Solvent Effects in Nuclear Magnetic Resonance Spectroscopy. II. Transmission of Substituent Effects by Three-Membered Rings[1,2]

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The nmr spectra of a series of *trans*-1-(substituted phenyl)-2-benzoyl-3,3-dideuteriocyclopropanes, *trans*-2-(substituted phenyl)-3-benzoyloxiranes, and *trans*- and *cis*-1-cyclohexyl-2-(substituted phenyl)-3-benzoylaziridines have been determined in deuteriochloroform and in benzene. The difference in chemical shifts in the two solvents, $\Delta = \delta_{CDCl_3} - \delta_{C_6H_6}$, has been correlated with substituent parameters, σ, σ^0, σ^+, and the Swain field and resonance parameters. Generally, good correlations were obtained using σ and σ^0 constants; however, correlations using F and R were usually better. Comparisons of ρ values obtained using σ constants indicate that the order of efficiency of transmission of substituent effects for the ring systems studied is cyclopropane $\sim$ oxirane > aziridine.

A number of reports have appeared which compare the transmission of electronic effects by the ethylene group, the cyclopropane ring, and the dimethylene group.[5] Only recently have reports appeared which include the small-ring heterocyclic systems, oxiranes[6] and aziridines,[6a] in these comparisons. As a continuation of our earlier investigations[1] of nmr solvent effects on three-membered ring ketones, we have studied the effect of substituents in these systems in an attempt to compare the relative abilities of various three-membered rings to transmit substituent effects.

Results

The nmr spectra of substituted phenylbenzoylcyclopropanes, -oxiranes, and -aziridines have been determined in deuteriochloroform and in benzene. Table I contains the proton chemical shift data for these three-membered ring ketones. The proton resonance values are expressed in hertz relative to tetramethylsilane (TMS) as an internal standard, and Δ is defined as $\delta_{CDCl_3} - \delta_{C_6H_6}$. Proton assignments were made by following conventional nmr rules and by deuterium labeling as indicated in Table I.

When Δ was plotted against the Hammett σ values,[7a] Brown's σ^+ constants,[7b] and the normal substituent constants, σ^0,[8] for the substituents of the various three-membered ring ketones, good linear relationships were obtained as shown by the correlation coefficients in Table II. Plots using σ constants are recorded in Figure 1 and the slopes ρ as determined by the method of least squares[9a] are given in Table II. The statistical treatments were carried out with the aid of a computer program.[9b] Table III contains the results of correlation of the nmr data with the Swain–Lupton expression.[10]

The 1-phenyl-2-benzoyl-3,3-dideuteriocyclopropanes were prepared by the synthetic method reported by Corey[11a] using dimethyloxosulfonium methylide-d_8 and substituted chalcones. In all cases, except for the reaction of 3,4-dichlorochalcone, substituted chalcones reacted at 55° with the ylide-d_8 to give the corresponding 3,3-dideuteriocyclopropane. The 3,4-dichlorochalcone gave 1-(3,4-dichlorophenyl)-2-benzoyl-2,3,3-trideuteriocyclopropane under the above conditions as demonstrated by its nmr spectrum and by the base-catalyzed exchange of the 2-deuterium atom in refluxing ethanolic sodium ethoxide. Presumably the 2-deuterium atom is incorporated into the molecule after cyclopropane formation by base-catalyzed exchange of the α proton. By raising the reaction temperature to 80°, trideuteriocyclopropanes were prepared for the *p*-F and *p*-Br derivatives. This approach provides a facile and potentially useful method by which trideuteriobenzoylcyclopropanes can be prepared. The designation of trans stereochemistry for these cyclopropanes is based on the assignment made by Griffin[11b] which was confirmed in our earlier work.[1]

The synthesis of oxiranes was accomplished by the sodium hypochlorite oxidation of the appropriately substituted chalcones.[12] In somewhat analogous fashion, the aziridines were prepared from chalcones by the method of Southwick.[13a] The cis and trans isomeric aziridines were separated by column chromatography. The stereochemistry for both the oxiranes[13b,c] and the aziridines[1,13d] has been previously established.

Discussion

We have recently shown that it is possible to make cis–trans configurational assignments for benzoylcy-

(1) For part I, see D. W. Boykin, Jr., A. B. Turner, and R. E. Lutz, *Tetrahedron Lett.*, 817 (1967).

(2) The work done at the University of Virginia was supported by Grant GP-5453 from the National Science Foundation.

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(8) R. W. Taft, Jr., *J. Phys. Chem.*, **64**, 1805 (1960).

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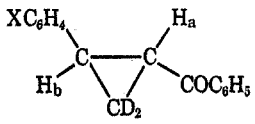
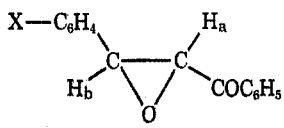
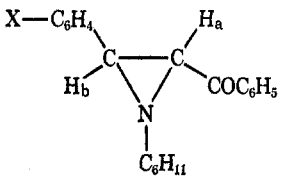
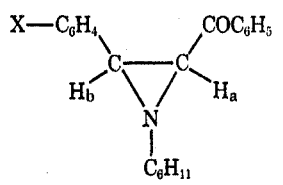
(10) C. G. Swain and E. C. Lupton, Jr., *J. Amer. Chem. Soc.*, **90**, 4328 (1968).

(11) (a) E. J. Corey and M. Chaykovsky, *ibid.*, **87**, 1353 (1965); (b) G. W. Griffin, J. Covell, R. C. Petterson, R. M. Dodson, and G. Klose, *ibid.*, **87**, 1410 (1965).

(12) S. Marmor, *J. Org. Chem.*, **28**, 250 (1963).

(13) (a) P. L. Southwick and R. J. Shozda, *J. Amer. Chem. Soc.*, **82**, 2888 (1960); (b) H. H. Wasserman and N. E. Aubrey, *ibid.*, **77**, 590 (1955); (c) H. O. House, *ibid.*, **78**, 2298 (1956); (d) N. H. Cromwell, R. E. Bambury, and J. L. Adelfang, *ibid.*, **82**, 4241 (1960).

TABLE I

X	No.	δ_{CDCl_3}, Hz[a] a	δ_{CDCl_3}, Hz[a] b	$\delta_{C_6H_6}$, Hz[a] a	$\delta_{C_6H_6}$, Hz[a] b	Δ[b] a	Δ[b] b
							
p-CH_3O	1	167.0	158.0	163.2	156.6	3.8	1.4
p-CH_3	2	169.7	158.3	161.3	158.1	8.4	0.2
H	3	172.6[c]	161.2	158.6[c]	162.2	14.0	−1.0
p-F	4	169.7[c]	160.1	156.7[c]	150.3	13.0	9.8
p-Cl	5	170.2[c]	159.0	149.6[c]	151.6	20.6	7.4
p-Br	6	171.0[c]	157.9	150.3[c]	150.3	20.7	7.6
m-Br	7	171.3	157.9	148.2	151.0	23.1	6.9
3,4-Di-Cl	8	171.1	157.7	145.4	145.4	25.7	12.3
							
p-CH_3O	9	253.5	238.1	239.9	235.3	13.6	2.8
p-CH_3	10	252.4	238.3	238.1	235.1	14.3	3.2
H	11	253.6	240.8	237.1	234.1	16.5	6.7
p-F	12	258.8	243.5	232.6	232.6	21.2	10.9
p-Cl	13	253.5	242.5	230.6	228.8	22.9	13.7
p-Br	14	251.4	239.6	227.0	225.1	24.4	14.5
m-Cl	15	254.2	242.6	227.4	227.4	26.8	15.2
m-Br	16	250.4	238.6	223.2	223.2	27.2	15.4
p-NO_2	17	256.8	252.0	219.3	226.9	37.5	25.1
							
p-CH_3O	18	211.2	208.0	209.9	218.0	1.3	−10.0
p-CH_3	19	211.5[c]	207.5	208.9[c]	217.1	2.6	−9.6
m-CH_3	20	213.3	208.5	211.0	218.3	2.3	−9.8
H	21	215.3[c]	211.9	209.9[c]	218.9	5.4	−7.0
p-F	22	212.9	210.5	204.2	212.8	8.7	−2.3
m-CH_3O	23	214.8	210.8	215.6	223.2	−0.8[d]	−12.4[d]
p-Cl	24	212.2[c]	208.6	202.6[c]	210.0	9.6	−1.6
p-Br	25	213.1	208.9	203.7	209.3	9.4	−0.4
m-Br	26	213.9	209.7	202.4	209.0	11.5	0.7
p-NO_2	27	217.2	216.2	202.9	209.7	14.3	5.5
							
p-CH_3O	28	192.1	187.9	171.9	167.7	20.2	20.2
p-CH_3	29	192.2[c]	187.4	171.7[c]	167.5	20.5	19.9
m-CH_3	30	192.5	188.3	171.2	165.0	21.3	23.3
H	31	193.2[c]	189.5	171.6[c]	167.2	21.6	22.3
p-F	32	194.2	188.8	170.4	160.2	23.8	28.6
m-CH_3O	33	191.7	187.1	171.4	166.8	20.3[d]	20.8[d]
p-Cl	34	194.9[c]	186.5	168.7[c]	155.7	26.2	31.2
p-Br	35	195.7	186.1	171.5	157.5	24.2	28.6
m-Br	36	195.1	186.3	169.8	156.0	25.3	30.3
p-NO_2	37	205.1	195.1	175.3	157.5	29.8	37.6

[a] Values in hertz relative to tetramethylsilane (TMS) as an internal standard. [b] $\Delta = \delta_{CDCl_3} - \delta_{C_6H_6}$. [c] Assigned by deuterium exchange. [d] These values of Δ were not used in the correlations.[e] [e] The Δ values for *m*-CH_3O compounds were not used in the calculations because they exhibited an excessively large negative shift. It is known that methoxy groups interact with benzene: J. H. Bowie, D. W. Cameron, P. E. Schutz, and D. H. Williams, *Tetrahedron*, **22**, 1771 (1966), and references cited therein. While the *p*-CH_3O substituents are also likely complexed, it is assumed that the complex is well removed from proton H_a and thus is expected to have little effect on it. Although the *p*-CH_3O points may be considered suspect, their deviations do not appear to warrant exclusion.

TABLE II

RESULTS OF STATISTICAL TREATMENT USING σ CONSTANTS[a,c]

		σ					σ^0					σ^+				
		n	ρ	s	c	i	n	ρ	s	c	i	n	ρ	s	c	i
Cyclopropanes	H_a	8	25.7	1.91	0.973	12.7	8	26.5	3.05	0.928	11.3	8	18.1	2.06	0.968	16.1
	H_b	8	13.3	3.13	0.798	3.79	8	15.8	2.51	0.875	2.71	8	7.81	3.89	0.662	5.56
Oxirane	H_a	9	23.3	1.18	0.989	18.5	9	25.1	0.72	0.996	17.2	9	15.4	3.03	0.926	21.5
	H_b	9	21.6	1.22	0.986	8.04	9	23.3	0.87	0.993	6.76	9	14.4	2.78	0.929	10.8
trans-Aziridines	H_a	9[b]	13.4	1.54	0.948	5.47	9[b]	14.0	1.52	0.949	4.8	9[b]	9.28	2.18	0.893	7.0
	H_b	9[b]	16.4	1.76	0.954	−5.99	9[b]	17.2	1.48	0.968	−6.78	9[b]	11.0	2.87	0.873	−4.1
cis-Aziridines	H_a	9[b]	9.47	0.86	0.967	22.4	9[b]	9.2	1.45	0.902	22.6	9[b]	6.35	1.57	0.883	23.5
	H_b	9[b]	17.7	1.90	0.954	24.6	9[b]	18.7	1.51	0.971	23.7	9[b]	11.9	3.05	0.887	26.6

[a] See ref 9a. [b] The value of Δ for the *m*-CH_3O compound was not used in the calculations. See footnote *e*, Table I. [c] n = number of points; ρ = slope as determined by method of least squares; s = standard deviation; c = correlation coefficient; i = intercept.

TABLE III

RESULTS OF STATISTICAL TREATMENT USING F AND R CONSTANTS[a,d]

		n	f	r	i	E	c	% R
Cyclopropanes	H_a	7[b]	18.2 ± 1.7	37.5 ± 3.8	14.4	1.4	0.987	45 ± 3
	H_b	7[b]	11.9 ± 2.3	3.56 ± 5.08	−0.11	1.86	0.935	11 ± 14
Oxiranes	H_a	9	15.7 ± 1.4	19.7 ± 2.9	17.2	1.51	0.985	33 ± 4
	H_b	9	14.9 ± 0.83	18.4 ± 1.68	6.71	0.86	0.994	33 ± 2
trans-Aziridines	H_a	9[c]	8.82 ± 1.30	10.05 ± 2.95	4.70	1.53	0.957	28 ± 7
	H_b	9[c]	11.3 ± 1.07	11.2 ± 2.44	−7.36	1.27	0.980	25 ± 4
cis-Aziridines	H_a	9[c]	6.03 ± 0.62	7.92 ± 1.41	22.1	0.73	0.979	31 ± 4
	H_b	9[c]	11.7 ± 1.4	12.6 ± 3.3	23.4	1.69	0.968	26 ± 6

[a] Swain field and resonance parameters; see ref 10. These correlations were made using the IBM multiple linear regression program REGRE (*cf.* ref 5a and 9b). [b] The value of Δ for the 3,4-di-Cl compound was not used in the calculations. [c] The value of Δ for the *m*-CH_3O compound was not used in the calculations. See footnote *e*, Table I. [d] n = number of points; f = regression coefficient for field parameter; r = regression coefficient for resonance parameter; i = intercept; E = standard error of estimate; c = multiple correlation coefficient; % R = resonance contribution, calculations as in ref 5a.

clopropanes and -aziridines by means of benzene-induced proton magnetic resonance chemical shift differences of the ring proton signals.[1] These differences ($\Delta = \delta_{CDCl_3} - \delta_{C_6H_6}$) were attributed to a time averaged benzene–substrate "complex"[14] in which the negative π system of the anisotropic solvent benzene is attracted to the positively charged carbon atom of the polarizable carbonyl group of the three-membered ring ketone and repelled by the negatively charged carbonyl oxygen atom. The exact nature of the solute–solvent interaction or attraction is the subject of continuing investigation.[15] For the purpose of discussing this work, it is convenient to consider the model proposed by Bhacca and Williams,[16] which has found widespread utility and which was assumed in our previous paper.[1]

In a given series of three-membered ring ketones reported in Table I, the only variables are the solvent (chloroform-d_1 or benzene) and the substituents attached to the phenyl ring. Other molecular parameters are assumed to remain essentially unchanged for a given series. Consequently, for a given solvent the difference between the chemical shifts of the ring hydrogens of the substituted and unsubstituted compounds can be considered as arising from the effects of the substituent as well as the interaction of the solvent with the substituent or remainder of the molecule, especially the carbonyl group.

The geometry of the "complex" between benzene and the trans isomers of each of the different three-membered ring systems is assumed to be similar, although

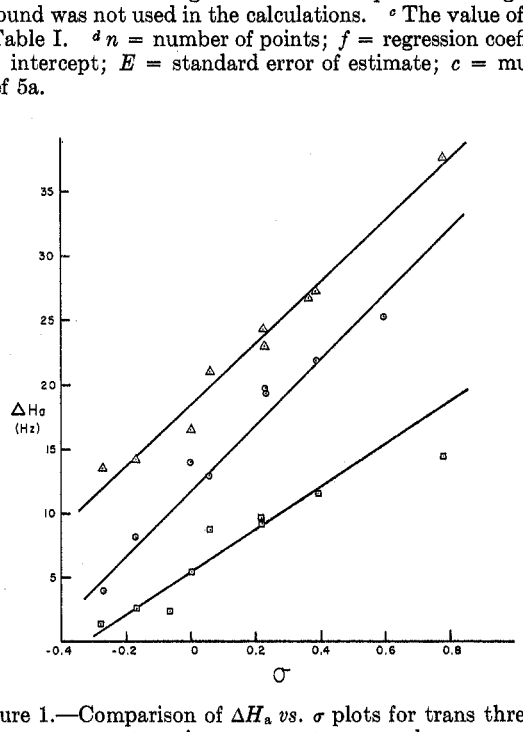
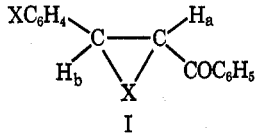


Figure 1.—Comparison of ΔH_a *vs.* σ plots for trans three-ring systems: △—△—△, oxiranes; ⊙—⊙—⊙, cyclopropanes; ⊡—⊡—⊡, aziridines.

the variances of X in I should cause some deviations in the geometry of the "complex." Deviations might be



I

expected to be most pronounced in the aziridines due to an added steric effect of the nitrogen substituent.[17] Furthermore, the geometry of the "complex" for the cis

(14) As have others,[15] we use the term "complex" for simplicity to describe the solute–solvent interaction; however, we do not attach any particular signifiance to the word as a description of this interaction.

(15) P. Laszlo in "Progress in Nuclear Magnetic Resonance Spectroscopy," Vol. 3, J. W. Emsley, J. Fenney, and L. H. Sutcliffe, Ed., Pergamon Press, Elmsford, N. Y., 1967, Chapter 6.

(16) N. S. Bhacca and D. H. Williams, *Tetrahedron Lett.*, 3127 (1964).

(17) D. H. Williams, J. Ronayne, H. W. Moore, and H. R. Shelden, *J. Org. Chem.*, **33**, 998 (1968).

isomers need not necessarily be the same as that for the trans isomers.

The effect of deviations in the geometry of the "complex" might be expected to be less pronounced at H_a than at H_b, since H_a is closer to the presumed interaction site. Consequently, information obtained from H_a is expected to be more significant than that obtained from H_b.

Figure 1 shows a fair linear relationship between σ constants of the meta and para substituents and the chemical shift differences Δ of the ring proton H_a of the cyclopropyl, oxiryl, and aziridyl rings. It can be seen from Table II by comparing correlation coefficients that slightly better correlations are obtained with σ^0 than with σ for the heterocyclic rings systems, whereas the opposite is the case for the cyclopropane ring system, suggesting the importance of inductive and field effects for transmission of substituent effects in the heterocyclic rings. Correlations with σ^+ generally are poorer for all rings systems; however, reasonable correlations are obtained for the cyclopropanes and oxiranes which indicate that resonance might play a role in the transmission in these systems. The correlation coefficients obtained using H_a are generally superior to those obtained from H_b.

Values of Δ for new three-membered ring ketones with substituents other than those reported in Table I may be calculated from the equation $\Delta = (\sigma, \sigma^0, \text{or } \sigma^+)\rho + i$ using the values of ρ and i given in Table II.

The ratio of ρ/ρ_0 has been used to estimate the effectiveness of the transmission of substituent effects by an intervening group.[5] If ρ_0 is defined as ρ for the *trans*-aziridine system and the ρ values in Table II for ΔH_a are compared, it is seen that the cyclopropane ring and the oxirane ring are not far different in their ability to transmit substituent effects, whereas the aziridine ring transmits less effectively. These results are in good accord with the recent results reported by Pews.[6a,b]

Pews has discussed an alternate interpretation of substituent effects relayed from a substituted aryl group through an intervening link to a reaction site in terms of a "modified substituent effect" which does not include transmission by conjugation.[5h] While our data above do not allow rigorous exclusion of such an interpretation, there is now considerable evidence that the cyclopropane ring transmits to an extent by conjugation[5e,h,6,18a] and some evidence that the oxirane[6a,b] and aziridine[6a] rings also transmit by conjugation. Further support for some contribution to transmission by conjugation in these systems is found in the % R values for the correlations in Table III (*vide infra*). The value of % R in systems reported by Swain which involved transmitting links which were incapable of participation by conjugation (*e.g.*, phenylacetic acids) showed very low % R values (>5%).

Treatment of the nmr data with the Swain–Lupton two-parameter expression[10] in general improved the correlations. The relative effectiveness of the different ring systems to transmit resonance effects as measured by the % R values for the H_a protons in Table III parallels the overall ability of the systems to transmit electronic effects as measured by the ρ/ρ_0 ratios. If the % R values are a reasonable measure of the transmission of resonance effects, then the results obtained for the cis and trans aziridines indicate that resonance effects are transmitted comparably by both isomers which is rather surprising. Comparison of ρ values for cis and trans isomers of vinylene sets has led to the conclusion that the major difference in transmission of substituent effects for geometric isomers is due to the field effect.[18b] Nevertheless, for the cis and trans aziridines, it seems reasonable to expect differences in effectiveness of transmission to arise from steric inhibition of resonance due to differences in overlap of the aromatic π system with the three-ring system. Yet, to the extent that % R calculations are a measure, these results suggest the resonance contributions to be similar for both the cis and trans isomers. It is also interesting to compare the % R values obtained from the three-membered ring systems with that obtained for the double bond system from infrared data on substituted chalcones.[5a] The % R value obtained for the double bond system, which is analogous to the three-ring systems reported herein, is 45. Surprisingly, this suggests that transmission of resonance effects by the cyclopropane ring and the double bond are comparable. The ultimate value of % R comparisons remains to be tested by additional experiments.

Experimental Section

The melting points were taken in a Thomas-Hoover capillary melting point apparatus and are corrected.

The nuclear magnetic resonance spectra were measured in $CDCl_3$ and C_6H_6 solutions (*ca.* 15% w/v) containing *ca.* 1% tetramethylsilane (TMS) as internal standard and using a Varian Associates Model A-60 and A-60A instrument near 33°. The spectra were first determined on the 500-Hz sweep width, and then the 100-Hz sweep width was employed to measure the chemical shift of the signals of the three-membered ring protons. Spectra at 100-Hz sweep width were calibrated with a Model 200 CD wide range oscillator and a 5521A electronic counter manufactured by the Hewlett-Packard Co. Reproducibility of band frequencies were within ±0.15 Hz; the estimated error is approximately ±0.3 Hz. The error for the dideuteriocyclopropanes is probably higher due to difficulty in measuring the band width which was broadened by deuterium coupling.

Deuterium exchange experiments to prepare the α-deuterio compounds shown by footnote *c* in Table I were carried out using $NaOCH_3$–CH_3OD with reflux times ranging from 4 days for the cyclopropanes to 2 min for the aziridines.[19]

Elemental analyses were obtained from Micro-Tech Laboratories, Skokie, Ill., and Galbraith Laboratories, Knoxville, Tenn. See Table IV.

***trans*-1-(Substituted phenyl)-2-benzoyl-3,3-dideuteriocyclopropanes.**[11]—To a stirred solution of 0.0037 mol of $(CD_3)_3S^+OI^-$[20a] dissolved in 5 ml of DMSO-d_6,[20b] NaH (0.0038 mol of NaH as a 58% dispersion in mineral oil) was slowly added portionwise at 30°. After addition was complete, the solution was stirred for 0.5 hr at room temperature and then 0.0036 mol of 1-phenyl-3-(substituted phenyl)-2-propen-1-one (substituted chalcone; see ref 5a for properties of these chalcones) dissolved in 5 ml of DMSO-d_6 was added dropwise. After addition was complete, the solution was stirred at 30° for 0.5 hr and then heated to 55–60° for 1 hr. If the reaction was heated at 80° for 1 hr, 2,3,3-trideuteriocyclopropanes were obtained. The higher temperature reaction was carried out only with *p*-F and *p*-Br isomers. The reaction mixture was poured into water and extracted with ether, and the ether layer was washed with water, dried ($CaSO_4$), and evaporated under reduced pressure. The resulting oil upon trituration with low boiling petroleum ether and cooling usually gave crystals. Occasionally, chromatography over Al_2O_3 was required to isolate the pure cyclopropane.

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TABLE IV

SUBSTITUTED PHENYL BENZOYL THREE-MEMBERED RING COMPOUNDS

No.[a]	Mp, °C[b]	Formula	Calcd, % C	Calcd, % H	Calcd, % N	Found, % C	Found, % H	Found, % N
1	41–42.5	$C_{17}H_{16}O_2$	80.92	6.39		80.72	6.44	
2	87–88	$C_{17}H_{16}O$	86.40	6.83		86.19	6.81	
3	43–44 (44.5–45.0)[c]							
4	54–55	$C_{16}H_{13}FO$	79.98	5.45		80.04	5.55	
5	59–60	$C_{16}H_{13}ClO$	74.85	5.10		74.61	5.28	
6	77–78	$C_{16}H_{13}BrO$	63.80	4.34		63.70	4.39	
7	63–64	$C_{16}H_{13}BrO$	63.80	4.34		63.60	4.32	
8	72–74	$C_{16}H_{12}Cl_2O$	66.00	4.15		65.87	4.00	
9	84–86 (85–86)[d]							
10	75–77 (77–78)[e]							
11	88–90 (89–90)[d]							
12	88–90	$C_{15}H_{11}FO_2$	74.37	4.58		74.23	4.63	
13	77–79 (78–80)[d]							
14	89.5–90.5	$C_{15}H_{11}BrO_2$	59.42	3.66		59.30	3.54	
15	66–68	$C_{15}H_{11}ClO_2$	69.64	4.29		69.55	4.37	
16	70.5–71.5	$C_{15}H_{11}BrO_2$	59.42	3.66		59.24	3.67	
17	148–150 (149.5–150)[e]							
18	94–96 (93–95)[f]							
19	110–111	$C_{22}H_{25}NO$	82.72	7.89	4.39	82.86	7.79	4.47
20	82.5–84	$C_{22}H_{25}NO$	82.72	7.89	4.39	82.90	7.89	4.46
21	106–108 (107–109)[g]							
22	100.5–102.5	$C_{21}H_{22}FNO$	77.99	6.86	4.33	78.23	6.79	4.33
23	83–84	$C_{22}H_{25}NO_2$	78.77	7.51	4.18	78.80	7.64	4.43
24	115.5–116.5	$C_{21}H_{22}ClNO$	74.21	6.52	4.12	74.45	6.58	4.19
25	126–127	$C_{21}H_{22}BrNO$	65.63	5.77	3.64	65.42	5.74	3.69
26	78–79	$C_{21}H_{22}BrNO$	65.63	5.77	3.64	65.41	5.75	3.82
27	108–109 (107–109)[h]							
28	115–116 (115–117)[f]							
29	120–121.5	$C_{22}H_{25}NO$	82.72	7.89	4.39	82.72	7.89	4.47
30	111–112	$C_{22}H_{25}NO$	82.72	7.89	4.39	82.77	7.96	4.40
31	127–128 (127–128)[g]							
32	113–114.5	$C_{21}H_{22}FNO$	77.99	6.89	4.33	77.96	6.86	4.23
33	117–117.5	$C_{22}H_{25}NO_2$	78.77	7.51	4.18	78.75	7.47	4.20
34	122–123.5	$C_{21}H_{22}ClNO$	74.21	6.52	4.12	74.10	6.50	4.22
35	121–122	$C_{21}H_{22}BrNO$	65.63	5.77	3.64	65.51	5.75	3.32
36	113–115	$C_{21}H_{22}BrNO$	65.63	5.77	3.64	65.60	5.75	3.75
37	127–129 (127–128)[h]							

[a] See Table I for the compound corresponding to number. All compounds were recrystallized from ethanol. [b] Literature melting points designated by parentheses. [c] See G. Wittig and F. Wingler, *Ber.*, 97, 2146 (1964). [d] See H. O. House and G. D. Ryerson, *J. Amer. Chem. Soc.*, 83, 979 (1961). [e] See ref 12, 13b,c.[b] [f] See ref 13a,d.[b] [g] See ref 13a,d. [h] See A. E. Pohland, R. C. Badger, and N. H. Cromwell, *Tetrahedron Lett.*, 4369 (1965).

trans-2-(**Substituted phenyl**)-3-**benzoyloxirane**.[12]—To a solution of 1.0 g (*ca.* 0.004 mol) of 1-phenyl-3-(substituted phenyl)-2-propen-1-one (substituted chalcone) dissolved in 15 ml of pyridine was added dropwise 11 ml of 5.25% sodium hypochlorite solution. It was found that a quantity of pyridine sufficient to keep everything in solution added simultaneously significantly improved the yields. After addition was complete, the resulting solution was stirred for an additional 15 min and then poured into 200 ml of a water–ice mixture. After standing for 2 hr, filtration gave the oxirane which was recrystallized from 95% ethanol.

1-**Cyclohexyl**-2-(**substituted phenyl**)-3-**benzoylaziridine**.[13a,d]—A solution of 5.08 g (0.020 mol) of iodine in 50 ml of anhydrous benzene was added slowly to a stirred solution of 0.020 mol of 1-phenyl-3-(substituted phenyl)-2-propen-1-one (substituted chalcone) and 7.9 g (0.080 mol) of cyclohexylamine in 15 ml of benzene, keeping the temperature between 15 and 25°. After the solution stood overnight, the precipitated cyclohexylamine hydriodide was removed by filtration. The resulting benzene solution was placed on a chromatographic column (320 g of Florisil, 60/100 mesh, packed in benzene; an Al_2O_3 column packed in hexane works similarly). Elution was by 250-ml portions of benzene–anhydrous ethyl ether mixture, beginning with 100% benzene, with ether concentration progressively increased by 3% increments (v/v) up to 21%, then to 25 and 30%, then by 20% increments up to 90% ether, and then to 100% ether; elution was continued with reagent grade acetone and finally with absolute methanol. Evaporation of the early fractions (usually *ca.* 9 to 15% ether) gave the cis isomer and evaporation of the succeeding fractions (usually 18 to 50%) gave the trans isomer.

Registry No.—**1**, 27729-87-9; **2**, 27729-88-0; **3**, 27729-89-1; **4**, 27729-90-4; **5**, 27729-91-5; **6**, 27729-92-6; **7**, 27729-93-7; **8**, 27729-94-8; **9**, 27729-95-9; **10**, 27729-96-0; **11**, 7570-86-7; **12**, 27729-98-2; **13**, 27729-99-3; **14**, 27730-00-3; **15**, 18873-05-7; **16**, 27730-02-5; **17**, 27730-03-6; **18**, 6531-10-8; **19**, 27730-05-8; **20**, 27730-06-9; **21**, 2211-61-2; **22**, 27730-08-1; **23**, 27730-09-2; **24**, 27730-10-5; **25**, 27730-11-6; **26**, 27730-12-7; **27**, 6372-30-1; **28**, 6450-55-1; **29**, 27730-15-0; **30**, 27730-16-1; **31**, 2211-65-6; **32**, 27730-18-3; **33**, 27730-19-4; **34**, 27730-20-7; **35**, 27730-12-8; **36**, 27730-22-9; **37**, 6667-81-8.

Chemistry of Enolates. VII. Kinetics and Orientation in Dimethyl Sulfoxide. Relative Nucleophilicities of Enolates[1]

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Lithium, sodium, and cesium enolates are prepared in dimethyl sulfoxide by titration of ketones with methylsulfinyl carbanion, $CH_3SOCH_2^-$. Rates of enolate alkylation in DMSO are 10^3-fold greater than in glyme solvents, and O-/C-alkylation ratios are substantially larger and more nearly independent of the cation. Carbon alkylation increases as the leaving group is varied from chloride to iodide. Enolate nucleophilicities calculated from the equation $\log k/k_0 = sn$ are obtained from partial rate constants for O- and C-alkylations by alkyl chlorides. Nucleophilicities increase with basicities of enolates as measured by pK_a values of the corresponding ketones.

The effect of dipolar aprotic solvents on the basicity and nucleophilicity of carbanions is an area of considerable recent interest.[2-9] Enhanced rates are explained by solvation of the accompanying cation[2-4] and by lack of solvation of the anion itself.[5] Of the common dipolar aprotic solvents, cation–solvent interactions are exceptionally strong in dimethyl sulfoxide.[2] Also, this solvent forms complexes with certain highly polarizable leaving groups such as iodide ion[10] and is effective in solvating extended, charged transition states, such as those encountered in SN2 and E2 mechanisms.[5-7] Finally, the strongly basic methylsulfinyl (dimsyl) carbanion, prepared in this solvent by the action of sodium hydride, provides a rapid quantitative conversion of weakly acidic compounds to their conjugate bases.[11]

In this solvent we find O-/C-alkylation ratios higher than in ethereal solvents and insensitive to variation of the cation. Also, improved bimolecular kinetics for the alkylation of sodium enolates are exhibited. Nucleophilicities of the anions are obtained from partial rate constants for O- and C-alkylation.

Results and Discussion

Sodium, lithium, and cesium enolates were prepared in DMSO by titration with dimsyl reagent to a triphenylmethane end point.[11] The success of this method depends on the relative acidities of DMSO, ketone, and indicator. The pK_a of DMSO is 31.3 compared with 27.3 for triphenylmethane. End points occurred when the calculated amounts of dimsyl reagent had been added to ketones with pK_a's in the range 16.1–20.3 (Table I). The quantitative conversions indicate the absence of condensation, for addition of enolate anion to another molecule of ketone would give rise to a premature end point. Glpc analysis of quenched aliquots eliminated the possibility of dimsyl addition to the carbonyl group; only the original ketones were recovered.

Alkylation of Sodium Enolates.—Second-order kinetics were observed for alkylations of sodium enolates by alkyl chlorides in DMSO. In Table II are listed second-order rate constants for the reactions of four sodium enolates with three alkyl chlorides. Figures 1 and 2 illustrate the second-order behavior and emphasize the rate dependence upon structure of enolate and alkylating agent.

Comparisons of alkylation rates in DMSO with those observed in ethereal solvents would be of interest. Unfortunately, most alkylations of sodium enolates in the ethers and glymes have been made with alkyl bromides and iodides and are too rapid in DMSO to be followed by conventional techniques. One comparison can be made. The rates of alkylation of sodiobutyrophenone by *n*-propyl chloride in monoglyme,[4] diglyme, and DMSO are 2×10^{-6}, 7×10^{-6}, and 7.6×10^{-3} sec^{-1} M^{-1}, respectively. Since diglyme is 5×10^3 times more effective than ethyl ether,[4] relative rates at 30° for alkylation in the four solvents are those given in parentheses: ether (1), monoglyme (10^2), diglyme (10^3), dimethyl sulfoxide (10^6).

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