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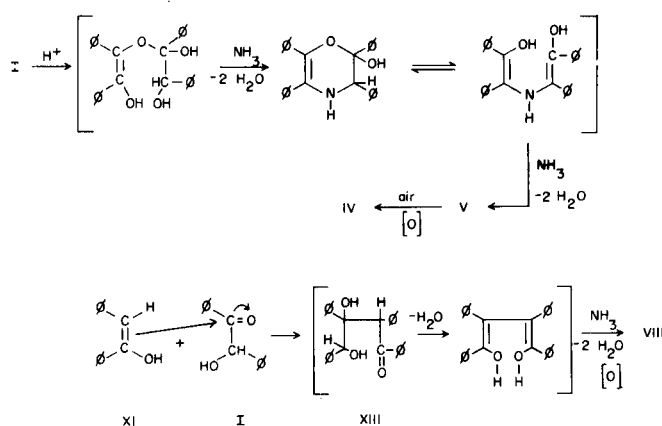
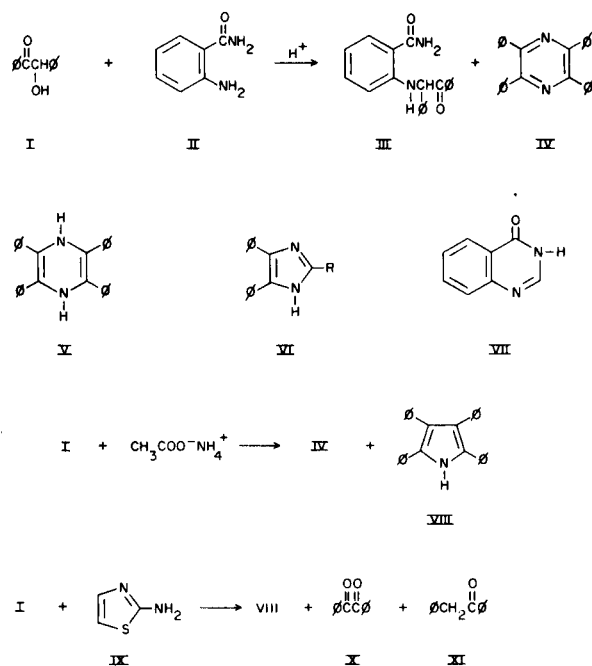
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Extension of the reaction time of benzoin (I) with anthranilamide (II) gave 2,3,5,6-tetraphenylpyrazine (IV) in addition to the expected benzamide III. Condensation of I with II in the presence of ammonium acetate or ammonium formate yielded IV, and IV with 4-quinazolinone (VII), respectively. Reaction of I with ammonium acetate only led to IV and 2,3,5,6-tetraphenylpyrrole (VIII). When I was heated with 2-aminothiazole, benzil, desoxybenzoin, and VIII were formed. A mechanism has been extended to explain the formation of IV and VIII.

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The acid-catalyzed reaction of benzoin (I) with anthranilamide (II) to form *o*-(α -benzoylbenzylamino)benzamide (III) was described earlier (1). When the prescribed forty-five minute reaction time was extended to eight hours in the current study, 2,3,5,6-tetraphenylpyrazine (IV) was isolated in small amounts in addition to the expected product, III. The reaction of ammonium salts with benzoin has been reported to form mainly compound IV, and lesser amounts of 1,4-dihydro-2,3,5,6-tetraphenylpyrazine (V) and a 2-substituted 4,5-diphenylimidazole (VI) (2). Apparently under our present conditions, ammonia, derived from II, reacted with I to form IV. To test this hypothesis further, ammonium acetate and ammonium formate were evaluated in the reaction of I with II.

When compounds I, II, and ammonium acetate were heated together, only compound IV was isolated, whereas a mixture of compounds I, II, and ammonium formate



heated similarly yielded compound IV and 4-quinazolinone (VII). Formation of the latter can be explained by the condensation of anthranilamide with formic acid, derived from ammonium formate. However, in neither case was the possible imidazole derivative (VI) formed, as suggested by earlier work (2).

The reaction of benzoin with ammonium acetate only was investigated next. Compound IV plus a small amount of the unexpected 2,3,4,5-tetraphenylpyrrole (VIII) was obtained when benzoin was heated with ammonium acetate. The possible imidazole derivative (VI, R = CH₃) was not detected.

Finally, in seemingly unrelated but significant experiments, benzoin was condensed with 2-aminothiazole (IX) in attempts to prepare 2-(α -benzoylbenzylamino)-thiazole. Instead, however, a gas (stench, probably hydrogen sulfide) was evolved and compound VIII, benzil (X), and desoxybenzoin (XI) were identified. Compound VIII has been prepared in 73% yield by refluxing benzoin, desoxybenzoin, and ammonium acetate together in acetic acid (3,4).

To account for the formation of compounds IV, VIII, X, and XI in the reactions described, a mechanism to explain the acid-catalyzed transformation of benzoin to tetraphenylfuran (5) has been extended to the present

work: compounds I and XI form a carbon to carbon bond (intermediate XIII), which in the presence of ammonia yields compound VIII.

EXPERIMENTAL

Melting points (uncorrected) were determined on a Thomas-Hoover melting point apparatus. ^1H -nmr spectra were recorded in deuteriochloroform, unless stated otherwise. Tms was used as the internal standard on a Varian A-60 spectrometer. All compounds were checked by tlc and gave superimposable ir spectra with those of the respective authentic compounds.

All reactions were conducted in air unless stated otherwise using oil baths which were preheated and maintained at the temperatures specified. No attempt has been made to optimize the yields of products in the described reactions. Progress of reactions was monitored by withdrawing, with open-end melting point capillary tubes, milligram quantities of the reaction mixture and examining them by tlc (Woelm GF silica gel). Visualization was by ultraviolet light followed by iodine and starch techniques (6). Column chromatography was executed on Mallinckrodt silicic acid (No. 2847) and/or Davison silica gel (grade 923, 100-200 mesh) and elution was monitored by tlc.

Isolation of IV During Preparation of III.

A mixture of 18.8 g. (0.09 mole) of I and 12 g. (0.09 mole) of II was moistened with two drops of concentrated hydrochloric acid and the product heated for eight hours at 150° . The amber glass was treated with about 150 ml. of hot chloroform and allowed to stand for one day during which time a precipitate formed. This precipitate was collected and consisted of 8.3 g. of III, m.p. $187\text{--}189^\circ$ (lit. (1) m.p. $185\text{--}188^\circ$). Concentration of the filtrate yielded another 1.6 g. of III, m.p. $185\text{--}187^\circ$ (total yield, 34%).

Tlc examination of the mother liquor showed another component. This liquor, concentrated by rotary evaporation, left 3 g. of a brown glass, which was dissolved in benzene and column chromatographed using a silica gel-silicic acid mixture (50/50; v/v). Benzene elution afforded 1 g. of impure IV, m.p. $239\text{--}243^\circ$ (lit. (7) m.p. 246°).

Reaction of I with II in Ammonium Acetate. Isolation of IV.

To a mixture of 10.6 g. (0.05 mole) of I and 6.8 g. (0.05 mole) of II, was added 20 g. of ammonium acetate and the product was heated at $126\text{--}130^\circ$ for forty-one hours. Tlc indicated the absence of I at this time and the presence of both a small amount of unreacted II and one other component. The product was cooled, diluted with water, and 15.7 g. of a brown solid was collected by filtration. It was dissolved in about 200 ml. of benzene and chromatographed on 375 g. of silica gel. Elution with benzene gave an off-white solid, which was recrystallized from carbon tetrachloride to give 6 g. of white, crystalline IV, m.p. $248\text{--}250^\circ$.

Anal. Calcd. for $\text{C}_{28}\text{H}_{20}\text{N}_2$: C, 87.5; H, 5.2; N, 7.3. Found: C, 87.4; H, 5.3; N, 7.2.

Reaction of I with II in Ammonium Formate. Isolation of IV and VII.

Twenty grams of ammonium formate were added to a mixture of 10.6 g. (0.05 mole) of I and 6.8 g. (0.05 mole) of II. The mixture was heated for one day at 125° . Tlc revealed that only a small amount of II remained. The product was processed as above to leave 14 g. of solid which was leached with warm benzene and

filtered to leave 5.4 g. of the buff solid VII, m.p. $212\text{--}213^\circ$ (lit. (8) m.p. $215\text{--}216^\circ$).

The concentrated benzene filtrate from above was dry-column chromatographed (9) on silica gel using chloroform as the developing liquid. Processing of the desired section of the chromatographic column produced 3 g. of the off-white solid IV, m.p. $247\text{--}250^\circ$.

Reaction of I with Ammonium Acetate. Isolation of IV and VIII.

A mixture of 10 g. (0.047 mole) of I and 20 g. of ammonium acetate was heated at 120° for one day. Compound I was essentially absent and two new spots were noted by tlc. The cooled reaction product was washed with water to leave 8.45 g. of a dry, yellow solid which was dissolved in hot carbon tetrachloride and chromatographed on Florisil[®] (100-200 mesh, Floridin Co., Pittsburgh, PA). Elution with carbon tetrachloride gave 0.8 g. of VIII, m.p. $212.5\text{--}215^\circ$ (lit. (3) m.p. 214°). Continued elution of the column with carbon tetrachloride led to 3 g. of IV, m.p. $248\text{--}250^\circ$. Both samples were recrystallized from carbon tetrachloride without further change in their respective melting points.

Reaction of I with 2-Aminothiazole (IX). Isolation of VIII and X.

A mixture of I (5.3 g., 0.025 mole) and IX (2.5 g., 0.025 mole) was heated at 150° for one day during which time a gas (stench probably hydrogen sulfide) was evolved. The cooled black-brown tar was leached with hot benzene and the leachate filtered through diatomaceous earth. The benzene filtrate was concentrated to about 75 ml. by rotary evaporation and chromatographed on silicic acid. The first benzene eluents afforded about 200 mg. of a pink-tan solid, m.p. $192\text{--}198^\circ$, which was dissolved in benzene and rechromatographed on silicic acid. Benzene elution gave an off-white material which was successively recrystallized (heptane) and sublimed ($190\text{--}200^\circ/0.1$ mm Hg). Heptane recrystallization of the sublimate led to the white product VIII, m.p. $213\text{--}214^\circ$ (lit. (3) m.p. 214°).

Anal. Calcd. for $\text{C}_{28}\text{H}_{11}\text{N}$: C, 90.5; H, 5.7; N, 3.8. Found: C, 90.9; H, 5.6; N, 3.6.

Continued elution with benzene of the original chromatographic column gave 200 mg. of impure, yellow crystalline X, m.p. $82\text{--}88^\circ$ (lit. (10) m.p. 96°).

Autoclave Reaction of I with IX. Isolation of VIII and XI.

Since IX sublimes readily, the reaction was conducted in a 110 ml. capacity pressure vessel (autoclave). The vessel, charged with 10.6 g. (0.05 mole) of I and 5 g. (0.05 mole) of IX, was flushed with nitrogen, sealed and heated at 150° for two days. Contents (hydrogen sulfide odor) of the autoclave were taken up in chloroform, filtered (diatomaceous earth), and the filtrate concentrated by rotary evaporation. The residue was dissolved in a small amount of benzene and chromatographed on silicic acid. Elution with carbon tetrachloride gave a faint pink solid which was further purified by sublimation ($190^\circ/0.1$ mm Hg) followed by heptane recrystallization of the sublimate to leave 0.2 g. of VIII, m.p. $214\text{--}215^\circ$.

Continued elution of the chromatography column with benzene followed by dichloromethane yielded 2.9 g. of a yellow solid. It was further purified by sublimation ($50\text{--}54^\circ/0.1$ mm Hg) followed by heptane recrystallization of the white sublimate to give 2.1 g. of XI, m.p. $55\text{--}56.5^\circ$ (lit. (11) m.p. $55\text{--}56^\circ$).

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REFERENCES AND NOTES

- (1) A. Mendel, *J. Heterocyclic Chem.*, **14**, 153 (1977).
- (2) D. Davidson, M. Weiss and M. Jelling, *J. Org. Chem.*, **2**, 328 (1937).
- (3) D. Davidson, *ibid.*, **3**, 361 (1938).
- (4) B. S. Tanascichuk, S. L. Vlasova, A. N. Sunin and V. E. Gavarilov, *Zh. Org. Khim.*, **5**, 144 (1969); *Chem. Abstr.*, **70**, 298 (1969).
- (5) S. K. Kar and A. Kar, *J. Org. Chem.*, **42**, 390 (1977).
- (6) E. Stahl, "Drug Analysis by Chromatography and Microscopy," Ann Arbor Science, Ann Arbor, Michigan, 1973.
- (7) F. R. Japp and W. H. Wilson, *J. Chem. Soc.*, **49**, 825 (1886).
- (8) W. L. F. Armarego, *J. Appl. Chem.*, **11**, 70 (1961).
- (9) A. Mendel, *J. Chromatogr.*, **87**, 236 (1973).
- (10) L. F. Fieser, "Organic Experiments," D. C. Heath, Boston, MA, 1964, p. 214.
- (11) C. F. H. Allen and W. E. Barker, *Org. Synth.*, Coll. Vol. **2**, 156 (1943).