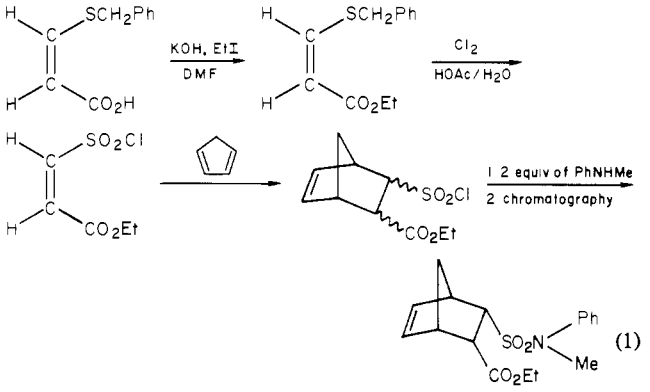
Experimental Section

Materials.[27] The sulfonamides **1–3** were synthesized as reported previously.[1a] Compound **4** was prepared according to standard procedures[28] starting from the ethyl ester of *N*-phenylglycine.

***N*-Phenyl-*N*-(methylsulfonyl)glycine (4)**: mp 151.0–152.7 °C; NMR ($CDCl_3$) 3.07 (s, 3 H), 4.50 (s, 2 H), 7.42 (s, 5 H), 8.20 (s, 1 H). Anal. Calcd for $C_9H_{11}NO_4S$: C, 47.15; H, 4.84; N, 6.11; S, 13.99. Found: C, 47.03; H, 4.83; N, 6.13; S, 14.13. The ethyl ester of compound **5** was prepared according to eq 1.[28,29]



(1)

6

2-*endo*-(Ethylcarboxy)-3-*endo*-(*N*-methyl-*N*-phenylsulfonamido)bicyclo[2.2.1]hept-5-ene (6): mp 81.2–82.6 °C; NMR ($CDCl_3$) 1.1–1.6 (m, 5 H), 3.0–3.5 (m, 3 H), 3.35 (s, 3 H), 3.9–4.3 (m, 1 H), 5.9–6.1 (m, 1 H), 6.4–6.6 (m, 1 H), 7.1–7.6 (m, 5 H). Anal. Calcd for $C_{17}H_{21}NO_4S$: C, 60.87; H, 6.31; N, 4.18; S, 9.56. Found: C, 61.17; H, 6.24; N, 4.21; S, 9.47. The X-ray structure[30] of **6** confirmed the endo position of both substituents at the ring.

2-*endo*-Carboxy-3-*endo*-(*N*-methyl-*N*-phenylsulfonamido)bicyclo[2.2.1]hept-5-ene (5). The preparation of the sodium salt of **5** was carried out as previously described[1a,31] for **1** and the salt was used as such in the kinetic measurements.

Kinetic Measurements. The kinetic data for hydrolysis of **4** and **5** have been determined by using the UV and NMR methods outlined in earlier studies.[1a]

Ab Initio Calculations. The closed-shell SCF ab initio calculations[16] were carried out by using Roos and Siegbahn's double-ζ contracted Gaussian basis set[17,18] with one 3d polarization function on sulfur. The orbital exponent for this polarization function was 0.54.[32] It has been shown that for compounds in which the sulfur atom is surrounded by electron-withdrawing groups, geometries can only be properly described by including sulfur d orbitals.[33] The molecular structure of Ib was optimized by sequentially varying the bond lengths to sulfur and the equatorial OSO angle. The sequence followed was[34] (1) S–O_e bond lengths, (2) OSO bond angle, (3) S–N bond length, (4) S–O_a bond length, (5) S–C bond length. Further iteration was not necessary. In Ia only the S–O_a and the S–N bond lengths were optimized, assuming that the equatorial bond lengths are less sensitive for the change in structure.[7] In order to save computer time, bond lengths and angles not involving the central sulfur atom were not optimized and standard values were taken from the literature.

All calculations were performed on a CDC Cyber 170/760 computer, using the program BIGMOL.[16,35]

Acknowledgment. We thank Dr. A. J. Kirby (University of Cambridge, England) for his interest in this work. We are indebted to Drs. B. T. Thole and H. Teeninga for their help in performing the calculations.

(27) Melting points were determined by using a Mettler FP1 apparatus. ^1H NMR spectra were recorded on a Hitachi Perkin-Elmer R24B high-resolution spectrometer. Me_4Si (δ 0) was used as an internal standard. IR spectra were taken on a Perkin-Elmer 257 spectrophotometer. Elemental analyses were performed by H. Draayer, J. Ebels, J. Hommes, and J. E. Vos of the analytical section of the Department.

(28) Details are available on request.

(29) Johnsson, H.; Allenmark, S. *Chem. Scripta* **1975**, *8*, 216–222.

(30) Unpublished work together with Professor H. Schenk, University of Amsterdam.

(31) Wagenaar, A.; Kirby, A. J.; Engberts, J. B. F. N. *Tetrahedron Lett.* **1976**, 489–492.

(32) Roos, B.; Siegbahn, P. *Theor. Chim. Acta* **1970**, *17*, 199–208.

(33) See, for example, Palmer, M. H.; Findlay, R. H. *J. Chem. Soc., Perkin Trans. 2*, **1975**, 1223–1230; (b) Keeton, M.; Santry, D. P. *Chem. Phys. Lett.* **1970**, *7*, 105–106; (c) Hillier, I. H.; Saunders, V. R. *Mol. Phys.* **1971**, *22*, 193. The same situation is encountered in open-shell sulfonyl systems: Teeninga, H.; Nieuwpoort, W. C.; Engberts, J. B. F. N. *Z. Naturforsch.* **1981**, *36b*, 279–281.

(34) As indicated by one of the referees, the protocol followed for Ib does not allow for a structural deformation along the coordinates for Berry pseudo-rotation (BPR). However, on the basis of the data for II–IV listed in Table II, we suggest that high energies are involved in structural perturbations which result from BPR for Ib.

(35) The program has been written by B. T. Thole and P. T. van Duynen (University of Groningen) and has been especially designed to perform calculations on large molecules.

Methylation of Lithioisobutyrophenone in Weakly Polar Aprotic Solvents. The Effect of Aggregation[1]

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Contribution from the Department of Chemistry, The Pennsylvania State University, University Park, Pennsylvania 16802. *Received January 30, 1981*

Abstract: The ratios (C/O) of C- and O-methylation of lithioisobutyrophenone in dioxolane and in dimethoxyethane have been determined over a wide temperature range and in the presence and absence of LiCl. Comparison of these results with those of earlier NMR studies has established that ion-pair aggregates are the true reactants. The effects of crown ethers, [2.1.1]cryptand, and hexamethylphosphoric triamide on both C/O and ^{13}C chemical shifts confirm these findings. The influence of the leaving group structure on rates and C/O has been established. Direct ESR evidence for the formation of a radical anion in the reaction of lithioisobutyrophenone with methyl *p*-nitrobenzenesulfonate is presented.

Enolate ions are ubiquitous intermediates in organic chemistry and are involved in many reactions of great synthetic utility. The factors controlling reactivity and product orientation in the reactions of these ambident anions with electrophiles have received wide attention.[2] Their behavior in aprotic solvents of high ionizing power (class C solvents[3]) is reasonably well understood[2,4] in terms

(1) This work was supported by Grant Nos. CHE76-20879 and CHE80-02426 from the National Science Foundation.

(2) L. M. Jackman and B. C. Lange, Tetrahedron Report No. 42, *Tetrahedron* **33**, 2737 (1977).

0002-7863/81/1503-4494$01.25/0

of the Pearson theory of hard and soft acids and bases (HSAB theory).[5] For weakly polar aprotic solvents (class B solvents), the situation is less clear even though the synthetic organic chemist frequently employs such solvents to suppress various side reactions which involve proton transfer between the enolate ion and ketonic products. The different behavior in class B solvents has been postulated by House,[6] by Zook[7a] and by Bram[7b] to be a consequence of the involvement of ion pairs and ion-pair aggregates, but the lack of precise knowledge of the structures of these entities has hampered a detailed understanding of mechanism in this area. We have recently reported[8,9] NMR studies of lithioisobutyrophenone (**1**) in class B solvents which have allowed the characterization of some of the ion-pair species present, and in this paper we examine the relation of these species to reactivity and orientation in the alkylation of this enolate ion.

The NMR studies have allowed the detection of only the principal species present under various conditions in class B solvents. Evidence will be presented which indicates that these species, rather than less aggregated ones present at low concentrations, are indeed reactants in the rate-controlling step of alkylation, and thus rates and orientation must ultimately be explicable in terms of their structures.

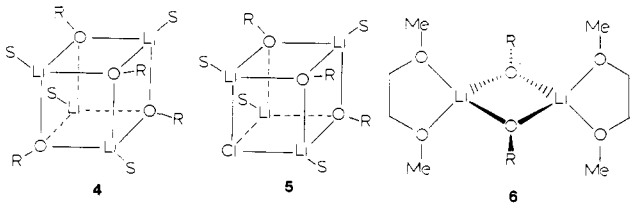
The enolate ion of isobutyrophenone was chosen because it is representative of simple enolates and because it has a unique structure and stereochemistry. It has the further advantage that it can only undergo monoalkylation. In the present study we have examined the reactions of a variety of methylating agents designed to provide a range of hardness of the leaving groups. We have also studied the effects of several cation complexing reagents on product orientation in these reactions.

$$\underset{\mathbf{1}}{PhC(OLi)=C(CH_3)_2} \rightarrow \underset{\mathbf{2}}{PhC(OCH_3)=C(CH_3)_2} + \underset{\mathbf{3}}{PhCOC(CH_3)_3}$$

Results and Discussion

Previously Characterized Species. In order to facilitate the discussion of the results presented below, we first catalog the species which we have characterized through NMR studies.[8,9]

Lithioisobutyrophenone in dioxolane exists as the tetramer, formulated as **4**, which occurs as two different solvates depending on temperature. The species predominating at low temperatures (<−8 °C) is more highly solvated although the absolute solvation numbers have not been established. The addition of lithium chloride converts the tetramer **4** to **5**.



4 **5** **6**

R = $(CH_3)_2C=C(Ph)-$

S = Solvent

Table I. Effect of Temperature and Added Lithium Chloride on Rate and C/O for the Methylation of Lithioisobutyrophenone by Dimethyl Sulfate in Two Solvents

dioxolane						dimethoxyethane					
no LiCl			1.23 equiv of LiCl			no LiCl			1.23 equiv of LiCl		
T, °C	$t_{1/2}$, min	C/O	T, °C	$t_{1/2}$, min	C/O	T, °C	$t_{1/2}$, min	C/O	T, °C	$t_{1/2}$, min	C/O
−20		1.56	−20		1.50						
−10	2000	1.27	−10		1.08						
0	720	1.22	2	420	1.04						
11	170	0.96	11	160	0.92						
23	80	0.89	25	60	0.92	25	6	1.22	24	9	0.92
40	14	0.89				40	<1	1.38			
50	8	0.79	50	5	0.82				55	1	0.89
62	3	0.82									
73	<1	0.79				83	<1	1.13			

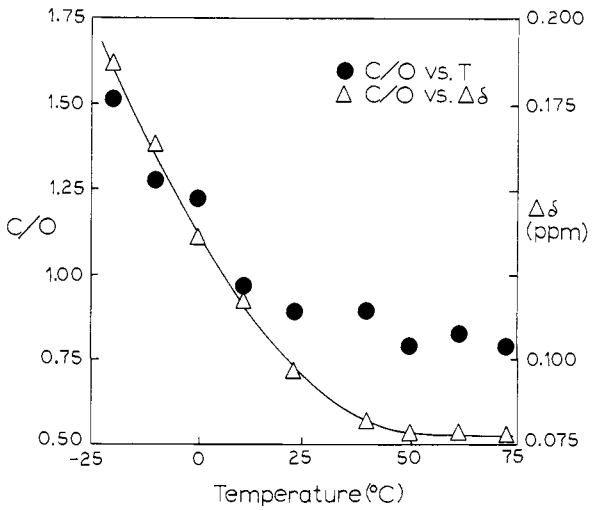


Figure 1. Plots of C/O and Δδ vs. temperature for the methylation of lithioisobutyrophenone by dimethyl sulfate in dioxolane.

In dimethoxyethane (DME), the major species is the dimer **6**, although significant amounts (~15%) of a tetramer presumably analogous to **4** are also present. Addition of lithium chloride converts both the dimer and tetramer into the aggregate **4**.

Evidence for the Direct Involvement of Aggregates in Methylation. The reaction of lithioisobutyrophenone in dioxolane with dimethyl sulfate yields comparable amounts of the methyl enol ether **2** (O-alkylation) and pivalophenone **3** (C-alkylation). It is expected that the product ratio (C/O ratio) should be characteristic of the particular species of lithioisobutyrophenone undergoing alkylation. Thus, whereas changes in conditions might well affect the rates of reaction by changing the concentration of a particular species, the C/O ratio should be relatively insensitive provided that the same species remains the true reactant.

Examination of the reaction of lithioisobutyrophenone in dioxolane at various temperatures reveals that the C/O ratio is essentially constant in the range 30–75 °C, but increases markedly below 30 °C (Table I, Figure 1). The onset of this change corresponds to the appearance of the more highly solvated ("low-temperature") aggregate. Indeed, Figure 1 reveals a good correlation between the C/O ratio and Δδ, the difference in chemical shift between the two methyl groups of the enolate ion. It is, in fact, the quantity Δδ which was used[8] to determine the relative concentrations of the two tetramers. Evidently, the more highly solvated species has a reactivity toward dimethyl sulfate which is comparable with or greater than that of the "high-temperature" tetramer so that in the temperature range in which the concentration of the former becomes significant it determines the observed product ratios. Unfortunately, it was not feasible to determine the limiting C/O ratio for the "low-temperature" aggregate since below −20 °C the reaction times were prohibitively

(3) A convenient rough classification of solvents in carbanion reactions has been suggested.[2] Briefly, the categories are: (A) nonpolar, (B) weakly polar (e.g., ethers), (C) polar aprotic, (D) polar protic.

(4) (a) A. L. Kurts, N. K. Genkina, A. Macias, I. P. Beletskaya, and O. A. Reutov, *Tetrahedron*, **27**, 4777 (1971); (b) W. J. LeNoble and H. F. Morris, *J. Org. Chem.*, **34**, 1969 (1969); (c) Y. Hara and M. Matsuda, *Bull. Chem. Soc. Jpn.*, **49**, 1126 (1976).

(5) R. G. Pearson and J. Songstad, *J. Am. Chem. Soc.*, **89**, 1827 (1967).

(6) H. O. House, M. Gall and H. D. Olmstead, *J. Org. Chem.*, **36**, 2361 (1971), and references cited therein.

(7) (a) H. D. Zook and W. L. Gumby, *J. Am. Chem. Soc.*, **82**, 1386 (1960); (b) F. Guibé, P. Sarthou, and G. Bram, *Tetrahedron*, **30**, 3139 (1974).

(8) L. M. Jackman and R. C. Haddon, *J. Am. Chem. Soc.*, **95**, 3687 (1973).

(9) L. M. Jackman and N. M. Szeverenyi, *J. Am. Chem. Soc.*, **99**, 4954 (1977).

Table II. Effect of Complexing Reagents on ^{13}C Chemical Shifts for Lithioisobutyrophenone in Dioxolane and Dimethoxyethane at 23 °C

complexing agent	mol equiv	chemical shifts (δ or $\Delta\delta^a$), ppm C(1)	C(2)	CH_3	CH_3	ipso	ortho	meta	para
				Dioxolane					
none		155.3	96.2	20.9	18.9	146.8	128.7	129.1	126.4
triglyme	5.02	0.1	*b*	0.3	0.0	0.0	−0.2	−0.1	−0.2
12-crown-4	5.00	0.0	*b*	0.1	0.1	0.1	0.0	−0.1	0.0
HMPT	4.41	1.6	−4.3	0.7	0.4	1.5	−1.4	0.3	−1.6
[2.1.1]cryptand	1.13	3.8	−7.7	1.6	1.3	3.1	−1.8	1.2	−2.4
				Dimethoxyethane					
none		156.0	93.6	21.3	18.9	147.7	127.8	129.2	125.5
triglyme	5.02	0.0	−0.1	0.1	0.0	0.0	−0.2	0.0	−0.2
15-crown-5	1.12	0.0	0.0	0.1	0.0	0.0	0.0	0.0	−0.1
12-crown-4	5.01	0.0	0.0	0.1	0.1	0.0	0.0	0.0	−0.2
HMPT	4.40	0.9	−1.9	0.4	0.4	0.6	−0.8	0.1	−0.9
[2.1.1]cryptand	1.11	2.7	−4.6	1.3	1.3	2.0	−1.1	1.2	−1.7

[a] $\Delta\delta = \delta$(complexing reagent) − δ(none). [b] Obscured by solvent absorption.

long. These findings demonstrate that at least the more highly solvated tetramer is directly involved in the alkylation by dimethyl sulfate at low temperatures and the less solvated species is strongly implicated at higher temperatures.

The addition of lithium chloride to the dioxolane solutions appears to cause a small increase in the half-lives of the reactions at various temperatures but, within experimental error, does not affect the C/O ratios (Table I) even though the concentration of lithium chloride was sufficient to effect essentially complete conversion of **4** to **5**. We therefore conclude that the reactivity of the tetramers are little affected by the replacement of RO^- by Cl^- at one of the corners of the cubic array. This is in accord with the observation[9] that the ^{13}C chemical shifts of all carbon atoms (including that in the sensitive β position) of the enolate ion are unchanged by the addition of LiCl, indicating that there is essentially no difference in the electron distribution in the enolate ion in the two environments (**4** and **5**).

Methylation by dimethyl sulfate is faster in dimethoxyethane than in dioxolane and leads to an increased C/O ratio (Table I). This behavior is probably characteristic of the dimer **6** which is the predominant species in the former solvent. In any event, addition of lithium chloride at concentrations sufficient to convert **6** to an aggregate analogous to **5** results in a reduction in rate and a decrease in the C/O ratio to a value characteristic of the tetramers in dioxolane. Thus, in the presence of lithium chloride, the direct involvement of the tetramer in alkylation is again strongly implicated. It is noteworthy that the species **5** is more reactive in dimethoxyethane than in dioxolane.

Effect of Li^+ Complexing Reagents. Another approach to the identification of the kinetically significant enolate species is provided by studies of the effect of the addition of lithium cation complexing reagents on the rate and orientation of methylation. House, Prabhu, and Phillips[10] examined the effect of several crown ethers on the ^{13}C spectra of alkali metal enolates in class B solvents, and the spectra showed that, if complexation occurred, it was to an extent insufficient to cause observable changes in the ^{13}C chemical shifts. We have performed a similar study of isobutyrophenone in dioxolane and dimethoxyethane with triglyme, 15-crown-5, 12-crown-4, hexamethylphosphoric triamide (HMPT), and [2.1.1]cryptand (**7**), the results of which are presented in Table II, and have confirmed the findings of House and his co-workers

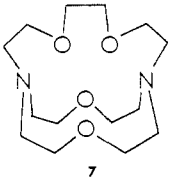


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Table III. Effect of Complexing Reagents on C/O[a] for Lithioisobutyrophenone (0.162 M) in Dioxolane and Dimethoxyethane at 23 °C

complexing agent	mol equiv	dioxolane C/O DMS	dioxolane C/O CH_3I	dimethoxyethane C/O DMS	dimethoxyethane C/O CH_3I
none		0.89[b]	>100[c]	1.22[d]	>200[e]
triglyme	1.26	0.70	49	1.04	>200[e]
	5.03	0.67			
15-crown-5	1.00	0.39	49	0.33[e]	49[e]
	1.26	0.35	19	0.37	49
12-crown-4	0.11	0.37		0.82	
	1.00	0.25		0.33	49
	1.26	0.27	24	0.28	49
	1.50	0.27	19	0.32	49
HMPT	0.41	0.39		0.37	
	4.00	0.15[e]	10	0.19	10
	4.40	0.15		0.15	
[2.1.1]-cryptand (7)	1.10	0.08[e]	6[e]	0.08[e]	8[e]

[a] See Experimental Section for discussion of the accuracy of the C/O ratios. [b] Half-life ($t_{1/2}$) at 23 and 40 °C is 80 and 14 min, respectively. [c] $t_{1/2}$ = 8 min. [d] $t_{1/2}$ = 6 min. [e] $t_{1/2}$ < 1 min.

regarding the crown ethers. The much more powerful lithium ion complexing agent, [2.1.1]cryptand, however, has a profound effect on the spectra. For example, in the solvent dioxolane, the resonance of the 2-carbon atom is shifted by almost 8 ppm to higher fields, corresponding to a substantial increase in charge density at that position. The X-ray structure of the [2.1.1]cryptand complex of lithium iodide reveals virtually complete dissociation of the LiI ionic bond, the lithium cation being completely encapsulated by the ligand.[11] Thus the ^{13}C spectrum of the lithium enolate in the presence of the cryptand presumably corresponds to that of the anion perturbed only slightly, if at all, by very weak ion pairing. The spectra in the two solvents studied are almost identical.

House et al.[10] showed that the addition of 4 equiv of HMPT caused significant upfield shifts of C(1) in the lithium enolate (**8**),

$$PhC(OLi)=CH_2$$
8

indicative of selective solvation of the lithium cation. We observe (Table II) similar behavior with lithioisobutyrophenone in dioxolane and dimethoxyethane. The absolute chemical shifts (δ) are the same in the two solvents and are unaffected by the further addition of 1 equiv of HMPT. The relative shifts ($\Delta\delta$), however, are less than those produced by [2.1.1]cryptand which shows that

(10) H. O. House, A. V. Prabhu, and W. V. Phillips, *J. Org. Chem.*, **41**, 1209 (1976).

(11) D. Moras and R. Weiss, *Acta Crystallog., Sect, B*, **29**, 400 (1973).

Table IV. Effect of Leaving Group on C/O Ratios for the Methylation of Lithioisobutyrophenone

methylating agent	dioxolane T, °C	dioxolane $t_{1/2}$, min	dioxolane C/O	DME T, °C	DME $t_{1/2}$, min	DME C/O	DME/[2.1.1]-cryptand[a] T, °C	DME/[2.1.1]-cryptand[a] C/O
CH_3I	42	<1	>100	42	<1	>100	24	8.1
CH_3Br	40	*b*	>100	24	*b*	100		
$(CH_3O)_2SO$				42	*c*	3-4	24	0.15
$(CH_3O)_3PO$	72	210	0.92	83	40	0.92	24	0.14
CH_3OTs	40	270	0.92				24	0.09
$(CH_3O)_2SO_2$	40	7	0.89	40	0.5	1.38	24	0.08

[a] 1.11 mol equiv. [b] Large excess of CH_3Br under reflux. [c] After 85 h.

Table V. Effect of the Para Substituent in Para-Substituted Methyl Benzenesulfonates on Methylation of Lithioisobutyrophenone in Dioxolane at 43 °C

X in p-$XC_6H_4SO_2OCH_3$	C/O	$t_{1/2}$, min	% yield
OCH_3	0.89	360	85
CH_3	0.92	270	78
H	0.89	160	83
Br	0.92	60	88
NO_2[a]	*b*		

[a] An electron-transfer reaction predominates. [b] Only trace amounts of alkylation products were observed.

there is still a significant interaction between the enolate ion and the HMPT solvated cation.

We have examined (Table III) the consequences of addition of the various complexing agents on the orientation of methylation by dimethyl sulfate (DMS) and methyl iodide. With the exception of triglyme, each of the complexing agents accelerated alkylation by dimethyl sulfate by a factor greater than 15. Thus, although the two crown ethers do not produce an observable change in the ^{13}C spectrum in either dioxolane or dimethoxyethane, it is clear that they do produce new species which are more reactive than either the tetramers (**4**) or dimers (**6**). This is also true for the additions of HMPT and [2.1.1]cryptand. As expected, the complexation of the cation exposes the oxygen terminus of the ambident anion and greatly decreases the C/O ratio.

Effect of Leaving Group. Table IV summarizes the data for the effect of the leaving group on the C/O ratio for methylation of lithioisobutyrophenone. The data for the reaction in the presence of [2.1.1]cryptand presumably characterize the reaction of the essentially free anion in dimethoxyethane, and the effects of the leaving groups are strikingly similar to those observed for the methylation[4c] and ethylation[4a,b] of the ethyl acetoacetate enolate ion in HMPT and for the tetrabutylammonium salt of ethyl acetoacetate in DME.[7b] This pattern of behavior has been interpreted[4,8] as a manifestation of the symbiotic effect[5] embodied in HSAB theory.

Reactions of the tetrameric (**4**) and dimeric (**6**) aggregates give substantially higher C/O ratios so that soft leaving groups (e.g., iodide) afford almost exclusive C-alkylation in both dioxolane and DME. This also parallels the behavior of ethyl lithioacetoacetate in DME[7b] even though this salt presumably has a chelated structure which is different from **6**. The C/O ratios do not parallel the overall rates of reaction but, again, they are in accord with the qualitative predictions of HSAB theory. Similarly, we have found that, while the rates of reaction of a series of para-substituted methyl benzenesulfonates (Table V) show a modest dependence ($\rho = 1.7$, $r = 0.944$) on the Hammett σ value of the substituent, the corresponding values of C/O are identical within experimental error.

Methyl p-nitrobenzenesulfonate was found to react rapidly and exothermically with lithioisobutyrophenone in dioxolane to give a dark red solution which on workup afforded a complex mixture of products containing less than a 10% yield of the expected

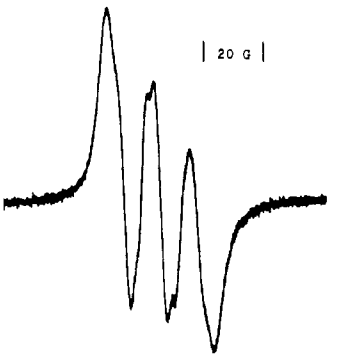
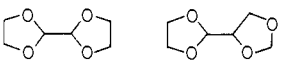


Figure 2. ESR spectrum of the reaction mixture of lithioisobutyrophenone and methyl p-nitrobenzenesulfonate in dioxolane at room temperature.

methylation products. The initial reaction appears to involve electron transfer from the enolate anion to the nitro ester to form a rather stable radical anion. The radical anion was characterized by its ESR spectrum (Figure 2) which consists of a triplet resulting from hyperfine splitting (12 G) by ^{14}N. The spectrum persisted for an appreciable time even at room temperature. A major component of the mixture of volatile products from the reaction consisted of two very similar compounds which were found by chemical ionization GLC–MS to have molecular weights of 146 and both of which showed a base peak at m/e 118 (–28) in their electron impact mass spectra. These are tentatively assigned as the epimeric bis(ethylene acetals) of glyoxal (**9**) which could be



9

expected to arise by hydrogen abstraction from the solvent followed by radical dimerization. The electron transfer between the enolate ion and the alkylating agent is reminiscent of reactions of p-nitrobenzyl chloride with enolate ions studied by Kornblum, Michel, and Kerber.[12] In their case, the radical anion is unstable to loss of chloride ion and the benzylation then occurs by coupling of the two neutral free-radical intermediates.

Effect of Aggregate Structure on Orientation. The major consequence of aggregation is seen to be a 10–20-fold increase in the C/O ratio and an overall decrease in rate of reaction by at least a factor of 100 in those cases where we have been able to determine it (Table III). A possible explanation is that O-alkylation of aggregates cannot occur because of the encumbrance of the oxygen atom of the enolate ion by the lithium cations. The formation of enol ether would then require dissociation of the aggregate in order to expose the oxygen terminus to the electrophile. A compelling argument against this postulate is provided, at least for the reactions with dimethyl sulfate, by the observation (Table I) that the C/O ratio is unaffected by the addition of lithium chloride which is known[8] to stabilize the tetramer as **5**. In fact, our earlier NMR studies[8] showed that dissociation of **5** is rate determining in the exchange of the enolate anion between **4** and **5**. Furthermore, the orientation in the methylation by dimethyl sulfate of the tetrameric species **5** is the same in dioxolane as in the better cation solvating solvent, DME, in which the reaction proceeds 5.5 times faster. Evidently, the electrophile is able to reach the enolate oxygen atom without dissociation of the complex. The precise mechanics of this process are not obvious but may involve unfolding of the cubic array. The possibility that some of the less reactive electrophiles listed in Table IV do require dissociation of the aggregate prior to O-alkylation has not been excluded.

It is interesting to note that C-alkylation is significantly favored in DME compared with dioxolane (Table I) even though it would seem that the enolate ion is more accessible in the dimer **6** than

(12) N. Kornblum, R. E. Michel, and R. C. Kerber, *J. Am. Chem. Soc.*, **88**, 5660, 5662 (1966).

in **4**. This is presumably due to the appreciably higher charge density at the 2-carbon atom in **6** as has been demonstrated by ^{13}C chemical shift studies[9] for the two solvent systems.

Experimental Section

Proton nuclear magnetic resonance (NMR) spectra were obtained at 60.00 MHz on a Varian A-60 spectrometer, using tetramethylsilane. Carbon NMR (^{13}C NMR) spectra of enolate solutions were recorded on a Varian CFT-20 instrument at 20.00 MHz, using a d_6-acetone-filled capillary as the field lock. The other ^{13}C NMR spectrum was taken on a JEOL JNM PS-100 spectrometer at 25.03 MHz. All chemical shifts are reported in parts per million (ppm) using the δ scale. Mass spectra were obtained with an MS-902 mass spectrometer, and, where separations of mixtures by gas–liquid chromatography (GLC) were required prior to mass spectral analysis, a Finnigan 3200 GLC-MS system was used. Electron spin resonance (ESR) data were acquired with a Varian E-Line spectrometer.

Materials. All ether solvents were purified by refluxing over and distillation from sodium benzophenone ketyl under nitrogen.[13] *n*-Butyllithium in hexane (Alfa) was assayed immediately before use. Triglyme and the anhydrous crown ethers were distilled prior to use. [2.1.1]Cryptand (PCR) was used without purification.

2,2-Dimethyl-1-phenylpropanone (3). A sample for use as a GLC standard was prepared by the method of Willemart[14] from *tert*-butyl chloride and benzonitrile. The product, bp 67.0 °C (1.25 mm), n^{24}_D 1.5072, has ^1H NMR (CCl_4) 1.28 (s, 9 H, methyls), 7.0–7.4 (m, 3 H, meta and para protons), and 7.4–7.8 (m, 2 H, ortho protons.

1-Methoxy-2-methyl-1-phenylpropene (2).[15] Racemic α-chloro-α-methoxytoluene (10.0 g, 0.064 mol) was added to triethyl phosphite (10.6 g, 0.064 mol) in a dry 100-mL flask fitted with a condenser and drying tube. Upon stirring at room temperature, a vigorous (Arbuzov) reaction ensued and a gas was evolved. The mixture was magnetically stirred at 25 °C for 1 h, then at 165 °C for 2 h to complete the reaction. After cooling, the crude oil (16.9 g) was washed with benzene (75 mL, distilled from sodium) into a dry, 300 mL three-necked round-bottomed flask fitted with a condenser, addition funnel, mechanical stirrer, thermometer, and an argon inlet–outlet system. The addition funnel was charged with a solution of *n*-butyllithium in hexane (38.0 mL of 1.67 M, 0.064 mol), which was added dropwise over 50 min with stirring at 25 °C under argon, to give the characteristic orange color of the ylide. After the mixture was stirred an additional hour at 25 °C, a solution of acetone (distilled, 3.8 g, 0.066 mol) in dry benzene (40 mL) was added dropwise over 30 min. An ice–water bath was used during addition to keep the reaction temperature at 25 °C. The mixture was stirred at 25 °C for another 2.5 h, then gently refluxed for 1.5 h. After cooling, the mixture was rinsed from the flask with benzene (150 mL), washed with water, and dried (potassium carbonate). The solvent was removed by atmospheric distillation and the residual oil was distilled to give the product (**2**, 3.6 g, 35% distilled), bp 37–38 °C (0.1 mm); n^{24}_D 1.5198; *m/e* 162; NMR (CCl_4) 1.61, 1.79 (two singlets, 6 H, vinyl methyls), 3.20 (s, 3 H, CH_3O), 7.27 (s, 5 H, aromatic protons).

Para-Substituted Methyl Benzenesulfonates. These compounds were prepared from the corresponding para-substituted benzenesulfonyl chlorides and sodium methoxide or potassium methoxide, as reported by Morgan and Cretcher.[16] Methyl *p*-toluenesulfonate was purchased and distilled before use.

Methyl *p*-methoxybenzenesulfonate was prepared on a 4.0×10^{-2} mol scale in 85% distilled yield, bp 126 °C (0.05 mm), n^{24}_D 1.5302, *m/e* 202. This material crystallized upon standing: NMR (CCl_4) 3.77, 3.90 (two singlets, each 3 H, CH_3OSO_2 and CH_3O protons), 7.10, 7.87 (two doublets, each 2 H, both J = 8.8 Hz, meta and ortho protons, respectively).

Methyl *p*-nitrobenzenesulfonate was prepared on a 2.5×10^{-2} mol scale from recrystallized (petroleum ether) *p*-nitrobenzenesulfonyl chloride in 41% recrystallized (diethyl ether) yield, mp 89–90 °C (a previous synthesis of this compound reports mp 53 °C, recrystallized from petroleum ether[17]): NMR ($CDCl_3$) 3.77 (s, 3 H, CH_3OSO_2), 7.98, 8.27 (two doublets, each 2 H, both J = 8.3 Hz, meta and ortho protons, respectively); *m/e* 217.

Methyl benzenesulfonate was prepared on a 0.10 mol scale in 34% distilled yield, bp 162 °C (18 mm); n_D^{24} 1.5158; NMR (CCl_4) 3.78 (s, 3 H, CH_3OSO_2), 7.4–8.0 (m, 5 H, aromatic protons).

Methyl *p*-bromobenzenesulfonate was prepared on a 0.10 mol scale from recrystallized (benzene) *p*-bromobenzenesulfonyl chloride in 21% recrystallized (*n*-pentane) yield, mp 59.5–60.0 °C (reported[18] mp 60.5 °C); NMR ($CDCl_3$) 3.80 (s, 3 H, CH_3OSO_2), 7.78 (s, 4 H, ortho and meta protons).

Stock Solutions of Lithioisobutyrophenone. A dry apparatus was assembled, consisting of a 500-mL, three-necked, round-bottomed flask fitted with a stir bar, addition funnel, thermometer, and an argon inlet–outlet system. To the flask were added *O*-trimethylsilylisobutyrophenone[8] (14.3 g, 6.50×10^{-2} mol) and dry diethyl ether (60 mL). The addition funnel was charged with a solution of *n*-butyllithium in hexane (40.5 mL of 1.60 M, 6.50×10^{-2} mol), which was added dropwise with stirring under argon at 0–5 °C over 30 min. The mixture was allowed to warm gradually for 1 h, the bath was removed, and the addition funnel and thermometer were replaced with glass stoppers. After the mixture was stirred another 6 h at 25 °C, a vacuum pump was attached and the solvent was carefully removed at 0.6 mm over 1 h with stirring to give a white solid. Argon was admitted to the flask, followed by dry dioxolane (40 mL). The mixture was stirred to give a clear, light yellow solution. The flask containing the enolate solution was transferred with 10 oven-dried, desiccator-cooled 10-mL ampoules, 10 small stoppers, and a pipet to an argon-filled glove bag, where the solution was distributed equally into the ampoules. The ampoules were stoppered, removed from the glove bag, and sealed as follows: a stream of nitrogen was directed into the neck of the ampoule while the contents was frozen in liquid nitrogen. When the contents was completely frozen, the ampoule neck was sealed.

Solutions in dimethoxyethane were prepared by the same procedure.

Methylation Reactions. A dry apparatus was assembled, consisting of a three-necked, 100-mL round-bottomed flask fitted with a stir bar, condenser, addition funnel, and an argon inlet–outlet system. Depending on the experiment, the contents of an ampoule of enolate stock solution (~4 mL, containing 1.0 g, 6.5×10^{-3} mol of enolate) in either dioxolane or DME was placed in the flask, followed by the respective dry ether solvent (20 mL). The addition funnel was charged with a solution of 1.10 equiv of the methylating agent in the appropriate dry ether solvent (15 mL). This solution was added in a stream over approximately 10 s with stirring under argon to give the reaction solution (ca. 40 mL; in each case the enolate concentration in the reaction mixture was ~0.162 M). Invariably, a white precipitate formed as the methylation reactions neared completion. In cases for which the desired reaction temperature was greater than 25 °C, an oil bath was applied to the reaction flask and heating tape was used on the addition funnel to bring both solutions to the appropriate temperature before addition. In the cases of low-temperature reactions which were complete within 1 day, the above apparatus and a cold-temperature (slush) bath in which the flask was partially immersed were used. For the cases in which the reactions were sufficiently slow so that competing hydrolysis of the enolate became a serious problem, it was found desirable to use a glass-sealed reaction flask.

Product Analysis. In general, the methylation reactions were monitored and crude kinetic data were provided by periodically assaying aliquots from the reaction mixture using analytical GLC at 185 °C. Relatively fast reactions ($t_{1/2}$ < 1 min) and reactions run in sealed flasks were assayed only after reaction completion.

In the assay procedure, approximately 0.2 mL of the reaction mixture was withdrawn from the flask by pipet, quenched with water (~0.5 mL), and extracted with carbon tetrachloride (distilled, GLC pure, ~0.5 mL). The resulting solution was injected into the GLC column (12 ft × $^1/_4$ in. glass column packed with 2.5% SE-30 on HMDS treated Chromosorb G) at 185 °C. The following retention times were observed: 110.9 (enol ether), 119.2 (isobutyrophenone), and 141.6 s (2,2-dimethyl-1-phenylpropanone). Because the first two components are incompletely resolved, a calibration curve was constructed from mixtures of known composition. This analytical procedure is estimated to give the yields of the C- and O-alkylation products for the completed reactions which are accurate to ±1%. It is less satisfactory in the initial phases of the reaction. All reported C/O ratios are the average of the results of at least three chromatograms.

Reaction of Lithioisobutyrophenone with Methyl *p*-Nitrobenzenesulfonate. When solutions of the title compounds in dioxolane were mixed at 43 °C, an immediate exotherm and formation of a deep red color occurred. Similar behavior was observed upon addition of Li-IBP/dioxolane solution to nitrobenzene. Following the exotherm, analysis of aliquots by GLC showed the steady formation of two major and several minor new peaks. None of these new peaks corresponded to either the C- or O-methylated compounds, although these products were shown to be present in trace amounts. The reaction mixture was poured into water and extracted with ether; the extracts were combined and

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washed with 1 N aqueous hydrochloric acid, 5% aqueous sodium bicarbonate solution, and water. The organic layer was dried (magnesium sulfate), the solvent was removed under reduced pressure, and the resulting brown oil was chromatographed on 60–200 mesh silica gel. The fraction eluted with 5:1 benzene:hexane was shown by GLC to contain the two major unknown products. Since the parent ions of neither compound could be detected with electron-impact GLC–MS conditions, chemical ionization (CI) GLC–MS was used with ethane ionizing gas. This method gave m/e 146 as the parent ion for both substances. In addition, a strong peak at m/e 118 was seen in each mass spectrum.

In an ESR spectroscopic study[19] of this reaction, stable baselines were obtained when separate solutions of the reactants in dioxolane solutions were scanned using a 9-GHz probe at −30 °C. However, mixing of the enolate solution with the solution of the nitro ester gave a mixture which immediately gave the deep red color and which exhibited a strong signal (triplet, splitting constant = 12 G), indicating the formation of radical species. Improved resolution of this spectrum gave evidence of overlapping peaks (Figure 2). However, the peaks could not be further resolved at −60°, at 25°, or by employing a 35-GHz probe at −100° to −35 °C.

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Redox-Photosensitized Reactions. 7.[1] Aromatic Hydrocarbon-Photosensitized Electron-Transfer Reactions of Furan, Methylated Furans, 1,1-Diphenylethylene, and Indene with *p*-Dicyanobenzene

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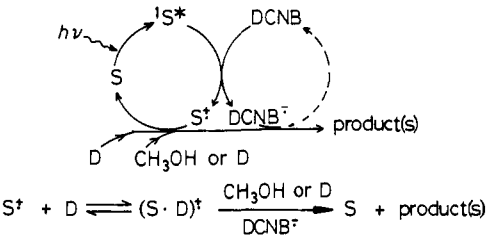
Abstract: Electron-transfer reactions of furan, 2-methylfuran, 2,5-dimethylfuran, 1,1-diphenylethylene, and indene with *p*-dicyanobenzene are photosensitized by several selected aromatic hydrocarbons. With the furan compounds are formed the dihydrofurans having both the *p*-cyanophenyl and the methoxy groups by the phenanthrene-photosensitized reaction in 4:1 acetonitrile–methanol, whereas the photodimerization or anti-Markovnikov addition of alcohols occurs with the olefins. Kinetic studies on the anti-Markovnikov addition of methanol to 1,1-diphenylethylene suggest that the cation radical of phenanthrene forms a π complex with the olefin as a key intermediate. The mechanisms of the photosensitized reactions are discussed.

Recently, photoreactions involving electron-transfer events have received much attention from synthetic and mechanistic aspects of organic photochemistry[2] and also for chemical conversions of solar energy.[3] In a variety of organic electron donor (D)–acceptor (A) pairs, photoexcitation of either A or D in polar media results in electron transfer from D to A, thus generating the cation radical of D and the anion radical of A.[4] Numerous photoreactions of A–D pairs in polar solvents have been reported to proceed via the ion radicals, involving adduct formation between A and D,[5] cyclodimerization of olefins,[6] cross-addition between olefins,[7] addition of nucleophiles to various substrates,[8-10] methanolysis of alcohols and benzoates,[11] reductive removal of a protecting group,[12] bond-cleavage reactions,[13] reduction of arenes[14] and carbonyl

Scheme I



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