dium bismuthate oxidation[11] of II. In the n.m.r. spectrum of V, a quartet signal at τ 5.48 corresponding to the proton on 11β-hydroxyl-bearing carbon and an AB-type quartet at τ 4.90 and 5.95 (J = 10.0 c.p.s.) arising from the 18-methylene group are found. The infrared spectra of this compound in the various states (KBr, $CHCl_3$, and CH_2Cl_2) were in agreement with those of an authentic specimen of $11\beta,18$-dihydroxyandrost-4-ene-17β-carboxylic acid 18,20-lactone.[12,13]

Incubation of III with *C. cassiicola* (IMI 56007) produced three crystalline compounds (VI, VII, and VIII; yields, 17, 3, and 2%, respectively). The main product [VI, m.p. 165–167°, $[\alpha]^{24}D$ +163.3°, λ_{max} 240.5 mμ (ϵ 16,600), $\nu_{max}^{CHCl_3}$ 3721, 3571, 3461, 1705, 1667, and 1618 cm.$^{-1}$] was identified as aldosterone[14] by mixture melting point determination and by comparison of infrared and n.m.r. spectra with those of an authentic specimen. Partial acetylation of VI gave a 21-mono-acetate [IX, m.p. 193–195°, $[\alpha]^{23.5}D$ +127.5°, $\nu_{max}^{CHCl_3}$ 3711, 3591, 3431, 1738, 1718, 1666, and 1617 cm.$^{-1}$], which was converted into a five-membered lactone [X, m.p. 202–204°, $[\alpha]^{23.5}D$ +118.4°, $\nu_{max}^{CHCl_3}$ 1772, 1750, 1728, 1669, and 1621 cm.$^{-1}$] by chromic acid oxidation. Physical constants as well as infrared and n.m.r. spectra of X agreed with those of an authentic specimen of 18-dehydroaldosterone 21-acetate prepared in our laboratory.[1d,9] The second product [VII, m.p. 208–213°, $\nu_{max}^{CH_2Cl_2}$ 3486, 1772, 1710, 1671, and 1621 cm.$^{-1}$] was identified as 18-dehydroaldosterone by both comparison of infrared spectra[15] and the preparation of X by usual acetylation. The remaining compound [VIII, m.p. 234–236°, λ_{max} 241 mμ (ϵ 15,800), ν_{max}^{Nujol} 3421, 1728, 1659, and 1624 cm.$^{-1}$] lacks the 20-carbonyl band and 21-methylene signal in its infrared and n.m.r. spectra, respectively, and instead has a carbonyl in a five-membered ring and only one tertiary hydroxyl group which shifts the 19-methyl n.m.r. signal downfield by about 0.2 p.p.m. from its position in III.[3,16] Furthermore, the 18-methylene signal appears at τ 5.97 and 6.58 as an AB-type quartet and the 11α-proton signal is found at τ 5.52 as a second-order tripletlike pattern. In addition, from other physical and chemical evidence[17] VIII was elucidated to be 9α-hydroxy-$11\beta,18$-epoxy-androst-4-ene-3,17-dione. The total yield of this synthesis of VI from I is about 2% at present, but a possible improvement for increasing the yield might be expected in the future.

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Acid-Catalyzed Reactions of Phenols with Dimethyl Sulfoxide and Dicyclohexylcarbodiimide

Sir:

One of the mildest methods available for the oxidation of alcohols to aldehydes and ketones consists of their acid-catalyzed reaction with dimethyl sulfoxide (DMSO) and dicyclohexylcarbodiimide (DCC).[1] We now wish to report similar reactions applied to phenols.[2]

The predominant reaction with most simple phenols is the introduction of thiomethoxymethyl groups in the available *ortho* positions. Thus, phenol itself reacts exothermally with 3 equiv. of DCC and 0.5 equiv. of anhydrous orthophosphoric acid in mixtures of DMSO and benzene to give 2-(thiomethoxymethyl)-phenol (Ia, 27%, λ_{max}^{MeOH} 278 mμ (ϵ 2900); $\lambda_{max}^{OH^-}$ 242 and 297 mμ (ϵ 8300 and 4100)) and 2,6-di(thiomethoxymethyl)phenol (Ib, 17%, λ_{max}^{MeOH} 283 mμ (ϵ 2870); $\lambda_{max}^{OH^-}$ 307 mμ (ϵ 5530)). Desulfurization of Ia and Ib with Raney nickel in methanol rapidly and quantitatively gave *o*-cresol and 2,6-dimethylphenol, respectively. Similar *ortho*-alkylation products were obtained from other phenols. Thus[3]: *o*-cresol gave 28% Ic; 2,5-dimethylphenol gave 35% Id; *o*-nitro-phenol gave 38% Ie (m.p. 78–79°); *p*-nitrophenol gave 26% If (m.p. 127.5–128.5°), 11% Ig (m.p. 76.5–77.5°), and 15% Ih (m.p. 148–149°); α-naphthol gave 2-(thiomethoxymethyl)-1-naphthol. Desulfurization of each of the unnitrated products gave an excellent yield of the appropriate methylphenol. The n.m.r. spectra of products of type I are characterized by three-proton singlets (SCH_3) at 112–124 c.p.s. and by two-proton singlets ($ArCH_2S$) at 221–231 c.p.s. A similar reaction with estrone gave both 2-(thiomethoxymethyl)estrone (m.p. 205–207°, two aromatic protons as singlets at 399 and 422 c.p.s.) and 4-(thiomethoxymethyl)estrone (m.p. 154–156°, two doublets with J = 8–9 c.p.s. centered at 403 and 429 c.p.s.).
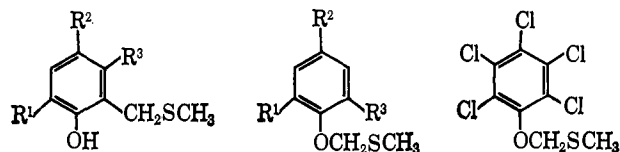
Several other types of products were also formed, depending upon the nature of the phenol. Thus, with more acidic phenols, O-alkylation was observed. In the case of *p*-nitrophenol 3% of IIa (m.p. 50–51°) and 14% of IIb (m.p. 61–62°) were obtained, while *o*-nitrophenol gave low yields of both IIc and IId as distillable oils. These products were nonphenolic (infrared and ultraviolet) and showed three-proton singlets (SCH_3) at 135–138 c.p.s. and two-proton singlets (OCH_2S) at 314–319 c.p.s. in their n.m.r. spectra. Acid hydrolysis readily gave the appropriate phenol, formaldehyde, and methyl mercaptan, and both IIa

(11) C. J. W. Brooks and J. K. Norymberski, *Biochem. J.*, **55**, 371 (1953).

(12) R. Neher and A. Wettstein, *Helv. Chim. Acta*, **43**, 623 (1960). We thank Drs. A. Wettstein and R. Neher of CIBA Aktiengesellschaft (Basel) for sending us copies of the infrared spectra of this compound.

(13) In a nitrogen atmosphere, treatment of II with aqueous acetic acid (refluxing) gave only a trace of the lactone V. From this result as well as that in the report by F. G. Péron, *Endocrinology*, **70**, 386 (1962), it might be considered that 18-hydroxycorticosterone derivatives are unstable in air.

(14) The infrared spectrum of VI was also identical with that reported by S. A. Simpson, J. F. Tait, A. Wettstein, R. Neher, J. V. Euw, O. Schindler, and T. Reichstein, *Helv. Chim. Acta*, **37**, 1163 (1954); the physical constants agreed well with those reported by R. E. Harman, E. A. Ham, J. J. DeYoung, N. G. Brink, and L. H. Sarett, *J. Am. Chem. Soc.*, **76**, 5035 (1954).

(15) E. Vischer, J. Schmidlin, and A. Wettstein, *Experientia*, **12**, 50 (1956).

(16) Also refer to K. Tori and E. Kondo, *Steroids*, **4**, 713 (1964).

(17) The detail of the structure determination of VIII will appear in our full paper.

(1) K. E. Pfitzner and J. G. Moffatt, *J. Am. Chem. Soc.*, **85**, 3027 (1963), and in press.

(2) Independently K. E. Pfitzner, J. P. Marino, and R. A. Olofson, *J. Am. Chem. Soc.*, **87**, 4658 (1965), have studied similar reactions.

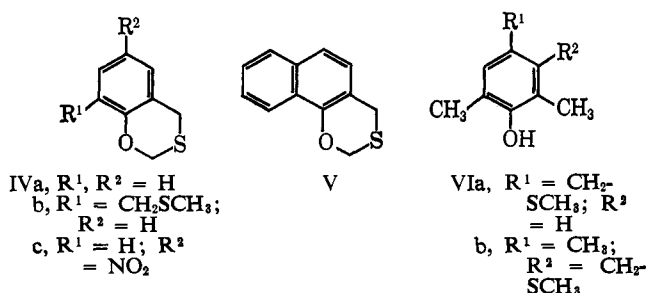(3) All compounds described gave correct elemental analyses.

and IIc were independently synthesized from the potassium salt of the nitrophenol and chloromethyl methyl sulfide. With pentachlorophenol O-alkylation became the only observed reaction and III (m.p. 85–87°, n.m.r. singlets at 142.5 and 315.8 c.p.s.) was isolated in 60% yield.

Ia, R^1, R^2, R^3 = H
b, R^1 = CH_2SCH_3;
   R^2, R^3 = H
c, R^1 = CH_3; R^2,
   R^3 = H
d, R^1, R^3 = CH_3;
   R^2 = H
e, R^1 = NO_2; R^2,
   R^3 = H
f, R^2 = NO_2; R^1,
   R^3 = H
g, R^1 = CH_2SCH_3;
   R^2 = NO_2;
   R^3 = H
h, R^1 = (C_6H_{11})-
   $(CONHC_6H_{11})N$;
   R^2 = NO_2;
   R^3 = H

IIa, R^2 = NO_2; R^1,
    R^3 = H
b, R^1 = CH_2SCH_3;
   R^2 = NO_2;
   R^3 = H
c, R^1 = NO_2; R^2,
   R^3 = H
d, R^1 = NO_2; R^3
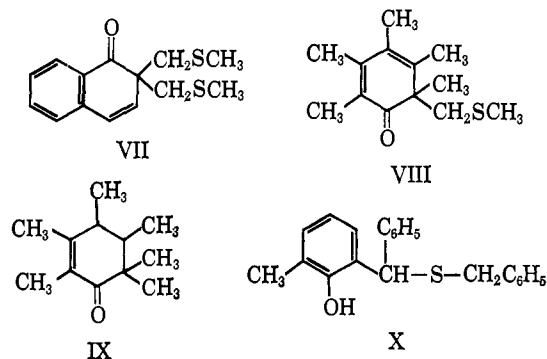   = CH_2SCH_3;
   R^2 = H

III

Small amounts (up to 5%) of cyclic products containing the previously undescribed 1,3-benzoxathian ring system were also encountered. Thus phenol gave both 1,3-benzoxathian (IVa) and 8-(thiomethoxymethyl)-1,3-benzoxathian (IVb) as distillable oils in 4% yield each, while p-nitrophenol gave 3% of the nitro analog IVc (m.p. 135–136°) and α-naphthol gave V (m.p. 60–62°). The n.m.r. spectra of these compounds showed two-proton singlets at 312–322 c.p.s. (OCH₂S) and at 230–236 c.p.s. (ArCH₂S). Treatment of V with Raney nickel in methanol gave exclusively 1-methoxy-2-methylnaphthalene.

Phenols without free ortho positions lead to para-alkylated products. Thus, 2,6-dimethylphenol readily reacts with DMSO, DCC, and anhydrous phosphoric acid to give 2,6-dimethyl-4-(thiomethoxymethyl)phenol (VIa, m.p. 38–40°) in high yield. VIa showed n.m.r. singlets at 118 c.p.s. (SCH₃), 131 c.p.s. (2-ArCH₃), 214 c.p.s. (ArCH₂S), 288 c.p.s. (phenol), and 415 c.p.s. (two aromatic protons). Desulfurization gave 2,4,6-trimethylphenol, m.p. 72–73°. An identical reaction with 2,4,6-trimethylphenol led to meta alkylation, giving an 88% yield of VIb (m.p. 85–86°) which was identified by its n.m.r. spectrum and by desulfurization to authentic 2,3,4,6-tetramethylphenol, m.p. 77–78°.
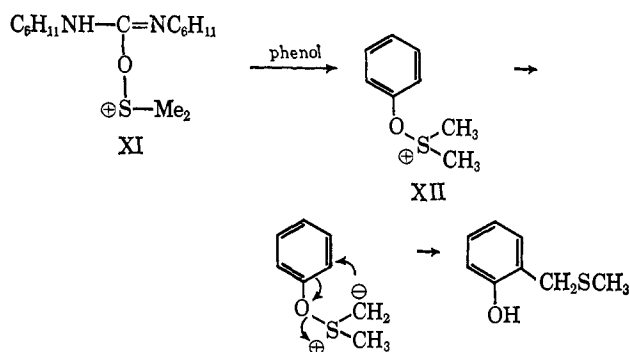

IVa, R^1, R^2 = H
b, R^1 = CH_2SCH_3;
   R^2 = H
c, R^1 = H; R^2
   = NO_2

V

VIa, R^1 = CH_2-
    SCH_3; R^2
    = H
b, R^1 = CH_3;
   R^2 = CH_2-
   SCH_3

Certain phenols lead to products with a disrupted aromatic system. Thus, the major product from α-naphthol proved to be VII (m.p. 50–51°; λ_{max}^{MeOH} 234 mμ (ε 32,800); ν_{max} (KBr) 1680 cm.$^{-1}$). The n.m.r. spectrum of XII showed two CH₂SCH₃ groups (122 and 178 c.p.s.), two styrenoid one-proton doublets (370 and 406 c.p.s., J = 10 c.p.s.), and four aromatic protons (430–485 c.p.s.). Desulfurization in methanol was accompanied by reduction of the styrene double bond and gave 2,2-dimethyltetralone identical with a synthetic sample.[4] Similarly, 2,3,4,5,6-pentamethylphenol gave a 30% yield of VIII as a distillable oil with λ_{max}^{MeOH} 336 mμ (ε 3973) and $\nu_{max}^{CHCl_3}$ 1630 and 1650 cm.$^{-1}$. The n.m.r. spectrum showed four vinyl methyl groups and an SCH₃ at 116–118 c.p.s., a singlet aliphatic methyl at 71 c.p.s., an SCH₃ at 127 c.p.s., and a CH₂S as a quartet[5] centered at 182 c.p.s. Desulfurization, once again accompanied by partial reduction, gave a compound (λ_{max}^{MeOH} 246 mμ (ε 8600) and ν_{max} 1660 cm.$^{-1}$) with an n.m.r. spectrum consistent with IX.

Similar reactions with other sulfoxides provide a route to various ortho-alkylated phenols. Thus o-cresol, dibenzyl sulfoxide, DCC, and phosphoric acid gave a satisfactory yield of X, which upon desulfurization gave 2-benzyl-6-methylphenol of m.p. 49–50° (reported[6] m.p. 51–52°).

VII

VIII

IX

X

We suggest that the mechanism of these reactions involves initial, acid-catalyzed addition of DMSO to DCC giving a sulfonium isourea (XI) which is irreversibly attacked by phenol giving the phenoxysulfonium salt XII. Loss of a proton from XII readily gives a 3d-orbital stabilized carbanion[7] which intramolecularly alkylates the available ortho position.
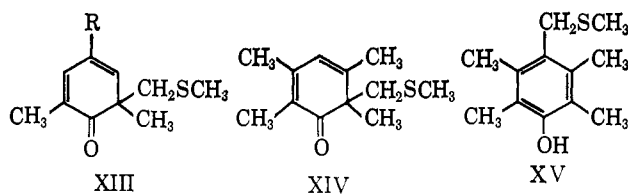

XI

XII

(4) M. Mousseron, R. Jacquier, and H. Cristol, Bull. soc. chim. France, 346 (1957).
(5) J. D. Roberts, "Nuclear Magnetic Resonance. Applications to Organic Chemistry," McGraw-Hill Book Co., Inc., New York, N. Y., 1959, p. 58.
(6) P. Shorigin, Ber., 58B, 2028 (1925).
(7) G. Cilento, Chem. Rev., 60, 147 (1960).

We also consider the observed *meta* and *para* alkylations to be intramolecular. This stems from our inability to detect any alkylation of large excesses of anisole, N,N-dimethylaniline, or furan present during *para* alkylation of 2,6-dimethylphenol. It is likely that both *meta* and *para* alkylation proceed *via* a cyclohexadienone (XIII). In support of this we have found that 2,3,5,6-tetramethylphenol reacts to give a good yield of XIV (λ_{max}^{MeOH} 325 mμ (ϵ 4,600); $\nu_{max}^{CHCl_3}$ 1640 and 1660 cm.$^{-1}$) as a distillable oil with the expected n.m.r. spectrum. Mild acidic treatment of XIV results in its rapid rearrangement to the *para*-alkylated phenol XV, m.p. 144–145°. Desulfurization of the latter gave 2,3,4,5,6-pentamethylphenol (m.p. 126–128°) identical with an authentic sample. If in XIII R = CH$_3$, however, a dienone–phenol type of arrangement similar to that observed with 6,6-dimethylcyclohexa-2,4-dien-1-one itself[8] can lead to the *meta*-alkylated phenol VIb.

Further studies designed to cast light upon the mechanism of these reactions are in progress.

(8) (a) E. N. Marvel and E. Magoon, *J. Am. Chem. Soc.*, 77, 2542 (1955); (b) H. Budzikiewicz, *Tetrahedron Letters*, 12 (1960).
(9) Receipt of a travel grant from the Welcome Trust is gratefully acknowledged.

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The Reactions of Phenols with Oxysulfonium Cations

Sir:

Several procedures for the oxidation of alcohols to aldehydes or ketones *via* oxysulfonium intermediates (ROS$^+$R$_2$) are known. These include: (1) reaction of the derived tosylate with dimethyl sulfoxide (DMSO) at high temperature,[1] (2) reaction of the alcohol with DMSO and dicyclohexylcarbodiimide (DCC) in the presence of a proton donor,[2] (3) reaction of the derived chloroformate with DMSO,[3] and (4) reaction of the derived alkoxide with a dimethylmethoxysulfonium salt.[4] In the present communication we wish to describe a few of the contents of a Pandora's box of new reactions and rearrangements discovered in an attempt to extend some of these oxidation procedures to vinylogous alcohols.[5] In particular we hoped to accomplish the transformation of *p*-cresol *via* a postulated quinonoid intermediate to *p*-hydroxybenzyl phosphate by treat-

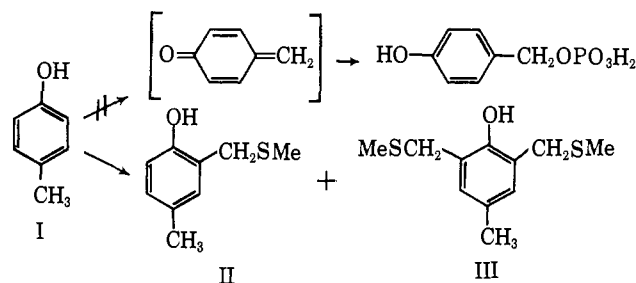(1) N. Kornblum, W. J. Jones, and G. J. Anderson, *J. Am. Chem. Soc.*, 81, 4113 (1959).
(2) K. E. Pfitzner and J. G. Moffatt, *ibid.*, 85, 3027 (1963).
(3) D. H. R. Barton, B. J. Garner, and R. H. Wightman, *J. Chem. Soc.*, 1855 (1964).
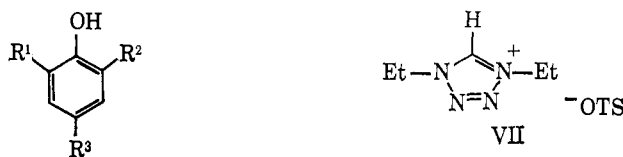(4) C. R. Johnson and W. G. Phillips, *Tetrahedron Letters*, 2101 (1965).
(5) M. G. Burdon and J. G. Moffatt have independently discovered similar reactions, and simultaneous publication has been arranged (*J. Am. Chem. Soc.*, 87, 4656 (1965)).

ment of I with DMSO, DCC, and H$_3$PO$_4$. The reaction however took a different course, and the major phenolic products are the thiomethoxymethyl compounds (II and III).[6]

From *o*-cresol we obtained a 65% yield of the 6-thiomethoxymethyl derivative (IV) and from phenol itself both V and VI were isolated. The highest yields (3 equiv. of DCC) of V (30%) and VI (18%) were

IV, R^1 = Me, R^2 = CH$_2$SMe, R^3 = H
V, R^1 = CH$_2$SMe, R^2 = R^3 = H
VI, R^1 = R^2 = CH$_2$SMe, R^3 = H
VIII, R^1 = COH, R^2 = CH$_2$SMe, R^3 = H
IX, R^1 = R^2 = Me, R^3 = CH$_2$SMe

obtained when pyridinium trifluoroacetate (0.5 equiv.) was used as the proton source, though under these conditions N-trifluoroacetyl-N,N'-dicyclohexylurea (m.p. 137–139°) and cyclohexyltrifluoroacetamide (m.p. 93–94°) were also isolated. Similar products are formed from other phenols, other sulfoxides with α-hydrogens, and other carbodiimides (*o*-cresol also gives IV on treatment with 1,4-diethyltetrazolium tosylate (VII) (an *in situ* source of carbodiimide[7]), Et$_3$N, and H$_3$PO$_4$ in DMSO). Salicylaldehyde in addition to yielding the expected *ortho* alkylation product (VIII, 18%) gave the decarbonylated species (V, 16%).

No isomers substituted *para* to the OH could be detected in these reaction mixtures, but, when the *ortho* positions are blocked as in 2,6-dimethylphenol, the *para* product (IX) is encountered in variable yield. Surprisingly, both α-naphthol (X) and β-naphthol yielded conjugated ketones and other extraordinary compounds in addition to the anticipated products. Compounds with the previously unknown 1,3-benzoxathian ring system (as in XIII and XV) are also formed in trace amounts from the simpler phenols including phenol itself, which gives XVI in 2% yield. *o*-Nitrophenol and the other nitrophenols yield oxygen alkylation products like XVII (5%) in addition to compounds of the types already described.

(6) The structures of the new compounds described in this communication were determined from a study of their infrared, ultraviolet (neutral and base), and n.m.r. spectra (see Table I), mass spectral fragmentation patterns, and by Raney nickel desulfurization (usually in almost quantitative yield) to the expected known products. Correct elemental analyses were obtained. The products were isolated by extraction followed by distillation or crystallization or, when necessary, preparative layer chromatography.
(7) R. A. Olofson, W. R. Thompson, and J. S. Michelman, *J. Am. Chem. Soc.*, 86, 1865 (1964).