Enolate Anions. III. Substituent Effects of Sodium Diethyl Alkylmalonates in DMSO[1)]

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The conformations of sodium enolate anions, derived from diethyl malonate and diethyl alkylmalonates (alkyl=methyl, ethyl, propyl, isopropyl, butyl, isobutyl, and *s*-butyl), have been determined to be *Z,Z*-type by the analysis of their ^{1}H-NMR spectra in DMSO. In the case of diethyl *t*-butylmalonate, such a *Z,Z* type contributes to the lesser extent to the conformations of the sodium enolate anion because of repulsion between the *t*-butyl substituent and the two ethoxyl groups, which exist in three types (*Z,Z*, *Z,E*, *E,E*) of conformation, as is evident in the ^{1}H-NMR spectra. The IR spectra of sodium diethyl malonate in DMSO showed two characteristic absorption bands at 1679 and 1556 cm^{-1}. The IR isotope shifts upon the use of the enolates of diethyl malonate-2-^{13}C and diethyl malonate-1,3-$^{13}C_2$ suggested that these two bands are attributable to the C$\doteq$O and C$\doteq$C$\doteq$C bonds. All sodium diethyl alkylmalonates except for the *t*-butyl derivative have two characteristic IR bands in the region of 1500—1700 cm^{-1}, the bands on the high-frequency side of which have nearly equal wave numbers, while those on the low-frequency side have a good correlation with the substituent constant, σ^*.

Since the reaction rates in the alkylation of enolate anions have been reported to be rapidly accelerated by the addition of dipolar aprotic solvents, such as DMSO and DMF,[2)] the effect of the difference in the solvation state on the reactivity has been investigated for various reactions.[3)] Because of the mutual electrostatic-interaction between a cation and an enolate anion, almost all enolate anions tend to be present as ion pairs.[4)] Moreover, it is generally expected that the degree of this ion-pairing association would be altered by the extent of the solvation of the cation.

Recently, Raban *et al.* discussed the effect of the ion-pairing on the structures of the enolate anions of β-diketones on the basis of their ^{1}H- and ^{13}C-NMR spectra.[5)] The relations between the reactivity of the enolate anions derived from β-diketones and the ion-pairing were reported in detail by DePalma *et al.*[6)] In order to evaluate the reactivity of the enolate anions with ester groups, which are very important for organic synthesis, various spectral studies of them have been continued.[1)]

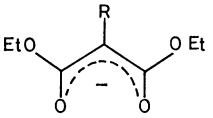
The substituent effects on the electron density at the delocalized anionic moiety of the enolate anions and on the conformations of them in DMSO were examined using the sodium enolates of ethyl substituted-phenylacetates.[1b)] The ^{13}C-NMR spectra of sodium diethyl alkylmalonates were shown to correspond to a single conformer except in the case of the *t*-butyl derivative.

This report deals with alkyl substituent effects on the electron density at the delocalized anionic moiety of sodium diethyl malonates and on their conformations by means of IR and ^{1}H-NMR measurements.

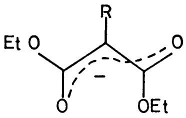
Results and Discussion

The enolate anions produced from acetylacetone were found to be 100% in the *Z,Z* conformation for lithium enolate and 34% in the *Z,Z* conformation for sodium enolate in methanol-d_4.[5a)] Further, the enolate anions from acetoacetaldehyde and ethyl acetoacetate exist exclusively in the *Z,Z* conformation for lithium enolates in DMF, and in the latter enolate anion, a *Z,Z* conformer is predominant even for sodium and potassium enolates.[7)] The sodium enolate of ethyl 2-methylacetoacetate in DMF was shown to exist 66% in the *Z,Z* conformation, which is slightly destabilized by the introduction of the α-methyl group.[7)]

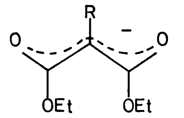
Three arrangements are possible for the structures of enolate anions derived from diethyl alkylmalonates. Compared with the stereomodels of other enolate anions, such as acetylacetonato-alkali metals, those of sodium diethyl alkylmalonates are so crowded that the most preferred conformation can not be presumed by the inspection of their stereomodels alone.



Z,Z



Z,E($\rightleftarrows$*E,Z*)



E,E

Table 1 shows the ^{1}H-NMR chemical shifts of diethyl alkylmalonates and their enolate anions in DMSO. The ^{1}H-NMR spectra of the enolates with the alkyl substituents other than the *t*-butyl group can be correlated to one conformation, as has been deduced from their ^{13}C-NMR spectra;[1a)] the number of conformers existing in the enolate anion can be determined simply by the inspection of the spectra of the ethoxyl groups. Upon enolate-anion formation, the chemical shifts of the methylene and methyl protons of the ethoxyl groups are shifted to a higher field, $\Delta\delta$ being +0.25—+0.30 and +0.09—+0.15 ppm respectively, while down-field shifts ($\Delta\delta$ −0.31—−0.81 ppm) are observed for the β-protons. The alkyl-substituent effects for these $\Delta\delta$ values can not, however, interpreted quantitatively.

On the other hand, the unusual chemical shifts of the enolate anion with a *t*-butyl substituent are very informative in estimating the structures of these enolate-anion series in DMSO. In this enolate anion, the chemical shifts of the methylene protons in ethoxyl groups are observed at 3.44 and 3.98 ppm, where the former is a quartet and the latter consists of two overlapping quartets. This result suggests the existence of three different conformers of the enolate anion in DMSO. In the case of the isopropyl substituent, the quartet

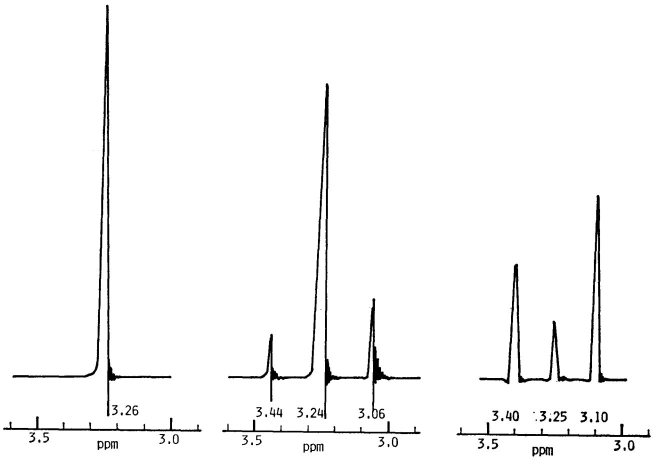
TABLE 1. ^{1}H-NMR CHEMICAL SHIFTS OF DIETHYL ALKYLMALONATES AND THEIR ENOLATES $(\underset{b}{CH_3}-\underset{a}{CH_2}-O-\underset{\overset{\|}{O}}{C}-)_2-\underset{\alpha}{CH}-\underset{\beta,\gamma,\delta,\varepsilon}{R}$

R	Chemical shifts (δ/ppm) a	b	α	β	γ	δ	ε
Hydrogen	4.15[a]	1.20	3.45				
	3.85[b]	1.09	3.66				
	+0.30[c]	+0.11	−0.21				
Methy	4.11	1.19	3.52	1.25			
	3.86	1.10		1.61			
	+0.25	+0.09		−0.36			
Ethyl	4.11	1.20	3.33	1.81	0.90		
	3.86	1.07		2.11	0.82		
	+0.25	+0.13		−0.30	+0.08		
Propyl	4.11	1.19	3.39	1.77		0.89	
	3.85	1.05		2.10		0.75	
	+0.26	+0.14		−0.33		+0.14	
Isopropyl	4.13	1.20	3.36	2.26	0.95		
	3.86[d]	1.06		3.07	1.00		
	+0.27	+0.14		−0.81	−0.05		
Butyl	4.11	1.19	3.38				0.87
	3.85	1.04					0.82
	+0.26	+0.15					+0.05
Isobutyl	4.09	1.18	3.49	1.70		0.88	
	3.84	1.03		2.01		0.75	
	+0.25	+0.15		−0.31		+0.13	
s-Butyl	4.13	1.21	3.28			0.86	
	3.85	1.06				0.70	
	+0.28	+0.15				+0.16	
t-Butyl	4.10	1.16	3.27	1.05			
	3.44 3.98[e]	1.13		1.03			
	+0.66 +0.12	+0.03		+0.02			

a) Parent esters. b) Enolate anions. c) Differences (a—b); a minus sign denotes down-field shift. d) After 24 h, the quartet at 3.86 ppm separated into two signals, at 3.45 (q) and 3.90 (dq) ppm. The integral intensity of the signal at 3.45 ppm was about half of that at 3.90 ppm. e) The ratio of the integral intensity of the signal at 3.44 ppm to that at 3.98 was about 2/3. The signal at 3.98 ppm is a multiplet similar to that at 3.90 ppm of the isopropyl derivative.

signal of methylene protons in the ethoxyl groups appeared at 3.86 ppm immediately after the enolate-anion preparation, but separated into two signals at 3.45 (a quartet) and 3.90 ppm (a double-quartet) after 24 h. This spectral change also suggests a change in the conformational distribution from a single conformational entity to a mixture of three different conformations closely related to the case of the *t*-butyl derivative. The conformational change might be attributable to the bulkiness of an alkyl group at α-carbon, which induces repulsions between the alkyl substituent and the ethoxyl groups.

If the same phenomenon could be observed for the sodium dimethyl alkylmalonate system, more precise information would be obtained, since far more simplified spectra are obtained for methoxyl groups. In practice, the ester-methyl parts of the ^{1}H-NMR spectra of the enolates were found to be in circumstances similar to those of the diethyl–ester system, as is illustrated in Fig. 1. The methoxyl parts of the ^{1}H-NMR spectra of the enolates with isopropyl or *t*-butyl substituents consisted of three singlet peaks with different intensities,



1) Ethyl derivative 2) Isopropyl derivative 3) *t*-Butyl derivative

Fig. 1. The methoxyl parts of the ^{1}H-NMR spectra of sodium enolates derived from dimethyl alkylmalonates in DMSO.

their chemical shifts closely corresponding to each other. On the other hand, only one singlet peak, corresponding to the central peaks of the three peaks described above, was observed in the enolate with an ethyl substituent. Again, in the case of the isopropyl derivative, methoxyl signals other than that at 3.24 ppm did not appear in the spectrum observed immediately after the enolate-anion preparation. The two signals at 3.44 and 3.06 ppm gradually appeared after the solution had been allowed to stand for 24 h at room temperature.

In order to determine the conformation to which the singlet peak in the case of ethyl derivative is to be ascribed, the spectral changes upon the addition of 18-crown-6 were investigated with the enolates of diethyl ethylmalonate, dimethyl isopropylmalonate, and dimethyl *t*-butylmalonate. Though the ^{1}H-NMR signal of 18-crown-6 and that of the lowest-field peak in the three singlet peaks of the enolates overlap each other, the integral intensities of the other two peaks could be measured and compared with those of the α-alkyl moieties. Thus, the intensities of the singlet peak in the ethyl derivative and of the central singlet peaks in the isopropyl and *t*-butyl derivatives were decreased by the addition of 18-crown-6. This spectral change caused by 18-crown-6 is a result of the dissociation of the ion pairs, facilitated by the ability of 18-crown-6 to capture the cation.5a)

Among the three possible arrangements, the most stable conformation for the non-dissociated ion pairs is thought to be the *Z*,*Z* type. Zaugg *et al.* have discussed how *Z*,*E* and *E*,*E* types are more dissociated than the *Z*,*Z* type.8) It has generally been accepted that, in the absence of compelling steric interactions, the *Z*,*Z* conformers exist only as ion pairs; chelation by the counter-cation is necessary to offset the coulombic repulsions between the two oxygen atoms.7) The small central peak in the case of the *t*-butyl substituent can also be assigned to the *Z*,*Z* conformer, while the outer two peaks may be ascribed to the *Z*,*E* and *E*,*E* conformers, although their assignment remains to be definitely settled.

Vibrational spectroscopy is useful in estimating the electron density of bonds. Zook *et al.* found that the typical C=O stretching frequency (1710 cm^{-1}) of pinacolone shifts to a much lower region (1575 cm^{-1}) on conversion to its sodium derivative.3a) A similar lower frequency shift, from 1724 to 1589 cm^{-1}, has also been observed when ethyl phenylacetate was converted to its sodium enolate.1b)

Table 2 shows the IR absorption frequencies of diethyl alkylmalonates and their sodium enolates in DMSO in the region of 1800—1500 cm^{-1}. These enolate anions have two characteristic absorption bands, except that the *t*-butyl substituent, which has a broad absorption band at 1600 cm^{-1}, presumably because its complex conformational composition is different from those with the other substituents. The enolate anions of *β*-dicarbonyl compounds have been established to have two absorption bands in this region.9) Acetylacetone forms a metal chelate, and the chelate ring (*Z*,*Z* conformation) is planar and symmetrical; the two C≃O bonds are equivalent, as are the C≃C bonds in the ring. The IR spectra of bis(acetylacetonato)copper(II) showed two bands (1578 and 1527 cm^{-1}) in the carbonyl region; they were assigned to the C≃O stretching and C≃C≃C stretching modes of vibration respectively, on the basis of their ^{13}C isotope shifts; the original 1578 and 1527 cm^{-1} absorptions were found to shift to frequencies lower by 30 and 7 cm^{-1} respectively in the 2,4-$^{13}C_2$ derivative and by 3 and 1 cm^{-1} respectively in the 1,3,5-$^{13}C_3$ derivative.10)

TABLE 2. IR SPECTRA OF DIETHYL ALKYLMALONATES AND THEIR SODIUM ENOLATES IN DMSO IN THE REGION OF 1800—1500 cm^{-1}

Alkyl	Wave numbers		
	Parent ester	Sodium enolate	
Hydrogen	1732	1679	1556
Methyl	1729	1677	1524
Ethyl	1731	1675	1521
Propyl	1729	1671	1519
Isopropyl	1728	1667	1512
Butyl	1727	1670	1517
Isobutyl	1728	1668	1516
s-Butyl	1732	1665	1509
t-Butyl	1731	1600	

a) The wave numbers were given as the mean values of two split absorptions, which were identified as symmetrically and *anti*-symmetrically coupled vibrations; R. A. Abramovitch, *Can. J. Chem.*, **36**, 151 (1958); **37**, 361 (1959).

TABLE 3. IR SPECTRA OF SODIUM DIETHYL MALONATES LABELED BY ^{13}C AND THE ISOTOPE-SHIFTS VALUES IN THE REGION OF 1700—1500 cm^{-1}

^{12}C Compound	1,3-^{13}C Compound	2-^{13}C Compound
1679	(1659 sh.) 1640a) (Δδ 39) 1630a)	1675 (Δδ 4)
(1564 sh.)		
1556	1519 (Δδ 37)	1552 (Δδ 4)

a) The intensity of the absorption at 1640 cm^{-1} is slightly smaller than that at 1640 cm^{-1}; this may be caused by combination vibrations.

Isotope-labeling experiments were employed to assign the two absorption bands of sodium diethyl malonate. In the IR spectrum of sodium diethyl malonate-1,3-$^{13}C_2$, the absorption bands at 1679 and 1556 cm^{-1} of the ^{12}C compound shifted to a frequency region lower by 39 and 37 cm^{-1} respectively, as is shown in Table 3. On the other hand, the sodium diethyl malonate-2-^{13}C gave only a small isotope shift (Δδ —4 cm^{-1}), which indicated that the C-2 carbon atom participates little in these two vibrations, such as in the case of the *β*-diketone system. Consequently, the two absorptions of sodium diethyl malonate at 1679 and 1556 cm^{-1} are assigned to vibrations of the C≃O and C≃C≃C bonds respectively.10) The assignment of the latter is further verified by the examination of the alkyl-substituent effect on the positions of the two absorptions of the sodium

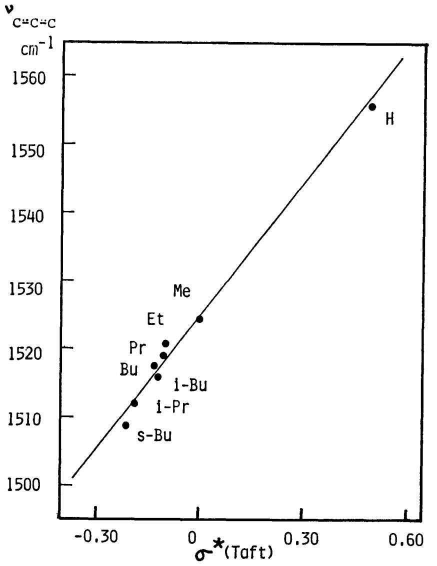


Fig. 2. Correlation of $\nu_{C=C=C}$ (cm^{-1}) in the IR spectra of sodium diethyl alkylmalonates in DMSO to Taft's σ*.

enolate of diethyl alkylmalonates. While the absorptions at higher frequencies of the two remain rather unaffected by the alkyl substituent, those at lower frequencies are nicely correlated (r=0.994) to the substituent constants, σ*, as is shown in Fig. 2. The inductive effect of α-alkyl substituents will affect the C=C=C group more intensely than the C=O group, a bond away from the α-carbon.

Experimental

The diethyl and dimethyl esters of alkylmalonic acids were synthesized according to the literature[12] and were identified by elementary analysis and by means of the ^{1}H-NMR spectra. Diethyl malonate-1,3-$^{13}C_2$ and diethyl malonate-2-^{13}C, from the British Oxygen Company, Limited, labeled with 93.0 and 92.0 atom% respectively, were used.

The preparation of enolate anions and the IR and ^{1}H-NMR measurements of them were carried out in a manner similar to that described in a previous report.[1b]

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