On the Mechanism of the Alkylative Decarboxylation of *N*-Carbalkoxypyrazoles

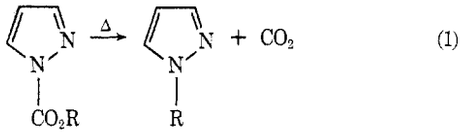
Joseph J. Wilczynski and H. W. Johnson, Jr.*

Department of Chemistry, University of California, Riverside, California 92502

Received August 20, 1973

The alkylative decarboxylation of *N*-carbalkoxypyrazoles reported by van Auwers has been shown to require a polar aprotic solvent and to be subject to catalysis by nucleophiles, *e.g.*, halide ions. The halide ion catalyzed reaction is first order in ester and in halide ion in DMSO solvent. The relative rates of reaction of the methyl, ethyl, and isopropyl esters of 4-bromo-3,5-dimethyl-1-pyrazolecarboxylic acid are 17.2, 1, and 0.0401, respectively, in DMSO at 99.85° with chloride ion catalyst. The relative rates of reaction for Cl^--, Br^--, and I^--catalyzed alkylative decarboxylations of 4-bromo-1-carbomethoxy-3,5-dimethylpyrazole are 5.12, 3.02, and 1, respectively, in DMSO. The same mixture of 30% 1,3-dimethyl-5-phenylpyrazole and 55% 1,5-dimethyl-3-phenylpyrazole is obtained from the decarboxylation of the isomeric 1-carbomethoxy-3-methyl-5-phenylpyrazole and 1-carbomethoxy-5-methyl-3-phenylpyrazole. The mechanism of the halide ion catalyzed reaction appears to involve rate-determining nucleophilic attack of halide ion on the alkoxy α-carbon atom to yield alkyl halide, pyrazolyl anion, and carbon dioxide. A rapidly decarboxylating *N*-pyrazolecarboxylate anion may intervene. Attack of pyrazolyl anion on the alkyl halide (or, more slowly, on the parent ester) leads to *N*-alkylpyrazole and halide ion (or *N*-alkylpyrazole, pyrazolyl anion, and carbon dioxide, if attack occurs on the ester). Methyl *p*-nitrophenylcarbonate and dimethyl malonate were shown to yield *p*-nitroanisole and methyl acetate, respectively, upon heating with sodium iodide in similar reactions.

This study was undertaken to determine the pathway by which carbon dioxide and *N*-alkylpyrazoles are generated thermally from *N*-carbalkoxypyrazoles (eq 1), a reaction originally described by von Auwers.[1] Although decarboxylation is a common reaction of acids, esters are not normally considered to undergo this reaction.[2] A few reactions of esters occur in which the major products of reaction result from alkylative decarboxylation.[3-13]



(1)

A variety of mechanisms were available *a priori*. Among others, internal nucleophilic attack *via* four- or five-center cyclic transition states, external attack by a nucleophile (or radical) at the carbonyl carbon atom or the α-carbon atom of the alkoxyl group, and electrophilic attack at one of the ring nitrogen atoms were possible. The reaction has been described only in the melt, and preliminary studies were necessary to define the gross character of the reaction.

The volume of carbon dioxide produced was used as the initial probe. The ester, the solvent, and any additional reagent were added to a Pyrex reaction vessel equipped with a mercury-filled gas burette in a constant temperature bath; rates of carbon dioxide evolution were reproducible to ±3%. The esters used were 1-carbomethoxy-3,5-dimethylpyrazole (**1**) and 4-bromo-1-carbomethoxy-3,5-dimethylpyrazole (**2**).

In both triglyme and dibutyl phthalate (DBP) at 195° 50% of the theoretical yield of carbon dioxide was evolved from **1** after 7 hr, while in mineral oil 6% of the CO_2 was formed after 23 hr. At 110°, reaction in dimethyl sulfoxide (DMSO) yielded 50% of carbon dioxide after 22 hr from **2** while in DBP no discernable reaction occurred. The solvent order in facilitating the reaction was DMSO ≫ DBP ≈ triglyme ≫ mineral oil. A polar mechanism seems likely.

Benzoyl peroxide, benzoquinone, and oxygen had no effect on the rate of decomposition of **2** in DBP at 195°. It is considered unlikely that radical intermediates are involved in this reaction.

Results obtained from the decarboxylation of **2** in the presence of other reagents are collected in Table I. The ester concentration was 0.6–0.7 *m* and the concentration of added reagent was 0.06–0.07 *m*. The time required for production of 50% of the theoretical yield of carbon dioxide in DBP at 195° with no added reagents was 900 min. Benzylamine gave a moderate increase in rate while tri-*n*-butylamine, iodide ion, and chloride ion effected large increases in the rate. The uncatalyzed decarboxylation of **2** in DMSO at 110° yielded 50% CO_2 after 22 hr, while addition of iodide ion (10% of the ester concentration) reduced this time by a factor of 17 and chloride ion reduced the "half-life" by a factor of 90 under the same conditions.

Decarboxylation of **2** in DBP at 195° had a "half-life" of 900 min; however, this reaction time included a 225-min induction period during which no carbon dioxide was evolved. Added nucleophiles eliminated the induction period. These data and the solvent dependence suggest a nucleophilic ionic mechanism. The induction period presumably reflects the time required to produce a nucleophile by secondary decomposition of the ester.

Having ascertained the gross character of the reaction, a more detailed study of the kinetics of the halide ion catalyzed reaction was undertaken. Rates of alkylative decarboxylation of esters of 4-bromo-3,5-dimethylpyrazole-1-carboxylic acid were determined by ultraviolet spectroscopy. The solution of catalyst ($1–5.5 \times 10^{-2}$ *M*) in DMSO was equilibrated in a constant temperature bath. Then 50–100 μl of a 0.2 *M* ester–DMSO solution was added to the catalyst solution through a stopcock *via* syringe. Samples were removed from the reaction vessel by syringe through the stopcock at intervals, and the absorbance of the solution was measured. All glassware and reagents were dried, since water and other protic species change the reaction products yielding quantities of unalkylated parent pyrazole. Reactions were usually run under pseudo-first-order conditions with 50–100-fold excess catalyst. In two experiments the volume of carbon dioxide produced was measured as described earlier. In these last two reactions, the molar catalyst to ester concentration ratio was 1:10, and both reactions yielded good pseudo-first-order kinetics to 60% reaction. The reaction studied by uv absorption yielded good pseudo-first-order kinetics to 70–80% completion. In reactions followed by carbon

Table I
Effect of Reagents on the Alkylative Decarboxylation of 4-Bromo-1-carbomethoxy-3,5-dimethylpyrazole[a]

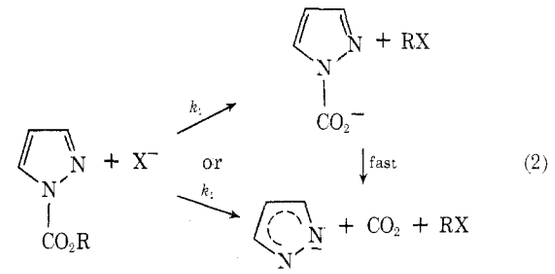
Reagent[b]	Solvent[c]	Temp, °C	$t_{1/2}$, min[d]
Tri-*n*-butylamine	DBP	195	11.5
I^- [e]	DBP	195	1
I^- [e]	DMSO	110	75
Cl^- [e]	DMSO	110	14
None	DMSO	110	1320
None	DBP	195	900

[a] Initial concentration, 0.6–0.7 *m*. [b] Initial concentration of added reagents, 0.06–0.07 *m*. [c] DBP, di-*n*-butyl phthalate; DMSO, dimethyl sulfoxide. [d] Time to yield 50% of theoretical carbon dioxide. [e] Tetra-*n*-butylammonium salts.

dioxide evolution, essentially quantitative recovery of unchanged halide was made after 80% reaction. The good pseudo-first-order plots obtained indicate that the assumption of constant halide ion concentration during these reactions is justified.

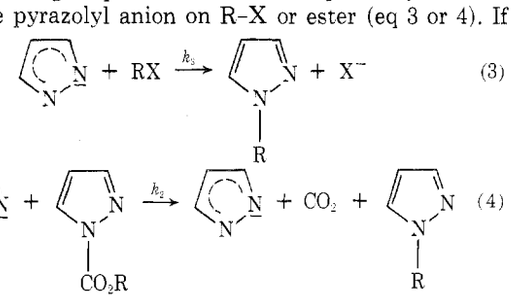
Table II contains data derived from the rate constants calculated for **2** at varying concentrations of sodium chloride. The data indicate that the reaction is first order in halide ion. Table III presents data with differing halide catalysts which suggest nucleophilic attack at the alkoxyl α-carbon atom. The ratio of the second-order rate constants k_{X^-}/k_{I^-}, was 5.12, 3.02, and 1.00 for the ions Cl^-, Br^-, and I^-, respectively, paralleling the relative nucleophilicities found in the displacement of tosylate from *n*-propyl tosylate in DMSO: Cl^-, 5.18; Br^-, 3.19; and I^-, 1.00.[14] The rate constant for the iodide-catalyzed reaction had to be determined by following the evolution of carbon dioxide rather than by uv because of the strong uv absorption of iodide ion, and molal concentrations were used. Data at 111 and 99.85° were combined to obtain these ratios; the assumption that k_{X^-}/k_{I^-} does not vary over the 11° range is implicit in this argument.

Changes in the structure of the alkoxyl group should have less effect on the rate of nucleophilic attack at the carbonyl carbon atom than on the rate of attack at the α-carbon atom of the alkoxyl function. In water or in 70% acetone–water, hydroxide ion attack on a series of alkyl acetates shows a very small change in the rate of reaction with changes in the alkoxy group. The relative rates of reaction of the series of acetates, methyl, ethyl, isopropyl, and benzyl, are all within a factor of 8 of each other in water.[15] Relative values are found in Table IV. In saponifications of the methyl and ethyl esters of aromatic acids in DMSO, the methyl ester reacted only 2.5 times faster than the ethyl ester.[16] Table IV also contains Streitwieser's values for the average relative rates of substitution (SN2) for compounds with changes in groups directly bonded to the reaction site. The ratio of rates of displacement from methyl, ethyl, and isopropyl halides was found to be 30:1:0.025.[17] The second-order rate constants for the reaction of the methyl, ethyl, isopropyl, benzyl, and (*R*)-(−)-α-methylbenzyl esters of 4-bromo-3,5-dimethyl-1-pyrazolecarboxylic acid with chloride ion in DMSO at 99.85° are given in Table IV. Comparison of the data in Table IV again suggests chloride ion attack at the α-carbon atom of the alkoxyl group (eq 2) rather than attack at the carbonyl carbon atom. The retardation of attack of chloride ion by successive methyl substitution at the α-carbon atom is of the order of magnitude seen in typical SN2 displacement reactions and larger than that of nucleophilic attack at the carbonyl carbon. Similar attack has been proposed by Warren and Williams[18] for the iodide-catalyzed decarboxylation of $(C_6H_5)_2POCO_2CH_2C_6H_5$.



(2)

The rate-determining step in the reaction is most likely attack of the nucleophile at the α-carbon atom of the alkoxyl group, yielding pyrazolyl anion, carbon dioxide, and alkylated nucleophile either in a concerted manner or *via* an intermediate *N*-pyrazolecarboxylate anion (eq 2). It is not possible to differentiate positively between the two modes of decarboxylation with the data at hand. The final product forming step in the reaction is probably SN2 attack of the pyrazolyl anion on R–X or ester (eq 3 or 4). If



(3) (4)

reaction proceeds through a *N*-pyrazolecarboxylate anion,[19] decarboxylation of this intermediate may potentially occur during or after a reaction with RX. In either of these schemes, an ester of an unsymmetrically substituted *N*-pyrazolecarboxylic acid would yield one *N*-alkylpyrazole (eq 5) while, if reaction of RX occurs with a pyrazolyl anion, two *N*-alkylpyrazoles will be formed (eq 6).

The iodide ion catalyzed decarboxylations of 1-carbomethoxy-3-methyl-5-phenylpyrazole (**3**) and 1-carbomethoxy-5-methyl-3-phenylpyrazole (**4**), in DMSO at 111°, gave two *N*-alkyl products in the same ratio: 30% 1,3-dimethyl-5-phenylpyrazole (**5**) and 55% 1,5-dimethyl-3-phenylpyrazole (**6**) from both **3** and **4**. The structures of compounds **3**–**6** were determined by von Auwers and Stuhlmann[1b] and the nuclear magnetic resonance (nmr)

Table II
Effect of Chloride Ion on the Rate of Decarboxylation of 4-Bromo-1-carbomethoxy-3,5-dimethylpyrazole in DMSO at 100°[a]

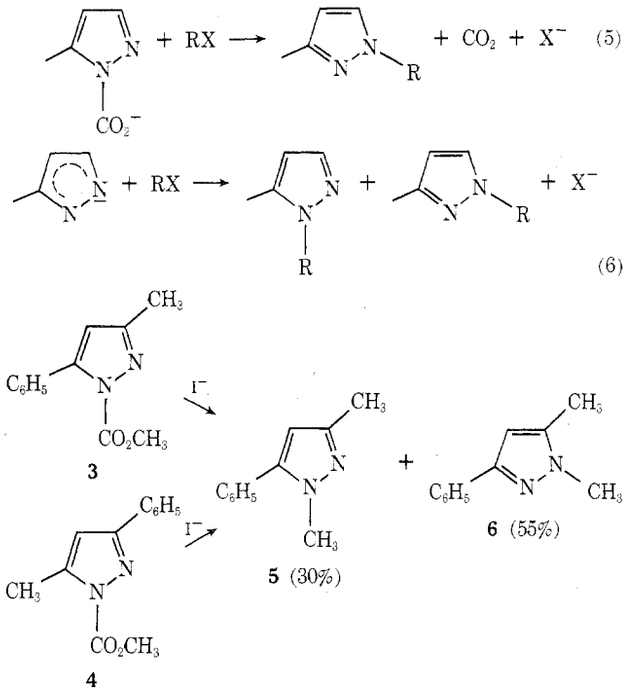
[NaCl], *M*	[$NaBF_4$],[b] *M*	k[c]	$k_1 = k/[Cl^-]$
5.42×10^{-2}	0	2.06×10^{-4} sec^{-1}	3.80×10^{-3} M^{-1} sec^{-1}
4.06×10^{-2}	1.355×10^{-2}	1.43×10^{-4} sec^{-1}	3.51×10^{-3} M^{-1} sec^{-1}
2.710×10^{-2}	2.710×10^{-2}	1.01×10^{-4} sec^{-1}	3.73×10^{-3} M^{-1} sec^{-1}
			Av 3.68×10^{-3} M^{-1} sec^{-1}
0	5.42×10^{-2}	0[d]	

[a] Temperature, 99.85 ± 0.04°; initial ester concentrations, 5–10 $\times 10^{-4}$ *M*. [b] $NaBF_4$ was used to keep the ionic strength constant. [c] Observed pseudo-first-order rate constant. [d] No reaction was observed after 4 hr.

Table III
Second-Order Rate Constants for the Decarboxylation of 4-Bromo-1-carbomethoxy-3,5-dimethylpyrazole in DMSO Catalyzed by Halide Ions

Halide	Temp, °C	Method of analysis	k_1[a]
Cl^-	99.85	Loss of uv absorption	3.80×10^{-3} M^{-1} sec^{-1}
Br^-	99.85	Loss of uv absorption	2.24×10^{-3} M^{-1} sec^{-1}
Cl^-	111	Evolution of CO_2	1.28×10^{-2} m^{-1} sec^{-1}
I^-	111	Evolution of CO_2	2.50×10^{-3} m^{-1} sec^{-1}

[a] Observed pseudo-first-order rate constant divided by halide ion concentration.



spectra of these compounds reconfirm their assignments (see Experimental Section, Table VII). The esters and products were shown to be stable to isomerization under the reaction conditions.[20,21]

The formation of **5** and **6** in the same ratio from both of the esters **3** and **4** suggests strongly that an intermediate common to both esters is produced during the reaction. Further, since ester **3** decarboxylates 3.2 times faster than does ester **4**, the common intermediate must be formed after or during the rate-determining step. The pyrazolyl anion is probably this intermediate. These results also exclude intramolecular reactions *via* cyclic transition states, mechanisms largely excluded by kinetic studies as well.

The final N-alkylation step may occur by reaction of the pyrazolyl anion with RX (eq 3) or with ester (eq 4). The relative importance of these reactions in the mechanisms may be estimated in the chloride ion catalyzed reaction. The pseudo-first-order rate constant for the chloride ion catalyzed alkylative decarboxylation of **2** was found to be 2.06×10^{-4} sec^{-1} at 99.85° in DMSO at 5.42×10^{-2} M chloride ion concentration. The pseudo-first-order rate constant for disappearance of ester is equal to k_1[chloride] + k_2[pyrazolyl anion] if eq 4 is also an important step in the mechanism. If step 4 is important, then the term k_2[pyrazolyl anion] must contribute an appreciable fraction to the pseudo-first-order rate constant. The value of k_2 may be determined from the rate of reaction of 4-bromo-1-carbomethoxy-3,5-dimethylpyrazole with independently prepared 4-bromo-3,5-dimethylpyrazolyl anion (as the sodium salt). This pseudo-first-order rate constant (k_2[pyrazolyl anion]) was 2.55×10^{-4} sec^{-1} at 99.85° in DMSO at a pyrazolyl anion concentration of 4.83×10^{-3} M. The value of k_2 derived from this rate constant is 5.29×10^{-2} l./(mol sec), 14 times greater than the value of k_1 calculated in Table II. To determine the contribution of k_2[pyrazolyl anion] to the pseudo-first-order rate constant for the chloride ion catalyzed reaction, an estimate of the pyrazolyl anion concentration must be made. The quantity of the pyrazolyl anion in solution cannot exceed the amount of the ester which has reacted. Since the kinetics were determined at a maximum ester concentration of 10^{-3} M, the concentration of the pyrazolyl anion cannot exceed 10^{-3} M in these solutions. Even at this concentration, the calculated value of k_2[pyrazolyl anion] is only 5.29×10^{-5} sec^{-1} or 25.7% of the observed pseudo-first-order rate constant of 2.06×10^{-4} sec^{-1}. At more reasonable lower concentrations of the intermediate anion, the contribution of k_2[pyrazolyl anion] to the total reaction rate should be negligible. The rate of reaction of methyl chloride with the pyrazolyl anion in DMSO was too fast to measure with conventional methods even at room temperature. The mechanism of the halide-catalyzed alkylative decarboxylation of *N*-carbalkoxypyrazoles therefore involves principally initial attack by the halide ion on the alkoxyl α-carbon atom of the ester with formation of an alkyl halide, carbon dioxide, and pyrazolyl anion. The attack of the pyrazolyl anion on the alkyl halide with formation of *N*-alkylpyrazole and regeneration of the halide ion completes the sequence.

Though the reaction of the pyrazolyl anion with the ester was unimportant in the halide ion catalyzed decarboxylation of *N*-carbalkoxypyrazoles, this reaction is thought to be the major pathway for the production of *N*-alkylpyrazole and carbon dioxide from the esters in the uncatalyzed reaction. The rate of decarboxylation of the methyl ester of 4-bromo-3,5-dimethyl-1-pyrazolecarboxylic acid (**2**) is very slow in DMSO, yielding only 50% of the theoretical amount of carbon dioxide after 22 hr. Assuming eq 4 to be the rate-determining step, the concentration of the pyrazolyl anion necessary to achieve this rate is 5×10^{-5} m or 0.008% of the initial ester concentration. It seems reasonable that this concentration of anion may be produced through a secondary decomposition of the ester during the induction period mentioned previously. Thus, the uncatalyzed reaction may involve a chain mechanism in which the pyrazolyl anion attacks the ester, forming *N*-alkylpyrazole, carbon dioxide, and a second pyrazolyl anion.

Table IV
Effect of Ester Structure on Rates of Nucleophilic Attack

Ester	k_R[a]	k_R/k_{Et}[b]	k_R/k_{Et}[c]	k_R/k_{Et}[d]
Methyl	3.80×10^{-3}	17.2	30	2.32
Ethyl	2.21×10^{-4}	1	1	1
Isopropyl	8.86×10^{-6} [e]	0.0401	0.025	0.151
Benzyl	2.94×10^{-3}	13.3	120	
α-Methylbenzyl[f]	1.28×10^{-3}	5.79		

[a] Rate of chloride ion catalyzed decarboxylation of 4-bromo-3,5-dimethyl-1-pyrazolecarboxylic acid ester, DMSO, 99.85°, M^{-1} sec^{-1}, this work. [b] Rate ratio for pyrazole ester decarboxylation relative to ethyl ester, this work. [c] Streitwieser's average values for displacement for SN2 displacements from alkyl halides, ref 17. [d] Relative rates of saponification of acetic acid esters in 70% acetone–water, ref 15. [e] Followed to 18% reaction. See Table V. [f] (*R*)-(−)-α-Methylbenzyl. See Table V.

Table V
Product Yields for the Halide Ion Catalyzed Decarboxylation of Esters of 4-Bromo-3,5-dimethyl-1-pyrazolecarboxylic Acid

Ester	Solvent	*N*-Alkyl-pyrazole, %	4-Bromo-3,5-dimethyl-pyrazole, %	Other products
CH_3	DMSO[a]	70–80	20–30	Dimethyl carbonate (10%)
CH_2CH_3	DMSO	70–80	20–30	
$(CH_3)_2CH$	DMSO	0	100[c]	
$PhCH_2$	DMSO	10	90	Benzaldehyde (90%)
$PhCHCH_3$	DMSO	1	99	Acetophenone (99%)
CH_3	DBP[b]	80–90	10–20	Dimethyl carbonate (5%)
CH_2CH_3	DBP	70–80	20–30	

[a] DMSO = dimethyl sulfoxide. [b] DBP = di-*n*-butyl phthalate. [c] At 18% total reaction.

Products. The products of alkylative decarboxylation of the *N*-carbalkoxypyrazoles in DMSO in the presence of halide ion are carbon dioxide, *N*-alkylpyrazole, the parent unalkylated pyrazole, and other products; see Table V. The yields of *N*-methyl- and *N*-ethylpyrazole from the respective esters are normally 70–90% under these conditions with unalkylated parent pyrazole forming the residue. In the case of the isopropyl ester, the nitrogen-containing product was solely the parent unalkylated pyrazole at 18% total reaction. When carried out in the presence of water or other proton donors, no *N*-alkylpyrazole was detected; all of the product was found as the parent unalkylated pyrazole. For example, decarboxylation of 4-bromo-1-carbomethoxy-3,5-dimethylpyrazole with chloride ion in 2.5% H_2O–DMSO gave no 4-bromo-1,3,5-trimethylpyrazole and 100% 4-bromo-3,5-dimethylpyrazole. The production of the unalkylated pyrazole presumably involves protonation of the intermediate pyrazolyl anion, and the yield of this product in the absence of added water probably reflects the concentration of the trace amounts of water in these reaction mixtures.

Further qualitative evidence for the premise that the production of unalkylated pyrazole depends on the presence of proton donors is found in Table VI. The yields of *N*-alkylpyrazoles are high (90%) when the methyl, ethyl, isopropyl, and benzyl esters of 4-bromo-3,5-dimethyl-1-pyrazolecarboxylic acid are heated at 200–300° with dry sodium iodide. When this reaction is carried out with moist sodium iodide (moisture derived from the atmosphere during storage) the yields of the *N*-alkylpyrazoles are reduced. As the alkyl groups increased in size, the SN2 displacement of iodide by the pyrazolyl anion will be retarded and more of the anion will react with water. Thus, the yield of *N*-alkylpyrazole from the isopropyl ester should be the lowest in the series methyl, ethyl, and isopropyl as it is.

In Table V, the yields of some other products are also given. The decarboxylations of the benzyl and the α-methylbenzyl esters give very high yields of benzaldehyde and acetophenone, respectively, together with high yields of the unalkylated pyrazole in DMSO. The reaction between water and the intermediate pyrazolyl anion cannot account for all of the unalkylated pyrazole. Benzylic halides react with dimethyl sulfoxide and base to produce carbonyl compounds and dimethyl sulfide.[22] This reaction could account for the production of both the carbonyl compounds and the unalkylated pyrazole in the decarboxylations of the benzyl and the α-methylbenzyl esters. The lack of formation of carbonyl compounds in the decarboxylations of the other alkyl esters is probably due to the relatively low reactivity of the intermediate alkyl halides with dimethyl sulfoxide.

Table VI
Products of the Decarboxylation of 4-Bromo-3,5-dimethyl-1-pyrazolecarboxylic Acid Esters[a]

Ester	Catalyst	*N*-Alkyl-pyrazole, %	Parent pyrazole, %
CH_3	NaI (dry)	90–100	0–10
CH_2CH_3	NaI (dry)	90–100	0–10
$(CH_3)_2CH$	NaI (dry)	80–90	10–20
$PhCH_2$	NaI (dry)	90–100	0–10
CH_3	NaI (moist)	78	22
CH_2CH_3	NaI (moist)	72	28
$(CH_3)_2CH$	NaI (moist)	41	59

[a] These reactions were carried out by heating the ester (1 g) and NaI (0.1 g) in a test tube over an open flame for 5–15 min without solvent.

In several of the reactions in which the methyl ester was decarboxylated, dimethyl carbonate was observed in the collected gases by glc and infrared spectroscopy. When *N*-pyrazole (carboxylic acid) methyl esters are treated with sodium methoxide in the DMSO solution, high yields of dimethyl carbonate are produced, based upon the quantity of methoxide added. The formation of dimethyl carbonate from the methyl ester in this reaction is almost surely due to attack of the methoxide ion on the carbonyl carbon atom of the ester, followed by elimination of a pyrazolyl anion. The formation of methoxide ion (and subsequently dimethyl carbonate) from the methyl ester in the absence of added methoxide ion could arise from the analogous attack of trace hydroxide ion at the carbonyl with production of the methoxide, the unalkylated pyrazole, and carbon dioxide.

The stability of the anionic residue from decarboxylation of the acid fragment of the ester is of prime importance in the prediction of alkylative decarboxylation reactions. An unrelated ester predicted on this basis to undergo alkylative decarboxylation catalyzed by nucleophiles is methyl *p*-nitrophenylcarbonate. This ester, when heated with tetra-*n*-butylammonium iodide (TBAI) above 200° without solvent, decarboxylates to give *p*-nitroanisole in 95% yield.[23] This result is consistent with the premise that the stability of the intermediate anion is important in the alkylative decarboxylation reactions but does not distinguish between attack at the carbonyl carbon atom or the methyl carbon atom.

Another ester which might alkylatively decarboxylate is dimethyl malonate. Refluxing dimethyl malonate with TBAI leads to the formation of carbon dioxide and methyl acetate instead of the expected methyl propionate. It is probable that the anion of methyl acetate formed initially reacts with the dimethyl malonate in a proton exchange to yield methyl acetate and the anion of dimethyl malonate.

Summary. The mechanism of the halide ion catalyzed alkylative decarboxylation of *N*-carbalkoxypyrazoles in polar aprotic solvents appears to involve initial rate-determining attack of halide ion at the α-carbon atom of the alkoxyl group of the ester, producing an alkyl halide, carbon dioxide, and a pyrazolyl anion either in a concerted manner or in a two-step process involving an intermediate *N*-pyrazolecarboxylate anion. The final step in the mechanism appears to be nucleophilic attack of the pyrazolyl anion on the alkyl halide to form the primary reaction product, *N*-alkylpyrazole, and to regenerate the catalyst halide ion. A secondary product, unalkylated pyrazole, was formed by pyrazolyl anion abstraction of a proton from trace amounts of water in the solution or by abstrac-

Table VII
Nmr[a] Data on Pyrazole Derivatives

Derivative	Pyrazole ring position 3	5	1	4	Registry no.
3,5-Dimethylpyrazole	7.76 (s)	7.76 (s)	−3.07 (s)	4.33 (s)	67-51-6
4-Bromo-3,5-dimethylpyrazole	7.78 (s)	7.78 (s)	−2.41 (s)		3398-16-1
3(5)-Methyl-5(3)-phenylpyrazole	7.80 (CH_3, s)	2.36 (Ph, m), 2.72 (Ph, m)	−2.55 (s)	3.78 (s)	3440-06-0
Derivatives of 4-Bromo-3,5-dimethylpyrazole					
1-Carbomethoxy-	7.82 (s)	7.55 (s)	6.05 (OCH_3, s)		28188-06-9
1-Carbethoxy-	7.80 (s)	7.55 (s)	5.60 (OCH_2, q), 8.57 (CCH_3, t)		51108-47-5
1-Carboisopropoxy-	7.79 (s)	7.50 (s)	4.87 (OCH, m), 8.60 (CCH_3, d)		51108-48-6
1-Carbobenzoxy-	7.80 (s)	7.50 (s)	4.66 (OCH_2, s), 2.62 (Ph, m)		51108-49-7
(*R*)-(−)-1-α-Methylbenzoxy-	7.81 (s)	7.56 (s)	4.07 (OCH, q), 8.32 (CCH_3, d), 2.71 (Ph, m)		51108-50-0
1-Methyl-	7.82 (s)	7.90 (s)	6.32 (NCH_3, s)		15801-69-1
1-Ethyl-	7.80 (s)	7.89 (s)	6.03 (NCH_2, q), 8.67 (CCH_3, t)		51108-51-1
1-Isopropyl-	7.81 (s)	7.88 (s)	5.70 (NCH, m), 8.62 (CCH_3, d)		51108-52-2
1-Benzyl-	7.86 (s)	8.04 (s)	5.02 (NCH_2, s), 2.93 (Ph, m)		51108-53-3
Derivatives of 3-Methyl-5-phenylpyrazole					
1-Carbomethoxy-	7.70 (CH_3, s)	2.69 (φ, s)	6.14 (OCH_3, s)	3.90 (s)	51108-54-4
1-Methyl-	7.80 (CH_3, s)	2.54 (φ, m)	6.38 (NCH_3, s)	4.05 (s)	10250-58-5
Derivatives of 5-Methyl-3-phenylpyrazole					
1-Carbomethoxy-	2.43 (Ph, m)	7.47 (CH_3, d)	6.05 (OCH_3, s)	3.65 (q)	51108-55-5
1-Methyl-	2.54 (Ph, m)	8.00 (CH_3, s)	6.48 (NCH_3, s)	3.88 (s)	10250-60-9

[a] Nmr spectra were obtained on CCl_4 solutions with internal tetramethylsilane standard reference using a Varian Associates Model A-60 analytical nmr spectrometer at ambient temperatures. The numbers in the table are chemical shifts in τ units relative to tetramethylsilane. The letters in parentheses refer to the multiplicity of the resonance as: s = singlet; d = doublet; t = triplet; q = quartet; and m = unresolved multiplet. All of the τ values given in the table are the centers of the resonances and all of the resonances integrated to the correct relative area.

tion of an α proton from an intermediate sulfoxonium salt formed by reaction of activated alkyl halides (benzylic halides) with the solvent, dimethyl sulfoxide. A carbonyl compound and (presumably) dimethyl sulfide were also formed in the latter case. Dimethyl carbonate was formed during the reactions of the methyl esters which produced some parent unalkylated pyrazole and was attributed to the formation of trace amounts of bases through reaction of the intermediate pyrazolyl anion with water in the reaction medium.

The uncatalyzed alkylative decarboxylation of *N*-carbalkoxypyrazoles appears to involve an initial induction period in which a small concentration of pyrazolyl anion is formed followed by a chain mechanism in which pyrazolyl anion attacks the *N*-carbalkoxypyrazole at the α carbon of the alkoxyl group yielding *N*-alkylpyrazole, carbon dioxide, and a second pyrazolyl anion.

Experimental Section

Acetylacetone and hydrazine hydrate were obtained from Matheson Coleman and Bell; methyl iodide, ethyl iodide, isopropyl iodide, methyl chloroformate, and ethyl chloroformate were obtained from the Aldrich Chemical Co. Phosgene was obtained from the Matheson Co. and (*R*)-(+)-α-methylbenzyl alcohol from Norse Laboratories. These reagents were used without further purification.

A Perkin-Elmer Model 137 sodium chloride spectrophotometer was used for ir spectra using films for liquids and Nujol mulls for solids. A Varian Associates Model A-60 analytical nmr spectrometer was used for nmr spectra of carbon tetrachloride solutions with internal tetramethylsilane at ambient temperatures. Melting points were obtained with a Thomas-Hoover capillary melting point apparatus. Gas chromatograms were obtained on a F & M Model 700 laboratory gas chromatograph (dual column) with columns of 20% Apiezon "L" on 60–80 Firebrick and 20% SE-20 on 100–120 Chromosorb W.

Nmr data on pyrazole derivatives appear in Table VII.

3,5-Dimethylpyrazole. The procedure of Knorr and Rosengarten[24] was used to prepare 3,5-dimethylpyrazole from acetylacetone and hydrazine hydrate: mp 106–108° (lit.[24] 107°).

4-Bromo-3,5-dimethylpyrazole. The procedure of Morgan and Ackerman[25] was used to prepare 4-bromo-3,5-dimethylpyrazole by the bromination of 3,5-dimethylpyrazole: mp 124–125°.[25]

3(5)-Methyl-5(3)-phenylpyrazole. The procedure of van Auwers and Breyhan[1c] was used to prepare 3(5)-methyl-5(3)-phenylpyrazole from benzoylacetone and hydrazine hydrate: mp 126–127° (lit.[1c] 128°).

Preparation of 4-Bromo-1-carbalkoxy-3,5-dimethylpyrazoles. A modified procedure of van Auwers and Breyhan[1c] was used to prepare 4-bromo-1-carbalkoxy-3,5-dimethylpyrazoles from 4-bromo-3,5-dimethylpyrazole and the respective alkyl chloroformate. To a solution of 0.037 mol of the alkyl chloroformate in 100 ml of benzene was added 3.0 g (0.017 mol) of 4-bromo-3,5-dimethylpyrazole dissolved in 50 ml of benzene. The solution was stirred for 2 hr and 6 g of sodium bicarbonate was added. The solution was allowed to stand at room temperature overnight and was then washed with two 100-ml portions of water. The benzene solution was dried over sodium sulfate and concentrated *in vacuo*. The residue was distilled (if liquid) and sublimed (if solid) at 1–2 Torr. The solid esters were then recrystallized from cyclohexane. Yields of esters based upon the quantity of pyrazole used ranged from 50 to 90%. The four esters prepared by this method follow.

4-Bromo-1-carbomethoxy-3,5-dimethylpyrazole: mp 63–64.5°; ir ν 1750, 1350, 1130, 1060 cm^{-1}. *Anal.* Calcd for $C_7H_9BrN_2O_2$: C, 36.08; H, 3.89; N, 12.02; Br, 34.29. Found: 36.10; H, 3.85; N, 11.92; Br, 34.75.

4-Bromo-1-carbethoxy-3,5-dimethylpyrazole: mp 32.5°; ir ν 1750, 1340, 1120, 1060 cm^{-1}. *Anal.* Calcd for $C_8H_{11}BrN_2O_2$: C, 38.89; H, 4.49; N, 11.34; Br, 32.34. Found: C, 38.76; H, 4.44; N, 11.17; Br, 32.86.

4-Bromo-1-carboisopropoxy-3,5-dimethylpyrazole: mp 31–33°; ir ν 1750, 1375, 1105, 1055 cm^{-1}. *Anal.* Calcd for

$C_9H_{13}BrN_2O_2$: C, 41.39; H, 5.02; N, 10.73; Br, 30.60. Found: C, 41.58; H, 4.80; N, 10.86; Br, 30.30.

4-Bromo-1-carbobenzoxy-3,5-dimethylpyrazole: mp 107–108°; ir ν 1740, 1340, 1270, 1120, 1060, 1010 cm^{-1}. *Anal.* Calcd for $C_{13}H_{13}BrN_2O_2$: C, 50.50; H, 4.24; N, 9.06; Br, 25.85. Found: C, 50.99; H, 4.49; N, 9.25; Br, 25.74.

(*R*)-(−)-4-Bromo-1-carbo-α-methylbenzoxy-3,5-dimethylpyrazole. To a solution of 3.7 g (0.03 mol) of (*R*)-(+)-α-phenylethanol ($[\alpha]^{20}D$ +37.5°, 93% optically pure) was added a solution of 6 g (0.06 mol) of phosgene in 100 ml of benzene. Dry nitrogen was bubbled through the solution for 2 hr, and the solution was warmed to remove excess phosgene. A solution of 5.3 g (0.03 mol) of 4-bromo-3,5-dimethylpyrazole dissolved in 50 ml of benzene was added and the solution was stirred at room temperature for 2 hr. To the solution was added 6 g of sodium bicarbonate. The mixture was stirred overnight at room temperature, washed with two 100-ml portions of water, dried over sodium sulfate, and concentrated *in vacuo*. Attempted distillation of the residue led to decomposition. The residue was chromatographed on silica gel and was eluted with dichloromethane. The yield of ester was 4 g of pale yellow liquid. This material was used in kinetic experiments without further purification: ir ν 1730, 1370, 1340, 1270, 1055, 760 cm^{-1}.

Preparation of 1-Carbomethoxy-5-methyl-3-phenylpyrazole. The modified procedure of van Auwers and Breyhan[1c] was used to prepare 1-carbomethoxy-5-methyl-3-phenylpyrazole from 3(5)-methyl-5(3)-phenylpyrazole and methyl chloroformate: mp 63–65° (lit.[1c] 74.5°); ir ν 1750, 1350, 1290, 1110, 947, 770, 693 cm^{-1}. The melting point difference is not resolved.

Preparation of 1-Carbomethoxy-3-methyl-5-phenylpyrazole. The procedure of van Auwers and Breyhan[1c] was used to prepare 1-carbomethoxy-3-methyl-5-phenylpyrazole from benzoylacetone and carbomethoxyhydrazine: mp 57.5–58.5° (lit.[1c] 58.9°); ir ν 1750, 1340, 1290, 1120, 830, 825, 778, 765, 727, 702, 678 cm^{-1}.

Preparation of 1-Alkylpyrazole Derivatives. The synthesis of 1-alkyl-4-bromo-3,5-dimethylpyrazoles and 1-methyl derivatives of 3(5)-methyl-5(3)-phenylpyrazole was accomplished through reaction of the sodium salt of the pyrazole with the alkyl halide in tetrahydrofuran solution. To a solution of 0.017 mol of the pyrazole in 50 ml of dry tetrahydrofuran (THF) was added 0.50 g (0.021 mol) of sodium hydride which had been previously washed with dry THF. The solution of 0.021 mol of the appropriate alkyl halide was added and the solution was stirred for 5 hr. The solution was filtered to remove the sodium halide and the solution was concentrated *in vacuo*. The residue was distilled at 1 Torr and compared spectrally with the respective products of the decarboxylations of the respective *N*-carbalkoxypyrazole. Compounds prepared are listed below.

4-Bromo-1,3,5-trimethylpyrazole: mp 34–36° (reported[26] liquid).

4-Bromo-3,5-dimethyl-1-ethylpyrazole: bp 56–57° (0.05 Torr). *Anal.* Calcd for $C_7H_{11}N_2Br$: C, 41.40; H, 5.46; N, 13.80; Br, 39.35. Found: C, 41.53; H, 5.46; N, 13.55; Br, 39.25.

4-Bromo-3,5-dimethyl-1-isopropylpyrazole: bp 65° (0.05 Torr). *Anal.* Calcd for $C_8H_{13}N_2Br$: C, 44.26; H, 6.04; N, 12.91; Br, 36.81. Found: C, 44.65; H, 6.31; N, 13.11; Br, 36.43.

1-Benzyl-4-bromo-3,5-dimethylpyrazole: bp ~210° (0.05 Torr). *Anal.* Calcd for $C_{12}H_{13}N_2Br$: C, 54.35; H, 4.94; N, 10.57; Br, 30.14. Found: C, 54.62; H, 5.19; N, 11.03; Br, 30.10.

Isolation of TBAI from Decarboxylation of Reaction Mixtures. Tetra-*n*-butylammonium iodide (TBAI) was recovered from two reaction mixtures by the following procedure. After 80% evolution of carbon dioxide from 0.131 g (5.65×10^{-4} mol) of 1-carbomethoxy-4-bromo-3,5-dimethylpyrazole catalyzed by 0.0561 g (1.52×10^{-4} mol) of TBAI at 110° in 1.884 g of dibutyl phthalate solvent, the reaction tube was removed from the constant temperature bath. To the reaction solution was added 10 ml of ligroine (bp 30–60°). The solution was washed into a beaker and was diluted with ligroine to a volume of 50 ml. The precipitated TBAI was collected by filtration and was washed with 10 ml of ligroin (bp 30–60°). The solution was washed into a beaker and 140–145° (authentic material melts at 145–146°); the ir spectrum (Nujol mull) was identical with that of authentic TBAI.

By the same procedure, 0.18 g (91% recovery) of TBAI was isolated from a decarboxylation involving 0.1989 g (5.40×10^{-4} mol) of TBAI and 0.934 g (4.325×10^{-3} mol) of 1-carbomethoxy-5-methyl-3-phenylpyrazole in 7.245 g of DBP and heated at 110°.

Kinetics. The constant temperature bath was of conventional design utilizing 5 gallons of Union Carbide L-45 silicone oil (200 cSt) as the bath liquid. Temperature control was ±0.04° at 100°. Ultraviolet spectra were recorded with a Beckman Model DB spectrophotometer equipped with a Sargent Model SRL recorder. The kinetic data were analyzed using a least-squares fit to the best straight line using an Olivetti Underwood Programma 101 desk computer.

Volumetric Kinetic Determinations. A weighed quantity of dry catalyst was placed in a 100 × 20 mm Pyrex test tube equipped with inner and outer standard taper joints. A weighed ester solution of known molal concentration in the appropriate solvent was added to the catalyst. The reaction tube was placed in a neck of a three-necked 500-ml flask in which 300 ml of toluene was vigorously refluxing. An insulated mercury gas buret was immediately attached to the reaction tube and the change in the volume of gas in the buret was measured as a function of time. Changes in room temperature and pressure during any kinetic run were negligible and variations in temperature (3°) and pressure (5 Torr) could have only produced a 1% error in the volume of gas which was observed. Volumes were corrected for the initial expansion of air in the reaction tube and for the initial temperature equilibration period. Duplicate runs were reproducible to ±3%.

Ultraviolet Kinetic Determinations. Kinetic experiments using ultraviolet maxima of the esters were conducted in DMSO solution. The esters exhibited a sharp absorption at 258 mμ where none of the products absorbed. Extinction coefficients of the esters were in the range 2×10^3–2.8×10^3 l./(mol cm).

A 20-ml portion of the halide catalyst solution (0.0543 *M*) was thermally equilibrated in the reaction vessel for 30–60 min at 99.85°. Then 50–100 μl of a 0.2000 *M* ester solution was added through the stopcock *via* a syringe. The initial ester concentration was in the range 5.0–10 × 10^{-4} *M* and the initial absorbance of the solution at 258 mμ was approximately 1.2. Samples of 1–2 ml were removed periodically from the reaction solution through the stopcock *via* syringe. The samples were cooled to room temperature, and the ultraviolet spectrum of the aliquot was recorded at least three times; the average of these values was used in the determination of the rate constant of the reaction. Reactions were followed for at least 2 half-lives with six to twelve samples being taken. Rate constants were reproducible to 1–2%, and all of the esters studied showed good first-order kinetics.

In the decomposition of the benzyl ester, one of the major products, benzaldehyde, absorbs at 258 mμ. The products were unalkylated pyrazole and benzaldehyde, and the ratio of the concentrations of the ester at time t to the initial concentration of the ester, $[E]_t/[E]_0$, was obtained from the expression

$$[E]_t/[E]_0 = (A_t - A_0)/(A_0 - A_\infty)$$

where A_∞ is the absorbance of the solution at infinite time and A_0 is the initial absorbance of the solution. Products are shown in Table V.

The kinetic reactions of the alkylative decarboxylation of the methyl ester catalyzed by the sodium salt of 4-bromo-3,5-dimethylpyrazole were followed by determining the change in the uv absorption of the solution as a function of time as were the halide-catalyzed reactions.

The sodium salt of the pyrazole was prepared by the reaction of 4-bromo-3,5-dimethylpyrazole with an excess of sodium hydride in tetrahydrofuran (THF) solution. A solution of the pyrazole salt resulted from this reaction, and, after filtration of the solution to remove the excess sodium hydride, the solution was concentrated *in vacuo*. The residual salt was then dried of residual THF in a bell jar at room temperature at 0.3 Torr for 2 days prior to use. The reaction solution of the catalyst was prepared just prior to use by dissolving 20.0 mg of sodium 4-bromo-3,5-dimethylpyrazole in 21.0 ml of dry DMSO to yield a 5.29×10^{-3} *M* solution. The reaction was then carried out exactly as were the halide-catalyzed reactions. A small amount of decomposition of the solution occurred but little problem was caused in determining the rate constant for the reaction. Analysis of the final reaction mixture showed essentially quantitative conversion of the 4-bromo-1-carbomethoxy-3,5-dimethylpyrazole to 4-bromo-1,3,5-trimethylpyrazole. The quantity of 4-bromo-3,5-dimethylpyrazole found after work-up was accountable to the hydrolysis of the sodium salt during the work-up procedure.

The kinetics of the decarboxylation of the (*R*)-(−)-α-methylbenzyl ester were determined by following the optical rotation of a DMSO solution. The instrument used was a Japan Spectroscopic Co., Ltd., Model ORD/UV-5 optical rotary dispersion spectrophotometer.

Into a 10-mm quartz curvette was placed 3.0 ml of the stock sodium chloride–DMSO solution. The curvette was capped with a

tight-fitting Teflon stopper and was then placed into the cell compartment of the ORD. The cell compartment was thermostated at 99.80 ± 0.5° through the use of an ethylene glycol filled circulating pump obtained from the Precision Scientific Co. The solution was allowed to equilibrate at this temperature for 30 min while the instrument was set at zero rotation at the sodium D line (5893 Å). The neat ester (5–15 mg) was introduced *via* a capillary tube and was stirred for 2 sec. The optical rotation of the solution was recorded continuously for a period of 6 hr (*ca.* 2 half-lives of reaction) and the rotation was found to decrease exponentially to a value of 0.00 after 20 hr. The products were acetophenone and 4-bromo-3,5-dimethylpyrazole in 99% yields by nmr and glc. A least-squares fit to the best straight line of ln (rotation) *vs.* time indicated that the decomposition of the ester was first order with a rate constant reproducible to ±3%.

Methyl 4-Nitrophenylcarbonate. Into the reaction vessel used for volumetric rate determinations was placed 0.540 g of methyl 4-nitrophenylcarbonate and 50 mg of tetra-*n*-butylammonium iodide. The reaction vessel was then placed into a flask containing vigorously boiling ethylene glycol (195°) and the gas buret was immediately attached to the reaction vessel. After 5 min 68 ml of carbon dioxide (identified by ir) was evolved, corresponding to 90% reaction. The reaction mixture was cooled to room temperature, and ether was added. The ether solution was washed with two 10-ml portions of water, dried over sodium sulfate, and concentrated *in vacuo*. The residue (0.375 g, 91% yield) was identified as 4-nitroanisole by comparison of the infrared and nmr spectra and melting point with those of authentic material.

Dimethyl Malonate Decarboxylation. Into a 50-ml round-bottom distilling flask was placed 25 g of dimethyl malonate and 1 g of tetra-*n*-butylammonium iodide. The mixture was heated with a heating mantle at atmospheric pressure with stirring. Near the boiling point of the malonate, evolution of carbon dioxide began and, after 30 min, methyl acetate began to distill from the reaction mixture. After 2.5 hr, 5 g of methyl acetate was collected (35% yield). The methyl acetate was identified by comparison of the ir and nmr spectra with those of authentic material.

Registry No.—Methyl chloroformate, 79-22-1; ethyl chloroformate, 541-41-3; isopropyl chloroformate, 108-23-6; benzyl chloroformate, 501-53-1; (*R*)-(+)-α-phenylethanol, 1517-69-7.

References and Notes

(1) (a) K. van Auwers and W. Daniel, *J. Prakt. Chem.*, **110**, 235 (1925); (b) K. van Auwers and H. Stuhlmann, *Chem. Ber.*, **59**, 1043 (1926); (c) K. van Auwers and Th. Breyhan, *J. Prakt. Chem.*, **143**, 259 (1935); (d) K. van Auwers and E. Cauer, *ibid.*, **126**, 146 (1930).
(2) (a) For a review of reactions of esters, see S. Patai, Ed., "The Chemistry of Carboxylic Acids and Esters," Interscience, London, 1969; J. March, "Advanced Organic Chemistry: Reactions, Mechanisms, and Structure," McGraw-Hill, New York, N. Y., 1968, pp 477–480.
(3) E. S. Lewis and W. C. Herndon, *J. Amer. Chem. Soc.*, **83**, 1955 (1961).
(4) (a) K. B. Wiberg and T. M. Shryne, *J. Amer. Chem. Soc.*, **77**, 2774 (1955); (b) A. H. J. Houssa and H. Phillips, *J. Chem. Soc.*, 1232 (1932).
(5) M. S. Newman and S. Mladenovic, *J. Amer. Chem. Soc.*, **88**, 4523 (1966).
(6) D. S. Tarbell and T. Parasaran, *J. Org. Chem.*, **29**, 2471 (1964).
(7) R. Oda, M. Miyanoki, and M. Okano, *Bull. Chem. Soc. Jap.*, **35**, 1915 (1962).
(8) J. L. Kice, R. A. Bartsch, M. A. Dankleff, and S. L. Schwartz, *J. Amer. Chem. Soc.*, **87**, 1734 (1965).
(9) S. M. Spatz, *J. Org. Chem.*, **26**, 4158 (1961).
(10) A. Padwa and R. Hartman, *Tetrahedron Lett.*, 2277 (1966).
(11) K. Schenker, Swiss Patent 385,887 (1965); *Chem. Abstr.*, **63**, 2930 (1965).
(12) (a) W. John, *Chem. Ber.*, **68**, 2283 (1935); (b) H. A. Staab, *Angew. Chem., Int. Ed. Engl.*, **1**, 351 (1962).
(13) R. C. L. Chow and D. S. Tarbell, *J. Org. Chem.*, **32**, 2188 (1967).
(14) R. F. Rodewald, K. Mahendran, J. L. Bear, and R. Fuchs, *J. Amer. Chem. Soc.*, **90**, 6698 (1968).
(15) E. K. Euranto, ref 2a, pp 505–588.
(16) W. Roberts and M. C. Whiting, *J. Chem. Soc.*, 1290 (1965).
(17) A. Streitwieser, *Chem. Rev.*, **56**, 571 (1956).
(18) S. Warren and M. R. Williams, *Chem. Commun.*, 180 (1969).
(19) Pyrazole-1-carboxylate salts have been isolated in the solid state: S. Trofimenko, *Chem. Rev.*, **72**, 4976 (1972).
(20) K. van Auwers and K. Dietrich, *J. Prakt. Chem.*, **139**, 65 (1934).
(21) J. Castello, *Chem. Commun.*, 709 (1972).
(22) H. R. Nace and J. J. Monagle, *J. Org. Chem.*, **24**, 1792 (1959).
(23) See also S. Inaba, M. Yamada, T. Yoshino, and Y. Ishido, *J. Amer. Chem. Soc.*, **95**, 2062 (1973).
(24) L. Knorr and G. D. Rosengarten, *Justus Liebigs Ann. Chem.*, **279**, 237 (1894).
(25) G. T. Morgan and I. Ackerman, *J. Chem. Soc.*, 123, 1316 (1923).
(26) R. Hüttel and E. Schön, *Justus Liebigs Ann. Chem.*, **625**, 55 (1959).

Kinetics and Mechanism for Chloromercuriolactonization of Esters of γ,δ-Unsaturated Acids[1]

Omar A. El Seoud,[2] Antonia T. do Amaral,[2] M. Moura Campos, and Luciano do Amaral*

Instituto de Quimica da Universidade de São Paulo, Caixa Postal, 20.780, São Paulo, SP, Brazil

Received August 17, 1973

The kinetics of the reaction of phenyl allylphenylacetate (I), phenyl allyl-*p*-tolylacetate (II), phenyl *p*-methoxyphenylacetate (III), phenyl allyl-*p*-chlorophenylacetate (IV), phenyl allyl-*p*-fluorophenylacetate (V), phenyl allyl-*p*-nitrophenylacetate (VI), phenyl allylacetate (VII), *p*-tolyl allylacetate (VIII), *p*-methoxylphenyl allylacetate (IX), *p*-bromophenyl allylacetate (X), *p*-nitrophenyl allylacetate (XI), and phenyl allyldiphenylacetate (XII) with mercuric chloride have been studied in 50% aqueous ethanol. The reaction follows the expression rate = k_2[ester][$HgCl_2$]. Rate constants for the reaction are increased by electron-withdrawing substituents in the phenyl allyl para-substituted phenylacetate moiety (compounds I–VI) and by electron-donating substituents in the para-substituted allylacetate moiety (compounds VII–XI). A mechanism is postulated and discussed in terms of the kinetic data.

In the course of a search for new mercurials of diuretic action, we have prepared δ-chloromercuri-γ-lactones by the reaction of various allyl para-substituted acids with mercuric chloride in 50% aqueous ethanol. The structure of these chloromercurilactones were established by chemical and spectroscopic means. Aside from the pharmacological importance of these products, we were interested in studying the reaction itself to determine its kinetic expression and the effect of structural changes on its rate. Such a kinetic study was particularly interesting because of the surprisingly small amount of kinetic data available on this reaction. We have therefore prepared several phenyl esters of allyl para-substituted phenylacetate acids (compounds I to VI) and several para-substituted phenylic esters of the allylacetic acid (compounds VII to XI). See Chart I for general structure of compounds I–XII. These esters react with mercuric chloride in ethanol–water solution to give δ-chloromercuri-γ-lactones and the corre-