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A SYNTHETIC APPROACH TO BENZENEDIAZONIUM-2-THIOCARBOXYLATE

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Diazotization of amino acids is not a general synthetic reaction. Aliphatic amino acids provide an array of products when diazotized in aqueous[1a] or aprotic[1b] media. Anthranilic acid is an exception and diazotizes to benzenediazonium-2-carboxylate,[2a] a compound of marginal stability.[2b] For aliphatic amino acids the diazoniumcarboxylate is not isolable being either not formed or highly unstable. A possible general solution to this problem involves conversion of amino acids to amino thioacids† with the expectation that the sulfur atom will stabilize the resulting diazotized system. Herein is reported the first successful attempt of this kind and some novel chemistry therefrom.

Synthesis of Thioanthranilic Acid -- If this synthetic idea is to be successful, anthranilic acid should undergo these reactions providing benzenediazonium-2-thiocarboxylate with increased stability over benzenediazonium-2-carboxylate. Accordingly a route to thioanthranilic acid was sought.[3] To an H_2S saturated KOH (.18 m in 500 ml) solution at 0° was added (2 hr) isatoic anhydride (.18 m, derived from anthranilic acid via N-carbobenzoxyanthranilic acid[4]). After 25 hr the stream of H_2S was removed and the solvent vacuum evaporated. The resulting residue was carefully acidified, extracted into chloroform and worked up to yield a yellow-brown oil (yield, 90%) of low stability (see below); ir (neat) 3500, 3370, 2560(broad), 1645, 1625, 1595, 1560, 1495, 1210, 1160, 945, 870, 790, 760 cm^{-1}; nmr (CCl_4) τ 2.4-3.48 (m, 4H), 4.7 (s, 3H). Treatment of this oil with p-bromophenacyl bromide afforded pale yellow needles, m.p. 118.5-120°(EtOH), which analyze correctly for the p-bromophenacylthioester of thioanthranilic acid:[5] ir (KBr) 3510, 3390, 1705, 1635(broad), 1590, 1500, 1210, 1190, 1160, 985, 915, 810, 753 cm^{-1}; nmr ($CDCl_3$) τ 2.2-2.9 (m, 6H), 3.3 (m,2H), 4.7 (broad s, 2H), 5.6 (s, 2H), m.s. 349,351

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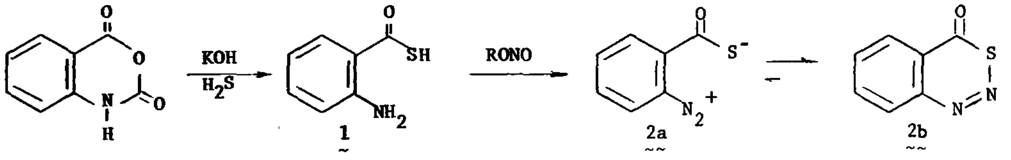
†Synthesis of amino thioacids, not a trivial task, has been reported. See T. Wieland and K. E. Euler, Chem. Ber., 91, 2305 (1958) and references cited therein.

(parent), 120 (base). The structure of this compound was therefore assigned as thioanthranilic acid, 1. Storage for 2-3 da. at R. T. deposits a yellow solid, m.p. 130-150,[3] with different ir and nmr. Therefore all transformations of 1 were carried out immediately.

Approach to Benzenediazonium-2-Thiocarboxylate -- A mixture of 1 (.18 m) and Cl_3CCO_2H (.5 g) in THF (250 ml) was added (1 hr) to isoamylnitrite (.3 m) in THF (50 ml) at -4 to +4°. After stirring 6 hr at 0° and 8 hr at R.T., the solvent was vacuum evaporated to 80 ml and diluted with 200 ml of ice-cold ligroin to yield a red-brown solid (raw yield 75%). Purification by sublimation (below 60°, 1 mm) or silica gel chromatography (pet. ether-ether) gave yellow crystals, m.p. 104-105.5°: ir (KBr) 1670(sharp), 1600, 1450, 1265, 1210, 920, 770 cm^{-1}; nmr ($CDCl_3$) τ 2.1-2.9 (m); UV λ_{max} 300 nm; mol. wt. (osmometry) 161 (calc. 164); m.s. m/e = 164 (parent), 136, 108, 104, 76 (base). This data[5] allows the assignment of this structure to be either benzenediazonium-2-thiocarboxylate, 2a, or 4-oxo-3,4-dihydro-3,1,2-benzothiadiazine, 2b. This compound is soluble in benzene, chloroform, and ether and insoluble in water in contrast to benzenediazonium-2-carboxylate. The sharp band at 1670 cm^{-1} and absence of broad $RCOS^-$ adsorption point to 2b as its structure. Apparently 2a forms first and readily ring closes to 2b. Although 2b slowly loses N_2 at about 60° (see below) in no case has a detonation been experienced. These results suggest that it may be possible to diazotize aliphatic amino thioacids to diazoniumthiocarboxylates. Experiments are underway to test this hypothesis.



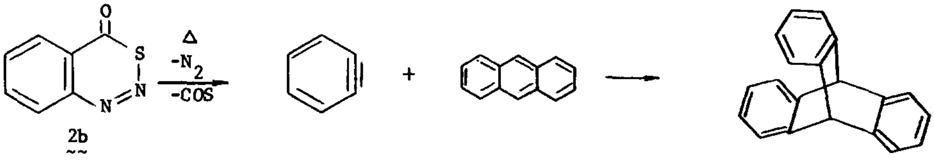
Thermolysis and Photolysis of 2b -- The m.s. data of 2b suggest fragmentation to 2-thiobenzpropiolactone[6] (m/e = 136 and 108) benzocyclopropenone[7] (m/e = 104) and/or benzyne (m/e = 76). Thus thermolytic and photolytic studies of 2b have been initiated. Although incomplete, preliminary data is reported here.

Gas evolution occurred during heating (1 hr) of 2b under N_2 at 166°. Sublimation (.25 mm) of the residue gave two fractions: At 50° (major amount) a mixture of 2b and 3H-1,2 benzodithiol-3-one,[8] 3 was obtained. At 50-170° (minor amount) dithiosalicylide, 4, was obtained.[9] The non-volatile residue (trace) was uncharacterized.

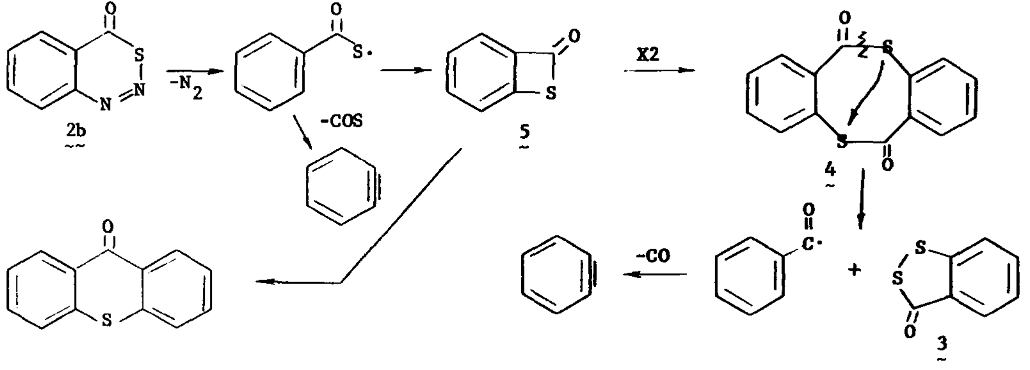
In a second thermolytic experiment a solution of 2b (.01 m) in triglyme (25 ml) was added slowly (1 hr, gas evolution followed each addition) to a solution of anthracene (.01 m) in triglyme (25 ml) held at 200°. Upon workup[10] 3, 4, and triptycene[11] (ca. 20%) were isolated. Work is continuing in this area in order to maximize yields of triptycene.

When 2b (.6 g) is irradiated[‡] in benzene (350 ml) under N_2 in quartz vessels until gas evolution ceases (47 hr), it is necessary to periodically filter the solution and dissolve ($CHCl_3$ first, then dimethylformamide, DMF) an insoluble brown product from the walls of the vessel. The benzene solution was vacuum evaporated and the residue chromatographed on silica gel to yield 3, 4 and thioxanthone.[12] The chloroform solution yielded 4 on workup. The tan solid m.p. 210-215d, filtered from the benzene solution during photolysis and identical with the DMF soluble product has ms parent peak at 272 and ir absorption bands at 1700, 1580, 1465, 1285, 1200, 890, 760, 740, 710, 690 cm^{-1}. The strong bands at 1700, 1200 and 890 cm^{-1} favor RCOS as a structural feature.[13] Efforts to identify this unknown are continuing.

Triptycene formation is most easily rationalized as the reaction of anthracene with benzyne. Current research should delineate the usefulness of 2b as a "benzyne precursor."



All of the other products require carbon-sulfur bond formation. An attractive intermediate which could be invoked in the mechanistic pathway to these products is 2-thiobenzpropiolactone, 5. Dimerization of 5 to 4 has been reported by Chapman and McIntosh.[6] Reaction



of 5 with benzyne is a possible route to thioxanthone. Cleavage of 4 α to the carbonyl followed by sulfur-sulfur bond formation may afford 3 and the elements of benzocyclopropenone (see

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[‡] 9 hr with a 550 watt Hanovia lamp, 38 hr with a circular bank of 16 G.E. G25T8 tubes.

mass spectral data above) or finally, with loss of CO, benzyne. Efforts are now underway using low temperature irradiation and ir scanning of **2b** to detect **5**. Independent synthesis and photolysis/thermolysis of **4** is also being studied.

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1a. A. T. Austin, J. Chem. Soc., 149 (1950). 1b. R. C. Neuman, Jr., J. Org. Chem., **29**, 2096 (1964).

2a. See R. W. Hoffman, "Dehydrobenzene and Cycloalkynes," Academic Press, New York, 1967, p 73f. 2b. F. M. Logullo, A. H. Seitz, and L. Friedman in "Organic Syntheses," V. **48**, P. Yates, Ed., J. Wiley, New York, 1969, p 12f.

3. This compound is reported by R. P. Staiger, G. F. Schlaudecker, and E. B. Miller, U. S. Patent 3,123,631 as having m.p. 130-155°. However, when our product deposits a solid with a m.p. in this range, the physical properties (ir, nmr) are changed. Further this solid does not give derivatives of thioanthranilic acid. Amino thioacids are known to condense to give higher molecular weight solids. (See reference in footnote †.)

4. Anthranilic acid and benzylchloroformate afford N-carbobenzoxyanthranilic acid (Adaptation of the method of H. E. Carter, R. L. Frank, and H. W. Johnson in "Organic Syntheses, Coll. Vol. III," E. C. Horning, Ed., J. Wiley, New York, 1955, p. 168f.) which reacts with thionyl chloride to yield isatoic anhydride (Adaptation of the method of Y. Go and H. Tani, Bull. Chem. Soc. Japan, **14**, 510 (1939).).

5. A satisfactory elemental analysis was obtained.

6. O. L. Chapman and C. L. McIntosh, J. Amer. Chem. Soc., **92**, 7001 (1970).

7. M. S. Ao, E. M. Burgess, A. Schauer, and E. A. Taylor, Chem. Comm., 220 (1969); J. Adamson, D. L. Forster, L. Gilchrist, and C. W. Rees, Chem. Comm., 221 (1969).

8. Separated by silica gel chromatography and shown to be identical with an authentic sample. S. Smiles and E. W. McClelland, J. Chem. Soc., **121**, 86 (1922).

9. Identical with an authentic sample. W. Baker, A. S. El-Nawawy and W. D. Ollis, J. Chem. Soc., 3163 (1952).

10. Following the method of F. M. Beringer and S. J. Huang, J. Org. Chem., **29**, 445 (1964).

11. Identical with properties reported.[10]

12. Identical in m.p. and spectral properties with that reported in the literature: ir, T. L. Brown, Spectrochim. Acta, **18**, 1065 (1962); nmr, R. H. Martin, N. Defoy, F. Geerts-Evrard, P. H. Givens, J. R. Jones and R. W. Wedel, Tetrahedron, **21**, 1833 (1965).

13. R. A. Nyquist and W. J. Potts, Spectrochim. Acta, **15**, 514 (1959).