(21%), 41 (23%), 30 (51%). Anal. Calcd. for $C_9H_{19}N_2O_2PCl_2$: C, 37.39; H, 6.62; N, 9.69; P, 10.71; Cl, 24.52. Found: C, 37.38; H, 6.65; N, 9.64; P, 10.96; Cl, 24.44.

2-(Dimethylamino)-2-oxo-3-phenyl-5,5-dimethyl-1,3,2-oxazaphosphorinane, 5. A mixture of *N*-phenyl-2-(hydroxymethyl)-2-methylpropylamine[14] (16.3 g, 91.1 mmol) and hexamethylphosphorous triamide (19.5 mL, 17.5 g, 91.1 mmol) in a solution of ethyl acetate (100 mL) and toluene (100 mL) was refluxed for 18 h. The solvents were removed in vacuo, and the residual liquid was dissolved in dichloromethane (250 mL). The reaction mixture was cooled to −20 °C, and the material was oxidized by dropwise addition of a saturated solution of N_2O_4 in CH_2Cl_2. The reaction mixture was warmed to room temperature and the solvent removed in vacuo, leaving a thick brown oil (41.7 g). A 5.75-g sample of the oil was chromatographed on a 20 × 700 mm column of silica gel (Baker, 60–200 mesh, 90 g), eluting with ethyl acetate/hexane (1:1). The first 700 mL of eluent was discarded and the next 400 mL collected. Removal of the solvent by rotary evaporation gave 2.48 g (73.6% yield) of 2-(dimethylamino)-2-oxo-3-phenyl-5,5-dimethyl-1,3,2-oxazaphosphorinane (**5**) as a pale yellow crystalline solid. A small sample of the compound was Kugelrohr distilled from bulb to bulb with an air bath temperature of 120 °C at 0.20 torr and then recrystallized from diethyl ether/pentane to give analytically pure product: mp 60–61 °C; ^{1}H NMR (90 MHz, $CDCl_3$) δ 1.00 (s, 3 H, CCH_3), 1.32 (s, 3 H, CCH_3), 2.63 (d, 6 H, NCH_3, J_{HP} = 10.2 Hz), 3.05–4.50 (m, 4 H, CH_2N, CH_2O), 7.3–7.7 (m, 5 H, C_6H_5); ^{31}P NMR (CD_3COCD_3) δ 8.28; IR (KBr) 2960, 2890, 2845, 2800, 1600, 1500, 1490, 1480, 1305, 1261 (s, P=O), 1230 (s, P=O), 1207, 1190, 1123, 1110, 1080, 1058, 1042, 994, 900, 810, 793, 757, 740, 696 cm^{-1}; mass spectrum, *m/e* 268 (48%, M^+), 213 (81%), 106 (100%), 105 (99%), 104 (29%), 77 (31%), 69 (25%). Anal. Calcd. for $C_{13}H_{21}N_2O_2P$: C, 58.20; H, 7.89; P, 11.54. Found: C, 58.14; H, 7.95; P, 11.68.

2-(Diisopropylamino)-2-oxo-5-*tert*-butyl-1,3,2-oxazaphosphorinanes, 6. A solution of (diisopropylamido)phosphoryl dichloride (6.20 g, 28.4 mmol) in anhydrous ethyl acetate (50 mL) was added slowly to a rapidly stirred solution of 2-(hydroxymethyl)-3,3-dimethylbutylamine (3.73 g, 28.4 mmol) and anhydrous triethylamine (7.92 mL, 5.75 g, 56.9 mmol) in anhydrous ethyl acetate (200 mL), cooled to 0 °C. The reaction mixture was allowed to warm to room temperature and stirred for 4 days. The triethylamine hydrochloride was filtered off and the solvents removed from the filtrate to give 8.24 g of a residual yellow solid. A 400-mg sample of this crude product was chromatographed by MPLC on silica gel, eluting with EtOAc/EtOH (9:1) to give 140 mg of pure *trans*-2-(diisopropylamino)-2-oxo-5-*tert*-butyl-1,3,2-oxazaphosphorinane (**6**) as a colorless crystalline solid which was recrystallized from Et_2O/pentane: mp 141 °C; ^{31}P NMR ($CDCl_3$) δ 13.70; IR (KBr), 3270 (s, b, NH), 2962, 2888, 1408, 1364, 1217 (sh), 1202 (s, P=O), 1158, 1130, 1088, 1037, 1030, 1014, 991, 840, 799, 774 cm^{-1}. Anal. Calcd. for $C_{13}H_{29}N_2O_2P$: C, 56.50; H, 10.58; P, 11.21. Found: 56.48; H, 10.61; P, 11.35; MS, (El) *m/e* 276 M^+ (5.0%), 262 (13%), 261 (100%), 233 (25%), 219 (70%), 135 (28%), 94 (13%), 86 (18%), 69 (11%). In addition 40 mg of the cis diastereomer was obtained and recrystallized from pentane: mp 80–82 °C; ^{31}P NMR ($CDCl_3$) δ 11.52; IR (KBr) 3210 (s, br, NH), 2920, 2870, 1404, 1367, 1249, 1214 (P=O), 1193 (sh), 1160, 1110, 1034, 1000, 968, cm^{-1}; mass spectrum, *m/e* 276 (M^+, 4%), 262 (14%), 261 (100%), 233 (23%), 219 (74%), 135 (29%), 94 (13%), 86 (19%), 69 (27%). Anal. Calcd. for $C_{13}H_{29}N_2O_2P$: C, 56.50; H, 10.58; P, 11.21. Found: C, 56.49; H, 10.54; P, 11.29. A further 160 mg of a pure mixture of diastereomers also was isolated, total 340 mg (89% yield).

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Registry No. 1, 88946-46-7; **2**, 94843-98-8; **3**, 94843-99-9; 4, 22089-27-6; **5**, 94844-00-5; *trans*-**6**, 94859-54-8; *cis*-6, 94844-01-6; **8**, 50-18-0; **9**, 94844-02-7; $Et_2NP(O)Cl_2$, 1498-54-0; *i*-$Pr_2P(O)Cl_2$, 23306-80-1; $EtO_2CC(CH_3)_2COCl$, 64244-87-7; $PhNH_2$, 62-53-3; 2-(hydroxymethyl)-2-methylpropylamine, 76733-32-9; (bis(2-chloroethyl)amido)-phosphoryl dichloride, 127-88-8; hexamethylphosphorus triamide, 680-31-9; 2-(hydroxymethyl)-3,3-dimethylbutylamine, 15521-17-2; *N*-phenyl-2-carboethoxy-2-methylpropionamide, 7507-43-9.

Ion Pairing and Reactivity of Enolate Anions. 6. Kinetics and Thermodynamics for Reaction of Alkali Acetylacetonates with Alkyl Halides in Dimethyl Sulfoxide

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Abstract: Rates and heats of reaction are reported for the C-alkylation of alkali salts of various symmetrical β-diketones with methyl and ethyl iodide in dimethyl sulfoxide (Me_2SO). Product analysis by FT-NMR established that the reactions were clean over the concentration range of the kinetic and thermochemical study and, with only one exception, gave 100% carbon alkylation within the limits of detection. The effects of ion pairing, temperature, and alkylating agent were probed to yield an extensive comparison of the effects of structural change on the kinetics of alkylation with methyl or ethyl iodide. The formation of 3-methyl-3-ethylacetylacetone by alternative routes (methylation of potassium 3-ethylacetylacetonate and ethylation of potassium 3-methylacetylacetonate) allows an unprecedented comparison of the energetics of each step along the reaction profile from isomeric reactants in the gas phase, through isomeric transition states, to a common product in Me_2SO solution.

From a pragmatic viewpoint, alkali enolates are probably the most important type of synthetic intermediate since they are involved in the many useful base-promoted alkylation and acylation reactions of carbonyl compounds. However, relatively few systematic physicoorganic studies have been aimed at elucidating the factors which control the rates or product distribution in these important reactions. From what has been done so far, it is clear that practically every variable in the system can influence the outcome. In recent years the sensitivity of many enolate reactions to the choice of alkali counterion has become appreciated and attributed to ion pairing. The notion that dissociated (i.e., "naked") anions are more reactive than those which are paired to alkali cations is attractive and has inspired the use of various strategies such as the use of dipolar nonhydroxylic solvents, polybasic cation ligands, and phase-transfer catalysis to help dissociate the ion pairs. Several excellent recent reviews have organized the literature that

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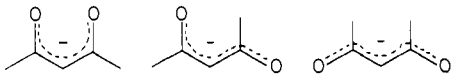
bears on the relation of ion aggregation to enolate reactivity.[1,2] From another angle, the deliberate use of highly aggregated lithium enolates (or their surrogates) now play a key role in stereocontrol of aldol-type condensations.[3-5]

The present paper continues our study of this problem by using preformed enolate salts of symmetrical β-diketones in Me_2SO at 25 °C. In the previous article[6] we compared the thermodynamic properties for formation of potassium enolates of various β-diketones and diesters by deprotonation in Me_2SO and also the ion-pairing association constants for their lithium, sodium, and potassium salts. In this paper we will use the association data to analyze the kinetics and thermochemistry of alkylation for several enolates of β-diketones by separating the observed rate constants into terms for reaction of the free ions and of the ion pairs.

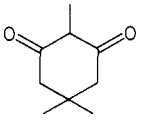
Our previous reactivity studies[7,8] employed salts of dibenzoylmethane and dipivaloylmethane which are assisted by steric hindrance to assume the U-shape (*Z,Z*) conformation that favors ion pairing through stabilization of the metal chelate. This raised



Z,Z *Z,E* *E,E*

the question of how cyclic diketones, such as dimedone, which are constrained to the W-shaped (*E,E*) conformation would behave relative to more flexible diketones, such as acetylacetone, which can assume the unsymmetric sickle-shaped (*E,Z*) arrangement. Although others have examined the effect of conformation on spectra[9-13] of enolates, we know of none which have systematically examined the effect of conformation on the ion pairing and alkylation of diketone or diester enolates. This paper extends our previous thermodynamic study of conformation and ionization by comparing the kinetics of alkylation of the enolates of methylacetylacetone with those of methyldimedone.

In approaching these problems we discovered that attack of methyl iodide on the enolates of unsubstituted parent compounds produced complex kinetics as dialkylation competed with monoalkylation. This problem was solved readily by using the per-



formed monoalkylated alkali salts as the nucleophiles. Careful product studies using ^1H and ^{13}C NMR showed that in most cases alkylation with methyl iodide or ethyl iodide occurred exclusively at the central carbon so that no allowance needed to be made for O-alkylation under these conditions. Thus, by careful choice of compounds and conditions, the reactivity of the central carbon of symmetrical enolate anions toward alkylating agents may be compared. Furthermore, since the energetics for converting the diketones to ions and ion pairs are in hand, a complete analysis of the effect of structural change on each step from the neutral carbon acid to the alkylated product is possible.

Experimental Section

All the compounds and solvents used here were purified and prepared as described in the previous article[6] except for the alkylating agents and chelating agents.

Methyl iodide (Aldrich) was dried over calcium chloride and then fractionally distilled from copper metal; bp 43.0 °C [lit.[14] bp 42.8 °C].

Ethyl iodide (Aldrich) was extracted with sodium thiosulfate to remove iodine and then dried over calcium chloride.[14] It was then fractionally distilled through a Vigreux column: bp 72–72.5 °C [lit.[14] bp 72.4 °C]. Dibenzo-18-crown-6 (Aldrich) was dried at 100 °C under vacuum and stored in a desiccator. [2.1.1]cryptand (E.M. Laboratories) was used without purification.

The technique for determining pK_a's and ion-pairing association constants were also presented previously with the results of such studies.[6] Further details are available in the doctoral dissertations of S.G.M. (University of Pittsburgh) and S.L.S. (Duke University).

Formation and Isolation of the Enolate Salt. Alkali enolates were prepared from the parent dicarbonyl compound and the appropriate alkali metal as follows. Approximately 25 mL of methanol was distilled from sodium into a 50-mL round-bottom flask. A clean piece of the alkali metal was then weighed under dry benzene and dissolved in the methanol. Next, a 1% molar excess of the dicarbonyl compound was added to the methanol solution along with several milliliters of dry benzene to azeotrope any water. The solvent was then removed by rotary evaporation. The solid enolate precipitate which formed was washed with several portions of benzene and dried under vacuum. Enolate salts were stored away from light under vacuum until used. The solid enolate salts remained good for at least 2 weeks if kept in a desiccator under vacuum.

Preparation of Enolate Solutions. Solutions of known enolate concentration were prepared immediately before use by weighing the enolate salt into a tared 50-mL volumetric flask purged with argon. Me_2SO was then added with stirring, and the flask and contents were reweighed after dissolution of the enolate salt was complete.

Enolate solutions would remain good for several hours if kept under argon. When exposed to air, however, the enolates decomposed rapidly, and the solution would discolor.

Calorimetry. Heats of solution and heats of reaction were measured with a Tronac 1250 solution calorimeter equipped with an ampule breaker as described in the previous article.[6]

Heats of Solution. The solute was sealed in an ampule and weighed. The reaction vessel was filled with pure Me_2SO and allowed to equilibrate. After an initial calibration of the system against an electrically generated increment of heat, the enthalpy change from solution of enolate was measured by breaking the ampule. This was followed by a second electrical calibration.

Heats of Alkylation. A weighed amount of the enolate was dissolved in 40 mL of Me_2SO under argon in the reaction vessel. An ampule was filled with an excess of the neat alkylating agent and sealed. The heat released upon breaking the ampule was determined as before and corrected for the heat of solution of the alkylating agent in pure Me_2SO. For reactions in the appropriate rate range (see below), heats and rates of alkylation were obtained from the same experiment.

Kinetics. Reaction rates reported here were determined by two methods. The thermokinetic approach, which permits simultaneous determination of the rate and enthalpy of reaction, was used for reactions with half-lives between 0.5 and 5 min. This technique has been described elsewhere (8) and is both convenient and elegant within the limited rate range where it can be applied.

For reactions which were too fast for thermokinetic analysis, an inexpensive homemade stopped-flow system was constructed which could be used for pseudo-first-order half-lives down to about 100 ms following an initial deadtime of about 100 ms required for mixing and stabilization.

Two gastight syringes (Glenco), one for the enolate solution (10 mL) and one for the neat alkylating agent (0.25–1.0 mL), were clamped into a hand-driven syringe drive (designed by Prof. Robert Henkens). The relative amounts delivered by the two syringes were calibrated by weighing water samples. From the syringes the reactants flowed through 0.8-mm Teflon tubing to a T-connector mixer and then through a 1-mm quartz flow cell (Hella) and into a third gastight syringe which acted as a deadstop. Slide valves were used to allow purging of the cell and refilling of the syringes from reservoirs. The flow cell was mounted in the thermostated cell compartment of a Gilford 242 (modified Beckman

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DU) spectrophotometer, whose output voltage was digitized by a Tekmar 12-bit A/D converter and stored for subsequent kinetic analysis by an Apple II+ microcomputer. In normal operation, the syringe drive was pushed by hand and the data collection triggered by a switch attached to the drive. All kinetic experiments were performed under pseudo-first-order conditions with a large excess of alkylating agent, typically 1–2 M compared to 0.001 to 0.05 M in the enolate.

The influence of varying ionic strength upon the activity coefficients, and, hence, the extent of dissociation of the enolate ions, was estimated by using the Debye–Hückel limiting law. Since the extent of dissociation affects the total ionic strength, such calculations were applied iteratively until the fractional amount of free ion changed by less than 0.01% per iteration.

Activation parameters were obtained by measuring the free ion rate constants as above at four different temperatures between 18.5 and 45 °C. Low concentrations of the potassium enolate with excess added dibenzo-18-crown-6 were used to ensure complete dissociation of the enolate anions.

Product Studies for the Alkylation of Enolate Anions with MeI and EtI. Enolate solutions in Me_2SO-d_6 were prepared as described above. They and their alkylation products were examined by ^1H FT-NMR over the concentration range (1–100 mM) used for the kinetic and thermochemical studies of enolate alkylation. These studies show that all the enolate anion salts and their alkylation products are stable in Me_2SO under the above conditions for at least 12 h as confirmed by ^1H NMR.

Methylation with MeI of the enolates listed in Tables I and II gave only carbon alkylation within the limits of detection. Ethylation with EtI of the alkali enolate salts, except for those of methyldimedone (MDD) and ethyldimedone (EDD) enolate anions, gave only carbon alkylation. In contrast to methylation, the ethylation of the enolates of methyldimedone and ethyldimedone gave 35% oxygen and 65% carbon alkylation over the concentration range of 3–30 mM, with the product distribution being independent of the initial enolate concentration and cation identity.

Results

The kinetic data presented in this paper are based on many rate measurements made over the past decade. All of them have been checked for reproducibility by repetition, often over periods of many months, with different batches of solvent, reagents, and addends. Many of the data have been cross-checked by several of the authors under different experimental conditions. In the course of making these comparisons, we confronted much greater difficulty in obtaining reproducible rates than was encountered in making the thermochemical measurements reported here and in the previous paper in this series.[6] Although it was shown that additions of water, dimethyl sulfide, or air to the purified Me_2SO solvent affected the rate, we have no final proof of what impurity led to erratic rates. More importantly, it was found that a routine of extended pumping for 4 to 5 days during purification, as previously described,[6] produced batches of solvent in which reproducible rates could be obtained.

All rate constants reported here are based on pseudo-first-order runs, usually monitored by the disappearance of UV absorbance of the enolate anion in the presence of a large excess of the alkylating agent. Table I demonstrates the effects of changing the nature and concentration of the enolate, the counterion, and various addends, all of which were used to probe the influence of ion pairing on the reaction rate.

In view of the fact that the reaction rate is highly sensitive to the enolate concentration, especially for lithium and sodium enolates which are most associated, one may ask why it was possible to get good first-order kinetics. We attribute this fortunate, but somewhat surprising, result to two facts that would reduce the possible influence of variable ion pairing. Firstly, the rate constant was usually determined over only one or two half-lives so that large concentration changes were not involved. However, even when an extended run could be followed over several half-lives, clean first-order behavior was seen. Secondly, since only the enolate anion was reacting, the concentration of the alkali counterion remained constant, and the original concentration of alkali enolate was steadily replaced by a compensating concentration of alkali iodide as the reaction proceeded. Since the alkali iodides are more dissociated than the corresponding alkali enolates, they provided a slightly increasing ionic strength. As will be noted below, this would assist dissociation and so would have its greatest effect on the early stages of reaction where ion-pairing is greatest, thereby providing a buffering effect on the complex coupling of ionic equilibria and rates.

Association constants listed in Table I were taken from our thermodynamic studies reported in the previous article[6] using conductance and Bordwell's indicator method and were used to calculate the degree of dissociation of the alkali enolates, α. An assumption which lies behind the application of these K_{assoc} values to the present kinetic study through the Acree equation is that the effect of replacing some of the Me_2SO solvent by up to 1.30 M alkyl iodide is negligible or constant within each series of runs where all other factors are varied. Table II gives a more limited set of data for the alkylation of methyldimedone (MDD), a cyclic analogue of MAA.

Although a competing pathway to alkylation involving formation of a highly reactive sulfoxonium ion (from prior alkylation of the solvent) was considered, no evidence for it was ever found when methyl or ethyl iodides were used. This contrasts with previous studies with methyl sulfate.[7,8]

Table III presents molar heats of reaction for the "isomeric reactions" of methyl iodide with ethylacetylacetonate and of ethyl iodide with methylacetylacetonate at 25 °C. The effects of ion pairing are clearly evident for the lithium enolates as the endothermic term for overcoming the enthalpy of association varies with concentration. Heats of alkylation, ΔH_{RI}, for the lithium enolates only approach the "free ion" values for the fully dissociated potassium salt at high dilution.

Table IV provides the Eyring activation parameters for the four possible alkylation reactions of methyl and ethyl iodide with the enolate anions of methyl- and ethylacetylacetone. Rate constants were obtained at four temperatures between 18 and 45 °C for the potassium enolates at concentrations mostly between 2.8 and 5.9 mM with an excess of dibenzo-18-crown-6 polyether added to ensure complete enolate dissociation.

Discussion

Introduction. Conditions have been found for obtaining reproducible rates for clean carbon alkylation of the enolate anions of β-diketones in dimethyl sulfoxide. We will now consider how these rates respond to perturbations of the system—variations in structure, concentration, temperature, and ion pairing. Table I presents such results for two closely related reactions: ethylation of the alkali enolates at 3-methylacetylacetone and the corresponding methylation of 3-ethylacetylacetonates.

This pair of processes allows the application of a strategy which gives an unusually complete comparison and analysis of the various states involved since both reactions go to a common product: 3-methyl-3-ethylacetylacetone. Unlike most kinetic and thermodynamic comparisons in which all the states from reactants to products have different structures and cannot be related on a common energy scale, these two reactions have one state in common. It is therefore feasible to work back from this point to place all other states, including their isomeric transition states, on a common energy diagram. We shall apply this "method of isomeric pathways" to the present case in point later after first discussing effects of the variables tabulated in the Results section.

Ion Pairing The simplest kinetic evidence for ion association is variation of the rate as the counterion is changed. Since the ion–ion interaction energy varies as the reciprocal of the ionic radii, the order of increasing ion association for alkali cations with a common anion is $Cs^+ < K^+ < Na^+ < Li^+$.[15,16] That order is clearly apparent for rates of the same enolate anion at equivalent concentrations if one makes the reasonable assumption that associated enolate ions are less reactive than "free" ones. A confirming probe of the cation effect is provided by addition of salts of the common cation with an unreactive and well-dissociating anion. Thus, a strong rate-retarding effect from adding LiI or $LiBF_4$ is seen on the ethylation of lithium 3-methylacetylacetonate.

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Table I. Rate Data for the Reaction of Alkali Salts of 3-Methylacetylacetone ($M^+MeAcAc^-$) with Ethyl Iodide (1.30 M) and of 3-Ethylacetylacetone ($M^+ETAcAc^-$) with Methyl Iodide, with and without Various Addenda in Dimethyl Sulfoxide

reactants M MeAcAc + EtI	T[g]	$[M^+MeAcAc^-]$[a]	addendum	[addendum][a]	α[b]	α_{corr}[c]	k_2, M^{-1} s^{-1}
$Li^+MeAcAc^-$ (log K_{assoc} = 3.33)		0.800			0.528	0.537	0.100 ± 0.003
		0.893			0.509	0.519	0.0891 ± 0.0009
		1.49			0.426	0.437	0.0534 ± 0.0008
		2.07			0.377	0.388	0.0420 ± 0.0011
		2.97			0.327	0.338	0.0335 ± 0.0008
		3.94			0.291	0.303	0.0229 ± 0.0004
		5.09			0.261	0.273	0.0186 ± 0.0002
		8.47			0.210	0.221	0.0111 ± 0.0002
		12.7			0.175	0.183	0.00705 + 0.00007
		1.08	Li^+I^-	1.85	0.187	0.205	0.0348 ± 0.0007
		1.37	$Li^+BF_4^-$	4.01	0.102	0.118	0.0185 ± 0.0006
		5.75	$Li^+BF_4^-$	18.4	0.024	0.035	0.00452 ± 0.00006
		3.01	$Pr_4N^+Br^-$	15.85	0.325	0.372	0.0422 ± 0.0008
		3.49	$Li^+BF_4^-$	6.69	0.306	0.337	0.0292 ± 0.0021
		2.91	crypt[b]	10.75	1.0	1.0	0.234 ± 0.006
		3.97	crypt[d]	8.57	1.0	1.0	0.230 ± 0.022
$Na^+MeAcAc^-$ (log K_{assoc} = 1.56)		2.97			0.911	0.921	0.211 ± 0.006
		3.57			0.896	0.909	0.216 ± 0.007
		4.53			0.875	0.890	0.212 ± 0.005
		4.66			0.872	0.888	0.207 ± 0.002
		7.42			0.820	0.845	0.175 ± 0.003
		8.02			0.810	0.837	0.182 ± 0.003
		10.0			0.780	0.813	0.165 ± 0.003
		12.2			0.751	0.789	0.161 ± 0.002
		4.39	$Na^+BPh_4^-$	14.9	0.612	0.689	0.149 ± 0.003
		9.23	$Na^+BPh_4^-$	5.49	0.699	0.751	0.146 ± 0.003
		9.52	$Na^+BPh_4^-$	12.8	0.600	0.677	0.134 ± 0.002
		10.5	$Na^+BPh_4^-$	37.8	0.398	0.328	0.114 ± 0.002
		13.0	$Na^+BPh_4^-$	14.2	0.563	0.648	0.131 ± 0.002
		6.98	$Na^+BPh_4^-$	7.06	0.827	0.862	0.188 ± 0.002
		10.9	Bu_4N+F^-	18.1	0.768	0.827	0.171 ± 0.003
$K^+MeAcAc^-$ (log K_{assoc} = 0.73)		4.23			0.978	0.981	0.243 ± 0.002
		6.51			0.967	0.973	0.220 ± 0.002
		11.98			0.942	0.955	0.201 ± 0.002
		3.41	$K^+BF_4^-$	38.6	0.816	0.884	0.200 ± 0.001
		6.66	$K^+BF_4^-$	99.1	0.640	0.806	0.163 ± 0.002
		7.21	$K^+BF_4^-$	46.5	0.779	0.866	0.174 ± 0.004
		3.71	crown	4.26	1.0	1.0	0.263 ± 0.003
	18.5	3.63	crown	5.50	1.0	1.0	0.177 ± 0.004
	35.0	3.08	crown	5.17	1.0	1.0	0.531 ± 0.016
	45.0	2.81	crown	3.21	1.0	1.0	1.007 ± 0.043

$M^+EtAcAc^-$ + MeI	T[g]	$[M^+EtAcAc^-]$[a]	[MeI], M	addendum	[addendum][a]	α[b]	α_{corr}[c]	k_2, M^{-1} s^{-1}
$Li^+EtAcAc^-$ (log K_{assoc} = 3.36)		0.690	1.70			0.543	0.550	0.764 ± 0.040
		1.262	1.70			0.441	0.451	0.545 ± 0.009
		2.17	1.70			0.360	0.371	0.389 ± 0.007
		5.51	1.70			0.245	0.256	0.166 ± 0.004
		10.64	1.70			0.183	0.194	0.0925 ± 0.0015
		3.79	1.70	Li^+I^-	8.115	0.050	0.063	0.0837 ± 0.0009
		3.01	1.70	Pr_4NBr[d]	25.64	0.316	0.376	0.391 ± 0.007
		2.014	1.70	crypt.	11.06	1.0	1.0	4.17 ± 0.72
$Na^+EtAcAc^-$ (log K_{assoc} = 1.48)		1.341	0.928			0.962	0.966	4.22 ± 0.11
		4.043	0.928			0.901	0.914	3.68 ± 0.18
		8.58	0.928			0.825	0.852	3.63 ± 0.14
		14.76	0.928			0.750	0.792	3.54 ± 0.04
		4.43	0.928	Na^+I^-	27.64	0.527	0.636	3.24 ± 0.07
		9.59	0.928	Na^+I^-	51.29	0.378	0.528	2.30 ± 0.10
		14.66	0.928	Na^+I^-	88.57	0.265	0.445	1.76 ± 0.03
$K^+EtAcAc^-$ (log K_{assoc} = 0.85)		3.47	0.928			0.976	0.979	4.30 ± 0.18
		9.08	0.928			0.943	0.954	4.09 ± 0.11
		3.09	0.928	K^+I^-	16.93	0.878	0.912	3.94 ± 0.17
		6.64	0.928	K^+I^-	23.68	0.829	0.883	3.58 ± 0.21
		10.92	0.928	K^+I^-	37.10	0.757	0.844	3.77 ± 0.10
		19.42	0.928	K^+I^-	60.75	0.658	0.796	3.29 ± 0.13
		3.471	0.487	crown[e]	5.31	1.0	1.0	4.12 ± 0.19
	18.5	3.314	0.487	crown	6.23	1.0	1.0	3.05 ± 0.07
	33.0	3.172	0.487	crown	4.36	1.0	1.0	6.11 ± 0.10
	41.5	3.197	0.487	crown	4.87	1.0	1.0	8.61 ± 0.43
		2.80	0.928	$Li^+EtAcAc^-$	2.53			0.893 ± 0.077
		4.48	0.928	$Li^+EtAcAc^-$	5.05			0.725 ± 0.043
		7.80	0.928	$Li^+EtAcAc^-$	2.66			3.77 ± 0.18

[a] Corrected ($\times 10^3$ mol L^{-1}) for dilution by RI. [b] Calculated from K_{assoc}. [c] Calculated by Debye–Huckel limiting law. [d] [2.1.1]Cryptand. [e] Dibenzo-18-crown-6 polyether. [f] Prof Lloyd Jackman has informed us that BF_4^- anion reacts with Me_2SO so that other species may be present with these salts. [g] Temperature (degrees) 25 °C unless shown otherwise.

Table II. Rates of Alkylation of Alkali Salts of Methyldimedone (M^+MDI^-) at 25 °C

M^+MDD^-	$[M^+MDD^-]$	RX	[RX]	addendum	[addendum][a]	α	k_2, M^{-1} s^{-1}
LiMDD	1.47	EtI	1.30				0.0252 ± 0.0005
	2.77						0.0232 ± 0.0003
	4.55						0.0194 ± 0.0004
	8.78						0.0148 ± 0.0003
	11.5						0.0144 ± 0.0002
NaMDD	1.66	EtI	1.30				0.0273 ± 0.0003
	2.68						0.0252 ± 0.0004
	3.90						0.0230 ± 0.0003
	5.30						0.0222 ± 0.0003
	6.59						0.0205 ± 0.0003
	8.11						0.0188 ± 0.0003
	4.61	EtBr	1.41			0.955	0.00107 ± 0.00003
	5.58					0.946	0.00157 ± 0.00002
	3.52	MeI	1.67			0.965	0.291 ± 0.003
	7.51					0.930	0.260 ± 0.005
	7.25			$NaBPh_4$	3.61	0.902	0.264 ± 0.006
	7.55				8.72	0.859	0.204 ± 0.007
	10.2				8.37	0.846	0.199 ± 0.004
	4.04				6.82	0.899	0.292 ± 0.005
LiMDD	2.25	EtBr	1.41				0.00242 ± 0.0001
KMDD	0.860	EtI	1.30			0.0365	0.0004
	1.54					0.0282	0.0004
	2.84					0.0245	0.0005
	4.50					0.0205	0.0003
	6.64					0.0192	0.0003
	9.23					0.0168	0.0004

Table III. Heats of Alkylation of the Alkali Enolates of Methylacetylacetone and Ethylacetylacetone with Methyl Iodide and Ethyl Iodide in Dimethyl Sulfoxide at 25 °C

cation	EtI[a] + $[MAA^-]$ × 10^3 M	$-\Delta H_{RI}$, kcal/mol	MeI[a] + $[EAA^-]$ × 10^3 M	[LiI] × 10^3 M	$-\Delta H_{RI}$, kcal/mol
K^+	3.33	37.49	1.63		39.53
	6.30	36.86	5.20		39.39
	7.98	37.54	7.10		38.93
	11.90	36.62	11.09		39.96
	13.43	37.98	16.78		39.34
	14.32	36.86			
Na^+	1.90	34.65	1.79		40.97
	4.86	36.26	3.78		41.98
	6.83	35.71	5.41		36.95
	8.36	35.66	5.76		43.09
	10.19	36.41	9.75		41.44
	13.09	35.79	13.53		38.97
Li^+	2.42	37.96	2.18		40.25
	4.47	35.36	4.32		40.59
	6.21	33.80	6.34		39.78
	7.50	31.70	8.33		35.27
	12.17	29.35	11.54		34.06
			12.92		34.59
			14.70		33.21
			17.72		33.51
			10.16	10.53	36.40
			10.09	47.27	35.29
			11.19	118.7	31.01

[a] Initial concentrations of alkyl iodide were about 0.1 M.

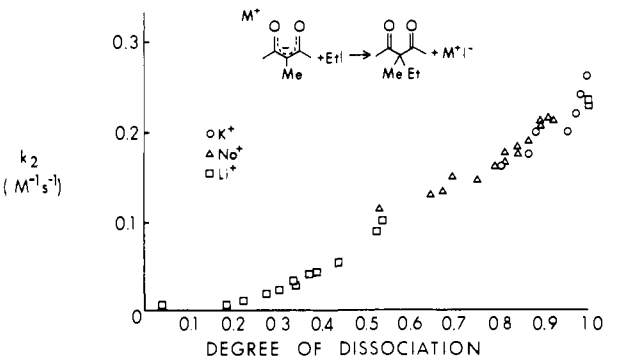

Figure 1. Acree plot of the observed second-order rate constant for ethylation of the alkali enolates of methylacetylacetonate vs. the calculated degree of dissociation.

A more modest concentration-dependent effect is produced by adding $NaBPh_4$ to the corresponding sodium enolate, while a much larger concentration of KBF_4 is needed to have any effect on the potassium enolate.

The effect of noncommon ion salts is interesting. Since the initial state (enolate ion plus alkyl halide) is charged and the transition state is too, the classical Brønsted ionic strength effect on rates[18] should be small. Yet, the addition of tetrapropylammonium bromide to the ethylation of Li MAA, for example, causes a 30% increase in rate (lines 5 and 13 in Table I) at equivalent concentrations of reactants. We interpret this as being due to an ionic strength effect on the ion–ion pair equilibrium which assists dissociation by lowering the activity of the enolate ions.

If ion association is truly the cause of rate reduction in the cases cited, there should be a marked increase in rate as a result of encapsulating the alkali cations in a neutral ligand such as a crown ether or cryptand. Such an effect is portrayed clearly in Table I.

A quantitative treatment of the effect of ion pairing on rates is provided by the Acree equation[17]

$$k_{obsd} = k_{ip}(1 - \alpha) + k_i\alpha$$

where k_{obsd} is the observed rate constant and k_{ip} and k_i refer to the components of the total rate contributed by the ionic pair and unassociated ("free") ion, respectively. The degree of dissociation, α, is obtained independently from conductance or indicator titration data as reported in our previous article.[6] If, as is often

(17) Acree, S. F. *Am. Chem. J.* **1912**, *48*, 352.

(18) Moore, J. W.; Pearson, R. G. "Kinetics and Mechanism", 3rd ed.; Wiley: New York, 1984; p 272.

Table IV. Thermodynamic and Kinetic Properties for Isomeric Reacting Systems in Me_2SO at 25 °C

property	system I ($K^+MeAcAc^-$ + EtI)	system II ($K^+EtAcAc^-$ + MeI)	$\Delta\Delta P$ ($\Delta P_I - \Delta P_{II}$)
$\Delta H_{R1}°$ (heat of reaction)	−37.07 ± 0.74	−39.43 ± 0.37	−2.36
k_{ion}, M^{-1} s^{-1}	0.263	4.12	
$\Delta G_{for}^{\ddagger}$, kcal/mol	18.22 ± 0.47	16.61 ± 0.62	1.61
$\Delta H_{for}^{\ddagger}$, kcal/mol	11.61 ± 0.34	7.70 ± 0.44	3.31
$\Delta S_{for}^{\ddagger}$, G/mol	−22.19 ± 1.13	−29.87 ± 1.47	7.68
$\Delta H_{rev}^{\ddagger}$, kcal/mol	48.68 ± 0.82	47.13 ± 0.58	1.55
	Heats of Formation and Solution of Reactants		
ΔH_f^1, kcal/mol of RI[a]	−9.72	−2.46	−7.26
$\Delta H_{sol}^{I\rightarrow Me_2SO}$, kcal/mol of RI	+0.988 ± 0.005	+0.441 ± 0.004	0.547
$\Delta H_f^{Me_2SO}$ of [RI], kcal/mol	−8.73	−2.02	−6.71
ΔH_f^{DMSO} [RAA^-] kcal/mol of enolate ion (rel to prod)	45.8	41.5	4.35
$\Delta H_D^{Me_2SO}$ RAA[b]	−31.7 ± 1.2	−32.7 ± 1.1	1.0
$\Delta H_{soln}^{Me_2SO}$ RAA[b]	0.461 ± 0.010	0.575 ± 0.008	−0.114
ΔH_{vap} RAA	11.9	12.3	−0.4
tot	88.94	85.93	3.01

[a] Reference 28. [b] Reference 6. See this reference also for thermodynamic of ionization of the diketones and association of the enolates.

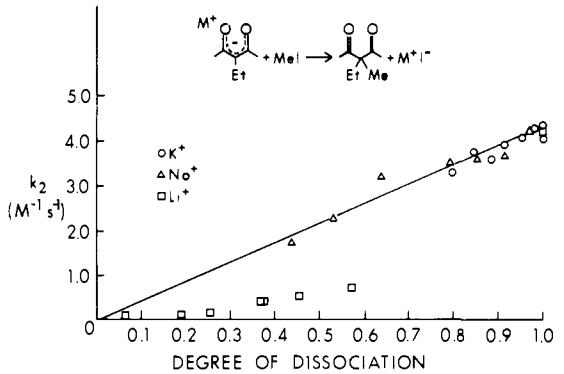

Figure 2. Acree plot of the observed second-order rate constant for methylation of the alkali enolates of ethylacetylacetonate vs. the calculated degree of dissociation.

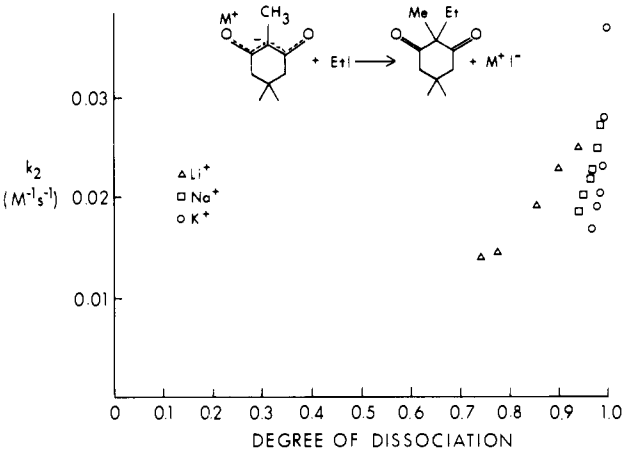

Figure 3. Plot of observed second-order rate constant for ethylation of the alkali enolates of methyldimedone vs. the degree of dissociation calculated from K_{assoc} from ref 6.

true, $k_{ip} \ll k_i$, a plot of k_{obsd} vs. α will be a stright line passing through the origin and giving k_i at $\alpha = 1.0$. More generally, this plot will give k_{ip} at $\alpha = 0$ and k_i at $\alpha = 1$. The line passes through the origin only if $k_i = 0$.

Figures 1 and 2 present the results from Table I in these terms. Reasonable agreement is found for points derived from the sodium and potassium enolates as has been seen for other enolate reactions.[7] In contrast, the rates for the lithium enolates fall far below what would be expected on the basis of a simple ion–ion pair analysis.

We have repeatedly observed a much stronger concentration dependence of conductance, enthalpy, and rate data for lithium enolates than for corresponding sodium or potassium salts. This behavior could be explained by the well-recognized tendency of lithium to form higher aggregates than simple 1:1 ion pairs. A very recent report from Reutov's group[19] documents exactly similar behavior for the reaction of fluoradene with alkali diphenylcarbinolates. The existence of triple ions is well-known in other solvents[9,10] and has been suggested in Me_2SO for the lithium enolate of 4-methyl-1,8-decalindione, which is locked in the (*Z*,*Z*) conformation.[20] Our data suggest, but do not prove, that significant amounts of triple ions or higher aggregates may exist in Me_2SO for the lithium enolates of conformationally free dicarbonyl compounds, even at concentrations as low as 10^{-3} M. However, several attempts to fit the experimental data with reasonable aggregation numbers failed. The source of this kinetic behavior is under further investigation. Confirmation that the lithium enolate is capable of providing reactive free ions is offered by addition of [2.1.1]cryptand to the lithium enolate which then yields a rate corresponding to the free ion rate extrapolated from the sodium and potassium enolate runs.

An interesting contrast to the behavior of the acyclic diketones is afforded by that of methyldimedone as seen in Table II and Figure 3. This cyclic diketone enolate is constrained to the W-shaped (*E*,*E*) conformation which prohibits formation of the chelated ion pairs commonly found for acyclic systems.

It is well-known that dimedone is a highly acidic diketone, and our previous report established that in Me_2SO at 25 °C, methyldimedone is considerably more acidic (pK_a = 11.73) than methylacetylacetone (pK_a = 15.07). One might expect that the lower stability of the MAA ion and the presumed chelation effect would cause it to be much more strongly associated with alkali cations than the more delocalized W-shaped methyldimedone anion. However, against the potassium ion, K_{assoc} for MAA is the same, within experimental error, as for MDD.[6] For sodium the factor is 3.4, and for lithium it is 40.3. Considering that the negative charge on the MAA anion is probably less delocalized than that of MDD, it is hard to tell how much of this modestly superior performance in ion association is really due to its chelation ability. Here it must be recognized that formation of a chelated ion pair, although favored by symmetry and geometry, involves an unfavorable component of aligning the carbonyl dipoles parallel to each other. Dipole–dipole repulsions will be greatest in the U-shaped (*Z*,*Z*) chelated arrangement, less so in the sickle-shaped (*E*,*Z*) configuration, and will be minimized in the W-shaped dimedone type of system. This is probably the main reason for the relatively high stability of the methyldimedone anion as reflected in its high pK_a and also (presumeably) in its ethylation rate, which is only one tenth of that of MAA.[21]

(19) Solov'yanov, A. A.; Karpyuk, A. D.; Beletskaya, I. P.; Reutov, O. A. *J. Org. Chem. USSR (Engl. Transl.)* **1983**, *19*, 2240; **1984**, 1952.
(20) Olmstead, W. N.; Bordwell, F. G. *J. Org. Chem.* **1980**, *45*, 3299.

Table V. Activation Parameters at 25 °C for the Reactions of Ethylacetylacetonate and Methylacetylacetonate with Ethyl Iodide and Methyl Iodide in Dimethyl Sulfoxide

enolate	RX	$\Delta G^{\ddagger}$, kcal/mol	$\Delta H^{\ddagger}$, kcal/mol	$\Delta S^{\ddagger}$, cal/mol K
MAA^-	MeI	16.52 ± 0.01	7.70 ± 0.16	−29.55 ± 0.53
MAA^-	EtI	18.25 ± 0.01	11.60 ± 0.34	−22.19 ± 1.13
EAA^-	MeI	16.61 ± 0.03	7.70 ± 0.44	−29.87 ± 1.47
EAA^-	EtI	18.23 ± 0.01	9.72 ± 0.14	−28.51 ± 0.47

Figure 3 shows an entirely different response of the observed second-order rate constant to change in concentration for the ethylation of MDD than was seen for the linear Acree plots going through the origin in Figures 1 and 2. The data for this reaction, Table II, are not so extensive as those in Table I but are sufficient to show the behavior when tested by the Acree equation.

We previously invoked the formation of higher aggregates as a possible reason for the failure of LiMAA and LiEAA to fit the simple Acree equation. If that is the reason for the behavior of LiMDD on Figure 3, one should also apply the same argument to the sodium and potassium salts of MDD. This possibility is not absurd, since triple ion (i.e., $A^-M^+A^-$ or $M^+A^-M^+$) occasionally are proposed to explain conductance data[22] and would be appealing for W-shaped dicarbonyl enolates on structural grounds. However, it seems far-fetched to propose that potassium would exhibit the greatest degree of multiple association and lithium, the least as Figure 3 appears to demand.

Another factor which differentiates the ethylation of M^+MDD^- from the other reactions reported here (Experimental Section) is that 35% alkylation on oxygen occurred. Presumably this change in the course of the reaction has a steric origin since methylation of LiMDD with MeI occurs 100% on carbon. One would scarcely be surprised to find that alkylation on oxygen responds quite differently to ion pairing than does attack at the less protected carbon atom, and this may be responsible for the different behavior seen in Figure 3 as compared to Figures 1 and 2.

Whatever the reason for the different reactivity behavior of the cyclic and acycyclic diketones, it is worth noting that even in cases as simple as this, the mechanistic analysis is complex and variable and precludes glib generalization.

Activation Parameters. The temperature variations for the reactions of MeI and EAA and of EtI with MAA which are reported in Table I have been used to calculated Eyring activation parameters and have been augmented with corresponding properties for the nonisomeric reactions of MeI with MAA and of EtI with EAA as shown in Tables IV and V.

From these data, the methylation of methylacetylacetone and the methylation of ethylacetylacetone appear to be very similar reactions energetically. The methylation of methylacetylacetonate is slightly faster than that of ethylacetylacetonate over the entire temperature range studied, but this rate difference translates into a free energy difference at 25 °C of less than 0.1 kcal/mol. Both the enthalpies and entropies of activation are identical within the experimental error of the measurements. Substitution of an ethyl group for a methyl group at the reactive site apparently has very little effect on the reactivity of the enolates with methyl iodide.

The ethylation of the free ions of methyl- and ethylacetylacetonate have nearly the same rate constant at 25 °C and, hence, the same free energy of activation. However, these reactions have different enthalpies and entropies of activation which lead to significant rate difference at other temperatures. The ethylation of methylacetylacetonate has an enthalpy of activation which is nearly 2 kcal/mol higher than that for the ethylation of ethylacetylacetonate. The entropies of activation differ by over 6 eu, with the ethylation of ethylacetylacetonate having the more negative activation entropy. The reason why these two ethylation reactions have different entropies and enthalpies of activation, while the corresponding methylation reactions have identical entropies and enthalpies of activation, is not understood at this time.

These entropies of activation are all in the range expected for an S_N2 reaction,[23] where solvent reorganization probably plays a large role.[24] It is amusing to note how easily one could be led into an arbitrary and erroneous interpretation of these "reactivities" if rates had been determined at a single and significantly different temperature. Above 25 °C, the ethylation of MAA^- is the faster reaction—below that temperature EAA^- is faster.

Formation of Ethylmethylacetylacetone by Isomeric Pathways. We are now in a position to analyze the formation of ethylmethylacetylacetone by two "isomeric" pathways through the reaction of ethyl iodide with methylacetylacetonate and of methyl iodide with ethylacetylacetonate. Since both reactions give the same final product, any differences in the two reactions must be due to differences either in their initial ground states, their intermediates, or their transition states. We know of no exact precedent for using such a strategy to analyze the effects of structural change on related reactions but note that it could be applied widely to any situation where the same product can be formed cleanly by alternative routes whose only difference is the arrangement of the atoms in the reacting components and the intermediate states leading to the products.

In effect, this is the reverse of the common practice of comparing the formation of isomeric products from common reactants. However, the latter approach is limited severely by analytical problems to competing reactions which have nearly the same energy profiles. If not, only one product is found.

A similar problem arises in applying the method of isomeric pathways to free energy analysis. Relatively few organic reactions can be studied under conditions of reversible equilibrium. Only if it were possible to equilibrate the product with both sets of reactants would it be possible to get equally good free energy terms for both pathways.

No such problem applies to enthalpy measurements. Heats of reaction as well as heats of solution and many other terms necessary to provide an extensive dissection of enthalpy terms are obtained readily by calorimetry.

Figure 4 shows the application of such a dissection of isomeric pathways to the formation of ethylmethylacetylacetone based on data summarized in Table IV. The most obvious difference between these two reactions is their rate constants, the methylation of ethylacetylacetonate being almost 16 times faster than the ethylation of methylacetylacetonate at 25 °C. This, however, is equal to a difference of only 1.64 kcal/mol in their free energies of activation. Furthermore, since we have seen that both enolates react with either methyl iodide or ethyl iodide at comparable rates, the rate differences for these isomeric reactions can be attributed largely to a difference in the reactivities of the alkylating agents. Methyl substrates always react faster than analogous ethyl substrates in S_N2 reactions,[25] and a 16-fold rate increase is within the normal range of the relative ratio for methyl vs. ethyl substrates.[25,26]

In a study of the Menschutkin reaction for a series of substituted pyridines in 2-nitropropane,[27] the relative rates of the methyl vs. ethyl substrate ranged from 15 to 20 with methyl and ethyl iodide. With methyl and ethyl fluorosulfonate, however, the methyl vs. ethyl ratio for the same pyridines ranged from 9.6 to 27.9. The average relative rate for methyl vs. ethyl substrates from a compilation of S_N2 reactions from many sources was 30, with values ranging from 11.1 to 129.[25]

A difference in the enthalpies of the two reaction is also observed, with the ethylation of methylacetylacetonate being about

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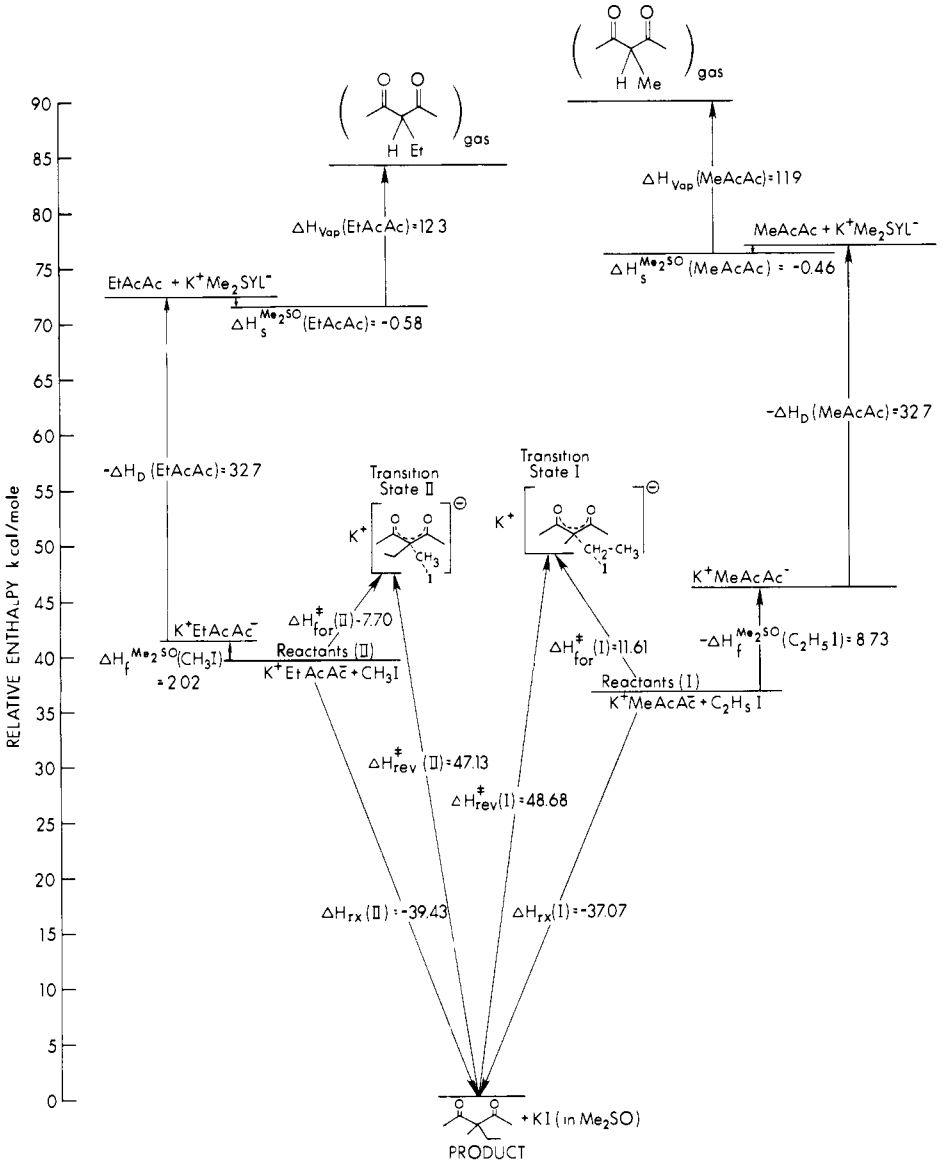

Figure 4. Diagram relating the enthalpies of precursors, reactants, and transition states for the isomeric reactions to the common product ethylmethylacetylacetone.

2.3 kcal/mol less exothermic than the methylation of ethylacetylacetonate. This difference must be due entirely to differences in the energies of the reactants and must lie mainly in differences in the energies of the bonds which are being broken or formed since the combined heats of solvation of the reactants are nearly the same.

Typically the entropy of activation for a displacement reaction is seen to become more negative as the substrate becomes more bulky.[25,26] In this pair of isomeric reactions, however, this is not the case. The methylation of ethylacetylacetonate has a more negative entropy of activation than the ethylation of methylacetylacetonate. In this case, however, the substrate becomes more sterically crowded as the enolate becomes less crowded. The difference in the entropies of activation must include these two compensating factors in addition to other contributions to the entropy of activation, including things such as solvation and (possibly) the enolate conformation.

The enthalpy of activation for the ethylation of methylacetylacetonate (reaction 1) is almost 4 kcal/mol more endothermic than it is for the methylation of ethylacetylacetonate (reaction 2). Much of this difference can be attributed to differences in the methyl iodide vs. ethyl iodide substrate in the transition state. The enthalpy of activation is identical for methylation of either methylacetylacetonate or ethylacetylacetonate while for ethylation, the enthalpy of alkylation for the two enolates differs by less than 2 kcal/mol. Again, the enthalpy of activation may be affected by factors such as the conformation of the enolate and solvation, which are impossible to sort out at this time.

Since the transition states for the reverse reactions must be the same as those for the forward reactions, it is possible to calculate the enthalpy of activation for the reverse reaction from the enthalpy of activation for the forward reaction and the total enthalpy of reaction. This has been included in Table IV. Here the values of the enthalpy analysis is clear since the corresponding rates needed to calculate ΔG_{rev} would be impossibly slow for such an endothermic step and related ΔG_{rev} too endergonic to measure.

As can be seen from Figure 4, the enthalpies of activation for the reverse reactions are quite close, differing by only 1.55 kcal/mol. It is interesting to note that while the displacement of ethylacetylacetonate from the methyl group by iodide would be the enthalpically faster reaction, the enthalpically more stable products would result from displacement of methylacetylacetonate from the ethyl group. The lower enthalpy of activation for the reverse of the methylation of ethylacetylacetonate is probably due to a less sterically hindered approach of iodide than is required to form its isomeric transition state. This is a reaction, however, where assignment of different products to kinetic vs. thermodynamic control of free energy terms will probably never be determined since both reactions are energetically so unfavorable.

It is also possible to make comparisons of any other states which can be related enthalpically to the reactants. In Table IV are presented the data necessary to carry back the analysis all the

way to the enthalpies of formation of the protonated dicarbonyl compounds in the gas phase.

The heat of solution of methyl and ethyl iodides in Me_2SO are listed in Table IV. Since their heats of solution were small, the relative energies of the two systems are still very nearly what they were as reactants. The standard enthalpies of formation of both methyl and ethyl iodide in the liquid phase have been tabulated and are listed in Table IV. The enthalpies of formation of methyl and ethyl iodide differ by 7.26 kcal/mol, a normal value for methyl and ethyl homologues.

After completion of these processes, we have brought the alkylating agents out of solution and to their elemental constituents. In Figure 4 these two processes have been combined and are represented as the heats of formation of the alkylating agents in Me_2SO.

We are now left with solutions of potassium methylacetylacetonate and potassium ethylacetylacetonate in Me_2SO. The next two steps involve protonating the enolates and taking the resulting diketones out of solution to give the neat diketones and solutions of $K^+Me_2SYL^-$. Since the heats of deprotonation ΔH_D have previously been determined,[6] heats of protonation are obtained by simply changing the sign for this value. After this correction, we are left with the relative enthalpies of hypothetical solutions of the undeprotonated β-diketones in $K^+Me_2SYL^-/Me_2SO$ solution. After subtracting the heats of solution of the diketones, which again are very similar, we are left with the neat β-diketones and $K^+Me_2SYL^-/Me_2O$ solutions. Since this solution is the same for both systems, we may neglect the enthalpy of the $K^+Me_2SYL^-$ solutions. Note that experimental determination of values for the heat of deprotonation involved by measuring the enthalpies for dissolving the neat diketones into a $K^+Me_2SYL^-/Me_2SO$ solution, which is exactly the reverse of what we have just accomplished in the previous two steps.

The enthalpies of vaporization and enthalpies of formation for methylacetylacetone or ethylacetylacetone have not been published. However, Irving and da Silva have measured enthalpies of vaporization for six closely related acyclic diketones and found an excellent correlation between these values and the boiling points of the compounds.[29] If one interpolates from the boiling points of methylacetylacetone (bp 170–172 °C)[30] and ethylacetylacetone (bp 177–178 °C), values for their heats of vaporization of 11.9 and 12.3 kcal/mol, respectively, are obtained.

By summing up the columns in Table IV for both systems, the energies of ethylacetylacetone and methylacetylacetone relative to each other are calculated to be 3.13 kcal/mol. Since these are isomeric systems, they contain the same number and types of atoms, and this difference of 3.13 kcal/mol is equal to the difference of the heats of formation of the two β-dicarbonyl compounds in the gas phase. The value obtained is in good agreement with the average difference for heats of formation of methyl-substituted compounds as compared to their ethyl-substituted homologue[28] and serves as a check on the energy bookkeeping.

Conclusions

This paper and its predecessor[6] provide an unusually detailed analysis of the effects of structure, temperature, and ion pairing on the thermodynamic stabilities and kinetic reactivities of some symmetrical enolate anions. Even for these greatly simplified systems, the effect of varying the conditions is complex and often not readily interpreted by us. For example the relative rates of two very similar reactions (ethylation of methylacetylacetonate and ethylacetylacetonate) are inverted above and below room temperature.

An apparently novel strategy (the method of isomeric pathways) for comparing clean reactions which give the same product permits an extensive comparison of many states of the reactants, products, and transition states on a common enthalpy scale.

The reactions of enolates constitute the largest family of processes in synthetic chemistry and have been fair game for ad hoc interpretations of even modest product differences in terms of stereoelectronic theories derived for isolated molecules in the gas paper. The occasionally complex relations of structure and reactivity reported here for carefully simplified systems provide a warning against the arbitrary and uncalled for interpretation of small differences in reactivity for base-promoted reactions of carbonyl compounds.

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Registry No. $Li^+MeAcAc^-$, 70902-15-7; $Na^+MeAcAc^-$, 34916-51-3; $K^+MeAcAc^-$, 72610-66-3; $Li^+EtAcAc^-$, 94904-86-6; $Na^+EtAcAc^-$, 18995-15-8; $K^+EtAcAc^-$, 94904-87-7; LiMDD, 22643-61-4; NaMDD, 17372-26-8; KMDD, 37892-21-0.

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Theory of Stereoselection in Conrotatory Electrocyclic Reactions of Substituted Cyclobutenes

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Abstract: Ab initio transition structures for the conrotatory electrocyclic ring openings of cyclobutene, *trans*-3,4-dimethylcyclobutene, and *trans*-3,4-dihydroxycyclobutene were computed using gradient techniques and the 3-21G basis set. For the disubstituted cyclobutenes, the transition structures leading to the *E,E* butadienes are more stable than those leading to the *Z,Z* isomer, consistent with the observed stereochemistries of related reactions. There is a very large preference for rotation of substituents "outward", which is shown to increase as the donor character of the substituent increases. Conventional steric effects are too small to explain these large effects. A theoretical rationale is provided to explain this effect and to predict the stereoselectivities of related reactions.

Cyclobutenes and butadienes interconvert thermally by a conrotatory process.[1,2] Brauman and Golden estimated that the allowed conrotatory process is 15.0 kcal/mol more favorable than the disrotatory process.[3] Various theoretical treatments predict

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