# Studies on 4-Quinazolinones. II.[1] Self-Condensation of Anthranilamide

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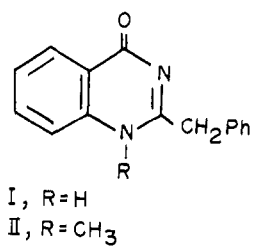
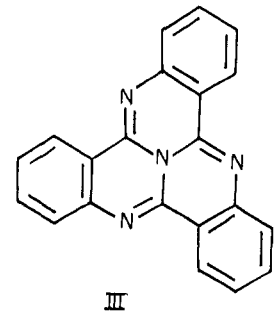
Condensation of phenylacetic acid with anthranilamide in xylene in the presence of phosphorus pentoxide furnished 2-benzyl-4-quinazolinone (I), *o*-aminobenzonitrile, tricycloquinazoline (III), 2-(*o*-aminophenyl)-4-quinazolinone (IV), 6,12-diaminophenohomazine (VI), and a compound, $C_{29}H_{21}N_5O$, mp 281°, for which the most probable structure VII has been advanced. The mass spectral fragmentation of III, IV, and VII are discussed.

In connection with some oxidation and reduction studies, we required glycosminine (I), one of the minor alkaloids[2,3] from *Glycosmis arborea* (Roxb) DC (*Rutaceae*), in quantities. Though a single-step synthesis[4] of arborine (II) from $N^1$-methylanthranilamide has been recorded in the literature, the condensation of anthranilamide with phenylacetic acid in boiling xylene in the presence of phosphorus pentoxide[5] afforded I in only *ca.* 10% yield. Among a number of side products (tlc), compounds A–E could be definitely characterized. Since the first four were obtained when anthranilamide alone was similarly treated, only compound E involved phenylacetic acid also. Thus, the modified general method of synthesis of 4-quinazolinones reported[1] from this laboratory appears to be the method of choice for the preparation of I.

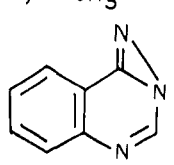
Compound A was *o*-aminobenzonitrile. Compound B was a trimer; the tricycloquinazoline structure III[6-10]



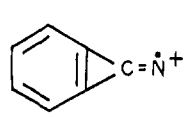
I, R = H
II, R = $CH_3$



III



a



b

(1) Part I: S. C. Pakrashi, A. De, and S. C. Chattopadhyay, *Indian J. Chem.*, **6**, 472 (1968).

(2) S. C. Pakrashi and J. Bhattacharyya, *Ann. Biochem. Exp. Med.*, **23**, 123 (1963).

(3) S. C. Pakrashi, J. Bhattacharyya, L. F. Johnson, and H. Budzikiewicz, *Tetrahedron*, **19**, 1011 (1963).

(4) A. Chatterjee and S. G. Majumdar, *J. Amer. Chem. Soc.*, **75**, 4365 (1953).

(5) S. K. Roy, S. G. Majumdar, and A. Chatterjee, *Proc. 47th Indian Sci. Congr.*, Part III, 145 (1960).

(6) R. W. Baldwin, K. Butler, F. C. Cooper, M. W. Partridge, and C. J. Cunningham, *Nature*, **181**, 838 (1958).

(7) R. W. Baldwin, C. J. Cunningham, and M. W. Partridge, *Brit. J. Cancer*, **13**, 94 (1959).

(8) P. Jacobson and L. Huber, *Ber.*, **41**, 660 (1908).

(9) J. Kozak and A. Kalmus, *Bull. Acad. Pol. Sci., Cl. Troisieme*, **10**, 532 (1933); *Chem. Abstr.*, **28**, 4424 (1934).

(10) F. C. Cooper and M. W. Partridge, *J. Chem. Soc.*, 3429 (1954).

was confirmed by its preparation from 2-(*o*-aminophenyl)-4-quinazolinone (IV). The infrared spectrum of the compound (Nujol) deserves comment in view of the varied observations[11] on the position of C=N stretching vibration particularly in conjugation in a cyclic system. The sharp and intense bands at 1618 and 1592 $cm^{-1}$ appear to be those for C=N stretching frequency, considerably lowered by conjugation with aromatic rings. Similarly, VI exhibits the corresponding bands at 1613 and 1567 $cm^{-1}$.

The mass spectrum of the compound is characterized by strong peaks for both M + 1 and M − 1. It, however, shows only a few major fragmentations and no metastable peak. The peaks at *m/e* 293 (M − 27) and at *m/e* 230 (M − 90) clearly result from the expulsion of a molecule of HCN and $C_6H_4N$ radical, respectively, supported by a prominent peak at *m/e* 90 in the latter case. Loss of a CN radical and HCN from *m/e* 230 would lead to the respective ions $204^+$ and $203^+$. Either further loss of HCN from *m/e* 204 or expulsion of a neutral $C_8H_5N_3$ fragment assigned to structure a directly from the $M^+$ appears to be the genesis of peak at *m/e* 177. Species b would account for *m/e* 102.

Compound C, $C_{14}H_{11}N_3O$, gave a crystalline acetyl derivative and is assigned the structure of 2-(*o*-aminophenyl-4-quinazolinone) (IV), which has been suggested[12,13] as the precursor of III. Further condensation of IV with anthranilic acid gave III, ruling out the other possible isomer V. The mass spectrum of IV showed a base peak at M + 1, compatible with a free amino group.

The first fragmentation step appears to follow that of the other 4-quinazolinones,[3] *viz.*, loss of atoms 2 and 3 with substituent, except hydrogen transfer has to be envisaged in this case. The ion peak at *m/e* 121 and a more intense one at *m/e* 120 could be assigned to species c and d or e, respectively. The observed metastable peaks at *m/e* 61.75 (calcd for $238^+ \rightarrow 121^+$, 61.52; $237^+ \rightarrow 121^+$, 61.79) and *m/e* 60.75 (calcd for $238^+ \rightarrow 120^+$, 60.50; $237^+ \rightarrow 120^+$, 60.77) favor the transition from $M^+$ rather than M + 1 ion. Species e may either lose a molecule of HCN to afford ion peak at *m/e* 93, corroborated by the metastable peak at *m/e* 72.0 (calcd for $120^+ \rightarrow 93^+$, 72.1), or species d may expel CO to lead to *m/e* 92.

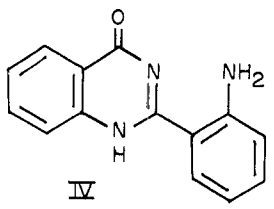
Compound D, mp 94°, retained a molecule of solvent of crystallization, but analysis of the base and the

(11) L. J. Bellamy, "The Infrared Spectra of Complex Molecules," Wiley, New York, N. Y., 1956, p 226; "Advances in Infrared Group Frequencies," Methuen, London, 1968, p 49.

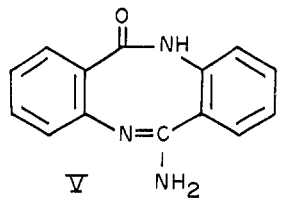
(12) K. Butler and M. W. Partridge, *J. Chem. Soc.*, 2396 (1959).

(13) M. W. Partridge, H. J. Vipond, and J. A. Waite, *ibid.*, 2549 (1962).

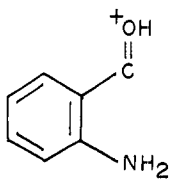
dihydrochloride were in agreement with the molecular formula, $C_{14}H_{12}N_4$. The physical constants are in accord with 6,12-diaminophenohomazine (VI) prepared by Cooper and Partridge[10] though, however, the slight discrepancy in the uv data reported by them cannot readily be explained.



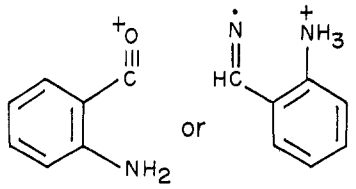
IV



V

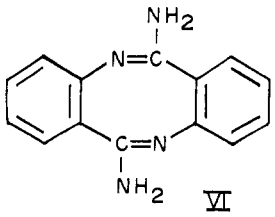


c, m/e 121



d or e

m/e 120



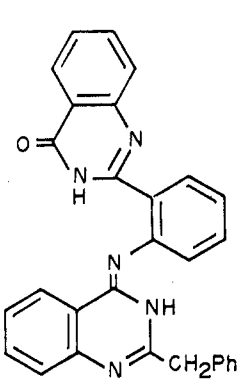
VI

The formula $C_{29}H_{21}N_5O$ was indicated by analysis of compound E, mp 280–281°. The $M^+$ and $M^{2+}$ ion peaks respectively at *m/e* 455 and 227.5 in the mass spectrum confirmed the molecular formula. To gain insight into the mode of combination of 3 mol of anthranilamide with 1 mol of phenylacetic acid, 2-(*o*-aminophenyl)-4-quinazolinone (IV) was condensed first with 2-benzyl-4-quinazolinone (I) and then separately with $N^4$-phenylacetylanthranilamide, the intermediate in the synthesis of I, in presence of phosphorus pentoxide. The desired compound was only obtained in the latter case along with I which was also recovered unchanged from the former reaction. Among a number of possible structures, VII and VIII (or their tautomers) appeared to be the most likely representation of compound E.

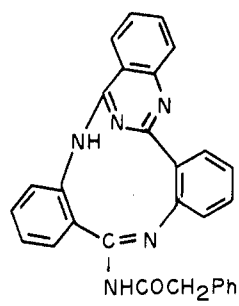
The infrared band at 3030 $cm^{-1}$ indicated the presence of a bonded NH, and a number of typical bands between 1681 and 1417 $cm^{-1}$ supported[3] the presence of an intact 4-quinazolinone rather than a phenyl acetamide moiety. The structure VII appears also to explain the mass spectral fragmentation pattern better.

The intense M − 1 ion peak and the corresponding peaks at *m/e* 91 and at *m/e* 364 (M − 91) are characteristic of a free benzyl substituent in the molecule in this series.[3] The two equally strong peaks at *m/e* 336 and *m/e* 335 must be due to the expulsion of species f from the 4-quinazolinone moiety of $M^+$ and M − 1 ions, respectively. The ion peak at *m/e* 119 and its protonated species at *m/e* 120 as well as the metastable peak at *m/e* 248.5 (calcd for $455^+ \rightarrow 336^+$, 248.1) corroborate the above transition.

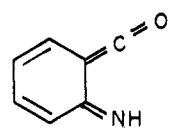
Primary loss of OH from the M − 1 peak (m* observed 420.5 − 0.5; calcd for $454^+ \rightarrow 437^+$, 420.6) followed by expulsion of 116 mass units assignable to radical g appears to be the genesis of the peak at *m/e* 321. The more important and intense peak at *m/e* 310 may result directly from the $M^+$ as evidenced by the presence of metastable peak at *m/e* 211 (calcd for $455^+ \rightarrow 310^+$, 211.2). Expulsion of the 4-quinazolinone moiety as such (loss of 145 mass units) would lead to a highly stabilized ion species h. Further loss of benzyl group would lead to ion at *m/e* 219 and subsequent expulsion of HCN to *m/e* 192.



VII



VIII



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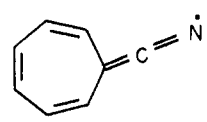
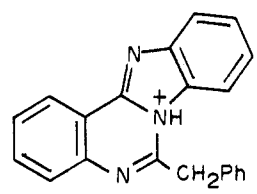


g



h

When, however, $N^1$-methylanthranilamide was condensed with phenylacetic acid in the presence of phosphorus pentoxide under similar condition, arborine (II) was indeed[4] obtained as the major product. The only recognizable side product was *o*-($N$-methylamino)-benzonitrile.

The above result was not unexpected in view of our observed[1] difference in the rate of dehydrocyclization between $N^1$-acylated anthranilamides and their $N^1$-methyl derivatives. The $N^1$-methylation has also been found to have remarkable influence on the oxidation[14] and reduction[15,16] of 4-quinazolinones.

(14) S. C. Pakrashi and S. C. Chattopadhyay, unpublished results.
(15) S. C. Pakrashi and J. Bhattacharyya, Abstracts, 3rd IUPAC Symposium on the Chemistry of Natural Products, Kyoto, Japan, April 12–18, 1964, p 74.
(16) S. C. Pakrashi, *J. Indian Chem. Soc.*, **44**, 887 (1967).

## Experimental Section[17]

**Condensation of Anthranilamide with Phenylacetic Acid.**—Anthranilamide (2 g) and phenylacetic acid (2 g) were dissolved in dry xylene (100 ml) and refluxed with excess phosphorus pentoxide for 1 hr under anhydrous conditions. After cooling, the reaction mixture was poured over crushed ice. The xylene layer was separated, extracted once with 2 *N* hydrochloric acid (50 ml), then washed, dried ($Na_2SO_4$), and evaporated to obtain the neutral fraction A (1.5 g). The pooled aqueous acid part was basified ($Na_2CO_3$) and filtered. The filtrate was thoroughly extracted with chloroform which yielded fraction B (1.43 g) as a viscous mass. The residue (0.15 g) was crystallized (five times) from chloroform–ethanol to afford compound E in granules: mp 280–281° dec; $R_f$ 0.42 (light brown); uv max (0.1 *N* HCl–EtOH) 201, 240, and 310 mμ (log ε 4.45, 4.43, and 4.20); ir (Nujol) 3030, 1681, 1631, 1608, 1570, 1538, 1490 (m), 1417, 1412, 1359, 1311, 1267, 950, 882, 760, 748, 722 $cm^{-1}$; mass spectrum (70 eV) *m/e* (rel intensity) 455 ($M^+$, 100), 454 (59.5), 437 (2.2), 364 (6), 336 (5.5), 335 (6), 322 (6), 321 (9), 310 (21), 309 (6), 308 (6), 234 (5.5), 227.5 ($M^{2+}$, 7.1), 219 (9), 218 (8.5), 192 (6), 120 (8.5), 119 (12), 102 (8.8), 92 (12), 91 (36). 90 (10.5).

*Anal.* Calcd for $C_{29}H_{21}N_5O$: C, 76.46; H, 4.65; N, 15.38. Found: C, 75.98; H, 4.64; N, 15.82.

Fraction B was subjected to column (1.5 × 12 cm) chromatography over alumina. After separation of phenylacetic acid (0.43 g), mp 77–78°, $R_f$ 0.53 (light pink, iodine chamber), benzene (1.5 l.) eluted fraction C (0.27 g), mp 210–215° (frothing), containing a mixture of components. Benzene–chloroform (4:1, 450 ml) separated a solid (0.1 g) which crystallized from ethanol in long white needles of glycosminine, mp 249°. Further increase in the polarity of solvents up to chloroform–methanol (98:2) eluted fraction D as a brownish yellow, viscous oil (0.5 g) responding positively to alkaloidal test.

Fraction C was resolved by preparative tlc into glycosminine (0.23 g) and two minor components, one of which could only be obtained crystalline, mp 240–241°.

Fraction D was converted to the picrate (0.23 g) in benzene solution, fractionally crystallized from methanol–benzene, and separately regenerated through ion-exchange resin (IRA-400). The bases liberated from the first two crops (0.12 g, yellow, mp 200–215°) were identified as unconverted anthranilamide (0.03 g), mp 107–109° (benzene), $R_f$ 0.27 (yellowish brown, iodine chamber). The regenerated bases from the third crop (0.1 g, brown, mp 225–230°) and the mother liquor of the above picrates on chromatography and crystallization from petroleum ether gave white long rods (0.25 g), mp 50–51°, identified as *o*-aminobenzonitrile through their alkaline hydrolysis to anthranilamide: $R_f$ 0.67 (orange); ir (Nujol) 2203 $cm^{-1}$.

*Anal.* Calcd for $C_7H_6N_2$: C, 71.25; H, 5.13; N, 23.74. Found: C, 70.67; H, 5.31; N, 23.92.

Fraction A (xylene layer) was chromatographed through an alumina column (1.2 × 15 cm). After the initial separation of an oil, petroleum ether eluates (total 550 ml) furnished a crude material (0.03 g) crystallizing (0.02 g) out of benzene–chloroform to give III in long yellow needles: mp 315–316°; $R_f$ 0.74 (light green); uv (dioxane) max 252, 284, 296, and 310 mμ (log ε 4.51, 4.26, 4.38, and 4.33); ir (Nujol) 1618, 1592, 1565 (m), 1475, 1333 (m), 1295 (w), 1280 (w), 1136, 768, 762, 755, 695 $cm^{-1}$; mass spectrum (70 eV) *m/e* (rel intensity) 321 (M + 1, 25.5), 320 ($M^+$, 100), 319 (M − 1, 7.7), 293 (1.1), 292 (0.8), 291 (0.5), 230 (0.5), 218 (0.6), 217 (0.65), 204 (1.3), 203 (0.9), 191 (0.5), 186 (0.5), 177 (1.1), 176 (0.6), 165 (0.5), 164 (0.7), 160.5 ($M^{2+}$, 5), 160 (19.4), 159.5 (1.9), 129 (0.6), 106.6 ($M^{3+}$, 0.8), 102 (6.2), 90 (1.3), 76 (5), 74 (4).

*Anal.* Calcd for $C_{21}H_{12}N_4$: C, 78.82; H, 3.78; N, 17.51. Found: C, 78.83; H, 3.75; N, 17.22.

Petroleum ether–benzene (3:1, 600 ml) eluted *o*-aminobenzonitrile, mp 50–51°, and benzene (650 ml) gave phenylacetic acid, mp 77–78°.

In one experiment, the xylene layer, after being extracted with acid and left overnight, deposited a substance (0.1 g) which recrystallized from benzene–chloroform in colorless needles: mp 187–188°; ir (Nujol) 1690, 1668, 1600, 1580, 1525, 1405 (m), 1261 $cm^{-1}$ (vs). In an attempted chromatography through neutral alumina, chloroform–methanol (98:2) eluted a compound (7 mg), mp 249°, while traces of the mother substance could only be separated from the benzene–acetic acid (5%) eluate. As such, it could not be further characterized.

**Self-Condensation of Anthranilamide.**—Anthranilamide (5 g) was dissolved in dry xylene (400 ml) and refluxed for 3 hr with an excess of phosphorus pentoxide under anhydrous conditions. Processed as before, the acid and xylene layers, respectively, furnished 3.67 and 1.15 g of viscous residues.

The basic fraction was chromatographed over alumina (1.5 × 22 cm). Petroleum ether–benzene (3:1, 150 ml) eluted *o*-aminobenzonitrile (0.85 g). The fractions eluted with benzene and chloroform, and their mixtures in various proportions (1.15 l.) gave an oil embedded with solid (2.4 g) which on crystallization several times from benzene–chloroform afforded light yellow needles (0.25 g), mp 240–241°, of 2-(*o*-aminophenyl)-4-quinazolinone. Another 0.35 g of the material was obtained from the filtrate: $R_f$ 0.5 (violetish brown); uv (EtOH) max 208, 242, and 286 mμ (log ε 4.25, 4.25, and 4.02); ir (Nujol) 3425 (sh), 3330, (3171, 3125 sh), 1670, 1613, 1577 (m), 1550, 1504 (w), 1480, 1337 (m), 1266, 950, 772, 764, 740, 692 $cm^{-1}$; mass spectrum (70 eV) *m/e* (rel intensity) 238 (M + 1, 100), 237 ($M^+$, 6), 121 (20.5), 120 (64), 119.5 ($M^{2+}$ + 1, 11), 119 (6.5), 103 (2), 93 (16), 92 (8), 91 (5), 77 (1.5).

*Anal.* Calcd for $C_{14}H_{11}N_3O$: C, 70.90; H, 4.70; N, 17.70. Found: C, 70.57; H, 4.94; N, 17.50.

It formed an acetate, mp 273–274° (lit.[12] mp 274–275°), with acetic anhydride and pyridine.

The acid extract was made ammoniacal, the base taken up in chloroform, and the residue (1.7 g) chromatographed. Benzene–chloroform (6:4, 1.5 l.) eluted anthranilamide (1.03 g), mp 109°; an increase in polarity up to chloroform yielded fraction E as an oil (0.45 g), while chloroform–methanol (98:2) separated an oil (0.32 g) containing a number (tlc) of unisolated alkaloidal components.

Fraction E was converted to the picrate, mp 230° (frothing) after repeated crystallizations from methanol. The regenerated base (0.4 g) was chromatographed (silica gel, column, 1 × 8 cm). Benzene and its mixture with chloroform (3:1) eluted a material (0.38 g) which on several crystallizations from benzene yielded Dragendorff-positive light yellow prisms (0.3 g) of 6,12-diaminophenohomazine: mp 93–94°; $R_f$ 0.48 (reddish brown); uv (EtOH) max 207, 250, 262 (sh), and 298 mμ [log ε 4.3, 4.3, 4.21, and 3.96 (calcd with 1 mol of $C_6H_6$ of crystallization), 4.17, 4.17, 4.08, and 3.8 (without)]; ir (Nujol) 3413, 3279, 3125, 1634, 1613, 1567, 1538 (m), 1497, 1480, 1359, 1307 (w), 1277 (w), 1244 (m), 1157 (m), 767, 748, 690 $cm^{-1}$ (vs).

*Anal.* Calcd for $C_{14}H_{12}N_4 \cdot C_6H_6$: C, 76.42; H, 5.78; N, 17.82. Found: C, 76.25; H, 5.70; N, 17.83.

It formed a hydrochloride which was crystallized from ethanol in yellow needles, mp 288° dec.

*Anal.* Calcd for $C_{14}H_{12}N_4 \cdot 2HCl$: C, 54.38; H, 4.57, N, 18.13. Found: C, 54.18; H, 4.41; N, 18.40.

The neutral part (xylene layer) on recrystallization from chloroform–benzene furnished yellow needles (0.14 g) of tricycloquinazoline, mp 315–316° dec; 15 mg more of the compound could be recovered from the mother liquor.

Petroleum ether–benzene (3:1, 500 ml) separated *o*-aminobenzonitrile (0.33 g).

**Condensation of *N*-Methylanthranilamide with Phenylacetic Acid.**—*N*-Methylanthranilamide (2 g) and phenylacetic acid (2 g) in dry xylene (150 ml) were refluxed over phosphorus pentoxide for 1 hr and worked up as described earlier.

The basic fraction (1.4 g) was chromatographed through a column (1.5 × 19 cm) of alumina. Benzene (150 ml) separated phenylacetic acid (0.2 g), mp 77°. With increasing proportions of chloroform and finally chloroform itself arborine was eluted (0.9 g), mp 156–157° (benzene).

The neutral part (2.5 g) was subjected to column (1.5 × 25 cm) chromatography. The only definite product (0.9 g) obtained was *o*-(*N*-methylamino)benzonitrile eluted by petroleum ether–benzene (9:1, 1.25 l.). It solidified on standing overnight

(17) All melting points are uncorrected. Column chromatography was carried out over acid-washed alumina (E. Merck), thin layer chromatography was run with benzene–ethyl acetate (6:4) for identification and ethyl acetate–methylene chloride–formic acid (5:4:1) for preparative purposes using silica gel G, iodine was used as spot developer, and Dragendorff's reagent was used as spraying agent. Identity with known compounds was established by direct comparison (tlc, mixture melting point, and ir) where possible. The mass spectra were recorded on a CEC 21-110 B mass spectrometer; samples were introduced through direct inlet system at 150, 140, and 230°, respectively, for the samples III, IV, and VII. The ionizing current used was 50 μA.

and crystallized from petroleum ether in colorless flakes: mp 72–73°; $R_f$ 0.68 (light orange); ir (Nujol) 2212 $cm^{-1}$.

*Anal.* Calcd for $C_8H_8N_2$: C, 72.79; H, 6.1; N, 21.2. Found: C, 72.55; H, 5.90; N, 21.5.

**Condensation of Anthranilamide with Anthranilic Acid.**—Thionyl chloride (3 ml) was added to a pyridine (3 ml) solution of anthranilamide (1 g) and anthranilic acid (1 g) and kept for 24 hr (i) at room temperature and (ii) at 0° in separate experiments. Crushed ice was then added; the reaction mixture was left for 2 hr and extracted with chloroform. The aqueous layer was filtered, an insoluble residue (0.4 g), not yet characterized, was kept aside, and the filtrate was mixed with the 2 *N* hydrochloric acid extract of the chloroform layer. The latter yielded a mixture of solid substances (1 g).

The combined acid aqueous solution was basified and extracted with chloroform, and the crude product (0.26 g) was chromatographed. Benzene–chloroform (9:1) eluted first an uncharacterized yellow crystalline compound (0.04 g), mp 208–212°, giving a positive test for alkaloid, and then 2-(*o*-aminophenyl)-4-quinazolinone (0.04 g), mp 240–241°. Further increase in the chloroform percentage (20%) eluted uncoverted anthranilamide (0.15 g) along with VI, mp 94°.

The reaction at 0° afforded the insoluble residue (0.8 g), solid substance (0.6 g) from the original chloroform layer, and a mixture of bases liberated from the acid aqueous part. The base on chromatography resolved into IV (0.09 g), mp 241°, anthranilamide (0.26 g), an uncharacterized compound (0.07 g), mp 210–212°, and trace amount of VI.

**Tricycloquinazoline (III) from IV.**—A mixture of 2-(*o*-aminophenyl)-4-quinazolinone (0.06 g) and an equal amount of anthranilic acid dissolved in xylene (25 ml) was refluxed in the presence of phosphorus pentoxide for 3 hr. The insoluble residue (0.01 g) left after being treated with crushed ice was filtered and chromatographed over acid-washed alumina. The benzene eluate (30 ml) afforded tricycloquinazoline, mp 316° (benzene–chloroform).

**Preparation of VII from IV.**—2-(*o*-Aminophenyl)-4-quinazolinone (25 mg) and $N^4$-phenylacetylanthranilamide (50 mg) in xylene were refluxed in the presence of phosphorus pentoxide for 3 hr. The acid layer, after usual work-up and chromatography with benzene–chloroform (8:2) as eluents, yielded VII (3 mg), mp 280–281°, identical in all repects with compound E, besides IV (8 mg) and I (6 mg).

On the other hand, equal proportions (40 mg) of IV and 2-benzyl-4-quinazolinone (I) on similar treatment led only to the recovery of the starting materials and not even a trace of VII could be detected.

**Registry No.**—*o*-Aminobenzonitrile (compound A), 1885-29-6; III (compound B), 195-84-6; IV (compound C), 27259-73-0; VI (compound D), 27259-74-1; VI 2HCl, 27259-75-2; VII (compound E), 27259-76-3; anthranilamide, 88-68-6; *o*-(*N*-methylamino)benzonitrile, 17583-40-3.

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# Reaction of 1-Acetyl-3-piperidinoindole with Acetylenic Esters

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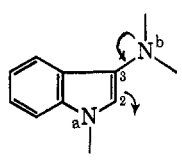
The reaction of 1-acetyl-3-piperidinoindole (**2**) with dimethyl acetylenedicarboxylate and methyl propiolate gave the benzazepine derivatives **3a** and **3b**, respectively. These products were subjected to a degradation sequence (**3** → **5** → **7** → **8**), each step of which was supported by spectral evidence; in the case of **8b**, direct correlation with authentic material was made. An alternative structure (**9**) for the product of the transformations **7** → **8** was ruled out by synthesis. Compound **11** was obtained and shown to be an intermediate for the formation of **3b**. Compounds **3a** and **3b** as well as a number of their degradation products exhibited geometrical isomerism due to restricted rotation about the *N*-acetyl function. In the case of **3b**, temperature-variable 100-Mc nmr spectra have been recorded and discussed.

Even a cursory reading of the literature of indole compounds reveals that the chemistry of simple 2- and 3-aminoindole derivatives has received scant attention.[1] The lack of activity in this area is undoubtedly related to the absence of versatile methods for the preparation of these compounds[2] and to their pronounced inherent instability.[1,3] Recent work dealing with new aspects of aminoindole chemistry[4,5] further emphasizes the latter point. The above survey gave impetus to devise new synthetic routes to ammoindoles[6] and to investigate some of their reactions. In particular, our intention was to put to experimental test the hypothesis that the system **1** may behave



**1**

to some extent like an enamine (arrows). This proposal had potentially important synthetic implications since enamine behavior of the $N^b$-enamine system would allow acylation and alkylation reactions to occur at

(1) A. Albert, "Heterocyclic Chemistry," 2nd ed, Oxford University Press, New York, N. Y., 1968, pp 205–206, and references to reviews therein.

(2) There are recent scattered investigations which may have a bearing on any new developments in aminoindole syntheses: (a) M. Colonna, P. Bruni, and G. Guerra, *Gazz. Chim. Ital.*, **99**, 3 (1969); (b) A. S. Bailey, M. C. Chum, and J. J. Wedgwood, *Tetrahedron Lett.*, 5953 (1968); (c) T. Hino, M. Nakagawa, and S. Akoboshi, *Chem. Commun.*, 656 (1967); (d) F. Yoneda, T. Miyamae, and Y. Nitta, *Chem. Pharm. Bull.*, **15**, 8 (1967); (e) D. Raileanu, V. Daniel, E. Mosanu, and C. D. Nenitzescu, *Rev. Roum. Chim.*, **12**, 1367 (1967). For an obvious but apparently unexplored approach, see E. Coxworth, *Alkaloids*, **8**, 40 (1965).

(3) J. Kebrle and K. Hoffmann, *Helv. Chim. Acta*, **39**, 116 (1956).

(4) J. Schmitt, M. Langlois, G. Callet, and C. Perrin, *Bull. Soc. Chim. Fr.*, 2008 (1969), and previous papers in this series.

(5) M. Colonna and L. Greci, *Gazz. Chim. Ital.*, **99**, 1264 (1969), and references cited therein.

(6) For an unsuccessful attempt, see V. Snieckus and M.-S. Lin, *J. Org. Chem.*, **35**, 3994 (1970).