

BASICITY AND STRUCTURE OF  $\alpha$ ,  $\beta$ -UNSATURATED  
HETEROCYCLIC KETONES. VII†. METHYL-SUBSTITUTED  
CHALCONES

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The protolytic equilibrium constants in the system  $\text{H}_2\text{SO}_4\text{-CH}_3\text{COOH}$  and the shifts in frequency of the OH stretching vibrations ( $\Delta\nu_{\text{OH}}$ ) of phenol and trifluoroacetic acid resulting from the perturbational effects of hydrogen bonding with the carbonyl group have been measured for  $\alpha$ -alkyl-substituted heterocyclic analogs of chalcone. It has been shown that introduction of a methyl group into the  $\alpha$ -position of five-membered heterocycles results in an increase in the proton-acceptor properties of chalcone analogs, and moreover, the influence of the methyl group on the polarization of the carbonyl group is substantially increased on passing from the furan ring to the thiophene and selenophene rings, perhaps as a result of the participation of the d-orbitals of sulfur and selenium in the electronic interactions. The benzene ring transmits the electronic effect of the methyl group to almost the same extent as the furan ring.

In continuation of an examination of the proton-acceptor properties of  $\alpha$ ,  $\beta$ -unsaturated heterocyclic ketones, it was decided to determine the basicity of heterocyclic analogs of chalcone containing an alkyl group (methyl or ethyl) in the  $\alpha$ -position of five-membered heterocycles (see Table 1). We assumed that it would be possible with this series of compounds to compare the transmission of the effect of the methyl group on the polarization of the carbonyl group through the benzene, furan, thiophene, and selenophene rings.

There is little information in the literature on which to estimate the comparative abilities of different heterocycles to transmit the electronic effects of substituents [2-6]. The most interesting work is on the NMR chemical shifts of heterocycles [5, 6], since the shielding of the nucleus is very sensitive to changes in electron density resulting from substituents and from variations in the conduction of these effects in systems with different heteroatoms.

Recently, two of us [7] have investigated the UV and IR spectra, and dipole moments, of methyl-substituted heterocyclic analogs of chalcone. It was shown that in the static state the heterocyclic systems were somewhat more sensitive to the effects of the methyl substituent than the benzene nucleus. It was not possible, however, to demonstrate clear differences resulting from the nature of the heteroatom. In order to compare the transmissibility of electronic effects in the various heterocycles in the dynamic state, we have measured the protolytic equilibrium constants in the system  $\text{H}_2\text{SO}_4\text{-CH}_3\text{COOH}$ , and the shifts in frequency of the hydroxyl stretching vibrations ( $\Delta\nu_{\text{OH}}$ ) of phenol and trifluoroacetic acid resulting from the perturbational effects of hydrogen bonding with the carbonyl group for alkyl-substituted heterocyclic analogs of chalcone. Since it is well known that the properties of 2,5-disubstituted five-membered heterocycles are reminiscent of those of para-disubstituted benzenes, we also determined the basicity of 4- and 4'-methyl-chalcones for comparison.

† For Part VI, see [1].

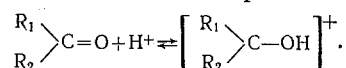
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TABLE 1. Protonation Constants and  $\Delta\nu_{\text{OH}}$  Values for Alkyl-substituted Chalcones  $\text{RCOCH}=\text{CHC}_6\text{H}_5$

Compound	Formula of ketone	$K \cdot 10^{10}$ *	$-\text{pK}_a$ *	$\Delta\nu_{\text{OH}}$ phenol, $\text{cm}^{-1}$	$\Delta\nu_{\text{OH}}$ $\text{CF}_3\text{COOH}$ , $\text{cm}^{-1}$
I	$\text{CH}_3\text{C}_4\text{H}_9\text{O}-\text{COCH}=\text{CHC}_6\text{H}_5^{**}$	$198 \pm 5$	$2,70 \pm 0,01$	$246 \pm 1$	$569 \pm 2$
II	$\text{CH}_3\text{C}_4\text{H}_9\text{O}-\text{CH}=\text{CHCOCH}_3$	$89 \pm 2$	$3,05 \pm 0,01$	$217 \pm 2$	$535 \pm 1$
III	$\text{CH}_3\text{C}_4\text{H}_9\text{S}-\text{COCH}=\text{CHC}_6\text{H}_5$	$34 \pm 1$	$3,47 \pm 0,01$	$213 \pm 2$	$531 \pm 3$
IV	$\text{C}_2\text{H}_5\text{C}_4\text{H}_9\text{S}-\text{COCH}=\text{CHC}_6\text{H}_5$	$72 \pm 2$	$3,14 \pm 0,01$	$216 \pm 2$	$534 \pm 1$
V	$\text{CH}_3\text{C}_4\text{H}_9\text{S}-\text{CH}=\text{CHCOCH}_3$	$74 \pm 3$	$3,13 \pm 0,02$	$211 \pm 1$	$527 \pm 2$
VI	$\text{CH}_3\text{C}_4\text{H}_9\text{Se}-\text{COCH}=\text{CHC}_6\text{H}_5$	$140 \pm 8$	$2,85 \pm 0,02$	$216 \pm 1$	$532 \pm 1$
VII	$\text{CH}_3\text{C}_4\text{H}_9\text{Se}-\text{CH}=\text{CHCOCH}_3$	$80 \pm 3$	$3,10 \pm 0,02$	$214 \pm 2$	$528 \pm 2$
VIII	$p\text{-CH}_3\text{C}_6\text{H}_4\text{COCH}=\text{CHC}_6\text{H}_5$	$17,3 \pm 0,7$	$3,76 \pm 0,02$	$215 \pm 2$	$522 \pm 1$
IX	$p\text{-CH}_3\text{C}_6\text{H}_4\text{CH}=\text{CHCOCH}_3$	$12,8 \pm 0,4$	$3,89 \pm 0,01$	$210 \pm 2$	$514 \pm 4$

\*K is the equilibrium constant for the protonation of the ketone



$\text{pK}_a$  is the dissociation constant for the conjugate acid of the ketone

\*\*  $\text{CH}_3\text{C}_4\text{H}_9\text{O}$  is 5-methyl-2-furyl;  $\text{CH}_3\text{C}_4\text{H}_9\text{S}$  is 5-methyl-2-thienyl; and  $\text{CH}_3\text{C}_4\text{H}_9\text{Se}$  is 5-methyl-2-selenenyl.

The values found for the protonation constants,  $\text{pK}_a$  values, and  $\Delta\nu_{\text{OH}}$  values for the alkyl-substituted chalcones are given in Table 1. Comparison of these results with those obtained previously for chalcone and its analogs [8, 9]† shows that the introduction of the methyl group either in the 4- or 4'-position of chalcone, or in the  $\alpha$ -position of the heterocyclic nucleus of its analogs, results in a considerable increase in the electron-acceptor properties. This is, of course, the result of the electron-donor properties of the methyl group which may, in general, arise from the positive inductive effect and the effect of hyperconjugation. From its protolytic equilibrium constant, 1-(5-ethyl-2-thienyl)-3-phenyl-1-propenone (IV) exhibits greater basicity than the analogous methyl-substituted compound (III). This can, however, hardly be taken as proof of the absence of the hyperconjugative effect in these compounds. A very likely reason for the significantly greater proton-accepting ability of IV in acid media, in comparison with III would be the more bulky nature of the ethyl group in comparison with methyl. This would shield the thiophene nucleus, reducing its solvation by acetic and sulfuric acid molecules, thereby increasing the interaction of the  $\pi$ -electron system of the heterocycle with the carbonyl group. It should be noted that, since in the formation of hydrogen bonds in an inert solvent (carbon tetrachloride), the effects of solvation are substantially reduced as compared with protonation in the system  $\text{H}_2\text{SO}_4\text{-CH}_3\text{COOH}$ , the ability of III and IV to associate with phenol and trifluoroacetic acid is virtually the same (the difference in the  $\Delta\nu_{\text{OH}}$  values lies within the limits of experimental error).

Comparisons of the changes in  $\text{pK}_a$  and  $\Delta\nu_{\text{OH}}$  of chalcones, resulting from the introduction of a methyl group into the aromatic ring or the heterocyclic ring (see Table 2), shows that the methyl group has a very considerable effect on the basicity of those isomers in which the carbonyl group is located in the direct vicinity of the methylated ring (1-propenones). This is in agreement with the generally accepted idea that the effects of atoms diminish with distance. However, the fact that, in the 3-propenones, the changes in  $\text{pK}_a$  and  $\Delta\nu_{\text{OH}}$  of trifluoroacetic acid are fairly large shows that the transmission of the effects of the methyl group through the carbonyl group conjugated with the carbon-carbon double bond is comparatively efficient. We came to a similar conclusion in [10, 11]. As far as the values of  $\Delta\nu_{\text{OH}}$  for phenol are concerned, however, they are much less sensitive to the electronic effects of the methyl group, as compared to the  $\text{pK}_a$  and  $\Delta\nu_{\text{OH}}$  for trifluoroacetic acid. Moreover, the influence of the methyl group on the values of  $\Delta\nu_{\text{OH}}$  for phenol in the 3-propenones is much reduced as compared with the 1-propenones (see Table 2). It is possible that dynamic effects play a considerable part in the protonation of the carbonyl group and the formation of hydrogen bonds with trifluoroacetic acid. Many workers include hyperconjugation of the methyl group in these effects. In addition, the ability of chalcones to form comparatively weak hydrogen bonds with phenol (as we have shown, [11],  $-\Delta H$  for the association of phenol with chalcones amounts to 4-5 kcal/mole) is basically determined by the static distribution of electron density in the molecules.

† The investigation of the hydrogen bonding of chalcone and its heterocyclic analogs with trifluoroacetic acid will be reported elsewhere.

TABLE 2. Changes in  $pK_a$  and  $\Delta\nu_{OH}$  as a Result of the Introduction of a Methyl Group into the Benzene or Heterocyclic Ring of the Chalcone

-R-	CH <sub>3</sub> -R-COCH=CHC <sub>6</sub> H <sub>5</sub> 1-Propenones			CH <sub>3</sub> -R-CH=CHCOC <sub>6</sub> H <sub>5</sub> 2-Propenones		
	$\Delta pK_a$	$\Delta(\Delta\nu_{OH})$ Phenol, cm <sup>-1</sup>	$\Delta(\Delta\nu_{OH})$ CF <sub>3</sub> COOH, cm <sup>-1</sup>	$\Delta pK_a$	$\Delta(\Delta\nu_{OH})$ Phenol, cm <sup>-1</sup>	$\Delta(\Delta\nu_{OH})$ CF <sub>3</sub> COOH, cm <sup>-1</sup>
-C <sub>6</sub> H <sub>4</sub> -	0,45	9	23	0,32	4	15
-C <sub>4</sub> H <sub>2</sub> O-	0,45	7	21	0,36	1	18
-C <sub>4</sub> H <sub>2</sub> S-	0,78	13	36	0,49	1	21
-C <sub>4</sub> H <sub>2</sub> Se-	0,62	10	32	0,44	3	20

Comparison of the values for  $\Delta pK_a$  and  $\Delta(\Delta\nu_{OH})$  resulting from the introduction of a methyl group into the  $\alpha$ -position of the heterocyclic radicals shows that transmission of the electronic effect of the methyl group increases considerably on passing from the furan to the thiophene and selenophene rings. The last two are not significantly different in their capacity to transmit electronic effects. In the 1-propenones, however, there is a tendency to a small reduction in the transmission of electronic effects when the sulfur atom is replaced by the heavier selenium. The benzene ring transmits electronic effects to almost the same extent as the furan ring (see Table 2).

The observed regularities in the changes in the transmissibility of the electronic effect of the methyl group in this series of five-membered heterocycles agrees with the results given in [4] for the trifluoroacetylation of furan and thiophene and their  $\alpha$ -methyl derivatives by the concurrent reaction method, in which introduction of a methyl group increases the rate of trifluoroacetylation of thiophene to a somewhat greater extent than it does in the case of furan.

It is interesting that the nature of the changes in the transmission of the electronic effects of substituents in the heterocycles which have been investigated are in agreement with the regularities noted for systems containing the same heteroatoms in open chains [12, 13]. The analogy is apparently due to the transmission of the electronic effects from the 2- to the 5-position of the heterocycles predominantly via the heteroatom, which is supported by the results given in [14].

The substantial increase in the transmission of electronic effects on passing from the furan ring to thiophene and selenophene may be explained by the participation of the d-orbitals of sulfur and selenium in these effects, as distinct from oxygen, in which there is no such possibility. It is, however, known [15] that the tendency of the vacant d-orbitals to participate in conjugation is reduced on passing from sulfur to selenium. It may be that this is also responsible for the reduction in the transmissibility in the selenophene ring in comparison with thiophene.

We have found that the order of change in transmissibility of the electronic effect of the methyl group in five-membered heterocycles in the dynamic state (furan < selenophene  $\leq$  thiophene) is not exactly the same as that for the static state. Thus, earlier investigations of the PMR spectra of carbonyl derivatives of furan, thiophene and selenophene [16] showed that, in the static state, the transmissibility of the electronic effects of substituents in five-membered heterocycles increased with increasing mass of the heteroatom (furan < thiophene < selenophene). A similar rule has also been noted for the spin-spin coupling constant for the 2 and 5 protons of the heterocycle [17]. The observed increase in the order of transmissibility of electronic effects in heterocycles in the static state corresponds to the increase in the polarizability of the heterocycles [18]. This factor apparently exerts a dominating effect in the static state.

From Table 1, it also follows that substitution in the 4- and 4'-methylchalcones of the methylated benzene ring by  $\alpha$ -methylated 2-furyl, 2-thienyl, and 2-selenenyl (compare VIII with I, III with VI, IX with II, and V with VII) is accompanied by a large increase in the protonation constant in acid media, and in the value for  $\Delta\nu_{OH}$  (particularly  $\Delta\nu_{OH}$  for trifluoroacetic acid). In this case, the electronic effect of the 5-methylated heterocycles decreases in the order: 2-(5-methyl)-furyl > 2-(5-methyl)-selenenyl > 2-(5-methyl)-thienyl. This is in agreement with the earlier conclusion [8, 9] on the similar order of reduction in transmissibility of electronic effects of unsubstituted heterocyclic radicals in  $\alpha$ ,  $\beta$ -unsaturated ketones.

## EXPERIMENTAL

The protolytic equilibrium constants were determined in sulfuric acid (monohydrate) in glacial acetic acid by the spectrophotometric method on an SF-4 instrument, in thermostated cells at  $20 \pm 0.2^\circ$ , as described in [1, 9, 19].

The  $\Delta\nu_{\text{OH}}$  values for phenol were measured in carbon tetrachloride solution on a UR-20 infrared spectrophotometer, as in [20].

The measurement of the  $\Delta\nu_{\text{OH}}$  shifts for trifluoroacetic acid were carried out in carbon tetrachloride solution on IKS-14 and UR-20 M instruments, at an acid concentration of 0.03 M and ketone concentration of 0.06 M. In the comparison cell there was placed the same concentration of the ketone in carbon tetrachloride. The reading was taken from the frequency of vibration of the free hydroxyl group of trifluoroacetic acid, which was found in separate experiments to be  $3500\text{ cm}^{-1}$ . In view of the hygroscopicity of trifluoroacetic acid, all the work with it was carried out in a dry box. Commercial trifluoroacetic acid was purified by distillation, taking the fraction bp  $71^\circ$ . Carbon tetrachloride, after treatment as in [21], was boiled for several hours over phosphorus pentoxide, followed by fractional distillation.

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