stance, which is related to fungi metabolites, could have been produced by the action of microorganisms. The problem of the nature of the original bitter principles of carrots, and in particular, of carrot seeds, remained open[4] until the isolation of the bitter crystalline "Gazarin" from the seeds of *D. carota* var. *boissieri* Schweinf. was reported.[5] This new compound melted at 113° and was assigned the molecular formula $C_{15}H_{18}O_6$. Its structure was not elucidated.

We have now isolated "Gazarin" by the published method[6] and proved its identity with 2,4,5-trimethoxybenzaldehyde (asaronaldehyde), already known as a natural constituent of the essential oil of *Asarum europaeum* L.[7,8]

Molecular weight determination (isopiestic method) and analysis, including methoxyl determination, made us revise the formula of "Gazarin" to $C_{10}H_{12}O_4$ or $C_7H_3O(OCH_3)_3$. The infrared spectrum suggested an aromatic carbonyl compound $C_6H_2(OCH_3)_3CHO$. The nuclear magnetic resonance spectrum[9] revealed three adjacent singlet peaks with τ-values: 6.20, 6.15, and 6.09 p.p.m. of equal area and in the correct region for methoxyl aromatic), two singlet peaks with τ-values: 3.57 and 2.78 p.p.m. (indicative of two non-adjacent protons on the benzene ring), and one peak with $\tau = -0.18$ p.p.m. (indicative of aldehyde). This pattern was closely parallel to that shown by anisaldehyde, 3,4-dimethoxybenzaldehyde, and 5,7-dimethoxy-6-formyl-2-methylchromone. The fact that the ring protons could not be adjacent and that the compound was not symmetrical restricted the choice to only two possibilities: 2,4,5- and 2,3,5-trimethoxybenzaldehydes. The latter melts at 71°[10], and therefore, "Gazarin" is 2,4,5-trimethoxybenzaldehyde (reported m.p., 114°[7]). Further confirmation was afforded by the identity of the melting points of two simple carbonyl derivatives of these two substances.

Experimental

Crushed seeds of *D. carota* L. var. *boissieri* Schweinf. were extracted by the method of D. Y. Haddad, *et al.*,[5] to give the natural product as colorless crystals, m.p. 113–114° (uncor.), soluble in hot water, and cold ethanol, ether, chloroform, and benzene. It gave a violet-blue spot (under ultraviolet light) of R_f 0.62 when chromatographed on Whatman No. 1 paper (temp., 27°, water used as eluent, ascending technique). Characteristic infrared bands were found at 6.01, 6.19, and 11.63 mμ. *p*-Nitrophenylhydrazone, m.p. 233–234° (reported m.p.: 234°[7]); semicarbazone, m.p. 209–210° (reported m.p. 208°[11]).

Anal. Calcd. for $C_{10}H_{12}O_4$: C, 61.21; H, 6.17; three OCH_3, 47.49; mol. wt., 196.20. Found: C, 61.52; H, 6.30; OCH_3, 45.33. mol. wt., 198 (modified isopiestic method with a Mechrolab Model 301 thermoelectric osmometer).

Acknowledgment.—The author is indebted to Dr. Jerry P. Heeschen for helpful advice.

(4) Comp. F. Korte, H. Barkemeyer, and I. Korte, *Fortschr. Chem. Org. Naturstoffe*, **17**, 124 (1959).

(5) D. Y. Haddad, S. M. Khafagy, and N. Nazmi, *Egypt. Pharm. Bull., Sci. Ed.*, **40**, 81 (1958).

(6) As extraction involved use of hot water, the possibility that 2,4,5-trimethoxybenzaldehyde exists in the intact seed as an easily hydrolysable complex with some other substances is not excluded.

(7) J. V. Alphen, *Rec. trav. chim.*, **46**, 195 (1927).

(8) I. Gerö, *Chem. Folyoirat.* **34**, 103, 115 (1928); *Chem. Abstr.*, **23**, 4943.

(9) N.m.r. spectra were recorded in deuterochloroform using tetramethylsilane as internal reference at +10 p.p.m. with a Varian Associates Model A-60 analytical n.m.r. spectrometer.

(10) L. E. Smith and F. B. LaForge, *J. Am. Chem. Soc.*, **53**, 3072 (1931).

(11) Y. Asahina and T. Tsukamoto, *J. Pharm. Soc. Japan*, **528**, 98 (1926).

Structure of the Alleged Diels–Alder Adduct from 2,3-Dimethylquinoxaline and Quinone[1]

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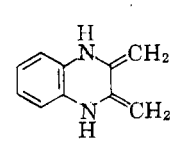
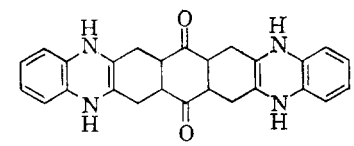
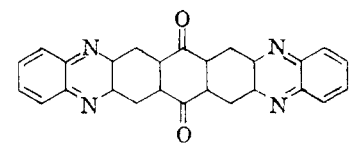
In discussions of quinoxalines, reference[2] is frequently made to the "Diels–Alder" reaction of 2,3-dimethylquinoxaline and *p*-benzoquinone in which the former compound is thought to react in its tautomeric form I. Schönberg and Mustafa,[3] who first reported this reaction, proposed structures II or III for the product on the basis of the finding that quinoxalines not capable of forming a diene system do not undergo this reaction. It



I



II

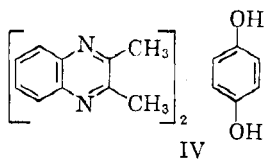


III

appeared to us that the dihydroquinoxaline systems present in either structure should be exceedingly sensitive towards air oxidation (which is apparently not the case) and that the structure of the "adduct" was therefore suspect. We have found that this alleged "Diels–Alder" product is in fact a complex

(1) This investigation was supported by a grant (CY-2551) to Princeton University from the National Cancer Institute, National Institutes of Health, Public Health Service.

(2) (a) E. H. Rodd, ed., "Chemistry of Carbon Compounds," Vol. IVB, Elsevier Publishing Co., Amsterdam, 1959, p. 1349; (b) J. C. E. Simpson, "The Chemistry of Heterocyclic Compounds: Condensed Pyridazine and Pyrazine Rings," Interscience Publishers, Inc., New York, 1953, p. 278; (c) R. C. Elderfield, ed., "Heterocyclic Compounds," Vol. VI, John Wiley and Sons, Inc., New York, 1957, p. 480.



IV

(IV) of two moles of dimethylquinoxaline and one mole of hydroquinone.

The "adduct," prepared according to the reported procedure,[3] had the correct melting point and could be sublimed. Treatment with potassium permanganate at room temperature led to the isolation of 2,3-dimethylquinoxaline, and treatment with acetic anhydride in the presence of either pyridine or sulfuric acid gave the diacetate of hydroquinone, as well as 2,3-dimethylquinoxaline. When the compound was shaken with chloroform and aqueous dilute potassium hydroxide, 2,3-dimethylquinoxaline was obtained from the organic layer, and after acidification of the aqueous layer, hydroquinone was obtained by ether extraction.

These several facile reactions, coupled with the chemical analysis of $C_{26}H_{26}N_4O_2$ and the infrared spectrum, which lacked carbonyl absorption but showed many bands in the region 3.2–4.3 μ, indicated that the "adduct" is, in fact, a complex of two moles of 2,3-dimethylquinoxaline and one mole of hydroquinone. When ethereal solutions of these two compounds are mixed, there is formed an immediate precipitate of a compound identical in all respects to that obtained from 2,3-dimethylquinoxaline and *p*-benzoquinone.

Since the ultraviolet spectrum of IV in ethanol is the same as (a) the sum of the spectra of 2 *M* 2,3-dimethylquinoxaline and 1 *M* hydroquinone solutions, and (b) the spectrum of a 2:1 *M* solution of the two components, but different from the sum of the spectra of the anion of hydroquinone and the cation of 2,3-dimethylquinoxaline, proton transfer cannot have taken place to any appreciable extent in the complex in solution. Such salt formation is also precluded on theoretical grounds, because quinoxaline hydrochloride[4] is a much stronger acid than hydroquinone.[5] The band positions in the infrared spectrum of IV in Nujol mull are remarkably similar to those of hydroquinone and 2,3-dimethylquinoxaline, but differ appreciably from those observed for 2,3-dimethylquinoxaline hydrochloride, so that even in the solid state a true salt has not been formed in IV.

Hydroquinone and other phenolic compounds are known to form complexes with many substances, among which amines are perhaps the most numerous.[6] In at least one other instance the hydroquinone complexes have been obtained when *p*-benzoquinone was heated with the amines.[7] The source of the hydroquinone in the present case is not known. Although *p*-benzoquinone can give rise to hydroquinone under various conditions,[8] it was recovered unchanged when treated under the conditions of complex formation but in the absence of 2,3-dimethylquinoxaline. The hydroquinone is therefore most probably formed by reduction of *p*-benzoquinone by 2,3-dimethylquinoxaline.

It is not surprising that Schönberg and Mustafa did not obtain a product from 2,3-diphenylquinoxaline and *p*-benzoquinone, for no complex could be obtained from hydroquinone in either alcohol or ether. Furthermore, it is difficult to conceive of 2,3-diphenylquinoxaline functioning as a reducing agent. 2-Methylquinoxaline, however, gave a 2:1 complex with hydroquinone which, in contrast to the complex formed from 2,3-dimethylquinoxaline, decomposed into its components upon attempted sublimation. 2,3-Dimethylquinoxaline also gave 1:1 complexes with resorcinol and catechol upon mixing ethereal solutions of the two components. The pure resorcinol complex could not be reisolated from an ethanol solution, and the complexes of hydroquinone with 2-methyl- and 2,3-dimethylquinoxaline were decomposed by chloroform.

Experimental[9]

2,3-Dimethylquinoxaline–Hydroquinone Complex (the Alleged Diels–Alder Adduct) (IV). Method A.—The following procedure is essentially that of Schönberg and Mustafa.[3] A mixture of 8.0 g. (51 mmoles) of 2,3-dimethylquinoxaline, 5.5 g. (52 mmoles) of freshly sublimed *p*-benzoquinone, and 50 ml. of toluene was heated under reflux for 2.5 hr. It was then cooled and filtered to give 4.5 g. of very dark product. The compound was purified to a brown solid by crystallization from ethanol, using large amounts of decolorizing charcoal. Sublimation at 130°/0.03 mm. afforded faintly yellow sturdy crystals, m.p. 189–190° (lit.[3] m.p. 190°). When the sublimed compound was recrystallized from chloroform, the melting point dropped to 150–190°. After recrystallization from toluene or ethanol, it melted at 188–190°.

Anal. Calcd. for $C_{26}H_{26}N_4O_2$: C, 73.21; H, 6.14; N, 13.14. Found: C, 73.22; H, 6.14; N, 13.18.

Its infrared spectrum showed a series of bands of decreasing intensity at 3.2 (broad), 3.70, 3.86, 4.05, and 4.25 μ as well as bands at 6.61, 6.70 μ and others. Its ultraviolet spectrum showed λ_{max}^{EtOH} 236 mμ (ϵ 47,800), 240 mμ (infl.) (ϵ 39,300), 298 mμ (infl.)(ϵ 11,200), 305 mμ (ϵ 12,500), 316 mμ (infl.) (ϵ 13,300), and 323 mμ (infl.) (ϵ 10,300).

Method B.—When a saturated ethereal solution of 1.1 g. (10 mmoles) of hydroquinone was added to an ethereal solution of 3.2 g. (20 mmoles) of 2,3-dimethylquinoxaline,

(3) A. Schönberg and A. Mustafa, *J. Chem. Soc.*, 654 (1943).

(4) The pK_a of quinoxaline is *ca.* 0.8 (A. Albert, R. Goldacre, and J. Phillips, *ibid.*, 2240 (1948).

(5) The pK_a of hydroquinone is 9.8 (J. D. Baxendale and H. R. Hardy, *Trans. Faraday Soc.*, **49**, 1140 (1953).

(6) *Cf.*, for example (a) C. H. Giles, T. J. Rose, and P. G. M. Vallance, *J. Chem. Soc.*, 3799 (1952); (b) J. T. Edward and R. Robinson, *ibid.*, 1080 (1952); (c) A. Baeyer and V. Villiger, *Ber.*, **35**, 1201 (1902).

(7) (a) F. Bell, *J. Chem. Soc.*, 348 (1953); (b) J. F. Cavalla, *ibid.*, 4701 (1954); (c) A. A. Bothner-By, *J. Am. Chem. Soc.*, **77**, 749 (1955).

(8) (a) B. Scheid, *Ann.*, **218**, 195 (1883); (b) O. Hesse, *ibid.*, **220**, 365 (1883); (c) W. N. Hartley and A. G. G. Leonard, *J. Chem. Soc.*, **95**, 34 (1909).

(9) All melting points are uncorrected. Microanalyses were performed by the Scandinavian Microanalytical Laboratory, Box 25, Herlev, Denmark.

colorless needles separated at once; yield, 4.0 g. (93%). Sublimation *in vacuo* gave faintly yellow, sturdy crystals, m.p. 189–190°. A mixture melting point determination with the material prepared by method A showed no depression, and infrared spectra were identical.

Treatment of the Complex (IV) with Acetic Anhydride.—A mixture of 1.1 g. of IV, 8 ml. of acetic anhydride, and 10 ml. of pyridine was heated on a steam bath for 40 min. and then evaporated to dryness under reduced pressure. Treatment of the crystalline residue with about 60 ml. of pentane and filtration gave a solid which was recrystallized from carbon tetrachloride to yield 0.46 g. (60%) of long needles, m.p. 115–120°. Sublimation raised the melting point to 118–120°. Diacetylhydroquinone is reported to melt at 123°.[10]

The infrared spectrum of the sublimed material [Nujol mull, principal bands at 5.49 (w), 5.67 (s), 5.80 (sh), and 6.66 μ] was identical with the spectrum of an authentic sample of hydroquinone diacetate.

The pentane filtrate was concentrated to a small volume, cooled, and filtered to give a solid (m.p. 91–104°) which was sublimed *in vacuo* to give 0.45 g. (70%) of 2,3-dimethylquinoxaline, m.p. 103–104° (lit.,[11] m.p. 106°). Its infrared spectrum was identical with the spectrum of an authentic sample of 2,3-dimethylquinoxaline.

Treatment of the Complex (IV) with Potassium Permanganate.—To a stirred mixture of the complex in aqueous acetone was added solid potassium permanganate until the purple color just persisted. The manganese dioxide was removed by filtration and rinsed with water followed by acetone, and the filtrate was extracted twice with ether. The ether extracts were dried over anhydrous sodium sulfate and evaporated to a small volume, whereupon long colorless needles, m.p. 103–104°, separated. A mixture melting point determination with authentic 2,3-dimethylquinoxaline showed no depression, and infrared spectra were identical.

Decomposition of the Complex (IV) with Base.—A mixture of 0.30 g. of IV in 20 ml. of 10% aqueous potassium hydroxide was extracted three times with chloroform, the chloroform extracts dried over anhydrous sodium sulfate and evaporated to give 0.23 g. of a colorless residue, m.p. 98–104°. Vacuum sublimation gave pure 2,3-dimethylquinoxaline, m.p. 103–105°, identical with an authentic sample. The aqueous basic layer was acidified with 2 *N* sulfuric acid and extracted three times with ether. The combined extracts were dried and evaporated to give 0.08 g. of a solid, m.p. 145–165°. Sublimation followed by crystallization from a mixture of carbon tetrachloride and ethanol gave hydroquinone, m.p. 171–172° (lit.[10] m.p. 169°). A mixture melting point determination with an authentic sample showed no depression, and infrared spectra were identical.

2-Methylquinoxaline–Hydroquinone Complex.—Mixing ethereal solutions of one equivalent of hydroquinone and two equivalents of 2-methylquinoxaline resulted in the separation of a pale yellow solid which was collected by filtration and recrystallized three times from ethanol. The complex melted at 137–138°.

Anal. Calcd. for $C_{24}H_{22}N_4O_2$: C, 72.34; H, 5.57; N, 14.06. Found: C, 72.07; H, 5.67; N, 13.91.

Two recrystallizations from chloroform yielded hydroquinone, m.p. 170–171°.

Resorcinol–2,3-Dimethylquinoxaline Complex.—An ethereal solution of 2.2 g. (20 mmoles) of resorcinol was added to an ethereal solution of 1.58 g. (10 mmoles) of 2,3-dimethylquinoxaline, and the precipitate which separated was collected by filtration; yield, 2.6 g., (95%), m.p. 179–182°. After three recrystallizations from benzene it melted at 180–182°.

Anal. Calcd. for $C_{16}H_{16}N_2O_2$: C, 71.62; H, 6.01; N, 10.44. Found: C, 71.78; H, 6.12; N, 10.63.

The material could be sublimed unchanged, but after recrystallization from ethanol it melted at 165–180°.

Catechol–2,3-Dimethylquinoxaline Complex.—Mixing ethereal solutions of equivalent amounts of catechol and 2,3-dimethylquinoxaline resulted in the immediate separation of long needles which, upon recrystallization from benzene, melted at 148–150°.

Anal. Calcd. for $C_{16}H_{16}N_2O_2$: C, 71.62; H, 6.01; N, 10.44. Found: C, 71.81; H, 6.02; N, 10.36.

(10) R. L. Shriner, R. C. Fuson, and D. Y. Curtin, "The Systematic Identification of Organic Compounds," 4th ed., John Wiley and Sons, Inc., New York, 1956, p. 326.

(11) Ref. 2b, p. 277.

Tris(thiocyclopropanone)

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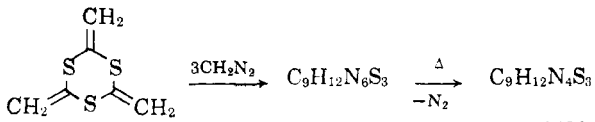
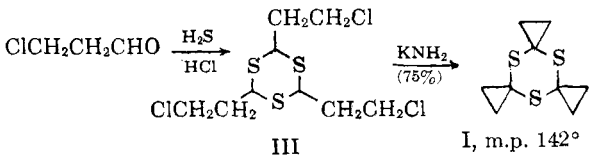
It seemed of some interest to us to prepare 2,4,6-tris(chloromethyl)-*s*-trithiane, an analog of sulfur mustard, bis(2-chloroethyl) sulfide, to investigate the possible properties of it and related compounds as potential biological alkylating agents. While our work was in progress, a number of these compounds were reported by Matlack, Chien, and Breslow.[2] We wish to report here principally on the successful synthesis of tris(thiocyclopropanone).

The first efforts in this direction involved the treatment of tris(methylene)-*s*-trithiane[2] with diazomethane.



II

In view of the reluctance of these products to eliminate nitrogen, the cyclization of tris(2-chloroethyl)-*s*-trithiane[2] by potassium amide in liquid ammonia was investigated and proved successful.



III I, m.p. 142°

Matlack, Chien, and Breslow[2] had reported that treatment of III with potassium *t*-butoxide in *t*-butyl alcohol gave a liquid identified by them as the ethylidene isomer of I. The structure of I was proven most conclusively by the n.m.r. spectrum

(1) Supported in part by U.S.P.H.S. Grant No. CY-2189. Abstracted in part from the doctoral dissertation of Jacqueline S. Vittimberga, June, 1961.

(2) A. S. Matlack, J. C. W. Chien, and D. S. Breslow, *J. Org. Chem.*, **26**, 1455 (1961).

(3) Th. J. DeBaer and H. J. Backer, *Rec. trav. chim.*, **73**, 229 (1954).