Society, for partial support of this research. Financial support from the Research Corporation is also gratefully acknowledged.

Registry No.—**1**, 62358-83-2; **2**, 10160-87-9; **3**, 62358-84-3; **4**, 62358-85-4; **5**, 6142-95-6; **6**, 62358-86-5; **7**, 62358-87-6; **8**, 62358-88-7; **9**, 62358-89-8; **10**, 62358-90-1; **11**, 62358-91-2; **12**, 62358-92-3; **13**, 766-82-5; CuI, 7681-65-4.

References and Notes

(1) National Science Foundation Undergraduate Research Participant, 1976.
(2) J. R. Sowa, E. J. Lamby, D. A. Benko, and A. Grodinier, *Org. Prep. Proced. Int.*, **7**, 137 (1975).
(3) J. Villieras, P. Perriot, and J. F. Normant, *Synthesis*, 458 (1975).
(4) E. J. Corey and P. L. Fuchs, *Tetrahedron Lett.*, 3769 (1972).
(5) K. Okuhara, *J. Org. Chem.*, **41**, 1487 (1976).
(6) H. A. Staab, A. Nissen, and J. Ipaktschi, *Angew. Chem., Int. Ed. Engl.*, **7**, 226 (1968); R. H. Mitchell and F. Sondheimer, *Tetrahedron*, **24**, 1397 (1968); *ibid.*, **26**, 2141 (1970).
(7) H. P. Hogan and J. Seehafer, *J. Org. Chem.*, **37**, 4466 (1972); T. B. Patrick, J. M. Disher, and W. J. Probst, *ibid.*, **37**, 4467 (1972); M. S. Newman and L. F. Lee, *ibid.*, **37**, 4468 (1972).
(8) I. Lalezari, A. Schafiee, and M. Yalpani, *Angew. Chem., Int. Ed. Engl.* **9**, 464 (1970).
(9) R. E. Atkinson, F. R. Curtis, D. M. Jones, and J. A. Taylor, *J. Chem. Soc. C*, 2173 (1969).
(10) I. Barrow and A. E. Pedler, *Tetrahedron*, **32**, 1829 (1976).
(11) (a) C. E. Castro and R. D. Stephens, *J. Org. Chem.*, **28**, 2163 (1963); (b) R. D. Stephens and C. E. Castro, *ibid.*, **28**, 3313 (1963); (c) D. C. Owsley and C. E. Castro, *Org. Synth.*, **52**, 128 (1972); (d) C. E. Castro, R. Havlin, V. K. Honwad, A. Malte, and S. Mojé, *J. Am. Chem. Soc.*, **91**, 6464 (1969); (e) C. E. Castro, E. J. Gaughan, and D. C. Owsley, *J. Org. Chem.*, **31**, 4071 (1966).
(12) H. O. House, D. G. Koepsell, and W. J. Campbell, *J. Org. Chem.*, **37**, 1003 (1972).
(13) J. S. Kiely, L. L. Nelson, and P. Boudjouk, *J. Org. Chem.*, **42**, 1480 (1977).
(14) M. W. Logue and G. L. Moore, *J. Org. Chem.*, **40**, 131 (1975).
(15) L. Brandsma, "Preparative Acetylenic Chemistry", Elsevier, Amsterdam, 1971, pp 118–119.
(16) E. Schmitz and I. Eichborn, "The Chemistry of the Ether Linkage", S. Patai, Ed., Interscience, New York, N.Y., 1967, pp 332–334.
(17) D. R. M. Walton, "Protective Groups in Organic Chemistry", J. F. W. McOwie, Ed., Plenum Press, London, 1973, p 7.
(18) G. Belil, J. Castella, J. Castells, R. Mestres, J. Pascual, and F. Serratosa, *An. R. Soc. Esp. Fis. Quim., Ser. B*, **57**, 617 (1961).
(19) R. Mantione, M. L. Martin, G. J. Martin, and H. Normant, *Bull. Soc. Chim. Fr.*, 2912 (1967).
(20) A. D. Allen and C. D. Cook, *Can. J. Chem.*, **41**, 1084 (1963).
(21) C. D. Cook and S. S. Danyluk, *Tetrahedron*, **19**, 177 (1963).

Chemistry of Enolates. 8. Kinetics and Mechanism of Alkylation of Lithium Enolates[1]

J. A. Miller and H. D. Zook*

Department of Chemistry, The Pennsylvania State University, University Park, Pennsylvania 16802

Received October 15, 1976

Alkylations of sodium and potassium ketone enolates exhibit second-order kinetics in ethereal solvents.[2] Although rates in Me_2SO are 10^4–10^6 times faster than in ethereal solvents and O/C product ratios are independent of metal cation for a given enolate and alkyl halide, the solvated cation is important in the transition state as shown by a pronounced effect on reaction rate.[3] In this paper, we describe similar second-order kinetics for the alkylation of lithium enolates by most halides but have observed surprisingly different behavior for alkylations by alkyl chlorides.

Alkylations of lithium enolates in Me_2SO by allyl chloride, alkyl bromides, and alkyl iodides exhibit good second-order kinetics over several half-lives regardless of whether rates are determined in excess halide or at moderate halide concentration (Figure 1). The usual order of reactivity for halides in bimolecular substitution (RI > RBr > $CH_2{=}CHCH_2Cl$) is shown in Table I.

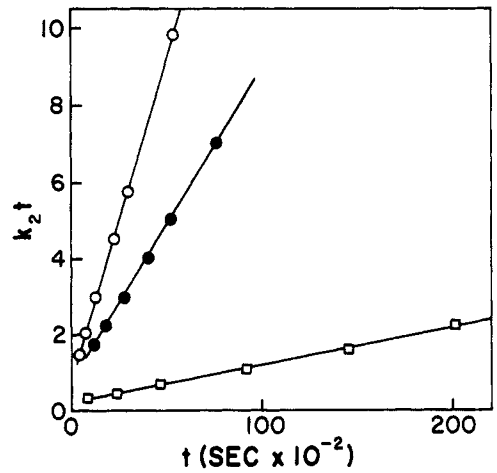

Figure 1. Alkylation of lithiobutyrophenone by *n*-propyl bromide (○), *n*-pentyl bromide (●), and allyl chloride (□).

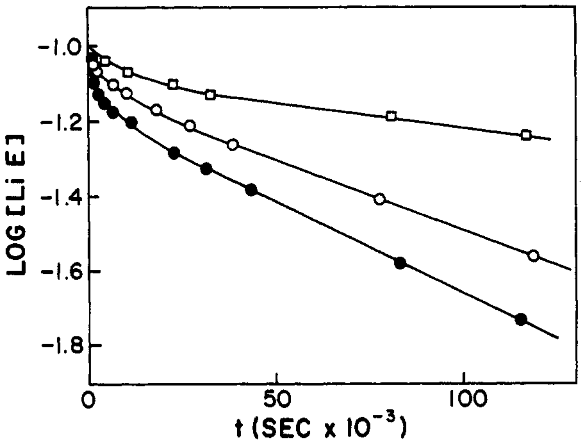

Figure 2. Alkylation of lithiobutyrophenone by *n*-pentyl chloride in Me_2SO (●); 0.074 M (○) and 0.66 M (□) LiCl added.

Table I. Second-Order Alkylations of Lithiobutyrophenone

Halide	$[RX]_0$, M	$[LiE]_0$, M	k_2 at 30 °C, $s^{-1}\,M^{-1} \times 10^4$
n-C_3H_7Br	0.26	0.14	15.3
	0.50	0.14	14.0
n-$C_5H_{11}Br$	0.16	0.13	7.4
	0.29	0.13	7.7
	1.18	0.11	6.5
	1.85	0.09	6.0
	0.22	0.13	63.5[a]
	0.34	0.13	64.0[a]
n-$C_5H_{11}I$	0.26	0.13	88.5
	0.34	0.13	85.0
C_2H_5I	0.26	0.14	200
$CH_2{=}CHCH_2Cl$	0.44	0.13	1.2
	0.87	0.13	1.0

[a] At 50 °C.

For alkyl chlorides, a very rapid rate over the first 20–30% of the reaction is followed by a much slower rate for the remainder of the reaction. This second phase is first order in enolate but independent of the concentration of the alkyl chloride (Figure 2). Second-order plots show considerable curvature, whereas alkylations in which the ratio of initial concentrations $[RCl]_0/[E]_0$ is as low as 2.3 obey the first-order

Table II. First-Order Alkylations of Lithium Enolates

Registry no.	$C_6H_5C(O^-)=CRR'$ R	$C_6H_5C(O^-)=CRR'$ R'	RCl R	$[RCl]_0$, M	$[LiE]_0$, M	k_1 at 30 °C, $s^{-1} \times 10^5$
	H	C_2H_5	n-C_3H_7	1.50	0.10	1.5
			n-C_5H_{11}	0.30	0.13	1.0
				0.73	0.11	1.2
				1.04	0.10	1.2
				1.07	0.11	1.2
				1.06[a]	0.10	0.9
				0.68[b]	0.10	0.4
				0.64	0.14	3.8[c]
				1.42	0.12	3.9[c]
				0.60	0.13	14.8[d]
				1.30	0.12	15.0[d]
			i-C_4H_9	0.61	0.10	1.3
				1.32	0.08	1.2
				1.51	0.09	1.2
62416-34-6	CH_3	CH_3	n-C_5H_{11}	1.36	0.09	2.3
			i-C_4H_9	1.30	0.08	2.1
62416-35-7	C_6H_5	C_6H_5	n-C_3H_7	1.62	0.10	5.5

[a] $[LiCl]_0$ = 0.074 M. [b] $[LiCl]_0$ = 0.66 M. [c] At 40 °C. [d] At 50 °C.

law, and a threefold increase in alkyl halide concentration has no effect on the rate constant (Table II).

The initial, rapid reaction of lithiobutyrophenone and n-pentyl chloride was investigated in detail. Preferential O- or C-alkylation during this phase was ruled out by measuring O/C product ratios on each titrated aliquot. The mean O/C ratio for the first third of the reaction was 1.33 and for the second two-thirds, 1.30. When lithium chloride, a reaction product, was added in varying amounts to the enolate solutions prior to alkylation, the initial, rapid reaction was suppressed, and the subsequent reaction, although still independent of alkyl chloride concentration, was appreciably slowed (Figure 2).

These results suggest that a reactive enolate such as the free ion, ion pair, or its aggregate is converted to a less active species by complexing with lithium halide; for example

$$\text{LiX(LiE)}_n \underset{-\text{LiX},\, k_{-1}}{\overset{+\text{LiX},\, k_1}{\rightleftharpoons}} \text{Li}^+\text{E}^- \xrightarrow[k_2]{\text{RX}} \text{RE} + \text{LiX}$$

A steady-state treatment of Li^+E^- leads to first-order alkylation kinetics when $k_2[RX] \gg k_{-1}[LiX(LiE)_n]$ and the dissociation of the complex is rate determining. The second-order kinetics observed with more reactive alkyl halides requires that $k_{-1}[LiX(LiE)_n] \gg k_2[RX]$ or that the alkyl halide is sufficiently reactive to directly alkylate the complex. The former explanation is in line with the observation that LiBr and LiI are not as effective as LiCl in decreasing the reactivity of phenyllithium as a polymerizing agent,[5] while the latter explanation best accounts for the results with allyl chloride where the complex is identical with that from alkylation by alkyl chlorides.

From the ratio of lithium chloride formed in the initial alkylation phase to the lithium enolate remaining, a stoichiometric $LiCl(LiE)_3$ complex is indicated. Such a complex may resemble the tetrameric alkyllithiums, where four lithium atoms occupy corners of a tetrahedron with the anions on the faces.[7] Lithium halide complexes have been postulated to account for decreased anionic activity of phenyllithium[5] and lithium piperidide,[4] and stoichiometric LiRLiX complexes have been suggested to explain the stability of the relatively unreactive solid product obtained by the action of alkyllithium compounds on alkyl halides.[6]

Activation parameters were determined for both the first- and second-order substitutions. A plot of log k vs. $1/T$ for the alkylation by n-pentyl chloride was linear and gave $\Delta H^{\ddagger}$ = 26.4 kcal/mol and $\Delta S^{\ddagger}$ = +6.0 cal/mol K. Dissociation of a complex in the rate-determining step would be expected to have a positive activation entropy, although a higher positive value was anticipated. Perhaps transition-state solvation by the Me_2SO with its accompanying negative entropy change becomes a leveling factor in this solvent. For the second-order alkylation by n-pentyl bromide, $\Delta H^{\ddagger}$ = 20.4 kcal/mol and $\Delta S^{\ddagger}$ = −6.4 cal/mol K. The latter result may be compared with $\Delta S^{\ddagger}$ values ranging from −13 to −40 cal/mol K for alkylations of sodium enolates of alkyl phenyl ketones in ethereal solvents[8] and values of −8 to −12 cal/mol K for hydroxide displacement of bromide from n-alkyl bromides in aqueous Me_2SO.[9]

Experimental Section

Kinetic measurements were made at 30.00 ± 0.05 °C unless otherwise indicated. Vacuum-line techniques for preparation, storage, and transfer of methylsulfinyl carbanion and enolate solutions, as well as analytical procedures for kinetic and product studies, have been previously described.[3] Disappearance of alkylatable enolate species was followed by quenching 12.4-mL aliquots from a pneumatic sampling buret and titrating the resulting hydroxide ion to a phenolphthalein end point. For product analysis, infinity samples were quenched in 0.1 M sodium hydroxide solution and extracted with carbon tetrachloride. O-Alkyl products were detected in the infrared (Beckman IR-8) by broad peaks near 1063 cm^{-1}, and C-alkyl products in the carbonyl stretching region near 1675 cm^{-1}. Enol ethers were confirmed by a repeat analysis on a second sample of carbon tetrachloride extract after shaking with dilute acid. Absorption at 1063 cm^{-1} disappeared and that in the carbonyl region increased. Quantitative analyses of the extracts of all 12 aliquots from an alkylation by n-pentyl chloride were made by GLC at 170 °C on a 5 ft × 0.3 mm column packed with GE SF-96 phenylsilicon on 100–140 mesh Gas Chrom Z. The O/C ratio was essentially constant at 1.3, a value in agreement with the infinity samples from all alkylations of lithiobutyrophenone and n-pentyl chloride. No products other than enol ether, alkylated ketone, and original ketone could be detected.

Registry No.—Lithiobutyrophenone, 62416-33-5; n-C_3H_7Br, 106-94-5; n-$C_5H_{11}Br$, 110-53-2; n-$C_5H_{11}I$, 628-17-1; C_2H_5I, 75-03-6; $CH_2{=}CHCH_2Cl$, 107-05-1; n-C_3H_7Cl, 540-54-5; n-$C_5H_{11}Cl$, 543-59-9; i-C_4H_9Cl, 14753-05-0.

References and Notes

(1) A grant from the National Science Foundation in support of this research is gratefully acknowledged.

(2) H. D. Zook, T. J. Russo, E. F. Ferrand, and D. S. Stotz, *J. Org. Chem.*, **33**, 2222 (1968); H. D. Zook and T. J. Russo, *J. Am. Chem. Soc.*, **82**, 1258 (1960); H. D. Zook and W. L. Gumby, *ibid.*, **82**, 1386 (1960).

(3) H. D. Zook and J. A. Miller, *J. Org. Chem.*, **36**, 1112 (1971).
(4) R. Huisgen and W. Mack, *Chem. Ber.*, **93**, 332 (1960).
(5) R. Waack and M. A. Doran, *Chem. Ind.* (*London*), 496 (1964).
(6) W. Glaze and R. West, *J. Am. Chem. Soc.*, **82**, 4437 (1960).
(7) P. D. Bartlett, C. V. Goebel, and W. P. Weber, *J. Am. Chem. Soc.*, **91**, 7425 (1969).
(8) Unpublished work of D. S. Stotz and W. L. Rellahan, The Pennsylvania State University.
(9) A. Kirrmann and J. Delpuech, *C. R. Acad. Sci.*, **257**, 127 (1963).

Decarbalkoxylation of Isohexylmalonates

J. Hodge Markgraf,* Mark S. Ibsen, John B. Kinney,
Jerry W. Kuper, Jonathan B. Lurie, David R. Marrs,
Cheryl A. McCarthy, Judith M. Pile, and Timothy J. Pritchard

Department of Chemistry, Williams College,
Williamstown, Massachusetts 01267

Received January 12, 1977

A decade ago Krapcho reported that a geminal diester could be converted to the corresponding monoester by a novel one-step method.[1] The original procedure of sodium cyanide and dimethyl sulfoxide (Me_2SO) was subsequently extended to include other salts in wet Me_2SO or wet dimethylformamide (DMF),[2] and it was further discovered that even the salt was unnecessary in the case of phenylmalonates.[3,4] While the pioneering work of Krapcho and co-workers served to define the structural range of diesters,[1–3] there has been no systematic study of the other reagents. In fact, a variety of conditions has been reported: sodium cyanide in Me_2SO,[5] lithium iodide and sodium cyanide in DMF,[6] and lithium chloride or sodium iodide[7a] or tetramethylammonium acetate[7b] in hexamethylphosphorictriamide. Recently, cyclic secondary or tertiary amines in hydrocarbon solvents have also been utilized for decarbalkoxylations.[8]

In connection with studies related to the synthesis of the gypsy moth sex pheromone, we required 1-bromo-6-methylheptane.[9,10] As an alternative to the published procedures, we have explored a route which involved the following reaction.

$$\underset{\textbf{1}}{Me_2CH(CH_2)_3CH(CO_2R)_2} \rightarrow \underset{\textbf{2}}{Me_2CH(CH_2)_4CO_2R}$$

a, R = Me; **b**, R = Et

The present work was undertaken to define the scope of this decarbalkoxylation step. Esters **1a** and **1b** were obtained by malonic ester syntheses. Hydrolysis, decarboxylation, and esterification gave authentic samples of **2a** and **2b** for calibration purposes. A standardized procedure for decarbalkoxylation was utilized to assess the effects of different salts, concentration, reaction times, and ester groups. The analytical procedure involved GLC determination of **1** and **2**; the isolated yield of crude product was 65–95%. The results are shown in Tables I and II. It is clear that an added salt is necessary; best results were obtained with 1 equiv. Previous work established that wet Me_2SO was necessary.[3] In the present study, 2 equiv of water proved satisfactory. The more facile reaction of methyl esters compared to the corresponding ethyl esters was also observed by Krapcho, who has considered the mechanistic aspects.[11] Although the present study was not designed to elucidate reaction pathways, our results do establish that acid catalysis generated in situ is not operative.[12]

Table I. Decarbalkoxylation of 1a by Various Salts in Me_2SO

Salt	Salt, mmol	Water, mmol	Reflux time, h	**2a**, %[a]
LiCl	4	8	1	>99
	4	8	0.5	99
NaCl	4	8	1	99
	4	4	1	99
KCl	4	8	1	98
$CaCl_2 \cdot 2H_2O$	4	0	1	>99
	4	0	0.5	99
NaBr	4	8	1	96
$LiI \cdot H_2O$	4	0	1	>99
NaI	4	8	1	97
NaCN	4	8	1	>99
	4	8	0.5	>99
	4	4	1	>99
	4	0	1	>99
	2	8	1	95
$Na_2CO_3 \cdot H_2O$	4	0	1	96
$Na_3PO_4 \cdot 12H_2O$	0.8	0	1	98
None		8	1	10
None		0	1	11

[a] Purity was determined by GLC and is based on **1a** and **2a**; no additional substances were detected. Values are the average (±1%) of duplicate runs.

Table II. Decarbalkoxylation of 1b by Various Salts in Me_2SO

Salt	Salt, mmol	Water, mmol	Reflux time, h	**2b**, %[a]
LiCl	4	8	2	>99
	4	8	1	88
NaCl	4	8	2	99
	4	8	1	81
KCl	4	8	2	>99
	4	8	1	83
$CaCl_2 \cdot 2H_2O$	4	0	2	98
	4	0	1	91
NaCN	4	8	2	>99
	4	8	1	99
	4	8	0.5	85
	4	4	1	95
	4	0	1	75
	2	8	1	93
$Na_3PO_4 \cdot 12H_2O$	0.8	0	2	>99
	0.8	0	1	90
None		8	1	2
		0	1	5

[a] Purity was determined by GLC and is based on **1b** and **2b**; no additional substances were detected. Values are the average (±1%) of duplicate runs.

Experimental Section

Melting points and boiling points are uncorrected. Infrared spectra were recorded on a Perkin-Elmer 237B spectrophotometer and calibrated by a polystyrene film. Gas–liquid chromatography (GLC) was carried out on a Varian 1400 chromatograph with a 12 ft × 0.125 in. column of 10% Dow-Corning 710 on Chromosorb W, the helium flow rate was 30 mL/min, and the column was operated at 210 °C. Elemental analyses were obtained from the Analytical Services Laboratory, University of California, Berkeley.

Materials. Dimethyl sulfoxide (Me_2SO; Fisher Certified), 1-bromo-4-methylpentane (Chemical Samples Co.), and all salts (reagent grade) were used without further purification.

Dialkyl Isohexylmalonates (1). The reaction of 1-bromo-4-methylpentane with dimethyl sodiomalonate by the method of Adams and Kamm[13] gave 69% of **1a**: bp 85–87 °C (2 Torr); IR (neat) 1757 and 1736 cm^{-1}.