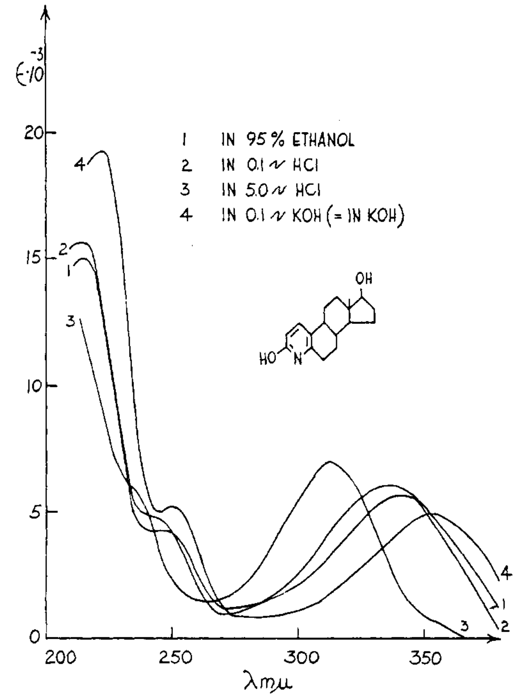

Figure 3

androst-5-en-3-one (I)[12] in 1000 ml. of dry benzene was introduced a stream of gaseous ammonia at room temperature, whereby a copious precipitate deposited. The crystals were filtered off and recrystallized from methanol. The 55 g. of colorless prisms had a m.p. 301–310°, dec. and the infrared and ultraviolet spectra were identical with those of a specimen obtained previously.[4]

17β-Hydroxy-19-nor-4-azaandrost-5-en-3-one (III) *from* II. The solution of 15 g. of II in 150 ml. of 2% sodium hydroxide in methanol was left overnight at room temperature, then a large amount of water was added, and the resulting suspension extracted with methylene chloride. The extract was washed with water, dried over anhydrous sodium sulfate, and evaporated to dryness. The residue was recrystallized from methanol to give 10.5 g. of III, m.p. 248–258° (transformations at 160–180° and 244–248°). $[\alpha]^{20}_{D}$ $-5°$ (*c*, 0.5 in $CHCl_3$); λ_{max} 234 mμ (ε 8800); infrared absorption ν_{max} 3600 and 1020 (hydroxyl), 3200 (NH-group) and 1660 cm.$^{-1}$ (amide carbonyl).

Anal. Calcd. for $C_{17}H_{25}O_2N$: C, 74.14; H, 9.15; N, 5.09. Found: C, 74.24; H, 9.28; N, 5.32.

Selenium dioxide oxidation of 17β-acetoxy-19-nor-4-azaandrost-5-en-3-one (**II**). To the solution of 5 g. of II in 900 ml. *tert*-butyl alcohol were added 9 ml. of acetic acid and 5.4 g. of selenium dioxide and the reaction mixture refluxed for 24 hr. After cooling, the liquid was decanted, the residue washed with ethyl acetate, and the combined solutions evaporated and chromatographed on silica gel. The fractions eluted with 25% ethyl acetate in benzene were pooled and rechromatographed (see below). The fractions eluted with 50% ethyl acetate–benzene gave, after recrystallization from ether, 650 mg. VII, m.p. >286°, dec.; $[\alpha]^{22}_{D}$ $-174°$ (*c*, 0.8 in chloroform), infrared absorption maxima ν_{max} 3520, 1200, and 1055 (tert. OH-group); 3180 and 3060 (NH-group); 1710 and 1250 (acetoxy group); 1664 cm.$^{-1}$ (amide carbonyl); ultraviolet absorption maximum λ_{max} 230 mμ (ε 16,000).

Anal. Calcd. for $C_{19}H_{27}O_4N$: C, 68.44; H, 8.16; N, 3.20. Found: C, 68.17; H, 8.08; N, 4.05.

The mixture which was eluted with 25% ethyl acetate–benzene (see above) was rechromatographed on silica gel, whereby the fractions with 15% ethyl acetate in benzene gave, after crystallization from methanol, 150 mg. VI, m.p. >320°, dec.; $[\alpha]^{21}_{D}$ $-3°$ (*c*, 0.25 in chloroform); λ_{max} 212 mμ (ε 23,000), 254 mμ (ε 16000); λ_{min} 220 mμ (ε 7600); unchanged in 0.1*N* HCl or 0.1*N* KOH.

Anal. Calcd. for $C_{21}H_{27}O_4N$: C, 70.56; H, 7.61; N, 3.92. Found: C, 70.60; H, 7.24; N, 4.10.

The fractions eluted with 25% ethyl acetate–benzene gave 300 mg. V, $[\alpha]^{21}_{D}$ $+31°$ (*c*, 0.4 in chloroform); λ_{max} 220 mμ (ε 7800)[13] and 288 mμ (ε 6600); λ_{min} 259 mμ (ε 3500), m.p. and infrared absorption as published previously; unchanged in 0.1 *N* HCl; 0.1 *N* KOH: λ_{max} 221 mμ (ε 16,100), 250 mμ (ε 6000) (shoulder), and 334 mμ (ε 5500); λ_{min} 281 mμ (ε 1200).

19-Nor-4-azaandrost-5-en-3,17-dione (IV) *from* III. To the solution of 3 g. of III in 200 ml. methylene chloride was added 40 ml. of 2% chromic oxide solution in 80% acetic acid and shaken overnight at room temperature. The methylene chloride layer was separated, washed with dilute sodium hydrogen sulfite solution, then with 2*N* sodium hydroxide solution and water, dried over anhydrous sodium sulfate, and evaporated. The crystalline residue was recrystallized from acetone to yield 2.6 g. of IV, m.p. 280–300°, dec.; $[\alpha]^{22}_{D}$ $+18°$ (*c*, 0.7 in $CHCl_3$): ultraviolet absorption λ_{max} 233 mμ (ε 9500) and 300–310 mμ (ε 800); infrared absorption ν_{max} 3200 (—HN), 1660 (amide carbonyl), 1740 cm.$^{-1}$ (>CO).

Anal. Calcd. for $C_{17}H_{23}O_2N$: C, 7 .69; H, 8.48; N, 5.12. Found: C, 74.59; H, 8.77; N, 4.92.

Attempted dehydration of VII. A solution of 20 mg. of VII in 8 ml. of acetic acid at 10° was saturated with hydrogen chloride and left for 2 hours at 5°. The solvent was evaporated *in vacuo* and the residue chromatographed on silica gel. The fractions eluted with 25% ethyl acetate in methylene chloride gave, after recrystallization from ether, 18 mg. prisms, m.p. >310°; λ_{max} 238 mμ (ε 630).

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[12] I. A. Hartman, A. J. Tomasewski, and A. S. Dreiding, *J. Am. Chem. Soc.*, **78**, 5662 (1956).

[13] Previously reported erroneously as λ_{max} 226 mμ (ε 6460).

Spectral Properties of Some Aromatic Thiols[1]

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As part of our broad concern with structure-reactivity correlations, we reported on the kinetics of addition of arylthiols (nucleophiles) to a series of ethyl phenylpropiolates (electrophiles).[2] Here we inquire whether there are independent measures of reactivity. Specifically, what relation, if any exists between the spectral properties of thiols and their nucleophilicity?

There are a few reports on ultraviolet spectral

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[1] (a) Supported by the Office of Ordnance Research, U. S. Army. (b) Abstracted in part from the Ph.D. thesis of G. S. Krishnamurthy, Illinois Institute of Technology, June 1960.

[2] G. S. Krishnamurthy and S. I. Miller, *J. Am. Chem. Soc.*, **83**, 3961 (1961).

TABLE I

Ultraviolet Spectra of Thiophenols and Thiophenolates

			$R_jC_6H_4SH$		$R_jC_6H_4S^-$	
R_j	σ	σ_R	λ_{max}	ϵ_{max}	λ_{max}	ϵ_{max}
p-t-C_4H_9	−0.197	−0.13	238.6	11,000	270.2	17,700
p-CH_3	−0.170	−0.12	237.0	9,500	270.2	16,000
m-CH_3	−0.07	−0.02	239.5	5,800	271.0	17,500
H	0.00	0.00	237.0	7,500	270.0	16,000
p-Cl	0.23	−0.24	247.5	11,000	279.0	19,500
m-$COOC_2H_5$	0.36	0.04	222.6	25,000	242.0	18,350
			244.0	8,300	280.5	11,500
p-NO_2	1.27	0.64	318.0	15,000	424.5	13,150

data of aromatic thiols.[3] Our own data are summarized in Table I. All of the undissociated thiols had a structureless symmetrical strong absorption and a much weaker broad absorption in the region 295–265 mμ.[3] In going from the thiols to the corresponding thiolates, there is an expected shift of λ_{max} to lower excitation energies. m-Carbethoxythiophenol also had a broad shoulder at *ca.* 244 mμ a band presumably overlapped by the 222 mμ band.

The effect of any substituent in benzenethiol appears to displace the main absorption band to lower excitation energies. Typical irregular U- or J-shaped curves[4] are obtained when $\Delta\lambda_{max}$ or ν_{max} are plotted against σ or σ_R values.[5] Contrary to the suggestions of Rao, we take the view that these plots point to complex rather than simple correlations. It has been reported, however, that in a limited series molar refraction does correlate with ν_{max}.[6]

We believed that substituents of benzenethiol would influence the infrared S—H stretching frequency in a simple and systematic fashion. Certainly similar series provided examples of correlations between Hammett or related substituent constants and frequency shifts.[7]

Our infrared data for the S—H stretching frequency of benzenethiols are given in Table II. The data of Josien *et al.* for a group of compounds not available to us are included.[8a] This is the most comprehensive table of such data and goes beyond that previously available.[8] Most strikingly these data point to little if any correlation between $\Delta\nu$ and Hammett σ (or. σ^+), a result in sharp contrast to a recent report.[8c]

TABLE II

Spectral Shifts of the S—H Stretching Frequency of Aryl Thiols RSH in the Solvent Carbon Tetrachloride

R^a	$\nu_R - \nu_H$	σ
C_6H_5	0.0	0.0
m-$CH_3C_6H_4$	−2.5	−0.07
Thioxylenol[b]	−2.5	−2.39
p-$NH_2C_6H_4$	−18.5	−0.66
p-$CH_3C_6H_4$	−2.5	−0.170
p-ClC_6H_4	3.5	0.23
p-t-BuC_6H_4[b]	−4.5	−0.197
C_6Cl_5[c]	15.5	3.493
m-$COOEtC_6H_4$	−10.5	0.363
p-$O_2NC_6H_4$	14.5	1.27
p-BrC_6H_4[d]	4.0	0.26
p-IC_6H_4[d]	1.0	0.28
m-BrC_6H_4[d]	16.0	0.38
m-ClC_6H_4[d]	15.0	0.37

[a] Commercial products except as noted. [b] Gift of Pitt-Consul Chemical Co., "Thioxylenol" is made up of isomers of dimethylbenzenethiol. [c] Gift of E. I. du Pont de Nemours and Co. σ is taken from P. J. Bray and R. G. Barnes, *J. Chem. Phys.*, **27**, 551 (1957). [d] Data of ref. 8a.

Our conclusion from this work is that the spectral data of thiols are not very promising as measures of nucleophilic reactivity.

EXPERIMENTAL

Materials. m- and p-Thiocresol were Eastman products. Benzenethiol and p-chlorothiophenol were gifts of Evans Chemetics Inc., while p-t-butylthiophenol was a gift of Pitt-Consul Chemical Co. These thiols were analyzed as 99.5 ±0.5% by amperometric titration with silver nitrate.[9]

p-Nitrothiophenol was prepared from p-chloronitrobenzene and sodium sulfide,[10a] m.p. 76–77° (lit.[10] 77.5°). Amperometric analysis with silver nitrate indicated a purity of 97.5 ±0.5%.

m-Carbethoxythiophenol was prepared by esterification of the zinc reduction product of m-carboxybenzenesulfonyl-

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(3) (a) A. E. Gillam and E. S. Stern, *An Introduction to Electronic Absorption Spectroscopy in Organic Chemistry*, Edward Arnold, London, 1954; (b) M. J. Murray, *Anal. Chem.*, **21**, 943 (1949); (c) American Petroleum Institute Research Project 44, *Ultraviolet Spectral Data*, Carnegie Institute of Technology, April 1959, Compound Serial Nos., 427, 435, 437; (d) R. N. Bapat, *Proc. Ind. Acad. Sci.*, **50A**, 183 (1959).

(4) C. N. Rao, *Chem. & Ind.* 1239 (1957); *J. Sci. and Ind. Res.*, **17B**, 56 (1958); *Current Sci.*, **26**, 276 (1957).

(5) R. W. Taft and I. C. Lewis, *J. Am. Chem. Soc.*, **81**, 5343 (1959).

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(7) (a) H. H. Jaffe, *Chem. Revs.*, **53**, 191 (1953); (b) J. Bellamy, *The Infra-red Spectra of Complex Molecules*, Wiley, New York, 1958, Ch. 22.

(8) (a) M. L. Josien, C. Castinel, and P. Saumagne, *Bull. soc. chim. France*, **423**, 648 (1957); (b) R. A. Spurr and H. F. Byers, *J. Phys. Chem.*, **62**, 425 (1958); (c) J. Jan, D. Hadzi, and G. Modena, *Ricerca Sci.*, **30**, 1065 (1960); (d) R. N. Bapat, *Ind. J. Phys.*, **33**, 295 (1959).

(9) I. M. Kolthoff and W. E. Harris, *Anal. Chem.*, **21**, 963 (1949); **18**, 161 (1946).

(10) (a) C. C. Price and G. W. Stacey, *J. Am. Chem. Soc.*, **68**, 499 (1946); (b) P. G. Bordwell and H. M. Andersen, *J. Am. Chem. Soc.*, **75**, 6019 (1953).

chloride.[11a] The reduction step gave *ca.* 3% yield of *m*-mercaptobenzoic acid, m.p. 146–147° (lit.[11] 146–147°). The thiol, 50 ml. of absolute alcohol, and 2 ml. of concentrated sulfuric acid were left for a week at *ca.* 25°. The crude ester was distilled through a small column to yield *m*-carbethoxythiophenol, b.p. 95–100° (0.1 mm.), n_D^{21} 1.5612 [lit.[11b] b.p. 147–149 (11 mm.)]. Amperometric analysis with silver nitrate indicated a purity of 97.5 ± 0.5%.

In the above thiols, any impurities were probably the disulfides. These would not interfere with the infrared measurements of the S—H frequency. Some errors could be introduced in the λ_{max} and ϵ_{max} values. For example, λ_{max} 238–241 mμ and log ϵ_{max} 4.2 have been reported[12] for diphenyl disulfide as compared to λ_{max} 237 mμ and log ϵ_{max} 3.88, which we have found for thiophenol. The ultraviolet spectra of seven undissociated thiols and their anions were taken on a Beckman DK2 recording spectrophotometer in the range 220–340 mμ. λ_{max} and ϵ_{max} were determined and are summarized in Table I. Matched pairs of quartz cells of 1-cm. path length were used. Absolute alcohol was the solvent. Its impurities could not be detected spectroscopically in a 1-cm. cell when run against the reference water. Typical thiol spectra have been given by others.[3]

To obtain the spectrum of an undissociated thiol, one drop of concentrated hydrochloric acid was added to 100 ml. of both the sample solution and the reference solvent. This was enough to suppress the ionization of the thiophenols since the yellow color of the most acidic thiol, *p*-nitrothiophenol, disappears completely. To obtain the spectrum of a thiolate ion, 1 ml. of 0.1*M* sodium ethoxide was added to 100 ml. of both the sample solution and the reference solvent.

The infrared spectra were taken on a Perkin-Elmer Model 21 spectrophotometer equipped with calcium fluoride optics. Sodium chloride or calcium fluoride cells of *ca.* 0.1 mm. thickness were used. The S—H region was scanned slowly at least three times. The scale on the infrared records was 5 cm.$^{-1}$ per cm. of chart. Spectrograde carbon tetrachloride was the usual solvent. As the S—H stretching frequency of benzenethiol shifted from 2570.5 cm.$^{-1}$ in the neat liquid to 2576.5 cm.$^{-1}$ when it was in dilute carbon tetrachloride solution, spectra for all thiols were taken on dilute solutions. Usually two such solutions of different dilutions were used. An internal standard spectrum of benzenethiol in carbon tetrachloride was repeatedly taken during these measurements. The precision of this standard was *ca.* 1.0 cm.$^{-1}$ while that of the other thiols was 1–2 cm.$^{-1}$

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Triphenylcarbethoxymethylphosphonium Chloride Dihydrate

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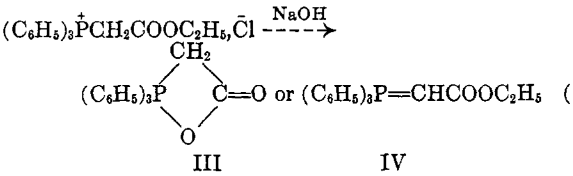
In a paper published in 1894 Michaelis and Gimborn reported[1] that the condensation of ethyl chloroacetate and triphenylphosphine[1] gave triphenylcarbethoxymethylphosphonium chloride (I). In the same paper they also report that treatment of I with sodium hydroxide (2) gave a compound formulated as the betaine (III). Recently Isler and co-workers[2] showed that the bromide analogue of I gives triphenylcarbethoxymethylene phosphorane (IV) on caustic treatment, rather than III. The discrepancy between these two reports led to a reinvestigation of the early work. Some of our results have been anticipated.[3]

$$(C_6H_5)_3P + ClCH_2COOC_2H_5 \dashrightarrow (C_6H_5)_3\overset{+}{P}CH_2COOC_2H_5,\bar{C}l\cdot nH_2O \quad (1)$$

I. $n = 0$
II. $n = 2$



III IV (2)

In following Michaelis's directions for the synthesis of the phosphonium chloride (I), difficulties were encountered. Attempts to recrystallize the crude product led invariably to decomposition. This problem was resolved when it became clear from interpretation of the infrared spectra, elementary analysis, and Karl Fisher determination that the product isolated was actually the dihydrate (II). This compound was best synthesized by simply mixing ethyl chloroacetate and a solution of triphenylphosphine in benzene. During standing at room temperature, a crystalline product was formed. The reaction was arbitrarily considered to be complete after a week and the product was filtered and washed with absolute ether. The crude salt was allowed to dry in air—*i.e.* in contact with water vapor—for one week. Under these conditions the dihydrate (II), of analytical purity, was obtained in high yield.

The dihydrate holds its crystalline water tenaciously. It survived recrystallization from methylene chloride–carbon tetrachloride. Long drying of II over phosphorus pentoxide *in vacuo* raised the melting point from 87° to 144°. This higher melting material is probably the anhydrous salt. On exposure to air, its melting point was soon lowered. Since the dihydrate was accessible, stable, and convenient for further work, no attempts were made to characterize the anhydrous salt.

An attempt to dehydrate the dihydrate (II) was made by refluxing with benzene. The products were found to be triphenylmethylphosphonium chloride (VI), carbon dioxide, ethanol and water. Formation of these products is represented by Equation 3. Reaction started as soon as the benzene

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