. Clemo and G. R. Ramage, *J. Chem. Soc.*, 440 (1931).

[CONTRIBUTION FROM THE RADIUM INSTITUTE OF THE UNIVERSITY OF PARIS]

β-Cyanoethylation of Phenoxazine and 7*H*-Benzo[c]phenothiazine

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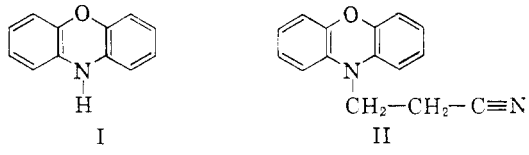
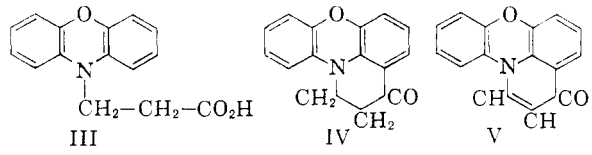
Phenoxazine and 7*H*-benzo[c]phenothiazine have been found to condense smoothly with acrylonitrile in the presence of organic alkaline catalysts; α-methylacrylonitrile failed to react. Friedel-Crafts cyclization of β-(10-phenoxazinyl)propionic acid has been performed, and its reaction products are investigated.

From the triad formed by phenoxazine, phenothiazine, and phenoselenazine, the behavior of the last two in β-cyanoethylation reactions has already been investigated, and both phenothiazine[1] and phenoselenazine[2] were found to give the corresponding *N*-propionic acid in good yields.

It is now shown that phenoxazine (I) likewise undergoes smooth β-cyanoethylation with acrylonitrile in the presence of benzyltrimethylammonium methoxide, to give β-(10-phenoxazinyl)propionitrile (II), the reaction being even more energetic than in the case of phenothiazine and phenoselenazine, probably because of its higher solubility in acrylonitrile. In similar and even more drastic experimental conditions, α-methylacrylonitrile failed to undergo condensation. Alkaline hydrolysis afforded β-(10-phenoxazinyl)propionic acid (III); cyclization of this acid could be effected, as in the case of the corresponding propionic acids derived from phenothiazine[1] and phenoselenazine,[2] with phosphorus pentoxide, but afforded two products, both of them yellow, the lower-melting one being 2,3-dihydro-3-keto-1H-pyrido[3,2,1-kl]phenoxazine (IV), as it possessed a reactive keto group and readily gave a phenylhydrazone. The higher-melting product, which did not form a phenylhydrazone in the same conditions, and which contained two atoms less of hydrogen, could be tentatively formulated as the *dehydro* derivative (V) of the former ketone. The differences in the degree of saturation of the two compounds are reflected in their infrared spectra (see Figure 1); in the case of ketone IV, the absorption band characterizing the ketone function is located at 1655 cm.$^{-1}$, while for compound V there are two ketone bands, one at 1630 cm.$^{-1}$ and the other at 1640 cm.$^{-1}$, a splitting resembling that observed with quinones. The infrared spectrum of ketone IV is similar to those of 2,3-dihydro-3-keto-1H-pyrido[3,2,1-kl]phenoselenazine and its 10-chloro- derivative (see Figure 2).

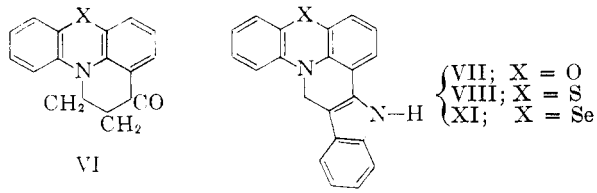


I II



III IV V

In the framework of our investigations on potential carcinogenic nitrogen-containing heterocycles, the phenylhydrazones of ketone IV and of its analogs 2,3-dihydro-3-keto-1H-pyrido[3,2,1-kl]-phenothiazine (VI; X = S) and 2,3-dihydro-3-keto-1H-pyrido[3,2,1-kl]phenoselenazine (VI; X = Se) were converted by Fischer cyclizations into indolo[3′,2′-2,3]-1H-pyrido[3,2,1-kl]phenoxazine (VII) and its phenothiazine and phenoselenazine analogs (VIII) and (IX). The Pfitzinger reaction of ketone (VI; X = S) with isatin afforded 4′-carboxyquinoleino[3′,2′-2,3]-1H-pyrido[3,2,1-kl]-phenothiazine (X; X = S), which underwent



VI

(1) N. L. Smith, *J. Org. Chem.*, **15**, 1125 (1950).

(2) P. Müller, N. P. Buu-Hoï, and R. Rips, *J. Org. Chem.*, **24**, 37 (1959).

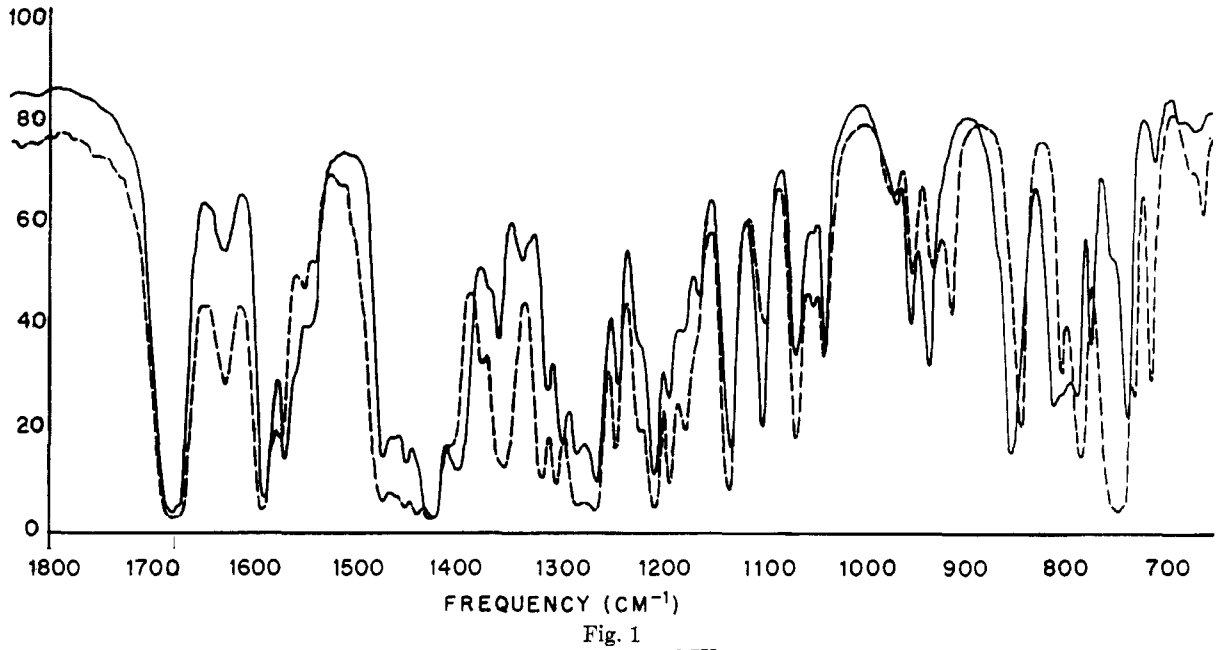
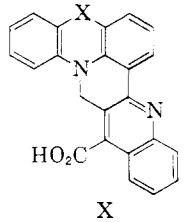
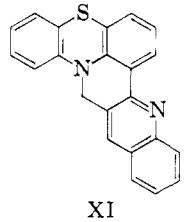


Fig. 1
- - - - compound IV
——— compound V

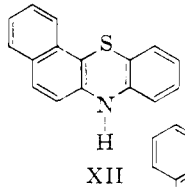
decarboxylation to the base (XI). A similar reaction with the phenoselenazine ketone afforded 4'-

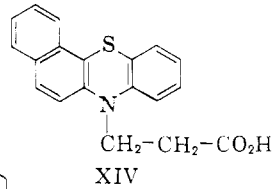

X

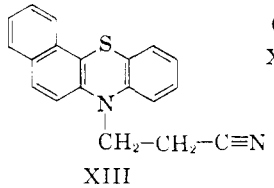

XI

carboxyquinoleino[3',2' - 2,3] - 1H - pyrido[3,2,1-kl]phenoselenazine (X; X = Se).

In the course of this work, 7H-benzo[c]phenothiazine (XII) was also found to undergo ready β-cyanoethylation, to give β-7-[7H-benzo[c]phenothiazinyl]propionitrile (XIII); this compound underwent hydrolysis to the corresponding acid (XIV), whose cyclization will be discussed in a later paper.


XII


XIV


XIII

EXPERIMENTAL

β-(10-Phenoxazinyl)propionitrile (II). To a mixture of 11 g. of phenoxazine and 15 ml. of acrylonitrile 0.5 ml. of benzyltrimethylammonium methoxide was added dropwise with stirring, whereupon an exothermic reaction set up accompanied by a deep red coloration. The mixture was then heated on a water bath for 30 minutes, the acrylonitrile in excess was distilled off *in vacuo*, and the solid residue taken up in benzene. The benzene solution was filtered, the solvent removed *in vacuo*, and the residue recrystallized from ether or ethanol, to form 33.5 g. of fine colorless needles, m.p. 123°, giving a red coloration in sulfuric acid.

Anal. Calcd. for $C_{15}H_{12}N_2O$: C, 76.3; H, 5.1; N, 11.9. Found: C, 76.2; H, 5.4; N, 12.1.

β-(10-Phenoxazinyl)propionic acid (III). A solution of 6.8 g. of the foregoing nitrile and 7.5 g. of sodium hydroxide in 100 ml. of ethanol was gently refluxed for 10 hr.; after cooling, water was added, and the solid precipitate of phenoxazine (m.p. 156°) was filtered off by suction. The filtrate yielded on acidification with dilute hydrochloric acid, 5 g. of an *acid*, crystallizing from cyclohexane in shiny colorless needles, m.p. 138°.

Anal. Calcd. for $C_{15}H_{13}NO_3$: C, 70.5; H, 5.1; N, 5.5. Found: C, 70.8; H, 5.2; N, 5.6.

Cyclization of β-(10-Phenoxazinyl)propionic acid (III). A solution of 3.5 g. of the above acid in 75 ml. of anhydrous benzene was refluxed for 1 hr. on a water bath with 19 g. of phosphorus pentoxide, and left overnight at room temperature. The reaction mixture, which consisted by then of a brownish solid and a supernatant benzene phase, was carefully poured onto ice, the benzene solution was washed with aqueous sodium carbonate, then with water, and dried over sodium sulfate, and the solvent distilled off *in vacuo*. The yield was 2.7 g. of a solid which was dissolved in a mixture of benzene and cyclohexane; the less soluble portion consisted of 0.5 g. of *3-keto-1H-pyrido[3,2,1-kl]phenoxazine* (V), bright yellow prisms which melted at 228° after recrystallization from ethanol. This compound gave in sulfuric acid a tawny coloration which rapidly turned yellow.

Anal. Calcd. for $C_{15}H_9NO_2$: C, 76.6; H, 3.8; O, 13.6. Found: C, 76.5; H, 3.7; O, 13.6.

The mother liquors were concentrated, and furnished on cooling, 2 g. of *2,3-dihydro-3-keto-1H-pyrido[3,2,1-kl]-phenoxazine* (IV), which was recrystallized from ethanol to yield orange yellow prisms, m.p. 144°, giving in sulfuric acid a deep blue coloration which turned yellow on heating.

Anal. Calcd. for $C_{15}H_{11}NO_2$: C, 75.9; H, 4.6; O, 13.5. Found: C, 75.8; H, 4.5; O, 13.5.

The corresponding *phenylhydrazone*, prepared in ethanol,

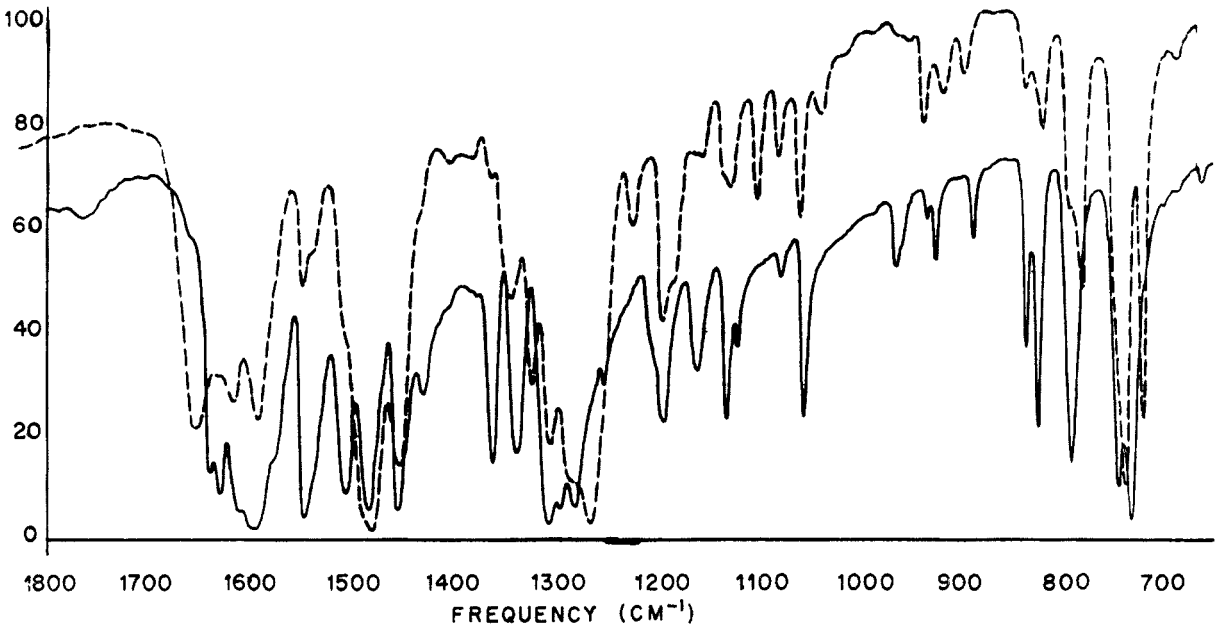


Fig. 2
- - - - compound (VI; X = Se)
——— 10-chloro derivative of compound (VI; X = Se)

crystallized from that solvent in pale yellow needles, m.p. 187°, giving a red coloration in sulfuric acid.

Anal. Calcd. for $C_{21}H_{17}N_3O$: N, 12.8. Found: N, 12.8.

Indolo[3',2'-2,3]-1H-pyrido[3,2,1-kl]phenoxazine (VII). The Fischer cyclization of the foregoing phenylhydrazone (0.25 g.) was effected by boiling for a few minutes its solution in 5 ml. of acetic acid saturated with hydrogen chloride. After cooling, water was added, and the deep yellow precipitate (0.18 g.) was recrystallized from ethanol, giving yellow prisms melting above 300° and containing 1.5 moles of ethanol (the analytical sample was dried for 30 minutes at 160°). This compound gave in sulfuric acid a yellow halochromy with a green fluorescence.

Anal. Calcd. for $C_{21}H_{14}N_2O$: C, 81.3; H, 4.6; N, 9.0. Found: C, 81.0; H, 4.3; N, 9.0.

Indolo[3',2'-2,3]-1H-pyrido[3,2,1-kl]phenothiazine (VIII). Similarly prepared from 2 g. of the phenylhydrazone of ketone (VI; X = S), this *compound* (1.5 g.) crystallized from ethanol in microscopic yellow needles, melting with decomposition at 275° and containing crystallization solvent (the analytical sample was dried at 160° as in the previous case). The halochromy in sulfuric acid was yellow.

Anal. Calcd. for $C_{21}H_{14}N_2S$: C, 77.3; H, 4.3; N, 8.5. Found: C, 77.0; H, 4.6; N, 8.4.

Indolo[3',2'-2,3]-1H-pyrido[3,2,1-kl]phenoselenazine (IX). Prepared as for the above from 0.3 g. of the phenylhydrazone of ketone (VI; X = Se), this *indole* (0.2 g.) crystallized from ethanol in yellow needles, m.p. 258°, giving a yellow halochromy in sulfuric acid.

Anal. Calcd. for $C_{21}H_{14}N_2Se$: N, 7.8. Found: N, 7.7.

4'-Carboxyquinoleino[3',2'-2,3]-1H-pyrido[3,2,1-kl]phenothiazine (X; X = S). A mixture of 2.5 g. of ketone (VI; X = S), 1.5 g. of isatin, and 1.7 g. of potassium hydroxide in 10 ml. of ethanol was refluxed for 40 hr.; after cooling, water was added, and the yellow potassium salt of the cinchoninic acid obtained was filtered off, suspended in water, and the free acid liberated by addition of acetic acid. Yield: 2.7 g. of reddish-brown microcrystals, m.p. 325°, giving a green coloration in sulfuric acid.

Anal. Calcd. for $C_{23}H_{14}N_2O_2S$: N, 7.4; S, 8.4. Found: N, 7.1; S, 8.1.

Quinoleino[3',2'-2,3]-1H-pyrido[3,2,1-kl]phenothiazine (XI), prepared by thermal decarboxylation of the foregoing acid, crystallized from ethanol in yellow prisms, m.p. 202°.

Anal. Calcd. for $C_{22}H_{14}N_2S$: N, 8.3; S, 9.5. Found: N, 8.3; S, 9.2.

4'-Carboxyquinoleino[3',2'-2,3]-1H-pyrido[3,2,1-kl]phenoselenazine (X; X = Se). Prepared and purified as for the sulfur analog, this *acid* crystallized from ethanol in brownish needles, melting with decomposition above 300°, and giving a dark green halochromy in sulfuric acid.

Anal. Calcd. for $C_{23}H_{14}N_2O_2Se$: C, 64.3; H, 3.3. Found: C, 64.0; H, 3.3.

β-7-[7H-Benzo[c]phenothiazinyl]propionitrile (XIII). To a suspension of 15.5 g. of 7H-benzo[c]phenothiazine (XII; prepared from N-phenyl-β-naphthylamine and sulfur in the presence of iodine[3]; the product was purified by distillation *in vacuo:* b.p. 235–240°/0.1 mm., m.p. 178°) in 25 ml. of acrylonitrile, 1 ml. of benzyltrimethylammonium methoxide was added dropwise, and the mixture heated for 30 minutes on a water bath. The paste obtained was left overnight at room temperature; the reaction product was then taken up in 250 ml. of hot benzene, the solvent was removed, and the residue recrystallized from acetone, to furnish 12 g. of colorless needles, m.p. 224°, giving a deep blue halochromy in sulfuric acid.

Anal. Calcd. for $C_{19}H_{14}N_2S$: C, 75.5; H, 4.7; N, 9.3. Found: C, 75.5; H, 5.0; N, 9.4.

β-7-[7H-benzo[c]phenothiazinyl]propionic acid (XIV). A suspension of 5.5 g. of the foregoing nitrile in 100 ml. of a 5% solution of sodium hydroxide in ethanol was refluxed for 10 hr.; after cooling, 200 ml. of water was added, and the precipitate of 7H-benzo[c]phenothiazine (2 g.) was filtered off. The filtrate yielded on acidification with dilute hydrochloric acid, 3.3 g. of a solid *acid*, crystallizing from ethanol in fine colorless needles, m.p. 190°. The halochromy in sulfuric acid was deep blue.

Anal. Calcd. for $C_{19}H_{15}NO_2S$: C, 71.0; H, 4.7; N, 4.4. Found: C, 71.0; H, 5.0; N, 4.1.

Acknowledgment. We thank Eastman Chemical Products Inc. (Kingsport, Tennessee) for the α-methylacrylonitrile used in this work.

PARIS V^E, FRANCE

(3) E. Knoevenagel, *J. prakt. Chem.*, [2] 89, 17 (1914).