benzene and about 9 for 1,2,4- and 1,3,5-triisopropenylbenzene. Using the $TiCl_4$–$Al(C_2H_5)_3$ catalyst, larger quantities of the symmetrical isomer have always been obtained, the ratio 1,3,5/1,2,4 being about 1.3 (when the total yield was at maximum).

The most important advantage offered by the $(Ph_3P)_2NiCl_2$–$NaBH_4$ system is the greater stability toward moisture and oxygen. Polymerization reactions carried out in nonanhydrous solvents and in air gave only slightly lower yields of aromatic products. Analogous conclusions were drawn by Luttinger and Colthup[3] from observations on similar catalytic systems.

Studies are continuing in order to find new more active catalysts and to define the mechanisms of the cyclization reactions.

Acknowledgment.—We are indebted to Professor G. Sartori for helpful discussions and to the Shell International Research Mij.N.V. for financial support of this work.

Preparation of 2,5-Bis(alkylamino)-3,6-dimethoxy-*p*-benzoquinones

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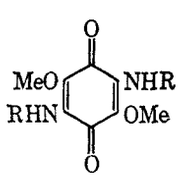
Reaction of tetramethoxyquinone[1] with primary amines yielded 2,5-bis(alkylamino)-3,6-dimethoxy-*p*-benzoquinones (1). Table I lists new quinones pre-



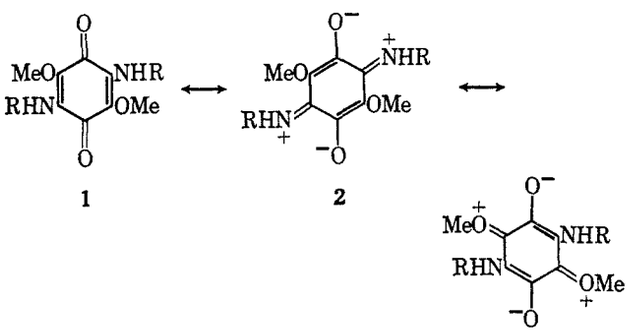
1

pared in this manner. Nonbasic amines such as *p*-nitroaniline, *o*-chloroaniline, and 2-bromo-4-methylaniline failed to react with tetramethoxyquinone. Sterically hindered amines did not react normally under the reaction conditions. For example, *t*-butylamine reacted with tetramethoxyquinone in aqueous solution to yield 2,5-dihydroxy-3,6-dimethoxy-*p*-benzoquinone as the main product. This behavior suggests that, in this case, hydroxide acts as a better nucleophile than the sterically hindered *t*-butylamine. Reaction under anhydrous conditions, however, yielded 2,5-bis(*t*-butylamino)-3,6-dimethoxy-*p*-benzoquinone.

The 2,5-bis(alkylamino)-3,6-dimethoxy-*p*-benzoquinones underwent amine exchange. For example, 2,5-bis(isopropylamino)-3,6-dimethoxy-*p*-benzoquinone (1, R = isopropyl) reacted with octylamine to yield 2,5-bis(octylamino)-3,6-dimethoxy-*p*-benzoquinone (1, R = octyl). In a similar manner, hexylamine displaced ethylamine from 2,5-bis(ethylamino)-3,6-dimethoxy-*p*-benzoquinone. The preferential displacement of an amino group over a methoxy group in this amine exchange reaction deserves some comment.

(1) B. Eistert and G. Bock, *Ber.*, **92**, 1239 (1959).

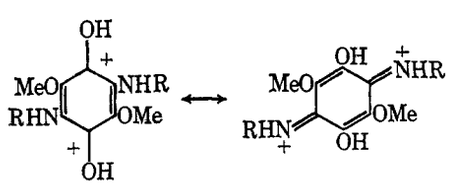
These quinones contain both vinylogous amide and vinylogous ester groupings. Since esters react with nucleophiles more readily than amides,[2] one might predict that reaction of 2,5-bis(alkylamino)-3,6-dimethoxy-*p*-benzoquinones with amines would yield 2,3,5,6-tetrakis(alkylamino)-*p*-benzoquinones, rather than yield quinones formed by amine exchange. Consideration of the resonance forms of 2,5-bis(alkylamino)-3,6-dimethoxy-*p*-benzoquinone offers an explanation of this paradox. Canonical form 2 would be expected



1 2 3

to contribute more to the structure of 2,5-bis(alkylamino)-3,6-dimethoxy-*p*-benzoquinone than canonical form 3, since from electronegativity considerations[3] nitrogen bears a positive charge more readily than oxygen. Because of this, positions 2 and 5 would suffer nucleophilic attack more readily than positions 3 and 6.

A related reaction occurred in acid solution. Reflux of 2,5-bis(isopropylamino)-3,6-dimethoxy-*p*-benzoquinone with 2 *N* hydrochloric acid yielded 2,5-dihydroxy-3,6-dimethoxy-*p*-benzoquinone instead of 2,5-bis(isopropylamino)-3,6-dihydroxy-*p*-benzoquinone. A similar rationale applies here. Acid-catalyzed attack of water probably occurs on resonance hybrid 4 in which positions 2 and 5 are most prone to nucleophilic attack.



4

An earlier report states that alkoxide displaces only two chlorines from chloranil.[4] Although treatment of chloranil with sodium methoxide in methanol at reflux did indeed yield 2,5-dichloro-3,6-dimethoxy-*p*-benzoquinone, heating the reactants in an autoclave yielded tetramethoxyquinone. Thus, all four chlorines of chloranil can be displaced by methoxide under forcing conditions. This procedure offers advantages over the literature procedure for the preparation of tetramethoxyquinone, methylation of tetrahydroxyquinone with diazomethane.[1]

A report of conversion of tetramethoxyquinone to 2,5-dihydroxy-3,6-dimethoxy-*p*-benzoquinone by treatment with sodium hydroxide has recently appeared.[1]

(2) R. C. Fuson, "Reactions of Organic Compounds," John Wiley and Sons, Inc., New York, N. Y., 1962, p 316.

(3) L. N. Ferguson, "The Modern Structural Theory of Organic Chemistry," Prentice-Hall, Inc., Englewoods Cliffs, N. J., 1963, p 314.

(4) K. Wallenfels and K. Friedrich, *Ber.*, **93**, 3070 (1960).

TABLE I. 2,5-BIS(ALKYLAMINO)-3,6-DIMETHOXY-*p*-BENZOQUINONES (1)

Amine	R	Mp, °C	Formula	Calcd, % C	Calcd, % H	Found, % C	Found, % H	Yield, %
Ethyl-	CH_3CH_2–	162	$C_{12}H_{18}N_2O_4$	56.7	7.1	56.8	7.1	90
Propyl-	$CH_3CH_2CH_2$–	161	$C_{14}H_{22}N_2O_4$	59.6	7.8	59.6	8.1	79
Isopropyl-	$(CH_3)_2CH$–	205	$C_{14}H_{22}N_2O_4$	59.6	7.8	59.8	7.9	74
Butyl-	$CH_3(CH_2)_3$–	113	$C_{16}H_{26}N_2O_4$	61.9	8.4	62.0	8.7	95
Isobutyl-	$(CH_3)_2CHCH_2$–	148	$C_{16}H_{26}N_2O_4$	61.9	8.4	62.1	8.3	89
sec-Butyl-	$CH_3CH_2CH(CH_3)$–	145	$C_{16}H_{26}N_2O_4$	61.9	8.4	61.9	8.6	61
t-Butyl-	$(CH_3)_3C$–	182	$C_{16}H_{26}N_2O_4$	61.9	8.4	61.9	8.3	91
Pentyl-	$CH_3(CH_2)_4$–	118	$C_{18}H_{30}N_2O_4$	63.9	8.9	63.6	8.8	90
Hexyl-	$CH_3(CH_2)_5$–	108	$C_{20}H_{34}N_2O_4$	65.5	9.3	65.7	9.6	88
Octyl-	$CH_3(CH_2)_7$–	86	$C_{24}H_{42}N_2O_4$	68.2	10.0	68.1	10.2	87
2,4-Dimethylaniline	$2,4\text{-}(CH_3)_2C_6H_3$–	245	$C_{24}H_{26}N_2O_4$	70.9	6.4	70.8	6.6	67
p-Methoxyaniline	$4\text{-}CH_3OC_6H_4$–	229	$C_{22}H_{22}N_2O_6$	64.4	5.4	64.5	5.5	98
p-Toluidine	$4\text{-}CH_3C_6H_4$–	277	$C_{22}H_{22}N_2O_4$	69.8	5.9	69.6	6.1	97

Tetramethoxyquinone also suffered cleavage to 2,5-dihydroxy-3,6-dimethoxy-*p*-benzoquinone under mild acid treatment.

Grateful acknowledgment is given to the Michigan Cancer Foundation for partial support of this research. Preliminary results indicate some aminoquinones of structure **1** show activity against Sarcoma 180.

Experimental Section

Melting points were determined on a Kofler micro hot stage and are corrected. The infrared spectra were obtained in Nujol mulls on a Perkin-Elmer Infracord, Model 137.

The procedure for the preparation of 2,5-bis(pentylamino)-3,6-dimethoxy-*p*-benzoquinone illustrates the general preparation of 2,5-bis(alkylamino)-3,6-dimethoxy-*p*-benzoquinones with the exception of 2,5-bis(*t*-butylamino)-3,6-dimethoxy-*p*-benzoquinone (*vide infra*) and of the last three quinones listed in Table I. These three quinones were prepared in methanol (30 ml of methanol/g of tetramethoxyquinone) with a reflux time of 24 hr. Table I lists the yields obtained under these conditions.

2,5-Bis(pentylamino)-3,6-dimethoxy-*p*-benzoquinone.—Tetramethoxyquinone (920 mg), pentylamine (5 ml), and water (3 ml) were warmed at 75° for 2 min. When the mixture was let stand overnight, crystals of 2,5-bis(pentylamino)-3,6-dimethoxy-*p*-benzoquinone separated, 1.23 g (90%), which crystallized from ethanol as blue-black needles. For physical data, see Table I.

Reaction of Tetramethoxyquinone and *t*-Butylamine in Aqueous Solution.—Tetramethoxyquinone (272 mg) was refluxed in a nitrogen atmosphere with 4 ml of *t*-butylamine and 4 ml of water. After the reaction was heated for 4 hr, solvent was stripped, 10 ml of water was added, and the aqueous solution was extracted with ether. Acidification of the aqueous layer yielded a red solution from which 83 mg (30%) of 2,5-dihydroxy-3,6-dimethoxy-*p*-benzoquinone, mp 236°, lit.[1] mp 236°, separated on concentration. The ether layer was extracted with several portions of 6 *N* hydrochloric acid. Neutralization of the acid extracts yielded 30 mg (8%) of 2,5-bis(*t*-butylamino)-3,6-dimethoxy-*p*-benzoquinone, mp 182°. Both 2,5-dihydroxy-3,6-dimethoxy-*p*-benzoquinone and 2,5-bis(*t*-butylamino)-3,6-dimethoxy-*p*-benzoquinone were identified with authentic samples (*vide infra*) by mixture melting point determination and comparison of the infrared spectra.

2,5-Bis(*t*-butylamino)-3,6-dimethoxy-*p*-benzoquinone.—Tetramethoxyquinone (187 mg) was refluxed for 40 hr with 10 ml of *t*-butylamine. When the mixture was let stand overnight, crystals of 2,5-bis(*t*-butylamino)-3,6-dimethoxy-*p*-benzoquinone separated, 231 mg (91%), which were purified by crystallization from ethanol.

Tetramethoxyquinone.—A slurry of 24.6 g (0.1 mole) of chloranil in 50 ml of methanol was added to a solution of 9.2 g (0.4 mole) of sodium in 200 ml of methanol. During addition the temperature was kept at 30° by means of an ice bath. The resulting mixture was autoclaved at 85° for 6 hr. The cooled reaction mixture deposited bright orange crystals which were collected and dissolved in methylene chloride. This solution was treated with charcoal and filtered, and the filtrate was evaporated to dryness. The residue crystallized from methanol to give 13.5 g (57%) of bright orange crystals, mp 135°, lit.[1] mp 135–136°. These were identified as tetramethoxyquinone by mixture melting point determination and comparison of infrared spectra with that of an authentic sample.[1]

2,5-Dihydroxy-3,6-dimethoxy-*p*-benzoquinone.—Tetramethoxyquinone (367 mg) was refluxed in a nitrogen atmosphere with 10 ml of 2 *N* hydrochloric acid for 1 hr. When the reaction mixture was cooled, black crystals separated, 249 mg (77%), mp 236°, lit.[1] mp 236°. These were identified as 2,5-dihydroxy-3,6-dimethoxy-*p*-benzoquinone by mixture melting point determination and comparison of infrared spectra with that of an authentic sample.[1]

Amine Exchange Reaction.—The following procedure illustrates the amine exchange reaction. A solution of 199 mg of 2,5-bis(isopropylamino)-3,6-dimethoxy-*p*-benzoquinone in 2 ml of octylamine and 3 ml of water was refluxed for 1 hr. When the reaction mixture was cooled, crystals separated, which were filtered and washed with dilute acetic acid and then with water. The 2,5-bis(octylamino)-3,6-dimethoxy-*p*-benzoquinone thus obtained, 260 mg (87%), proved to be identical with an authentic sample prepared from tetramethoxyquinone.

7-Hydroxy-11,12-dimethoxycoumestan. Characterization and Synthesis

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A new compound, $C_{17}H_{12}O_6$, isolated from alfalfa has been characterized. Analysis of the compound, its acetate, and methyl ether indicated that it was a dimethoxy derivative, containing one hydroxyl group. Its methyl ether was identical with authentic 7,11,12-trimethoxycoumestan.[2] Since λ_{max} 346 mμ in ethanol underwent a bathochromic shift in the presence of sodium acetate to 367 mμ, the hydroxyl group must be located at the 7-position.[3] Thus, the structure of the new compound is 7-hydroxy-11,12-dimethoxycoumestan, closely related to medicagol.[2]

This structure assignment was confirmed by its synthesis from 7,11,12-trihydroxycoumestan (Ia) in the following manner. The 11,12-positions of Ia were first blocked by the formation of the diphenylmethylenedioxy derivative IIa. Benzoylation to IIb, followed by acid hydrolysis, regenerated the 11,12-

(1) A laboratory of the Western Utilization Research and Development Division, Agricultural Research Service, U. S. Department of Agriculture.

(2) A. L. Livingston, S. C. Witt, R. L. Lundin, and E. M. Bickoff, *J. Org. Chem.*, **30**, 2353 (1965).

(3) L. Jurd, *ibid.*, **24**, 1786 (1959).