[CONTRIBUTION FROM THE SCHOOL OF CHEMISTRY OF THE UNIVERSITY OF MINNESOTA]

Heterocyclic Vinyl Ethers. XVII. Benzo-1,4-oxathiadiene-2-aldehyde, 2-Methylbenzo-1,4-oxathiadiene and 3-Methylbenzo-1,4-oxathiadiene[1]

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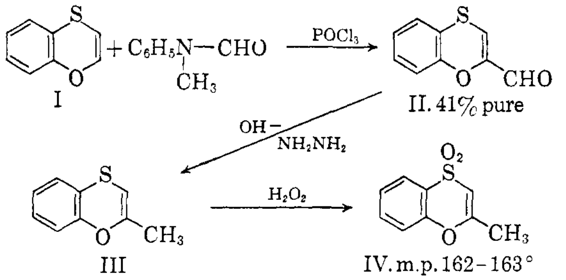
The electrophilic formylation of benzo-1,4-oxathiadiene (I) has been shown to give benzo-1,4-oxathiadiene-2-aldehyde (II). This orientation of substitution is somewhat anomalous in view of known electrical effects of oxygen and sulfur. The synthesis of 2-methyl- and 3-methylbenzo-1,4-oxathiadiene, as well as derivatives of these new heterocycles, is described.

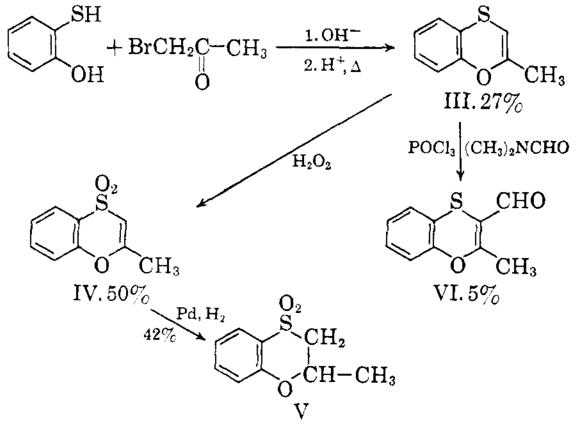
We have now examined the structure of the aldehyde, obtained[3] by reaction of benzo-1,4-oxathiadiene (I) with *N*-methylformanilide or *N*,*N*-dimethylformamide and phosphorus oxychloride (the Vilsmeyer Reaction), and have established the structure benzo-1,4-oxathiadiene-2-aldehyde (II) for this product.

Reduction of the aldehyde II with hydrazine and alkali (Wolff-Kishner) afforded an oil (22% calculated as III), which was characterized by conversion into the solid sulfone IV by oxidation. This sulfone was subsequently shown to be identical with an authentic sample of 2-methylbenzo-1,4-oxathiadiene sulfone.

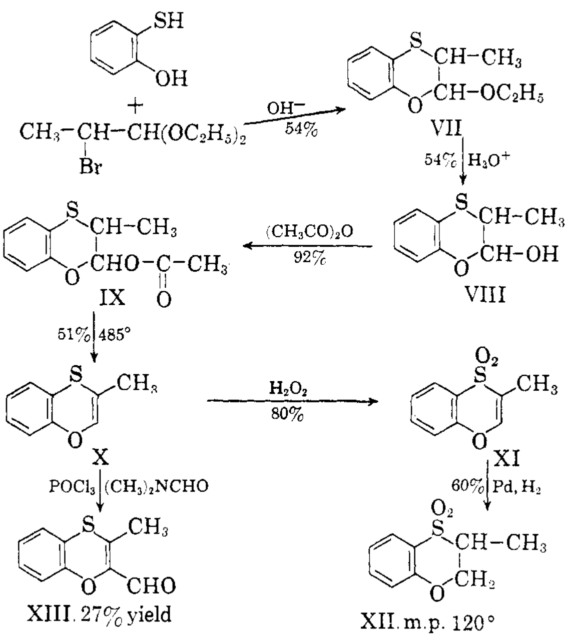


The independent synthesis of 2-methylbenzo-1,4-oxathiadiene (III), the sulfone IV, 3-methylbenzo-1,4-oxathiadiene (X), as well as other derivatives of these new heterocyclics is summarized in the following equations.

2-Methylbenzo-1,4-oxathiadiene (III)



3-Methylbenzo-1,4-oxathiadiene (X)



The structures of the aldehydes VI and XIII were not established; however, the preferential formylation of benzo-1,4-oxathiadiene (I) in the 2-position (I→II) is considered convincing evidence for the assignment of structure XIII, and is also consistent with the significant difference in yield noted for the formylation of the 2-, and 3-methyl derivatives (5 and 27%, respectively).

The syntheses employed for 2- and 3-methylbenzo-1,4-oxathiadiene (III and X), from monothiocatechol, were not considered unambiguous. Final confirmation of these structures was obtained by the alkaline hydrolysis of XI, together with the reactions summarized in the following equations. The two samples of XV were identical.

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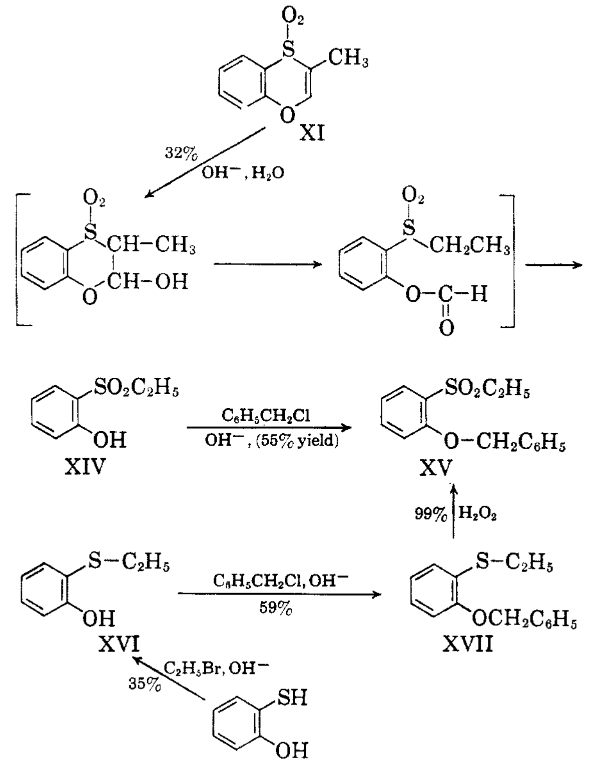
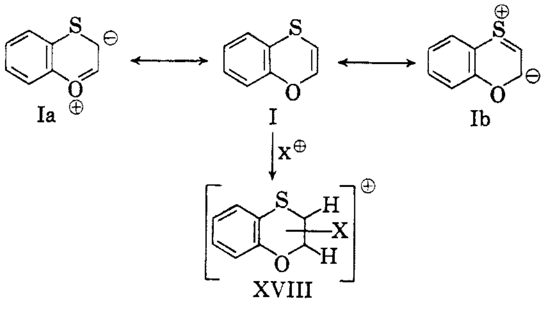
[1] (1) Supported in part by Office of Ordnance Research, U. S. Army, Contract No. DA-11-022-ORD-571.

[2] (2) Sinclair Oil Co. Fellow, 1958–59. From the PhD. Thesis of Gordon L. Willette, The University of Minnesota, 1959.

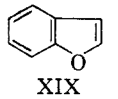
[3] (3) W. E. Parham and John D. Jones, *J. Am. Chem. Soc.*, 76, 1068 (1954).

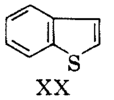


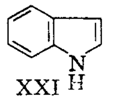
The Vilsmeyer Reaction is an example of an electrophilic substitution reaction.[4] The formation of II from I establishes the fact that simple p-orbital stabilization of the ground state of I (Ia-Ib) or the transition state XVIII, is not sufficient to explain the observed orientation, since it is well established that the oxygen-carbon $2p2p$ π-bond is stronger than the sulfur-carbon $3p2p$ π-bond (*i.e.*, Ia is more important than Ib).



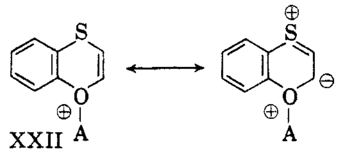
Electrophilic substitution of benzofuran (XIX), benzothiophene (XX), and iodole (XXI) occurs preferentially in the 2-, 3-, and 3- positions, respectively.[5] Although the oxygen-carbon and nitrogen-carbon resonance intergrals are thought to be higher than the sulfur-carbon resonance intergral,[6] resonance in the ground or transition states would seem to predict the same orientation for each of these heterocycles. Substitution of benzo-1,4-oxathiadiene in the 2- position is consistent with the orientation observed for benzofuran and benzothiophene; however, the differences noted are not readily explained.


XIX


XX


XXI

Attention may be called to the fact that the orientation observed for I is consistent with the possibility that the species undergoing substitution is a conjugate acid of I involving the oxygen atom, as shown in XXII.



EXPERIMENTAL

3-Methylbenzo-1,4-oxathiadiene (X) *and derivatives. 2-Ethoxy-3-methylbenzo-1,4-oxathiene* (VII). This reaction was carried out under nitrogen and with vigorous stirring. Diethyl α-bromopropionacetal[7] (162.5 g., 0.770 mol.) was added dropwise to a solution prepared from potassium hydroxide (56.7 g., 0.770 mol.) in absolute ethanol (400 ml.) and monothiocatechol (97.0 g., 0.770 mol.). The resulting mixture was heated at the reflux temperature for 2 hr., then cooled, treated with anhydrous magnesium sulfate (*ca.* 10 g.), and finally filtered. The salts were washed with absolute ethanol, and the combined filtrate and washings were concentrated at reduced pressure. The cooled residue was treated with saturated ethereal hydrogen chloride, and the resulting mixture was allowed to stand, out of contact with air, for 34 hr. The acidic solution was neutralized with sodium carbonate, water was then added, and the organic material was separated with ether. The ether solution was dried over magnesium sulfate and distilled, affording 88 g., 54% yield, of 2-ethoxy-3-methylbenzo-1,4-oxathiene (VII, b.p. 125–130°/2 mm.).

2-Hydroxy-3-methylbenzo-1,4-oxathiene (VIII). A mixture of VII (122 g., 0.576 mol.) and 3% aqueous sulfuric acid (500 ml.) was heated at the reflux temperature for 39 hr., and the resulting mixture was distilled with steam until the distillate was clear. The residue remaining from the steam distillation was cooled (25°), made basic by addition of solid sodium bicarbonate, and was then extracted with ether. The solid obtained from the dried ether extract was recrystallized from methylene chloride–petroleum ether (60–68°), and pure VIII was obtained (56.0 g., 53.5% yield, m.p. 64–64.5°).

Anal. Calcd. for $C_9H_{10}O_2S$: C, 59.32; H, 5.53. Found: C, 58.96; H, 6.03.

2-Acetoxy-3-methylbenzo-1,4-oxathiene (IX). The procedure employed was essentially identical with that previously descirbed for acetylation of 2-hydroxybenzo-1,4-oxathiene.[3] From VIII (56.0 g., 0.308 mol.) there was obtained 63.5 g. (92% yield) of IX (b.p. 105–115°/0.7 mm.).

Anal. Calcd. for $C_{11}H_{12}O_3S$: C, 58.91; H, 5.39. Found: C, 59.14; H, 5.67.

3-Methylbenzo-1,4-oxathiadiene (X). The deacetoxylation of 2-acetoxy-3-methylbenzo-1,4-oxathiene (IX, 10.0 g., 0.045 mol.) in dry benzene was carried out by pyrolysis at

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(4) G. F. Smith, *J. Chem. Soc.*, 3842 (1954).

(5) *Heterocyclic Compounds*, Vol. 2, R. C. Elderfield, editor: Chapter 1, p. 18 by R. C. Elderfield and V. B. Meyer; Chapter 4, p. 147 by D. K. Fukushima; Vol. 3, Chapter 1, by P. L. Julian, E. W. Meyer, and H. C. Printy, John Wiley & Sons, New York, N. Y.

(6) *Cf.* H. H. Jaffe, *J. Chem. Phys.*, **20**, 279 (1950).

(7) A. H. Williams and F. N. Woodward, *J. Chem. Soc.*, 38 (1948).

a temperature of 480–490°, by a procedure essentially identical with that previously described for the deacetoxylation of 2-acetoxybenzo-1,4-oxathiene.[3] 3-Methylbenzo-1,4-oxathiadiene (X, 3.76 g., 51% yield, n_D^{26} 1.5890) was collected at 74–91°/0.75 mm. by distillation. A sample was redistilled for analysis (b.p. 77°/1 mm., $n_D^{26.7}$ 1.5965).

Anal. Calcd. for C_9H_8OS: C, 65.85; H, 4.91. Found: C, 65.62; H, 5.24.

3-Methylbenzo-1,4-oxathiadiene sulfone (XI) was prepared from X (0.73 g., 0.0044 mol.) by oxidation in the usual manner[3] with 30% hydrogen peroxide in hot glacial acetic acid (15 ml.). The crude product (0.7 g., 80% yield, m.p. 107°) was purified by recrystallization from ethanol. Pure XI melted at 115–115.5°.

Anal. Calcd. for $C_9H_8O_3S$: C, 55.10; H, 4.11. Found: C, 55.15; H, 4.22.

3-Methylbenzo-1,4-oxathiene sulfone (XII). A mixture of XI (0.1 g.), absolute ethanol (25 ml.), and palladium black (0.05 g.) was stirred for 3 days in an atmosphere of hydrogen at room temperature. 3-Methylbenzo-1,4-oxathiene sulfone was isolated from the ethanol solution, and was recrystallized from carbon tetrachloride-petroleum ether (60–68°); 0.05 g., 60% yield, m.p. 119–120.5°.

Anal. Calcd. for $C_9H_{10}O_3S$: C, 54.54; H, 5.09. Found: C, 54.40; H, 5.21.

3-Methylbenzo-1,4-oxathiadiene-2-aldehyde (XIII). The procedure employed was essentially identical with that described below for the formylation of 2-methylbenzo-1,4-oxathiadiene. The aldehyde (XIII), obtained from 3-methylbenzo-1,4-oxathiadiene (X, 3.76 g., 0.023 mol.), was purified by isolation as the bisulfite adduct, and by final recrystallization frm petroleum ether (60–68°); 1.1 g., 27% yield, canary-yellow, m.p. 66–68°.

Anal. Calcd. for $C_{10}H_8O_2S$: C, 62.50; H, 4.20. Found: C, 62.44; H, 4.30.

The infrared spectrum of this product showed carbonyl absorption at 1655 cm.$^{-1}$

The 2,4-dinitrophenylhydrazone of 3-methylbenzo-1,4-oxathiadiene-2-aldehyde was prepared in the usual way from a solution of the corresponding bisulfide addition product (0.5 g.) in ethanol (20 ml.). The derivative melted at 243–244° (from nitromethane).

Anal. Calcd. for $C_{16}H_{12}O_5SN_4$: C, 51.62; H, 3.25; N, 15.05. Found: C, 52.38; H, 3.40; N, 14.82.

2-Methylbenzo-1,4-oxathiadiene (III) *and derivatives.* A solution of potassium hydroxide (25.5 g. assaying 85% KOH, 0.395 mol.) in absolute ethanol (200 ml.) was added slowly to monothiocatechol[3] (50 g., 0.395 mol., b.p. 72–76°/3 mm., $n_D^{25.5}$ 1.6072) in an atmosphere of nitrogen. Bromoacetone (54.12 g., 0.395 mol.) was then added dropwise, and the resulting solution was heated at the reflux temperature under nitrogen, and with stirring, for 2 hr. The mixture was then cooled to 25°, anhydrous magnesium sulfate (5 g.) was added, and the resulting mixture was filtered. The precipitate was washed with absolute ethanol, and the combined filtrate and ethanol washings was concentrated at reduced pressure. The residue was cooled (25°), and saturated ethereal hydrogen chloride (30 ml.) was added. The acidic solution was allowed to stand (out of contact with air) for 24 hr., and was then neutralized with solid sodium carbonate. The mixture was filtered, and the filtrate was distilled. Crude *2-methylbenzo-1,4-oxathiadiene* (III, 17.10 g., n_D^{27} 1.6020, 26.5% yield) was collected at 78–90°/1.1 mm.). A higher boiling fraction (10.8 g., b.p. 92–120°/1.4 mm.) was not examined.

A sample of crude III (1 g., 0.006 m.) was oxidized with 30% hydrogen peroxide (15 ml.) in boiling glacial acetic acid. The crude sulfone (0.6 g., 50% yield) was obtained as a solid when water was added to the cold acetic acid solution. Pure 2-methylbenzo-1,4-oxathiadiene sulfone (IV, m.p. 162–163°) was obtained by recrystallization of the crude sulfone from methylene chloride-petroleum ether (60–68°).

Anal. Calcd. for $C_9H_8O_3S$: C, 55.10; H, 4.11. Found: C, 55.03; H, 4.12.

A solution of IV (0.1 g., 0.005 mol.) in ethanol (25 ml.) was reduced with palladium and hydrogen at atmospheric pressure (48 hr.). The product, presumably *2-methylbenzo-1,4-oxathiene sulfone* (V), was recrystallized from petroleum ether (60–68°) to give a white solid (0.04 g., 40% yield) melting at 67–69°. This product was not analyzed further.

Formylation of 2-methylbenzo-1,4-oxathiadiene (III). A mixture of *N,N*-dimethylformamide (22.5 g., 0.308 mol.) and phosphorus oxychloride (25.0 g., 0.163 mol.), which had been allowed to stand overnight,[8] was cooled in an ice bath, and 2-methylbenzo-1,4-oxathiadiene (III, 18.74 g., 0.113 m., b.p. 73.5–86°/0.07 m., $n_D^{26.5}$ 1.5920–1.5950) was added slowly in portions. The mixture, after being allowed to stand at 25° for 24 hr., was dissolved in chloroform (200 ml.), and the resulting solution was added to a mixture of ice and water (*ca.* 300 g.). After the ice had melted, the chloroform layer was separated and washed with dilute sodium carbonate until all acid was removed. The chloroform layer was dried over magnesium sulfate, concentrated to 50 ml., and shaken with a mixture of ether (100 ml.) and saturated sodium bisulfite (200 ml.). The bisulfite adduct (*ca.* 2 g.) which formed was collected and washed with cold absolute ethanol, then washed again with cold ether. The pale yellow adduct was suspended in water, and sodium carbonate was added until the solution was basic to litmus. The resulting mixture was then extracted with ether, the ether extract was dried with magnesium sulfate and finally concentrated. The crude aldehyde (1.1 g., 5% yield, m.p. 136–139°) was recrystallized from methylene chloride-petroleum ether (60–68°), and then sublimed under vacuum, affording a product tentatively assigned structure VI (m.p. 140–141°).

Anal. Calcd. for $C_{10}H_8O_2S$: C, 62.50; H, 4.20. Found: C, 62.37; H, 4.36.

The infrared spectrum of the aldehyde showed carbonyl absorption at 1650 cm.$^{-1}$

Proof of structure of 2- and 3-methylbenzo-1,4-oxathiadiene. Hydrolysis of 3-methylbenzo-1,4-oxathiadiene sulfone (XI). A solution prepared from XI (0.8 g., 0.004 mol.), ethanol (10 ml.), and potassium hydroxide (3*N*, 10 ml.) was heated at the reflux temperature for 5 hr. The cold solution was dried with magnesium sulfate and distilled. 2-Ethylsulfonylphenol (XIV) was obtained as a colorless oil (0.24 g., 32% yield, b.p. 122–125°/1 mm.). A sample (0.15 g.) of this product was treated with phenylisocyanate (3 ml.) and pyridine (1 drop) and the mixture was heated at 100° for 15 min. The precipitate was treated with chloroform, the insoluble urea was removed, and the *phenylurethane* of XIV was recrystallized from carbon tetrachloride. The resulting urethane melted at 149–151°.

Anal. Calcd. for $C_{15}H_{15}O_4SN$: C, 59.01; H, 4.95; N, 4.59. Found: C, 59.75; H, 5.11; N, 5.19.

2-Benzyloxyphenyl ethyl sulfone (XV). (a) A solution containing XIV (2 g., 0.017), prepared as described above, potassium carbonate (1 g.), benzyl chloride (1 g., 0.008 mol.), and acetone (25 ml.) was heated at the reflux temperature for 16 hr. Water (10 ml.) was then added to the cold mixture, and the resulting mixture was extracted with ether. 2-Benzyloxyphenyl ethyl sulfone (1 g., 55% yield, m.p. 107–108° from 95% ethanol) was obtained from the ether extract.

Anal. Calcd. for $C_{15}H_{16}O_3S$: C, 64.95; H, 5.82. Found: C, 64.88; H, 5.81.

(b) Monothiocatechol (23.22 g., 0.184 mol.) in ethanol (100 ml.) was added dropwise to a solution, under nitrogen, of potassium hydroxide (11.79 g., 0.183 mol.) in ethanol (100 ml.). The solution was stirred, ethyl bromide (20.06 g., 0.184 mol.) in ethanol (50 ml.) was added slowly, and the resulting mixture was stirred at 25° for 2 hr. The mixture was filtered, and the filtrate was concentrated at reduced pressure. Water and sulfuric acid were added to the residue,

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(8) A. H. Weston and R. J. Michaels, Jr., *Org. Syntheses*, **31**, 108 (1951).

which was then distilled with steam. The ether-soluble material from the distillate was extracted with 10% sodium hydroxide, and the alkaline layer was then acidified with 10% sulfuric acid. The oil which separated was collected in ether, and the extract was dried with magnesium sulfate and distilled. *2-Ethylmercaptophenol* (XVI, 10 g., 35% yield, $n_D^{25.5}$ 1.5681) was collected at 59–60°/0.6 mm.

A sample of 2-ethylmercaptophenol (5.57 g., 0.0362 mol.) was benzylated with benzyl chloride by a procedure essentially identical with that described above. 2-Ethylmercaptophenol benzyl ether (XVII, 5.16 g., 58% yield, $n_D^{25.5}$ 1.5960) was collected at 148–149°/1 mm.

Ethylmercaptophenyl benzyl ether was oxidized in hot glacial acetic acid with hydrogen peroxide (30%) by a procedure identical with that described elsewhere in this report. 2-Benzyloxyphenyl ethyl sulfone (XV) was obtained in quantitative yield; m.p. 106–107.5° (from ethanol).

Anal. Calcd. for $C_{15}H_{16}O_3S$: C, 64.95; H, 5.82. Found: C, 64.85; H, 5.70.

Samples of 2-benzyloxyphenyl ethyl sulfone, prepared by procedures (a) and (b) showed no depression of melting point upon admixture. Furthermore, X-ray diffraction patterns of these materials were identical.

Proof of structure of benzo-1,4-oxathiadiene-2-aldehyde (II). *Reduction to 2-methylbenzo-1,4-oxathiadiene* (III). A mixture of benzo-1,4-oxathiadiene aldehyde[3] (II, 2.5 g., 0.014 mol.), hydrazine (8 ml., 95%), triethylene glycol (50 ml.), and pulverized potassium hydroxide (1 g.) was heated at the reflux temperature for 2 hr. Material was then allowed to distill until the temperature of the solution reached 120°.

(a) The aqueous distillate was extracted with ether (100 ml.), the ether was dried with magnesium sulfate and concentrated. The residue (0.5 g., 22% calcd. as C_9H_8OS) was oxidized with 30% hydrogen peroxide (5 ml.) in hot glacial acetic acid. The solid sulfone, obtained from the acetic acid by addition of water, was recrystallized from 95% ethanol. The sulfone weighed 0.4 g. and melted at 161–162.5°. This material caused no depression in melting point when admixed with authentic 2-methylbenzo-1,4-oxathiadiene sulfone (m.p. 162–163°).

(b) In one experiment the residue from the steam distillation was extracted with ether, and the extract was dried and distilled. The organic distillate (b.p. 54–62°/1.3 mm., *ca.* 2 g.) was washed with water and the insoluble oil (1 g.) was oxidized with hydrogen peroxide, as described above. The resulting product was recrystallized from methylene chloride–petroleum ether (60–68°). This procedure afforded a small amount of white solid melting at 63.5–64.5°.

Anal. Calcd. for $C_8H_8O_3S$: C, 52.16; H, 4.37; S, 17.38; M.W. 184.21. Found: C, 52.29, 52.52; H, 4.76, 4.05; S, 16.99, 17.91; M.W. (freezing point of benzene) 203, 203; M.W. (Rast in camphor), 117, 201.

The identity of this material was not established.

MINNEAPOLIS 14, MINN.

[CONTRIBUTION No. 184 FROM THE RESEARCH CENTER OF THE UNITED STATES RUBBER CO.]

The Chemistry of Maleimide and Its Derivatives.
I. *N*-Carbamylmaleimide

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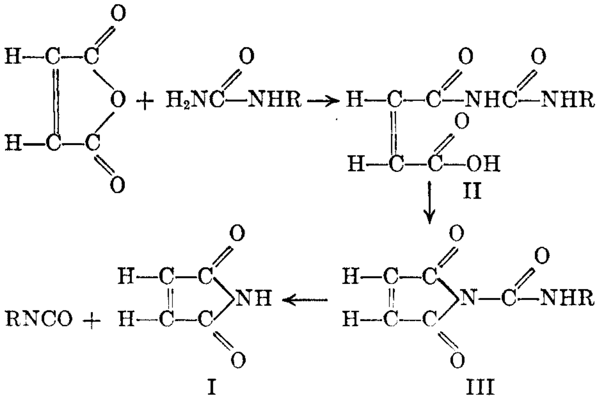
Carefully controlled condensation of maleic anhydride with urea or monosubstituted ureas, and cyclization of the maleuric acids to *N*-carbamylmaleimides followed by decomposition in dimethylformamide provide a practical route to maleimide. *N*-Carbamylmaleimides react with primary and secondary alcohols to yield esters of maleuric acid. *N*-Carbamylmaleimide and the maleurate esters have been copolymerized with several vinyl-type monomers.

Interest in the chemistry of maleimide (I) and its derivatives, and more particularly in their polymerizability, has been limited by the lack of a practical method of preparing such compounds. Until recently, the synthesis of maleimide was usually effected by chromic acid oxidation of pyrrole[1] or by acid-catalyzed cyclization of maleamide.[2] We have noted that these methods provide low yields and that neither is suitable for the preparation of appreciable amounts of maleimide. In our search for a more satisfactory method, we have devised the synthesis outlined in Chart A wherein the desired compound is obtained by thermal decomposition of the new structure, *N*-carbamylmaleimide (IIIa). Homologs of IIIa such as IIIb, c, and d are also readily available from this sequence of reactions.

CHART A



IIa. R = H
IIb. R = C_6H_5
IIc. R = n-C_4H_9
IId. R = $(CH_3)_3C$

IIIa. R = H
IIIb. R = C_6H_5
IIIc. R = n-C_4H_9
IIId. R = $(CH_3)_3C$

It is the purpose of this paper to describe the synthesis of III and to point out some of its reactions.

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(1) G. Plancher and F. Cattadori, *Atti reale accad. naz. Lincei*, [5] **13**, I, 489 (1904).

(2) I. J. Rinkes, *Rec. trav. chim.*, **48**, 961 (1929).