chromatogram of the unhydrogenated photolysate is shown in Figure 1. Assays of this photolysate were made periodically until the peak B (Figure 1) had disappeared (25 days). The results are given in Table I.

**Assay of Formaldehyde.** Hantzsch's reagent solution was prepared as described.[5] The molar absorbtivity of diacetyldihydrolutidine (the product of reaction of Hantzsch's solution with formaldehyde) was determined in aqueous DME as follows. A solution of 2.46 mg ($8.2 \times 10^{-2}$ mmol) of paraformaldehyde was made in 100 mL of Hantzsch's solution, and this was diluted to 200 mL with DME. The mixture was incubated at 45–50 °C for 12 h and diluted appropriately with a 50:50 mixture of Hantzsch's solution and DME for spectrophotometry at three dilutions. The molar absorptivity was $7.48 \pm 0.06 \times 10^3$. Nash reports a molar absorptivity of $8.0 \times 10^3$ in aqueous solutions.[5] Assays of formaldehyde in photolysis solutions were carried out before and after hydrogenation in the same way. This means necessarily that the assay before hydrogenation refers to free formaldehyde plus that obtained by hydrolysis of **4c** by Hantzsch's reagent. Assay after hydrogenation refers to free formaldehyde only.

***N*-Methylbutane-*p*-cyanosulfenanilide.** There are two possible adducts of BuSH to the *N*-methylene amine **4c**. One of these is *N*-methylbutane-*p*-cyanosulfenanilide, $NCC_6H_4N(SBu)CH_3$ (**10**), and the other is *N*-[(butylthio)methyl]-*p*-cyanoaniline, $NCC_6H_4NHCH_2SBu$ (**11**). The former (**10**) could arise from ionic addition and the latter (**11**) from free-radical addition of BuSH to **4c**. It was thought that either one could be responsible for the new unidentified peak which appeared in the HPLC chromatograms when **1c** was photolyzed in the presence of BuSH. The preparation of **10** was carried out by reaction of *N*-methyl-*p*-cyanoaniline with butanesulfenyl chloride according to the procedure of Ainpour and Heimer.[10] The product [bp 132–136 °C (0.03 mmHg] was found by $^1H$ NMR and high-pressure LC to contain some *N*-methylaniline. The retention time of **10** in the high-pressure LC was greater than that of the unidentified peak. Attempts to make **11** for high-pressure LC comparison with the unidentified peak were not successful.

**Registry No.** **1c**, 79121-25-8; **1d**, 5579-27-1; **1e**, 74763-65-8; **2c**, 79121-26-9; **2d**, 14996-70-4; **2e**, 74763-66-9; **3c**, 4714-62-9; **3d**, 100-61-8; **3e**, 6911-87-1; **4c**, 79121-27-0; **5c**, 873-74-5; 1-methyl-1-(*p*-cyanophenyl)hydrazine, 79121-28-1.

(10) Ainpour, P.; Heimer, N. E. *J. Org. Chem.* **1978**, *43*, 2061.

# Cation–Anion Combination Reactions. 20.[1] Reactions of Nucleophiles with *trans*-3-Methoxy- and *trans*-3-(Methylthio)acrylophenones

Calvin D. Ritchie* and Atsushi Kawasaki

*Department of Chemistry, State University of New York at Buffalo, Buffalo, New York 14214, and College of General Education, Shinshu University, 3-1-1 Asahi, Matsumoto 390, Japan*

*Received June 19, 1981*

The reactions of a number of nucleophiles with *trans*-3-methoxyacrylophenone (MeOAcr) and with *trans*-3-(methylthio)acrylophenone (MeSAcr) in water and methanol have been studied. The reactions of amines produce enamines as the first observable products, and primary amines show simple kinetics: first-order with respect to amine and first-order with respect to the acrylophenone. Piperidine reactions show kinetics which are consistent with a change in the rate-determining step with a change in amine concentration. Methoxylamine reactions produce the monooximes, and semicarbazide reactions produce the monosemicarbazone with MeOAcr but the disemicarbazone with MeSAcr. The reactions of hydroxide ion produced the enolate of benzoylacetaldehyde, which, at the high base concentration used in the MeSAcr reaction, was further converted to acetophenone and formate ion. Methoxide and cyanide ion reactions given addition across the double bond. Rate constants for the reactions of MeOAcr are 20–1000 times greater than those for corresponding reactions of MeSAcr. There is a very good correlation of the rate constants for reactions of nucleophiles with MeOAcr and those with 2,4-dinitrophenyl acetate in both water and methanol solution.

Some years ago, Friedman and his co-workers[2,3] showed that the relative rates of reactions of a series of amines and thiolates with a variety of compounds of the type $CH_2{=}CHX$, with X = CN, $CONH_2$, $CO_2R$, $PO(OR)_2$, and $SO_2R$, are independent of the identity of X. The Brønsted slopes for the reactions of amines are all very close to 0.4, and the thiolate/amine rate ratios are ca. 150. These characteristics are very similar to those which we have reported for reactions of these nucleophiles with a range of electrophiles.[1]

Fedor and his co-workers[4] have carried out mechanistic studies of the reactions of amines with a series of para-substituted *trans*-3-methoxyacrylophenones which support the addition–elimination mechanism proposed by Rappoport[5] for these types of reactions and which indicate that attack of amine is the rate-determining step of the reactions.

We became interested in these latter reactions for two primary reasons: first, we wished to examine further cases of neutral electrophiles reacting with nucleophiles in different solvents in order to gain further information on the variations in relative reactivities of electrophiles with change in solvent[6]; second, the replacement of the methoxy group with a methylthio group offered the opportunity of investigating the effect of this change from a group with high to a group with low polarizability directly bonded to the electrophilic reaction site. The first reason above was strengthed by Hoz's recent report[7] that the reactions of nucleophiles with $\alpha,\alpha$-dinitromethylenefluorene in several different solvents followed the $N_+$ relationship based on

(1) Previous paper in this series: C. D. Ritchie, A. A. Kamego, P. O. I. Virtanen, and C. Kubisty, *J. Org. Chem.*, **46**, 1957 (1981).
(2) M. Friedman, J. F. Cavins, and J. S. Wall, *J. Am. Chem. Soc.*, **87**, 3672 (1965).
(3) M. Friedman and J. S. Wall, *J. Org. Chem.*, **31**, 2888 (1966).
(4) J. H. Chu, B. S. R. Murty, and L. Fedor, *J. Am. Chem. Soc.*, **98**, 3632 (1976).
(5) Z. Rappoport and P. Peled, *J. Am. Chem. Soc.*, **101**, 2682 (1979), and earlier papers cited therein.
(6) C. D. Ritchie and M. Sawada. *J. Am. Chem. Soc.*, **99**, 3754 (1977).
(7) S. Hoz and D. Speizman, *Tetrahedron Lett.*, 1775 (1978).

0022-3263/81/1946-4704$01.25/0 

carbonium ion reactions. We have also been intrigued by Bernasconi's recent work[8] aimed at examining the similarities in nucleophilic additions to activated double bonds and the proton transfers of similarly activated alkanes.

The results of our studies of the reactions of nucleophiles with *trans*-3-methoxyacrylophenone (MeOAcr) and with *trans*-3-(methylthio)acrylophenone (MeSAcr) in water and methanol solution are presented here.

## Experimental Section

**Materials.** *trans*-3-Methoxyacrylophenone was prepared by the reaction of 3-chloroacrylophenone with sodium methoxide in methanol as described by Matsumoto.[9] Repeated distillation from a small amount of potassium bisulfate gave the pure material, bp 113–115 °C (0.5 mm) [lit[9]. bp 112 °C (1.8 mm)].

*trans*-3-(Methylthio)acrylophenone was obtained by the reaction of sodium thiomethoxide in methanol with 3-chloroacrylophenone: bp 143–144 °C (0.7 mm); $^1$H NMR in $CDCl_3$ $\delta$ 2.35 (s, 3, $SCH_3$), 6.65 (d, $J$ = 14 Hz, 1, =CHCO), 7.45 (m, 3, arom), 7.9 (m, 2, arom), 7.93 (d. $J$ = 14 Hz, 1, =CHS).

The sources of all other reagents have been described in earlier papers.[1]

**Apparatus.** UV spectra were recorded on a Cary Model 14 or a Shimadzu Model UV-300 spectrophotometer. Kinetic studies utilized either a Gilford Model 140 spectrophotometer or the single-wavelength stop-flow apparatus described in earlier papers. In all cases, the reacting solutions were thermostated at 25.0 ± 0.1 °C. NMR spectra were obtained with a Varian A-60 spectrometer.

**Preparation of Solutions.** Stock solutions of the 3-substituted acrylophenones were prepared by weighing samples of ca. 160–170 mg in a 10 mL volumetric flask and filling the flask with acetonitrile to give solutions ca. 1. × $10^{-2}$ M. Microliter pipets were used to dilute these solutions into the aqueous or methanolic solutions of nucleophiles to give final concentrations ranging from 5 × $10^{-5}$ to 1 × $10^{-3}$ M.

Sodium or potassium hydroxide solutions were standardized with potassium hydrogen phthalate with phenolphthalein as indicator. These solutions were then used for the standardization of hydrochloric acid solutions and for the preparation of buffers.

Sodium methoxide solutions in methanol were prepared by the addition of small pieces of freshly cut sodium to anhydrous methanol under nitrogen in a glovebag. In a few experiments, commerical 0.5 M sodium methoxide titrant (Eastman) was employed and gave the same results as the freshly prepared reagent. The methoxide solutions, after 25-fold dilution with water, were standardized with potassium hydrogen phthalate.

Buffers for the reactions of amines were prepared from solutions of the amine hydrochlorides by partial neutralization with hydroxide (water) or methoxide (methanol) solutions described above. The solutions of glycine ethyl ester were prepared immediately before use.

Cyanide buffer solutions were prepared immediately before use by partial neutralization of potassium cyanide solution with hydrochloric acid.

**Kinetic Studies.** All reactions were studied under pseudo-first-order conditions with the nucleophile in large excess. Ionic strength of all solutions was adjusted to 0.10 M by the addition of either NaCl or $NaClO_4$, in water, and $NaClO_4$ in methanol. The amine and cyanide solutions were buffered with the conjugate acid of the nucleophile. Methoxide and hydroxide solutions were unbuffered.

At least one experiment was carried out for each reaction in which all the UV spectral changes during reaction were followed. With the exceptions of the reactions of semicarbazide with MeOAcr and of hydroxide with MeSAcr, the spectral changes indicated simple conversion of reactant to product with no intermediates, and the kinetics were then studied by following either the absorbance of the acrylophenone (275 nm for MeOAcr and 330 nm for MeSAcr) or that of the products (330–340 nm for enamine products). Pseudo-first-order rate constants were calculated by the nonlinear least-squares method described in earlier papers.[1]

Table I. Summary of Experimental Conditions Employed[a]

| nucleophile | concentration range, M: in water | concentration range, M: in methanol | comment |
|---|---|---|---|
| A. Reactions of *trans*-3-Methoxyacrylophenone | | | |
| hydroxide ion | 0.01–0.05 | | |
| methoxide ion | | 0.005–0.05 | |
| cyanide ion | 0.02–0.20 | | *b* |
| piperidine | 0.002–0.05 | 0.0025–0.025 | *c* |
| morpholine | 0.02–0.05 | 0.005–0.030 | *c* |
| *n*-propylamine | 0.02–0.05 | 0.0025–0.040 | *c, d* |
| glycine ethyl ester | 0.03–0.05 | 0.01–0.025 | *c* |
| ethylenediamineH$^+$ | 0.01–0.05 | | *c* |
| 2,2,2-trifluoroethylamine | 0.02–0.05 | 0.010–0.10 | *c* |
| methoxylamine | 0.005–0.05 | 0.020–0.025 | *c* |
| semicarbazide | 0.02–0.05 | | *c, e* |
| B. Reactions of *trans*-3-(Methylthio)acrylophenone | | | |
| hydroxide ion | 0.06–0.50 | | *f* |
| methoxide ion | | 0.01–0.10 | |
| cyanide ion | 0.03–0.04 | | *b* |
| piperidine | 0.005–0.05 | | *c* |
| morpholine | 0.01–0.05 | | *c* |
| *n*-propylamine | 0.02–0.05 | | *c* |
| glycine ethyl ester | 0.03–0.05 | | *c* |
| ethylenediamineH$^+$ | 0.02–0.05 | | *c* |
| 2,2,2-trifluoroethylamine | 0.03–0.05 | | *c* |
| methoxylamine | 0.05–0.10 | | *c* |
| semicarbazide | 0.02–0.05 | | *c, g* |

[a] All reactions were studied at 25.0 ± 0.1 °C, and the ionic strength was 0.10 M unless otherwise noted. [b] Solutions contained equal concentrations of HCN and $CN^-$. In the one experiment with [$CN^-$] above 0.1 M, the ionic strength was 0.20 M. [c] Solutions contained equal concentrations of the amine hydrochloride. [d] The reactions of *n*-butylamine in methanol employed the same range of concentrations. For both the *n*-propylamine and *n*-butylamine reactions, the amine/amineH$^+$ was varied from 0.25 to 4.0. [e] Rate constants were calculated from the first half-life because of interference from further reaction at longer times, as discussed in the Experimental Section. [f] The rate constant reported in Table II was calculated for concentrations of hydroxide ion below 0.10 M and was based on data for the first half-life of the reactions because of further reaction as discussed in the Experimental Section. [g] The disemicarbazone was the observed product of the reaction.

The reaction of MeOAcr with semicarbazide buffers showed a decrease in the absorbance at 275 nm (MeOAcr) followed by a slower increase in absorbance at 285 nm (disemicarbazone), with isosbestic points appearing at 252 and 315 nm for the slower reaction. The slow reaction did not occur with unbuffered semicarbazide solutions, and the monosemicarbazone was the observed product. A prepared sample of the monosemicarbazone[10] reacted with buffered semicarbazide to produce the disemicarbazone,[10] with spectral characteristics confirming the above assignment. In the reaction of MeSAcr with semicarbazide buffers, the disemicarbazone is formed without detectable amounts of the monosemicarbazone present at any time.

The reaction of MeOAcr with hydroxide ion yielded the enolate ion of benzoylacetaldehyde whose further conversion to acetophenone and formate ion[11] was negligible under the reaction conditions. In the more basic solutions used for the reaction of MeSAcr, the further reaction of the benzoylacetaldehyde enolate was competitive with its formation. Three-point analyses of the

(8) C. F. Bernasconi and S. Fornarini, *J. Am. Chem. Soc.*, **102**, 5329 (1980), and earlier papers cited therein.
(9) T. Matsumoto and H. Shirahama, *Bull. Chem. Soc. Jpn.*, **38**, 1289, 1293 (1965).
(10) K. V. Auwers and B. Ottens, *Chem. Ber.*, **58B**, 2072 (1925).
(11) J. Rahil and R. F. Pratt, *J. Am. Chem. Soc.*, **99**, 2661 (1977).

Table II. Rate Constants for Reactions of Nucleophiles With MeOAcr and MeSAcr[a]

| nucleophile (solvent) | $k_2$, $M^{-1}$ $s^{-1}$ MeOAcr | $k_2$, $M^{-1}$ $s^{-1}$ MeSAcr | $k_{MeOAcr}/k_{MeSAcr}$ |
|---|---|---|---|
| piperidine (water) | 40.9 | 0.630 | 65 |
| morpholine (water) | 3.8 | 0.11 | 33 |
| *n*-propylamine (water) | 3.4 | $2.1 \times 10^{-2}$ | 161 |
| glycine ethyl ester (water) | 0.39 | $4.0 \times 10^{-3}$ | 98 |
| ethylenediamineH$^+$ (water) | 0.31 | $2.2 \times 10^{-3}$ | 138 |
| 2,2,2-trifluoroethylamine (water) | $3.3 \times 10^{-2}$ | $2.4 \times 10^{-4}$ | 137 |
| methoxylamine (water) | $2.8 \times 10^{-2}$ | $1.8 \times 10^{-3}$ | 16 |
| semicarbazide (water) | $3.5 \times 10^{-2}$ | $4.2 \times 10^{-4}$ | 84 |
| cyanide ion (water) | $3.3 \times 10^{-2}$ | $1.5 \times 10^{-4}$ | 223 |
| hydroxide ion (water) | 0.61 | $5.3 \times 10^{-4}$ | 1157 |
| methoxide ion (MeOH) | 1.1 | $3.1 \times 10^{-3}$ | 347 |
| piperidine (MeOH) | 3.2 | | |
| morpholine (MeOH) | 0.90 | | |
| *n*-butylamine (MeOH) | 0.43 | | |
| *n*-propylamine (MeOH) | 0.37 | | |
| glycine ethyl ester (MeOH) | $9.4 \times 10^{-2}$ | | |
| 2,2,2-trifluoroethylamine (MeOH) | $6.4 \times 10^{-3}$ | | |
| methoxylamine (MeOH) | $1.3 \times 10^{-2}$ | | |

[a] At 25.0 ± 0.1 °C and ionic strength of 0.10 M.

spectra confirmed the expected reaction scheme. The identity of the benzoylacetaldehyde enolate intermediate was further confirmed from the spectral changes on acidification of a partially reacted solution as compared to those of an authentic sample of benzoylacetaldehyde.

The experimental conditions utilized for the study of the reactions are summarized in Table I.

## Results

**Reactions of Primary Amines.** Under the conditions employed for the reactions of amines, the pH of the solutions was sufficiently low that the reactions of hydroxide or methoxide ion were negligible. The reactions followed good pseudo-first-order kinetics and cleanly produced the corresponding enamines as products.[4] Variation of the buffer ratio in the reactions of *n*-propylamine and of *n*-butylamine with MeOAcr in both water and methanol produced no deviations from linear dependence of rate on amine concentration. The second-order rate constants reported in Table II were calculated by division of the pseudo-first-order rate constants by the amine concentration and showed precision of better than ±10% in all cases.

**Reactions of Secondary Amines.** The reactions of morpholine and of piperidine with both MeOAcr and MeSAcr exhibited good pseudo-first-order kinetics with clean production of the enamines. The pseudo-first-order rate constants were not, however, proportional to amine concentrations. In the reactions of morpholine, the deviations of the calculated second-order rate constants were only slightly outside of expected experimental error, with a clear trend toward smaller values at the lowest concentrations of amine used. For the piperidine reactions, the second-order rate constants showed the behavior expected of a change in rate-determining step of the reaction from amine attack, at high amine concentrations, to proton transfer, at low amine concentrations, as found by Fedor[12] for the reaction of morpholine with *trans*-4-(*p*-methoxyphenoxy)-3-buten-2-one. The double-reciprocal plot of second-order rate constant vs. amine concentration[12] was accurately linear for the reactions with MeOAcr in both water and methanol ($r$ = 0.999 and 0.982, respectively) and with MeSAcr in water ($r$ = 0.991). The slopes and intercepts of the plots gave values of $k_a$ and $k_{-a}/k_b$ for the Scheme I as follows: MeOAcr in water, $k_a$ = 40.9 $M^{-1}$ $s^{-1}$, $k_{-a}/k_b = 2.65 \times 10^{-3}$ M; MeOAcr in methanol, $k_a$ = 3.25 $M^{-1}$ $s^{-1}$, $k_{-a}/k_b = 1.64 \times 10^{-4}$ M; MeSAcr in water, $k_a$ = 0.630 $M^{-1}$ $s^{-1}$, $k_{-a}/k_b = 3.14 \times 10^{-3}$ M. The values of $k_a$ thus obtained are those reported in Table II.

**Scheme I**

$$\mathrm{PhCOCH{=}CHX + R_2NH} \underset{k_{-a}}{\overset{k_a}{\rightleftharpoons}} \mathrm{PhCOCH^-{-}CHXNR_2H^+}$$

$$\mathrm{PhCOCH^-{-}CHXNR_2H^+ + R_2NH} \xrightarrow{k_b} \text{products}$$

**Reactions of Methoxylamine and Semicarbazide.** The reactions of methoxylamine with both MeOAcr and MeSAcr produced the ω-oxime of benzoylacetaldehyde in clean reactions which were first-order with respect to both acrylophenone and nucleophile. The second-order rate constants were calculated by division of the pseudo-first-order rate constants by the nucleophile concentrations and were precise to better than +10%.

The reaction of semicarbazide with MeSAcr produces the disemicarbazone of benzoylacetaldehyde cleanly, and the kinetics are accurately first-order with respect to both MeSAcr and semicarbazide. The second-order rate constant was calculated by division of the pseudo-first-order rate constants by semicarbazide concentrations and was precise to better than ±10%.

As discussed in the Experimental Section, the reaction of semicarbazide with MeOAcr produces the ω-semicarbazone which is further converted to the disemicarbazone of benzoylacetaldehyde under the experimental conditions utilizing semicarbazide buffer. Pseudo-first-order rate constants calculated from the data obtained before appreciable appearance of the disemicarbazone showed the expected dependence on semicarbazide concentration, and the derived second-order constants were precise to better than ±10%.

**Reactions of Hydroxide Ion.** The reaction of hydroxide ion with MeOAcr exhibited good pseudo-first-order kinetics and the reaction cleanly produced the enolate of benzoylacetaldehyde under the reaction conditions employed. Rate constants were proportional to hydroxide ion concentration, and the derived second-order rate constants were precise to better than ±10%. The value obtained, 0.61 $M^{-1}$ $S^{-1}$ at 25 °C and ionic strength 0.1 M, is in reasonable accord with the value of 0.31 $M^{-1}$ $s^{-1}$ reported[4] for reaction at 30 °C and ionic strength 1.0 M.

The reaction of hydroxide ion with MeSAcr is complicated by the conversion of the initial product, benzoylacetaldehyde enolate, into acetophenone and formate ion at a rate comparable to the initial reaction. Pseudo-

(12) P. A. Lartey and L. Fedor, *J. Am. Chem. Soc.*, **101**, 7385 (1979).

first-order rate constants were calculated from the reactions at the lower hydroxide concentrations shown in Table I by using data for early stages of reaction before appreciable hydrolysis of the initial product. The calculated second-order rate constants were precise to better than ±10%. A further check was carried out by analysis of the spectra during reaction of 0.5 M hydroxide ion to determine the concentrations of all three absorbing species as functions of time. The disappearance of MeSAcr followed pseudo-first-order kinetics and the calculated second-order rate constant was only slightly lower than that obtained at the lower ionic strength, as expected.

**Reactions of Methoxide Ion and Cyanide Ion.** These reactions showed simple spectral changes consistent with addition across the double bond. The reactions followed good pseudo-first-order kinetics with the rate constants proportional to nucleophile concentrations. Second-order rate constants were precise to better than ±10%.

All rate constants obtained in the present study are reported in Table II.

## Discussion

The present data for the reactions of primary amines with MeOAcr and with MeSAcr are quite similar to that reported by Fedor[4] for reactions with the *p*-(dimethylamino)-substituted MeOAcr. For both the MeOAcr and MeSAcr reactions, the Brønsted slopes are ca. 0.4 as compared to 0.37 reported by Fedor. The behavior of the reactions of piperidine with MeOAcr and with MeSAcr, showing a change in rate-determining step with concentration of amine, provides strong evidence for the addition–elimination mechanism which Fedor proposed for these[4] an similar[12] reactions. The fact that MeOAcr is more reactive than MeSAcr toward all of the amines is also in accord with the addition–elimination mechanism since any appreciable bond-breaking to the leaving group should favor MeSAcr over MeOAcr.

In this last regard, the present data also support the conclusion[4] that the reaction of hydroxide ion proceeds with rate-determining attack of hydroxide on the double bond. This is somewhat surprising since, in the case of MeOAcr, one might expect methoxide ion to be a poorer leaving group than hydroxide ion.[13] If this were true, we should have expected that the rate ratio for the reaction of hydroxide ion with MeOAcr and MeSAcr would be smaller than for the reactions of amines and perhaps that MeSAcr would be more reactive than MeOAcr. As shown in Table II, the data are not in accord with this expectation; the rate ratio is actually larger for hydroxide reactions than for the amine reactions.

The reactions of cyanide ion, methoxide ion, semicarbazide, and methoxylamine with MeOAcr and MeSAcr give products in which the 2-carbon is protonated. The kinetics of these reactions, with the second-order rate constants having no dependence on buffer concentration, and the greater reactivity of MeOAcr than of MeSAcr indicate that the rate-determining step is the attack of the nucleophile.

The last column of Table II shows clearly that the change from $OCH_3$ to $SCH_3$ groups attached to the electrophilic center significantly changes the relative reactivities of the nucleophiles in the present reactions. The hydroxide/methoxylamine rate constant ratio changes from 22 for MeOAcr to 0.3 for MeSAcr, the largest variation shown. We can offer no rationalization of these changes, but note that they are not in accord with polarizability arguments.[14] The MeOAcr/MeSAcr rate ratio is essentially the same for the polarizable cyanide ion as for the less polarizable amines or methoxide ion.

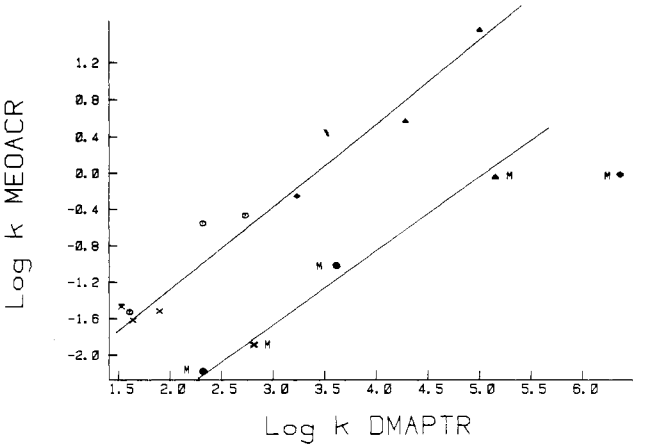



**Figure 1.** Plot for reactions of nucleophiles with MeOAcr vs. those with [*p*-(dimethylamino)phenyl]tropylium cation. The points marked with "M" are for methanol solution.

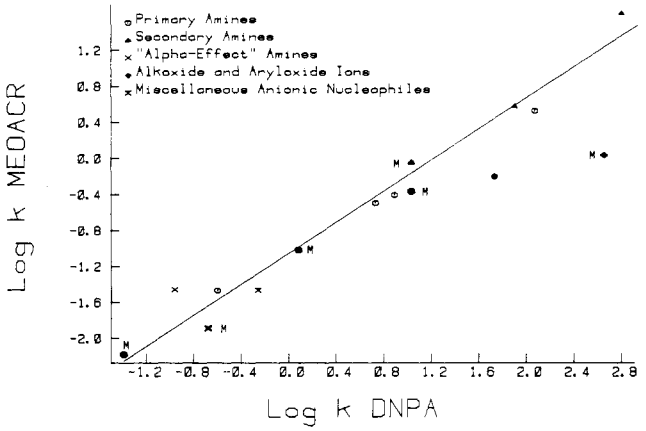



**Figure 2.** Plot for reactions of nucleophiles with MeOAcr vs. those with (2,4-dinitrophenyl)acetate. The points marked with an "M" are for methanol solution.

The change of solvent from water to methanol also changes the relative reactivities of nucleophiles toward MeOAcr as compared with other electrophiles studied in earlier work.[1] The data for reactions of MeOAcr vs. those of the [*p*-(dimethylamino)phenyl]tropylium ion are shown in figure 1. The dispersion of the data into separate lines for the two solvents is similar to, but more pronounced than, that seen in our earlier study of nucleophilic aromatic substitution reactions.[6] Figure 2 exhibits the data for reactions of MeOAcr vs. those of 2,4-dinitrophenylacetate.[15,16] In this latter case, the similarity of the relative reactivities in the two solvents is quite striking and must be due to similarities in the transition states for the reactions (i.e., Fedor's "vinylogous ester" analogy[4,12] for these

(13) In fact, cases can be found in which methoxide is a better leaving group than is hydroxide [C. K. Sauers, W. P. Jencks, and S. Groh, *J. Am. Chem. Soc.*, **97**, 5546 (1975)] or a poorer one [L. H. Funderburk, L. Aldwin, and W. P. Jencks, *ibid.*, **100**, 5444 (1978)].

(14) G. Bartoli and P. E. Todesco, *Acc. Chem. Res.*, **10**, 125 (1977), and earlier work cited therein.

(15) The data for the aqueous solution are from W. P. Jencks and M. Gilchrist, *J. Am. Chem. Soc.*, **90**, 2622 (1968).

(16) The data for reactions of nucleophiles with 2,4-dinitrophenyl acetate in methanol solution were obtained in our laboratories by Mr. D. W. Hamp. The reactions were followed by the production of the aryloxide ion, and the techniques used were analogous to those reported in ref 6 above. For the reactions at 25.0 °C and an ionic strength of 0.01 M, the logarithms of the rate constants ($M^{-1}$ $s^{-1}$) are as follows: *n*-$BuNH_2$, 1.03; ethyl glycinate, 0.08; $CF_3CH_2NH_2$, −1.39; morpholine, 1.03; methoxylamine, −0.68; $CH_3O^-$ 2.65.

types of reactions). It should be noted, however, that this similarity does not apply in the comparison of MeOAcr/MeSAcr vs. oxy ester/thioester reactivities since the thioesters are generally somewhat more reactive than the corresponding oxy esters.[17]

**Acknowledgment.** This work was supported by grants from the National Institutes of Health, Public Health Service (GM 12832), and from the National Science Foundation (CHE77-24701A).

(17) For example, see D. J. Hupe and W. P. Jencks, *J. Am. Chem. Soc.*, **99**, 451 (1977).

**Registry No.** *trans*-3-Methoxyacrylophenone, 40685-20-9; *trans*-3-(methylthio)acrylophenone, 79134-84-2; (*trans*)-3-chloroacrylophenone, 15724-86-4; piperidine, 110-89-4; morpholine, 110-91-8; propylamine, 107-10-8; glycine ethyl ester, 459-73-4; ethylenediamine $H^+$, 26265-69-0; 2,2,2-trifluoroethylamine, 753-90-2; methoxylamine, 67-62-9; semicarbazide, 57-56-7; cyanide ion, 57-12-5; hydroxide ion, 14280-30-9; methoxide ion, 2143-68-2; butylamine, 109-73-9.

# Mechanistic Evidence regarding the Magnesium Halide Transformation of Cyclopropylmethanols into Homoallylic Halides

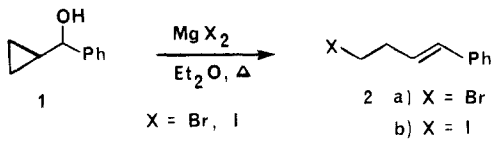
J. P. McCormick,* Alan S. Fitterman, and Donald L. Barton

*Department of Chemistry, University of Missouri, Columbia, Missouri 65211*

*Received July 21, 1981*

Cyclopropylmethanols are converted into homoallylic halides in high yield by treatment with magnesium bromide or iodide in refluxing, anhydrous diethyl ether. For uncovering of the details of the reaction mechanism, (cyclopropylphenylmethoxy)magnesium bromide (**3a**) was prepared by treatment of cyclopropylphenylmethanol (**1**) with hydridomagnesium bromide. Alkoxymagnesium bromide **3a** was stable in refluxing diethyl ether and was not changed when treated with tetrabutylammonium bromide but was transformed into 4-bromo-1-phenyl-1-butene by treatment with hydrogen bromide or magnesium bromide. These results, together with first-order kinetics for the reaction of magnesium halide with 1, suggest a mechanism involving rapid formation of an intermediate ion pair (**4**), a magnesium oxonium bromide, which undergoes rate-determining ring opening to give homoallylic halide. A Hammett study of the reaction of substituted cyclopropylphenylmethanols with magnesium iodide provided a $\rho$ value of −1.82, revealing substantial positive charge development on the carbinol carbon in the latter step. This investigation provides one of only a very few reported examples of Hammett studies used to probe positive charge development for a reaction carried out in anhydrous diethyl ether.

Since the early development by Julia of the hydrogen bromide promoted opening of cyclopropylmethanols as a method for the preparation of homoallylic bromides[1] and the modification by Johnson which involves intermediate formation of cyclopropylmethyl bromides,[2] this methodology has become a common route to homoallylic bromides. More recently, it has been found that cyclopropylmethanols are transformed into homoallylic bromides or iodides by treatment with the corresponding magnesium halide in refluxing, anhydrous diethyl ether.[3] The salient




(1)

features of this efficient synthetic transformation can be summarized: generally, the homoallylic halide is the sole isolated product; the relative rates of reaction of the alcohols follow the order of the expected stabilities of the carbocations at the carbinol carbon; generally, the relative rates of reaction of a given alcohol with the various magnesium halides follows the order iodide > bromide > chloride, an order which parallels the relative nucleophilicities of the halides but is opposite to the probable relative acidities of the reagents; additional halide, added as tetrabutylammonium iodide, has no effect on the rate of reaction.

Related chemistry has been reported, including the alkylation and subsequent opening of cyclopropyl ketones when treated with Grignard reagents under certain conditions,[4] an outcome which was plausibly envisioned as a ring-opening reaction of intermediate (cyclopropylmethoxy)magnesium halides (**3**).[5] Other reactions which involve use of magnesium halides to accomplish carbon–halogen bond formation together with carbon–oxygen bond cleavage include conversion of alkyl tosylates into iodides by magnesium iodide[6] and the action of the latter on propargyl acetates to give mixtures of iodides which include iodoallenes.[7] As well, the action of magnesium bromide on cyclic ethers can lead to ring opening with bromide displacement of oxygen, as in the case of oxiranes[8] or functionalized oxiranes,[9] and cyclic ethers can be effectively transformed into acyclic bromoacetates by magnesium bromide in acetic anhydride.[10]

(1) (a) Julia, M.; Julia, S.; Guegan, R. *Bull. Soc. Chim. Fr.* **1960**, 1072. (b) Julia, M.; Descoins, C.; Risse, C. *Tetrahedron Suppl.* **1966**, *8*, 443. (c) Julia, M.; Paris, J.-M. *Tetrahedron Lett.* **1974**, 3445.

(2) (a) Brady, S. F.; Ilton, M. A.; Johnson, W. S. *J. Am. Chem. Soc.* **1968**, *90*, 2882. (b) Johnson, W. S.; Li, T.; Faulkner, D. J.; Campbell, S. F. *Ibid.* **1968**, *90*, 6225.

(3) McCormick, J. P.; Barton, D. L. *J. Org. Chem.* **1980**, *45*, 2566.

(4) Yovell, J.; Sarel-Imber, M.; Sarel, S. *Isr. J. Chem.* **1966**, *4*, 21p.

(5) Sarel, S.; Yovell, J.; Sarel-Imber, M. *Angew.* Chem., *Int. Ed. Engl.* **1968**, *7*, 577.

(6) Gore, J.; Place, P.; Roumestant, M. L. *J. Chem. Soc., Chem. Commun.* **1973**, 821.

(7) Coulomb, F.; Gore, J. *J. Organomet. Chem.* **1975**, *87*, C23.

(8) Cope, A. C.; Hecht, J. K. *J. Am. Chem. Soc.* **1962**, *84*, 4872.

(9) (a) Hudrlik, P. F.; Misra, R. N.; Withers, G. P.; Hudrlik, A. M.; Rona, R. J.; Arcoleo, J. P. *Tetrahedron Lett.* **1976**, 1453. (b) de Reinach-Hirtzbach, F.; Durst, T. *Ibid.* **1976**, 3677.

(10) Goldsmith, D. J.; Kennedy, E.; Campbell, R. G. *J. Org. Chem.* **1975**, *40*, 3571.

0022-3263/81/1946-4708$01.25/0 