*Tetrahedron* Vol 27, pp. 2651 to 2669. Pergamon Press 1971. Printed in Great Britain

# NUCLEOPHILIC SUBSTITUTION AT AN ACETYLENIC CARBON

## COMPETING PROCESSES IN THE REACTIONS OF SODIUM METHOXIDE WITH PHENYLBROMOACETYLENE OR PHENYLCHLOROACETYLENE IN METHANOL*

R. TANAKA, M. RODGERS, R. SIMONAITIS,† and S. I. MILLER‡

Contribution from the Department of Chemistry, Illinois Institute of Technology, Chicago, Illinois 60616

(*Received in USA* 22 *February* 1971; *Received in the UK for publication* 16 *March* 1971)

**Abstract**—Phenylhaloacetylenes are triphilic towards methoxide ion in methanol. With phenylchloroacetylene (**1'**), methoxide attacks ~0·2% on chlorine, ~99% on carbon 1, and ~1% on carbon 2; with phenylbromoacetylene (**1**), methoxide attacks ~5% on bromine, ~83% on carbon 1, and ~11% on carbon 2. The first detectable products, phenylacetylene, phenylmethoxyacetylene (**2**), (**E**)-β-bromo-β-methoxystyrene, and (**Z**)-β-bromo-α-methoxystyrene lie on discrete mechanistic paths and are not interconvertible under the reaction conditions. Comparable amounts of alkynyl and alkenyl ethers are formed by attack on carbon 1. The element effects for attack on halogen, $k(Cl)/k(Br) \simeq 0{\cdot}4$, and on carbon 1, $k(Cl)/k(Br) \simeq 1\,6$ are consistent with the notion of independent competing processes. Phenylmethoxyacetylene is a short-lived transient; its formation and decay (with methoxide) rate constants at 78° are $k_{1\cdot2}$ (Cl) $0{\cdot}6 \times 10^{-4}$ or $k_{12}$ (Br) $0{\cdot}5 \times 10^{-4}$ and $k_{2l}$ $1{\cdot}7 \times 10^{-3}\,M^{-1}\,sec^{-1}$. Previously, the intermediacy of alkoxyacetylenes under analogous conditions has only been surmised. In the course of this work, five of the six bromomethoxystyrenes were prepared and some of their distinctive chemistries, as well as those of the corresponding carbonyl compounds, were worked out (eq 2–4).

IT is well known that nucleophilic substitution at certain unsaturated carbon centers, alkene, alkyne, and aryl can often be difficult. Success with several nucleophiles has been reported from several laboratories.[1,2] In this work, the feasibility of nucleophilic substitution by alkoxide at an sp carbon site was explored.

$$C_6H_5C{\equiv}CX + RO^- \rightarrow C_6H_5C{\equiv}COR + X^- \qquad (1)$$

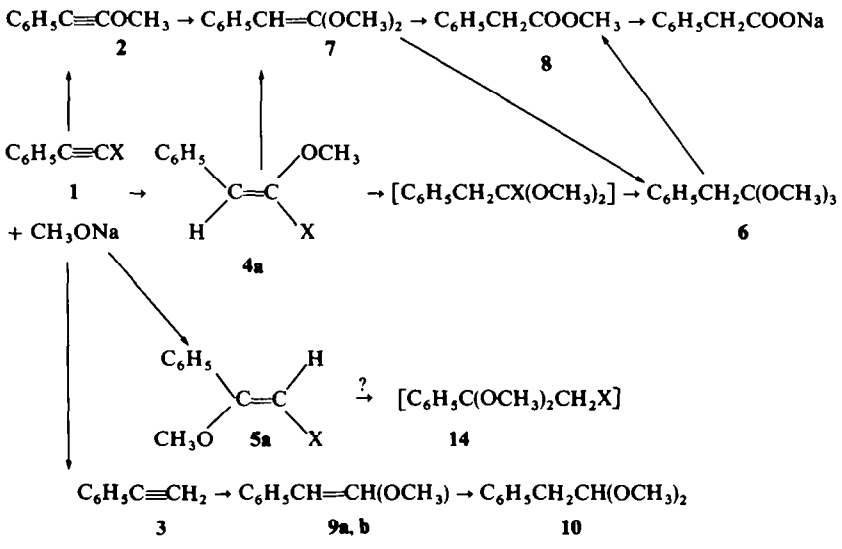
Heretofore, the syntheses of alkoxyalkynes have usually involved routes leading through β-halovinylethers.[3] Process 1, however, does seem to be the last step in a sequence in which fluorochloroalkenes react with alkoxides to form ethynyl ethers.[3,4] As indicated in Scheme 2, we have found that reaction 1 was only one of several that had to be considered for the systems we chose. Nevertheless, the possibility of process 1 was established, rate data for the first steps in Eq. 2 were obtained, and the fate of several intermediates could be described. In the course of working out the timing of the various steps, we also investigated the possible links of the halomethoxystyrenes (**4**, **5**) to related compounds. In the bromo series, these are given in Eqs. 3 and 4.

Literature on the reactions of oxygen nucleophiles with haloalkynes is limited.

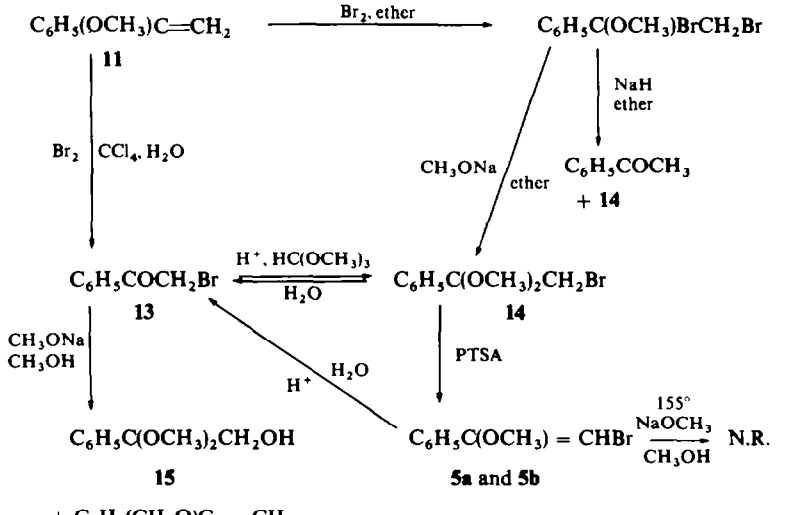
* This research was supported by the National Institutes of Health grant GM 07021, abstracted in part from the Ph.D. thesis of R.T., and presented at the 159th ACS Meeting, Houston, Texas, February, 1970, ORGN 119.

† National Science Foundation Undergraduate Research Participant

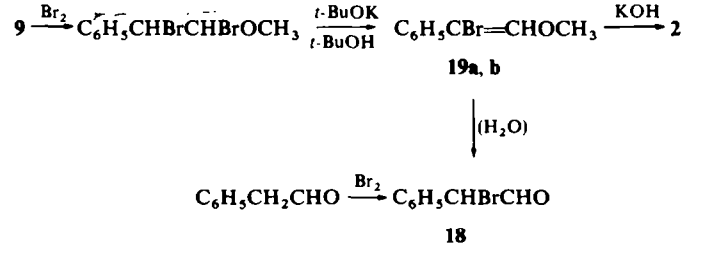
‡ Author to whom inquiries should be addressed.


C6H5C≡COCH3 → C6H5CH=C(OCH3)2 → C6H5CH2COOCH3 → C6H5CH2COONa
2
7
8
C6H5C≡CX
1
+ CH3ONa
C6H5
OCH3
C=C
H
X
4a
→ [C6H5CH2CX(OCH3)2] → C6H5CH2C(OCH3)3
6
C6H5
H
C=C
CH3O
5a
X
?
[C6H5C(OCH3)2CH2X]
14
C6H5C≡CH2 → C6H5CH=CH(OCH3) → C6H5CH2CH(OCH3)2
3
9a, b
10

(2)


C6H5(OCH3)C=CH2
11
Br2, ether
C6H5C(OCH3)BrCH2Br
NaH
ether
Br2
CCl4, H2O
CH3ONa
ether
C6H5COCH3
+ 14
C6H5COCH2Br
13
H+, HC(OCH3)3
H2O
C6H5C(OCH3)2CH2Br
14
CH3ONa
CH3OH
H+
H2O
PTSA
C6H5C(OCH3)2CH2OH
15
C6H5C(OCH3) = CHBr
5a and 5b
155°
NaOCH3
CH3OH
N.R.
+ C6H5(CH3O)C——CH2
O
16

(3)


9
Br2
C6H5CHBrCHBrOCH3
t-BuOK
t-BuOH
C6H5CBr=CHOCH3
19a, b
KOH
2
(H2O)
C6H5CH2CHO
Br2
C6H5CHBrCHO
18

(4)

Indeed, a useful route *to* the haloalkynes requires strong base and a source of positive halogen.[2] An index of the low reactivity of haloalkynes and hydroxide ion is found in the following observation: when 1-bromo-1-heptyne was heated with hydroxides of silver, lead or calcium in various solvents at *ca.* 310° for several days in an auto-

$$R{-}C{\equiv}CH \underset{H^+}{\overset{OH^-}{\rightleftharpoons}} R{-}C{\equiv}C^- \xrightarrow[OH^-]{X_2 \text{ or } HOX} R{-}C{\equiv}C{-}X \qquad (5)$$

clave, *ca.* 50% of the starting material, somewhat purified by the treatment, could be recovered.[5] When heated with alcohol–alkoxide, haloalkynes show an interesting crossover in mechanism:[4, 6, 7] the upper branch of Eq. 6 is simple addition and the lower branch of Eq. 6 is the reverse of Eq. 5. The detailed description of Scheme 2, of which Eqs. 1, 5, and 6 are just parts, is the major theme of this paper.

$$R{-}C{\equiv}C{-}X \xrightarrow[C_2H_5OH]{C_2H_5O^-} \begin{cases} \xrightarrow{X = Cl, Br} RCH = C(X)OC_2H_5 + RCH_2COOR' \\ \xrightarrow{X = Br, I} RC{\equiv}C{-}H \end{cases} \qquad (6)$$

## EXPERIMENTAL

IR spectra were obtained with a Beckman IR 8 spectrophotometer. NMR spectra were taken on a Varian A 60 instrument with TMS as an internal reference. A Varian MAT CH7 spectrometer was used to obtain mass spectra.

*Materials.* A stock NaOMe soln was prepared under $N_2$ from freshly-cut Na, and washed with hexane and then MeOH.

Most of the compounds required in this study were known. Additional novel procedures or new compounds are described below. IR and NMR spectral data were particularly useful for screening and characterization of our product mixtures. Confirmation of components of a mixture was usually performed by adding an authentic sample and checking for an increase in the intensity of relevant NMR peaks. Key spectral data, which supplement but do not overlap the following sections, as well as citations for preparative methods and physical properties, are given in Table 1.

*α-Bromo-β-methoxystyrenes* (**19**). These were prepared from **9** by $Br_2$ addition followed by dehydrobromination[8] and had bp 84–90° (0·5 nm). Traces of a contaminant, **18**, were removed by chromatography on alumina. The bromoether mixture had $n_D^{20}$ 1·5889 (lit[8] $n_D^{25}$ 1·585–1·590); IR (neat) 1645 (C=C), 1447, 1265, 1127, 1012, 883, 765, and 700 $cm^{-1}$; NMR (neat) $\delta$ for **E** 3·55 ($OCH_3$) and 6·82 (=C<u>H</u>$OC_3$), and for **Z** 3·42 ($OCH_3$) 6·66 (=C<u>H</u>$OCH_3$). These bromoethers were readily converted to **18**, when exposed to the atmosphere for a day.

*Phenylmethoxyacetylene* (**2**). Dehydrobromination of **19** gave **2** in *ca* 20% yield.[9] Further purification yielded a sample which still contained *ca* 5% of **8** and had bp 38° (0·1 mm) $n_D^{25}$ 1·5510 (lit.[9] $n_D^{25}$ 1·5481); IR (neat) 1065 $cm^{-1}$; NMR (neat), $\delta$ 3·63 (C<u>H</u>$_3$) and 6·85–7·45 ($C_6$<u>H</u>$_5$).

*α-Bromophenylacetaldehyde* (**18**) *from β-methoxystyrene dibromide* (**9**). An ethereal soln of the dibromide prepared from **9** (43·5 g),[9] was added dropwise to a stirred suspension of pulverized KOH (1·2 mole) in refluxing ether (1·2 l). After work-up and two fractional distillations, **18** (*ca* 25 g), bp 55–57° (0·3 mm), was obtained.

*α-Bromoacetophenone dimethylketal* (**14**). α-Bromoacetophenone **13** (19·9 g, 0·1 mole) and trimethyl orthoformate (11 g, 0·104 mole) was refluxed in abs MeOH (50 g) in the presence of small amount of *p*-toluenesulfonic acid (PTSA) for 24 hr. The mixture was made slightly alkaline toward phenolphthalein with methanolic NaOMe and MeOH was removed under vacuum at ~25°. Slightly grayish ketal was obtained in almost quantitative yield; this almost pure ketal was used directly in further syntheses. On recrystallization from MeOH–water, the ketal reverted in part to **13**, mp 50°. Sublimation (0·25 mm) of the crude ketal gave white crystals of **14**: mp 46·0 ~ 46·9° (new compound); IR (KBr) 1448, 1285, 1207, 1150, 1127, 1070, 1030 (vs), and 968 $cm^{-1}$; NMR ($CCl_4$) $\delta$ 3·18 (s, 6H), 3·53 (s, 2H, –C<u>H</u>$_2$Br) and 7·35 ~ 7·55 (m, 5H).

*α-Methoxy-β-bromostyrenes* (**5**). Crude **14** (8 g) in tetraethyleneglycol dimethyl ether was refluxed under vacuum for 11 hr in the presence of a catalytic amount of PTSA. MeOH (1 equiv) was eliminated from the

TABLE 1. SPECTRAL DATA FOR COMPOUNDS OF THIS STUDY AND A TEST OF A PMR CORRELATION (Eq 15)

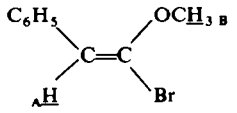
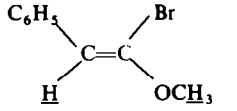
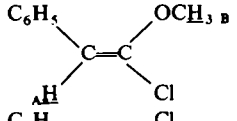
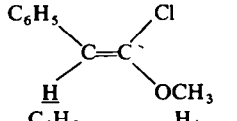
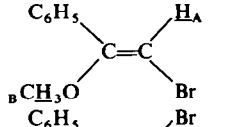
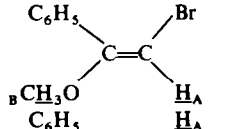
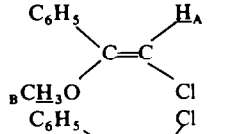
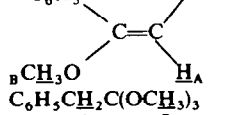
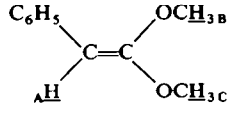
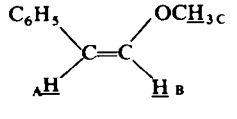
| No.[a] | Compound | $\delta_{obs}$ ($J$, Hz),[b] ppm | $\delta_{calc}$, ppm[c] | $\delta_{calc} - \delta_{obs}$ | ir, $cm^{-1}$[d] | Ref.[e] |
|---|---|---|---|---|---|---|
| **1** | $C_6H_5C{\equiv}CBr$ | | | | 2220 | *f* |
| **1′** | $C_6H_5C{\equiv}CCl$ | | | | 2210 | *g* |
| **2** | $C_6H_5C{\equiv}COCH_3$ | 3·89 | | | 2275, 2225 | *h* |
| **3** | $C_6H_5C{\equiv}CH$ | 2·92 | | | 3300, 2105 | *i* |
| **4a** |  | A 5·87<br>B 3·69 | 5·87 | 0·00 | | *j* |
| **4b** |  | | 6·11 | | | |
| **4′a** |  | A 5·68<br>B 3·81 | 5·60 | −0·08 | 1643, 1071 | *j* |
| **4′b** |  | | 5·74 | | | |
| **5a** |  | A 5·79<br>B 3·59 | 5·47 | −0·32 | | *j* |
| **5b** |  | A 5·43<br>B 3·66 | 5·18 | −0·25 | | *j* |
| **5′a** |  | A 5·79<br>B 3·61 | 5·48 | −0·31 | | *j* |
| **5′b** |  | A 5·50<br>B 3·61 | 5·19 | −0·31 | | *j* |
| **6** |  | A 2·96<br>B 3·21 | | | 1240, 1152, 1092, 1014, 1000 | *k* |
| **7** |  | A 4·65<br>B 3·61<br>C 3·69 | 4·35 | −0·30 | 1651 | *l* |
| **8** | $C_6H_5CH_2CO_2CH_3$ | A 3·51<br>B 3·62 | | | 1725 | |
| **9a** |  | A 5·10 (d, 7·1)<br>B 5·90 (d, 7·1)<br>C 3·48 | 5·42<br>6·40 | 0·32<br>0·50 | | *m, n* |

TABLE 1—*Continued*

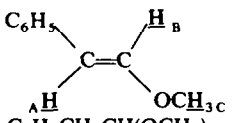
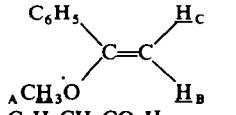
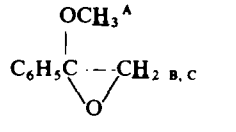
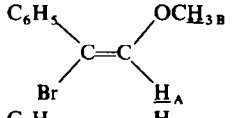
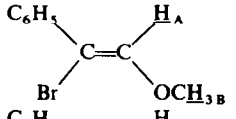
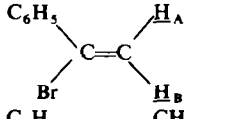
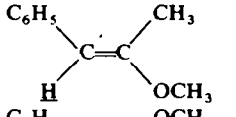
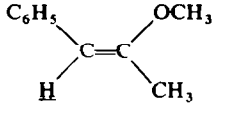
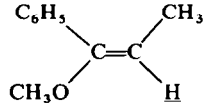
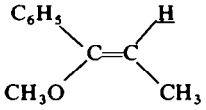
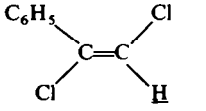
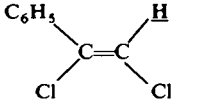
| No.[a] | Compound | $\delta_{obs}$ ($J$, Hz),[b] ppm | $\delta_{calc}$, ppm[c] | $\delta_{calc} - \delta_{obs}$ | ir, $cm^{-1}$[d] | Ref.[e] |
|---|---|---|---|---|---|---|
| **9b** |  | A 5·68 (d, 13·0)<br>B 6·91 (d, 13·0)<br>C 3·48 | 5·56<br>6·83 | −0·12<br>−0·08 | | [n] |
| **10** | $C_6H_5C\underset{A}{H_2}C\underset{B}{H}(O\underset{C}{CH_3})_2$ | A 2·77 (d, 5·8)<br>B 4·39 (d, 5·8)<br>C 3·20 | | | | [n] |
| **11** |  | A 3·54<br>B 3·94 (d, 2·55)<br>C 4·39 (d, 2·55) | 4·11<br>4·40 | 0·17<br>0·01 | 1640 | [n, o] |
| **12** | $C_6H_5C\underset{A}{H_2}CO_2\underset{B}{H}$ | A 3·56<br>B 11·97 | | | 3300, 1695 | |
| **13** | $C_6H_5COC\underset{}{H_2}Br$ | 4·11 | | | 1710, 1690 | |
| **13′** | $C_6H_5COC\underset{}{H_2}Cl$ | 4·53 | | | | |
| **14** | $C_6H_5C(O\underset{A}{CH_3})_2C\underset{B}{H_2}Br$ | A 3·18<br>B 3·53 | | | | [j] |
| **14′** | $C_6H_5C(O\underset{A}{CH_3})_2C\underset{B}{H_2}Cl$ | A 3·15<br>B 3·64 | | | | [j] |
| **15** | $C_6H_5C(O\underset{A}{CH_3})_2C\underset{B}{H_2}O\underset{C}{H}$ | A 3·21<br>B 3·65<br>C 1·2 | | | 3460, 1150,<br>1085, 1045 | [j, p] |
| **16** |  | A 3·14<br>B 4·39 (d, 9·5)<br>C 4·26 (d, 9·5) | | | | [j, p] |
| **17** | $C_6H_5C(O\underset{A}{CH_3})_2C\underset{B}{H}Br_2$ | A 3·31<br>B 5·84 | | | 1095, 1041<br>713 | [q] |
| **18** | $C_6H_5C\underset{A}{H}BrC\underset{B}{H}O$ | A 5·14 (d, 3·7)<br>B 9·41 (d, 3·7) | | | 1726 | [k, r] |
| **19a** |  | A 6·60 (6·52)<br>B 3·59 (3·48) | 6·85 | 0·25 (0·33) | | [k, s] |
| **19b** |  | A 6·52 (6·60)<br>B 3·48 (3·59) | 7·38 | 0·86 (0·78) | | [k, s] |
| |  | A 6·04<br>B 5·71 | 6·16<br>5·63 | 0·12<br>−0·08 | | [j, t] |
| |  | 5·32 | 5·22 | −0·10 | | [u] |
| |  | 5·50 | 5·17 | −0·33 | | [u] |

TABLE 1—*Continued*

| No.[a] | Compound | $\delta_{obs}$ ($J$, Hz),[b] ppm | $\delta_{calc}$, ppm[c] | $\delta_{calc} - \delta_{obs}$ | ir.cm$^{-1}$[d] | Ref.[e] |
|---|---|---|---|---|---|---|
| |  | 4·69 | 4·56 | −0·13 | | [v] |
| |  | 5·22 | 4·85 | −0·37 | | [v] |
| |  | 6·45 | 6·37 | −0·08 | | [w] |
| |  | 6·63 | 6·68 | 0·05 | | [w] |

[a] Compounds **2–8** and **12**, but not **5b**, were present in the phenylbromoacetylene-methoxide product mixtures. Chloro analogs of the bromo compounds are assigned primed numbers. Substituted styrenes following **19** are listed for the test of PMR correlation and are not directly related to the mechanistic discussions. [b] PMR spectra were taken on *ca* 10% solutions in $CCl_4$. [c] Group contributions were taken from Ref. 35. When bromine is *cis* to phenyl, the "tilted phenyl" values in Ref. 36 were used. [d] Neat liquid film spectra, except for solid compounds for which KBr tablets were used. [e] Citation for previous preparation and some properties. [f] S. I. Miller, G. R. Ziegler, and R. Wielesek, *Org. Syn.* **45**, 86 (1965). [g] Ref. 6. [h] Ref. 8, 9. [i] J. C. Hessler, *Org. Syn.* Coll. Vol. **1**, 438 (1941). [j] This study. [k] S. M. McElvain and C. L. Stevens, *J. Am. Chem. Soc.* **68**, 1917 (1946). [l] S. M. McElvain and J. T. Venerable, *Ibid.* **71**, 1668 (1950); J. E. Baldwin and L. E. Walker, *J. Org. Chem.* **31**, 3985 (1966). [m] R. Huisgen, L. Möbius and G. Szeimies, *Chem. Ber.* **98**, 1147 (1965). [n] Ref. 16. [o] S. Winstein and L. L. Ingraham, *J. Am. Chem. Soc.* **77**, 1738 (1955). [p] Ref. 11. [q] Ref. 13. [r] H. Erlenmeyer, C. Becker, E. Sorkin, H. Bloch, and E. Suter, *Helv. Chim. Acta.* **30**, 2058 (1947); P. Z. Bedoukian. *J. Am. Chem. Soc.* **66**, 1325 (1944). [s] S. M. McElvain and M. J. Curry, *Ibid.* **70**, 3784 (1948). Our structural assignment is uncertain. [t] (a) C. A. Grob and G. Cseh, *Helv. Chim. Acta* **47**, 194 (1964); (b) W. Taylor, *J. Chem. Soc.* 343 (1937). [u] A. J. Kresge and H. J. Chen, private communication. [v] G. A. Russell and E. T. Sabourin, *J. Org. Chem.* **34**, 2336 (1969). [w] R. R. Lii, private communication.

ketal and condensed in a dry ice trap. The residue in the flask was distilled: bp 80 ~ 85°/1·5 mm; IR (neat) 1616 (νC=C), 1496, 1448, 1302, 1206, 1124, 1080 (vs), 773, 740 and 700 cm$^{-1}$; mass spectrum *m/e* 214 and 212 $(P)^+$, 169 and 171 $(C_7H_6Br)^+$ 133 $(P - Br)^+$, 118 $(C_8H_7O)^+$, 103 base peak $(C_8H_7)^+$, 90 $(C_7H_6)^+$ and 77 $(C_6H_5)^+$. This isomeric mixture changed into **13** completely when it was exposed to the vapor of hydrochloric acid for 1 min, when a few crystals of PTSA were placed on the liquid film of this mixture, or when the liquid was exposed to laboratory atmosphere for *ca* 12 hr.

*Bromomethoxystyrenes* (**4**, **5**) *from phenylbromoacetylene and sodium methoxide.* Phenylbromoacetylene **1** (36·2 g, 0·2 mole) in NaOMe (2 M) in MeOH (250 ml) was refluxed for 5 hr. The mixture was worked up to give an oil, which was distilled (0·1 mm). Phenylacetylene **3** and most of unreacted **1** went over to the cold trap, while three fractions (47 ~ 55°, 55·5 ~ 57·5°, 58 ~ 64°/0·1 mm) were collected.

The second fraction was chromatographed on alumina (1·5 × 18 cm) with pentane as eluant. **6**, one of the major components, was completely retained in the column. The early fractions of the eluate were found to be almost free of **8** and consisted chiefly of **4a** and **5a**; IR (neat) 1640 (s, νC=C), 1620 (shoulder),

1456, 1075 (vs), 960, 763, 730 and 700 $cm^{-1}$; NMR ($CCl_4$) two sets of methoxyvinylic pairs existed: $\delta$ 3·58 (s, $OCH_3$, **5a**), 3·69 (s, $OCH_3$, **4a**), 5·79 (s, vinylic, **5a**) and 5·87 (s, vinylic, **4a**), **4a**/**5a** = 1·6 based on integration of both methoxy and vinylic proton peaks; mass spectrum *m/e* 212 and 214 (P and P + 2)$^+$ 169 and 171 $(C_7H_6Br)^+$, 118 $(C_8H_7O)^+$ and 103 base peak $(C_8H_7)^+$. Another component was partly eluted with the above two isomers. This component had NMR peaks at $\delta$ 3·18 (s) and 3·50 (s) with intensity 3:1. Judging from its IR and NMR spectra, we tentatively assume this to be **14**. It should be noted that the third component was not observed in small scale preparations.

*α-Methoxystyrene dibromide.* This compound is sensitive to moisture and its preparation must be carried out under anhydrous conditions, i.e. from carefully dried reagents and in baked glassware under $N_2$. To a 3-necked flask (500 ml) containing **11** (20 g, 0·15 mole) in ether (200 ml) and cooled in an ice-water bath, $Br_2$ (24 g) was added over a period of 1·5 hr. The soln was stirred magnetically for another hr. At this point, a 10 ml aliquot was quickly taken and the ether was removed under vacuum. The residual oil had NMR (10% in $CCl_4$) $\delta$ 3·48 ($C\underline{H}_3O$), 4·10 (d, 1H, $J$ = 11·5 Hz, $-C\underline{H}HBr$), and 4·22 (d, 1H, $J$ = 11·5 Hz, $-CH\underline{H}Br$).

*Attempted dehydrobromination of α-methoxystyrene dibromide.* Freshly prepared ethereal soln of α-methoxystyrene dibromide was treated with NaOMe (34 g) in MeOH (200 ml) at *ca* 25° for 4 hr, worked up and distilled. The main fraction (75–80°/0·3 mm) turned out to be **14** contaminated by *ca* 5% of **13**. A second fraction (86–90°/0·35 mm) solidified in the receiver. It turned out to be **13**; mp 49·5–50·2°, from EtOH. Incidentally, if an ether extract of the original crude product was allowed to stand for 2 weeks, **13** was the sole product. When the whole reaction was repeated with NaH and α-methoxystyrene dibromide in dry ether, and water was not used in the work up, substantially the same compounds, **13** and **14**, were detected along with acetophenone. The ease of the formation of α-bromoacetophenone in the addition of bromine to α-alkoxystyrene had previously been noticed in the case of *p*-nitro-α-methoxystyrene.[10]

*The reaction of phenacyl bromide* (**13**) *with sodium methoxide.* Our findings differ from those of previous workers,[11] in part because of differences in the experimental conditions. Phenacyl bromide (9·9 g, 0·05 mole) was refluxed in 2M NaOMe (100 ml) for 36 hr. Work-up yielded an oil which contained two major and several minor products. Fractional distillation gave a colorless cut, 85–90° (0·25 mm) which was further purified by treatment with K in pentane. The most abundant product was identified as **15**: IR (neat) 3460 (OH), 1450, 1300, 1291, 1220, 1200, 1180, 1150, 1085, 1045, and 980; NMR ($CCl_4$), $\delta$ 3·21 ($C\underline{H}_3O$), 3·65 ($C\underline{H}_2OH$), and 1·2–1·8 ($O\underline{H}$); mass spectrum, no $P^+$ (182), 151 $(P—CH_3O)^+$, 119 $(C_8H_7O)^+$, and 105 (base peak, $C_7H_5O)^+$.

Chromatography of the original oil on alumina, with pentane left the above ketal on the column and yielded a somewhat impure sample of the second major component. On the basis of spectral data, we suppose this to be **16**: NMR ($CCl_4$), $\delta$ 3·14 (s, 3, $C\underline{H}_3O$), 4·39, 4·26 (d, 2, $C\underline{H}_2$, $J$ = 9·5 Hz).

*Attempted reaction of α-methoxy-β-bromostyrene* (**5**) *with sodium methoxide.* The isomeric mixture of **5** was subjected to three different treatments. (1) The isomeric pair was mixed with excess methanolic NaOMe (1·8M) at ~25°, and immediately the soln was poured into cold water. (2) The isomeric mixture was refluxed in excess NaOMe (1·8M) in MeOH for 2·5 hr and worked up similarly. (3) The isomeric mixture was mixed with an excess of conc NaOMe (3·9M) and introduced into a pyrex ampule (10 ml) and heated to 155° in an electric furnace for 3·5 hr. All produce mixtures were worked up similarly with water and $CCl_4$. It was found that both isomers (**5**) were very stable toward methanolic NaOMe. In all three cases there was little indication of the consumption of the reactant, nor was there any production of another neutral organic species.

*The reaction of phenylacetylene* (**3**) *with methyl hypobromite.* Methyl hypobromite was prepared by mixing $Br_2$ (3·3 g) with MeOH (75 ml) cooled to 0–3°.[12] Our experiments were intended to simulate the reaction conditions of the phenylbromoacetylene-methoxide system. The hypobromite soln (15 ml) was added to excess **3** (*ca* 0·8 g) in MeOH (10 ml) at *ca* 25°. After 4·5 hr, the soln was worked up (**3** was evaporated off) to give an oily residue. This contained **17** mp 69·1–69·6° (lit.[13] 68–69°) from pentane; IR (KBr) 1493, 1453, 1295, 1095, 1070, 1041, 1030, 988, 776, 755, and 713 $cm^{-1}$. Chromatography of the remaining residues over alumina gave an oil which appeared to be phenylacetylene tetrabromide: IR (neat) 1490, 1448, 1270, 1169, 873, 795, 700, and 684; NMR ($CCl_4$) $\delta$ 6·77 ($C\underline{H}Br_2$) and ~7·4 (m, $C_6\underline{H}_5$); mass spectrum *m/e* 260, 262, and 264 $(P-2Br)^+$. 181 and 183 $(P-3Br)^+$ and 102 (base peak. $P-4Br)^+$. The possibility that this was dibromostyrene was excluded because of the absence of the IR band at 1680 $cm^{-1}$.[14]

Repetition of the previous reaction in the presence of 0·4M NaOMe yielded the same combination of products. In a third experiment, the hypobromite soln was added to a boiling soln of excess **3** in 2M NaOMe methoxide. This time, no neutral products, aside from **3**, were obtained.

*The reaction of phenylbromoacetylene* (**1**) *and methyl hypobromite.* The hypobromite soln (15 ml) was added to a refluxing soln of **1** (1 g) in 2M NaOMe (20 ml). After 4 5 hr, work-up and analysis of the mixture indicated no features that differed from reactions without added hypobromite.

*The reaction of phenylbromoacetylene* (**1**) *with sodium methoxide in methanol.* This system was studied in several ways. A stock soln (100 ml) of **1** and NaOMe in MeOH was distributed as aliquots (10 ml) among ampules. These were sealed, kept in constant temp baths for desired periods, cooled, opened and quenched in water. For bromide analyses, 0·35M AcOH (10 ml) was added to this soln and it was titrated with standard $AgNO_3$. Otherwise, the quenched soln was extracted with light petroleum. The extract (10 ml) was dried over $CaCl_2$ and 1–1·5 μl was analyzed by GLC on a column 5'QFl on firebrick at 100° and a He flow rate of 20 ml/min. The quantities of **3** and **1** were obtained relative to a marker compound, benzyl methyl ether. The retention times were 4·20, 19·70 and 9·28 min respectively. The data are given in Table 2.

TABLE 2. RATE DATA FOR THE APPEARANCE OF BROMIDE AND CONSUMPTION OF PHENYLBROMOACETYLENE IN THE REACTION OF PHENYLBROMOACETYLENE (**1**) WITH SODIUM METHOXIDE IN METHANOL

| $(C_6H_5C{\equiv}CBr)$ M | $(CH_3O^-)$ M | Temp. °C | $k$(Br) × $10^5$ $M^{-1}$ $sec^{-1}$ | $k_{1i}$ × $10^5$ $M^{-1}$ $sec^{-1}$ |
|---|---|---|---|---|
| 0·02018 | 0·2116 | 100·2 | 38·8 | 53·6 |
| 0·02018 | 0·2116 | 100·2 | 38·5 | 64·2 |
| 0 02029 | 0·2116 | 100·2 | 39·8 | 56·0 |
| 0·02018 | 0 2116 | 100·1 | 38·0 | |
| 0·02018 | 0·2116 | 100·3 | 38·5 | |
| 0·004036 | 0·04228 | 100·1 | 42·2 | |
| 0·02018 | 0·2116 | 84·0 | 8·38 | 16·6[a] |
| 0·02018 | 0·2116 | 74 8 | 3·35 | |
| 0·02029 | 0·2116 | 69·2 | 1·89 | |

[a] At 85·85°.

Detailed product studies were made as follows. Typically, **1** (3·6 g) was refluxed in 2M NaOMe in MeOH (50 ml) under $N_2$. Aliquots (5 ml) were removed at intervals and treated with water (10 ml) and spectrograde $CCl_4$ (5 ml). The organic layer was washed 4 times with distilled water, dried with $CaCl_2$, and stored in a capped NMR tube in dry ice until required for analysis. The IR spectrum was taken of the film deposited

TABLE 3. RATE DATA FOR THE REACTION OF PHENYLBROMOACETYLENE (0·3 M), **1**, IN METHANOLIC SODIUM METHOXIDE (1·95 M) AT 78°[a]

| Time, min | $[1]/[1]_0$ | $[2]$ × $10^3$ M | $k_{12}$ × $10^3$ $min^{-1}$ | $[4a]$ × $10^2$ M | $[5a]$ × $10^2$ M | $k_{15}$ × $10^3$ $min^{-1}$ | $[3]$ × $10^{3b}$ M | $k_{13}$ × $10^{5b}$ $min^{-1}$ |
|---|---|---|---|---|---|---|---|---|
| 0 | 1·000 | -- | - | - | -- | --- | - | - - |
| 10·0 | 0·845 | 7 0 | 5·84 | 0·60 | 0 04 | -- | 0·9 | |
| 20 0 | 0·818 | 6 7 | 5·46 | 1·24 | 0·03 | -- | 1 9 | - |
| 35·1 | 0·661 | 6·5 | 6 22 | 1 95 | 1·16 | 1·37 | 3·5 | 4 13 |
| 50·0 | 0·558 | 5·3 | 6·03 | 2·02 | 1·21 | 1·10 | 4·8 | 4·34 |
| 67·5 | 0 467 | 4 9 | 6·90 | 2·54 | 1·58 | 1·19 | 6·4 | 4·80 |
| 84 6 | 0·426 | 3 6 | 6 23 | 2·82 | 2·08 | 1·45 | 9·3 | 6·48 |
| 100 5 | 0·299 | 1·7 | -- | 2·40 | 1·85 | 1·06 | 9·6 | 5·48 |
| 127 5 | 0 241 | - - | --- | 2·71 | 3·01 | 1 59 | 12 1 | 6 38 |
| 164·0 | 0·197 | --- | -- | - - | 3·22 | 1·60 | 17·5 | 8·72 |
| | | | Mean 6 | | | Mean 1·3 | | Mean 6 |

[a] $k_{1i}$ 1·2 × $10^{-2}$ $min^{-1}$.

[b] Early values may be unreliable.

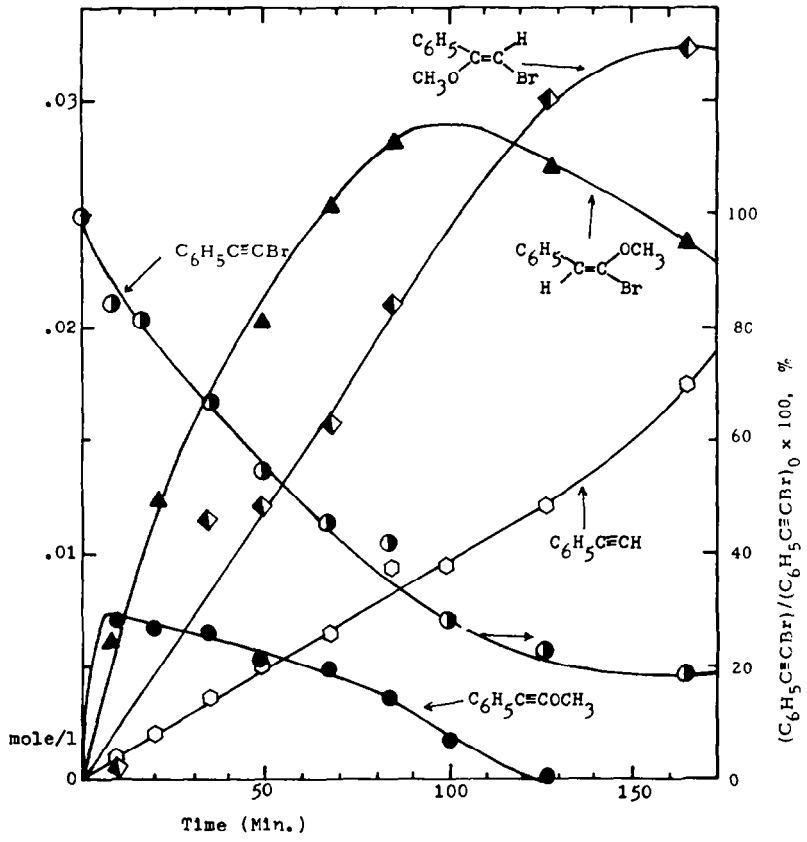



FIG 1. A Reaction Profile of Phenylbromoacetylene (0·30M) and Sodium Methoxide (1·95M) in Methanol at 78°

on a NaCl plate, when several drops of the $CCl_4$ soln were allowed to evaporate on it. The water layer from the above extraction was washed twice with $CCl_4$, acidified with HCl, and then extracted with ether. Evaporation of the dried ether layer yielded solid phenylacetic acid.

In another approach, we used a soln 1·95M in NaOMe, 0·3M in **1** and 0·05M in t-butylbenzene in abs MeOH (100 ml). Ten ml aliquots were distributed among ampules which were sealed and immersed in an 80·0° bath for given intervals. Again, IR and NMR spectra were used in identification. The areas of characteristic proton peaks in the NMR were determined relative to the Me protons of t-butylbenzene on an expanded scale (Fig 3). In this way, the concentrations of **2**, **3**, **4a**, **5a**, **6** and **8** were determined. The effect of the work-up procedure on the relative concentration of each component was examined by using the known amounts of pure samples. Most of **8** and part of **6** were found to be lost into the water during the extraction, but the other components were not affected and gave reproducible relative concentrations. The progress of the reaction was also estimated from the VPC peak areas of unreacted **1** and t-butylbenzene on a 6′ SF 96 column at 130° at a helium flow rate of 85·6 ml/min. Typical data are given in Fig 1.

Since NaOMe is present in excess, we can regard our system (see Eq. 2) as a collection of pseudo first order processes, provided that the kinetic order in each organic species is unity. If each process also is first order in NaOMe, we can estimate its $k$ value. The rate constant for the disappearance of **1** is composite, as in Eq. 7. Since the half-life of **1** at

$$k_t = \Sigma k_{1i} = k_{12} + k_{13} + k_{14} + k_{15} \tag{7}$$

78° is 60 min, $k_t = 0{\cdot}012\ min^{-1}$. Under the reaction conditions of our analysis at 80°, **3** and **5a** are stable. Therefore, Eq. 8 apply and the rate constants of Table 3 were obtained.

$$k_{13}/k_t = [3]/([1]_0 - [1]) \text{ and } k_{15}/k_t = [5]/([1_0] - [1]) \quad (8)$$

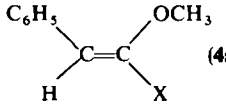
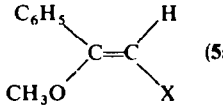
In order to obtain $k_{12}$, we had to work with the portion of Scheme 2 related to species 2. Now $[1] = [1]_0 \exp(-k_t t)$ and Eq. 9 leads to Eq. 10, on integration.

$$d[2]/dt = k_{12}[1] - k_{2j}[2] \quad (9)$$

$$[2] = (k_{12}[1]_0/(k_{2j} - k_t))\,[\exp(-k_t t) - \exp(-k_{2j} t)] \quad (10)$$

Fortunately, $k_{2j}$ could be estimated from the phenylchloroacetylene results to be described below. The value of $k_{12}$ was extracted from Eq. 10, and now $k_{14}$ could be evaluated from Eq. 7. Since the growth and decay of **4a** is given by an expression similar to Eq. 10, its total decay constant $k_{4t}$ can now be found. All of the rate constants are collected in Table 4.

TABLE 4. RATE CONSTANTS × $10^4$ IN $M^{-1}$ $SEC^{-1}$ OF THE INDIVIDUAL REACTION PATHS IN PHENYLBROMO- AND PHENYLCHLOROACETYLENE REACTIONS WITH SODIUM METHOXIDE IN METHANOL AT 78° IN SCHEME 2

| | $k$[a] | X = Cl | X = Br | $k$(Cl)/$k$(Br) |
|---|---|---|---|---|
| $C_6H_5C{\equiv}CX$ (1) | $k_{1i}$ | 1·63 | 1·03 | 1·6 |
| $C_6H_5C{\equiv}COCH_3$ (2) | $k_{12}$ | 0·60 | 0·51 | 1·2 |
| | $k_{2j}$ | 17·1 | 17·1 | 1·0 |
|  (4a) | $k_{14}$ | 1·03 | 0·34 | 3·0 |
| | $k_{4t}$ | ~1 | ~2 | 0·5 |
|  (5a) | $k_{15}$ | 0·004 | 0·11 | 0·036 |
| **5a** | | | | |
| $C_6H_5C{\equiv}CH$ (3) | $k_{13}$ | 0·02 | 0·05 | 0·4 |
| α-Carbon | $k_{12} + k_{14}$ | 1·63 | 0·85 | 1·9 |

[a] Pseudo first order constants of the text have been converted into second order constants here. The constants are self consistent, but any individual value may be uncertain (10–20%). The subscripts on $k$ indicate reactant and product, respectively.

*α-Chloroacetophenone dimethylketal* (**14'**). A procedure analogous to that for **14** was employed. Since the reaction was a little slower, the reflux was continued for 30 hr until the NMR peaks for the starting material disappeared. After MeOH was removed under reduced pressure, a slightly turbid colorless oil was obtained. The yield was quantitative, and there was no indication of byproducts; IR (neat) 1455, 1292, 1216, 1131 (vs), 1080 (vs), 1059 (vs) and 987 $cm^{-1}$; NMR ($CCl_4$) 3·15 (s, 6H) 3·64 (s, 2H) and 7·15, 7·55 (m, 5H).

*α-Methoxy-β-chlorostyrenes* **5'a** *and* **5'b**. A mixture of **14'** (20 g, 0·1 mole) and tetraethyleneglycol dimethyl ether (20 ml) was refluxed under reduced pressure (*ca* 2 mm) for 14 hr in the presence of PTSA (0·1 g). After the system was brought to *ca* 25°, a distillation column was mounted in place of the reflux condenser and vacuum distillation was carried out. Four fractions (~76°, 77–80°, 80–82° and 82–88°/1·75 mm) were practically identical in spectra and thus were combined (10·9 g, 65% yield); IR (neat) 3198, 1625 (νC=C), 1450, 1320, 1238, 1218 (vs), 1130, 1085 (vs) and 758 $cm^{-1}$; NMR ($CCl_4$). (**5'a**) 3·61, 5·79 and 8 (**5'b**) 3·61, 5·50. Separation of the two OMe resonances was effected in DMSO-$d_6$; δ 3·60 (s, $OCH_3$, **5'a**), 3·68 (s, $OCH_3$, **5'b**), 5·90 (s, vinyl, **5'b**) and 6·33 (s, vinyl, **5'a**). **5'a**/**5'b** = 2·9 based on integration for both vinylic and OMe protons: mass spectrum *m/e* 168 $(P)^+$, 170 $(P+2)^+$, 133 $(P-Cl)^+$, 127 (isotopic peak of 125, 125) $(C_7H_6Cl)^+$, 103 base peak $(C_8H_7)^+$, 91 $(C_7H_7)^+$, 89 $(C_7H_5)^+$, and 77 $(C_6H_5)^+$.

*Product analysis of the reaction between phenylchloroacetylene with sodium methoxide in methanol.* The sampling, work-up and analyses were exactly parallel to those described for **1**. Phenylchloroacetylene (2 g) was refluxed in 2M NaOMe in abs MeOH (50 ml) for 4 hr. The soln was cooled, neutralized with excess $NaHSO_4$, and worked up. The oily product was chromatographed over alumina (1·5 × 18 cm) with pentane as eluant. The early fractions were essentially free of contaminants and found to contain one of the isomers of chloromethoxystyrenes; $n_D^{20}$ 1·5715; decomposes at 145° in air; IR 1453, 1349, 1195, 1089, 1071, 973, 920, 830, 781, 755 and 700 $cm^{-1}$; NMR ($CCl_4$) ~7·3 (m, 4·9 H); mass spectrum *m/e* 168 and 170 $(P)^+$, 136 and 138 $(P - CH_3OH)^+$, 125 and 127 $(C_7H_6Cl)^+$ base peak, 118 $(C_6H_5CHCO)^+$ and 101 $(C_6H_5C{\equiv}C)^+$. Since the NMR coincided with neither of the two α-methoxy-β-chlorostyrenes (Table 1), the isomer was assigned as (**4'a**). When **4'a** was refluxed in 2M NaOMe for 5 hr, the products which appeared in the mixture were **6** and **8**; on acidification of the water layer from the work-up, followed by ether extraction, pure phenylacetic acid was obtained. These products presumably arise from **4'a** and **2**.

After 20 or 35 hr reflux periods with NaOMe (2M) in MeOH, **4'a** is completely transformed into sodium phenylacetate and **8**, in small amounts; compounds **6** and **8** were probably lost into the aqueous layer

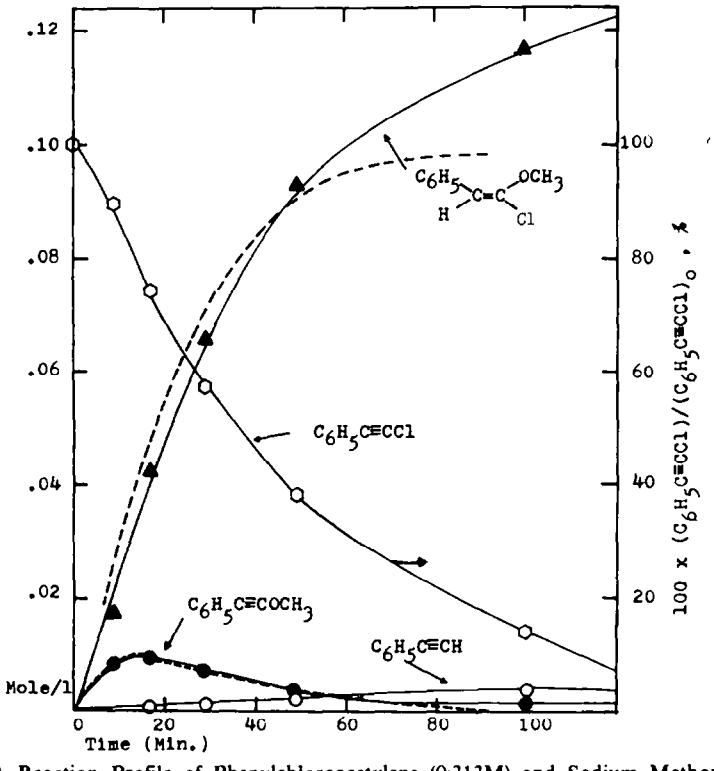



FIG 2. A Reaction Profile of Phenylchloroacetylene (0·313M) and Sodium Methoxide (1·95M) in Methanol at 78°. The curves computed with the rate constants (Table 4) are shown as broken lines. For all curves but the one indicated, the left ordinate applies.

during our workup. Examination of the $CCl_4$ extract revealed a set of NMR peaks (δ 5·79 and 3·61, 1:3 ratio, both singlet), which had been only barely distinguishable in the crude product. Close comparison of the NMR and IR spectra indicated that this component was identical with **5'a**. We estimate by NMR that **5'a** was produced in $<1\%$ yield in the original products.

To obtain a detailed picture of the progress of the reaction, the ampule method was used, as described. The results at 78° for **1'** (0·3128M), NaOMe (1·95M), and t-butylbenzene (0·0155M) in MeOH are given in Table 5 and in Fig 2.

Since the production of **3** and **5'a** is ~1%, it is practical to set $k_{1'3} = k_{1'5'} = 0$ in Eq 7, so that $k_t \simeq k_{'2} + k_{1'4'}$. The half-life of **1'** under these conditions is ~36 min; therefore, $k_t$ is known. The growth and

TABLE 5. CONCENTRATIONS OF THE PRODUCTS OF THE REACTION BETWEEN PHENYLCHLOROACETYLENE (0·3128 M) AND SODIUM METHOXIDE (1·95 M) IN METHANOL AT 78°[a]

| Time, min | $[1']/[1']_0$ | [2] M | [4'a] M | [3] M | [6] M | [8] M |
|---|---|---|---|---|---|---|
| 0 | 1·000 | -- | -- | 0·0006[b,c] | -- | -- |
| 9·10 | 0·897 | 0·0084 | 0·0175 | 0·0007[b] | 0·0008 | -- |
| 17·40 | 0·738 | 0·0091 | 0·0428 | 0·0011[b] | 0·0007 | 0·0062 |
| 29·35 | 0·571 | 0·0070 | 0·0655 | 0·0013 | 0·0028 | 0·0100 |
| 49·30 | 0·380 | 0·0038 | 0·0935 | 0·0019 | 0·0091 | 0·0079 |
| 100·00 | 0·137 | 0·0017 | 0·1164 | 0·0035 | 0·0136 | 0·0067 |

[a] The concentrations are calculated from values relative to *t*-butylbenzene (0·0155M), by NMR.
[b] Roughly estimated with VPC, because NMR peaks were too small.
[c] Phenylacetylene present in the reactant.

decay rate constants, $k_{1'2}$ and $k_{2j}$ of Eq 10, were adjusted by trial and error until a fit to the data was obtained. Once $k_{1'2}$ is known, $k_{14'}$ and then $k_{4'k}$ can be calculated. The values of $k_{1'3}$ and $k_{1'5}$ were obtained as described for **1**. Note that the computed curve for **4'a** in Fig 2 does match the experimental data but that the curves does deviate at high conversions.

## RESULTS AND DISCUSSION

*Products and mechanism.* Preliminary kinetic studies on the phenylbromoacetylene–methoxide reaction in methanol indicated that *more* sodium methoxide was consumed than bromide was produced. Under pseudo first order conditions it was found that the bromide ion appeared more slowly than would be anticipated by Eq 1. Moreover *ca* 10% of the expected bromide ion was still missing at long reaction times. These kinetic results are given in Table 2. We were then led to a careful examination of the product mixtures and their changes with time from both **1** and **1'**. Typical runs are illustrated in Figs 1 and 2. From these data we were able to formulate Scheme 2 and approximate rate constants from the early to the middle stages of reaction (Table 4). The accumulation of the haloethers (**4**, **5**) in the middle stages of reaction and of methyl orthophenylacetate, methyl phenylacetate, and sodium phenylacetate in the later stages of the reaction provides a rationale for our kinetic observations. We now consider Scheme 2 in detail, leaving to a later section the chemistry of the haloalkoxystyrenes.

The general features of the nmr spectrum of a crude product mixture can be seen in Fig. 3. Its IR spectrum showed the existence of the terminal acetylenic structure (3300, 2103 $cm^{-1}$), of another kind of triple bond (2275 $cm^{-1}$), of carbonyl function (1740 $cm^{-1}$) and of double bonds (1638 $cm^{-1}$, broad). The existence of many intense absorption bands in 1000–1300 $cm^{-1}$ region corresponds to the diversity of NMR OMe singlets. Comparison of each individual spectral (NMR, IR) detail with that of authentic samples of plausible products, aided by the technique of admixture spectra and GPC analysis, led to identification of nearly all of the components. Compounds relevant to our product analyses are found in Table 1.

The spectroscopic approach made it possible to detect the compound, phenylmethoxyacetylene **2**, which is a transient. Although **2** was not isolated from the reaction, its detection provides the first example of the nucleophilic acetylenic substitution

caused by oxygen nucleophiles. The fact that **2** was not found previously should be obvious from Figs. 1 and 2. This ether is presumed to be converted to phenylketene dimethylacetal (**7**) which, in turn, rapidly undergoes further attack by methoxide to become the ortho ester (**6**). Here this reaction route probably merges with the path via the addition of methanol to β-methoxy-β-halostyrene (**4**). The formation of analogs of **6** and **7** has been postulated or found with ethoxyethyne.[3, 15]

Right from the early stages it was evident that two bromomethoxystyrenes were formed in the phenylbromoacetylene reaction. Suffice it to say here that **4a** and **5a**

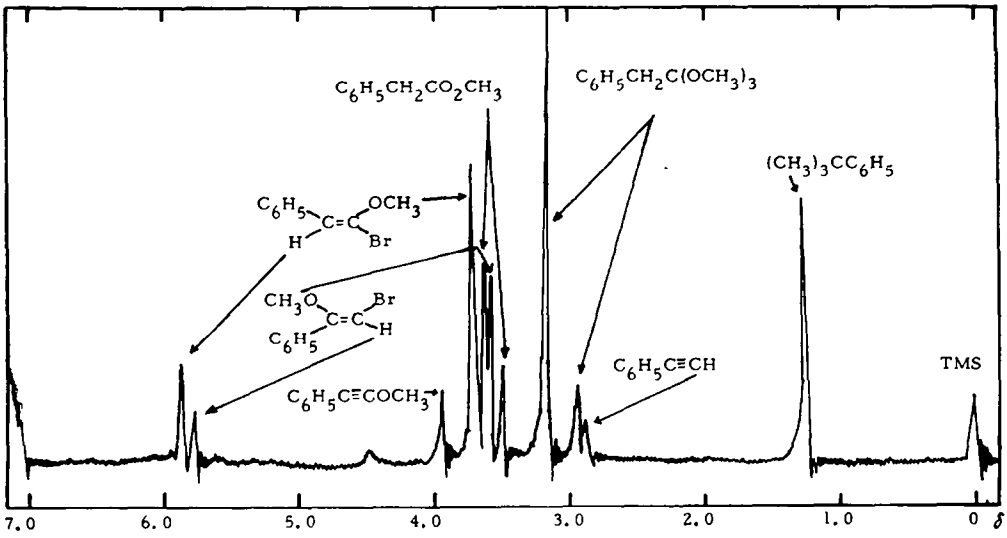



FIG 3. NMR Spectrum of the Product Mixture (*ca* 10% in $CCl_4$) of Phenylbromoacetylene–Sodium Methoxide Reaction. Concentrations were determined relative to t-butylbenzene.

were primary products of the reaction of **1** and that they were not precursors of **2**. Path 1 to **3** is minor, and it presumably involves abstraction of "positive" halogen, as in scheme 5, and the formation of methyl hypobromite. In separate experiments, we found that process 11 took place at ~ 25°, but that no neutral products could be isolated at 80°. In methanolic-methoxide at reflux temperature, in the presence or

$$3 + CH_3OBr \rightarrow C_6H_5C(OCH_3)_2CHBr_2 + C_6H_5CBr_2CHBr_2 \qquad (11)$$

**17**

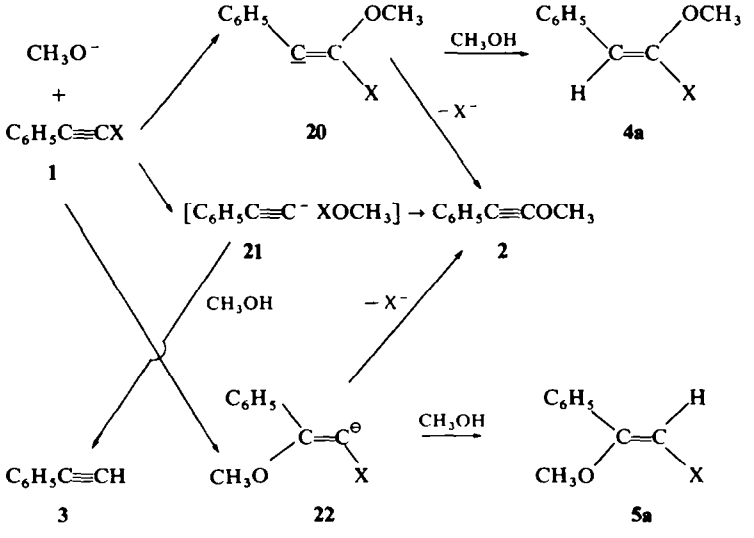
absence of sodium hypobromite, the range of products from **1** by our usual analysis, did not change. It is possible, but unlikely, that the methyl hypobromite was scavenged by **1** and led to undetected products. As for **3**, it survived our usual reaction conditions, 50–80°, and even treatment at 100°; none of **9a**, **9b**, **10** and **11** were detected. Conditions for the interconversions among these compounds are known to be more strenuous.[16]

The phenylchloroacetylene-methoxide system displays the same overall pattern in long term products as that we have found for phenylbromoacetylene-methoxide. Qualitative differences do arise in the primary products because of differences in rates of formation and in stability of intermediates. Now the formation of **3** and **5'a** is only barely detectable while that of **4'a** is dominant; since **4'a** is more stable than **4a**, this retards the production of long term products in the phenylchloroacetylene reaction.

The identification of the first products as **2**, **3**, **4a**, (**4'a**), and **5a** (**5'a**) indicates that there are three points of nucleophilic attack on the phenylhaloacetylene, namely at halogen, or carbon one (terminal), and carbon two (internal). Since recent mechanistic proposals for reaction 1 have evoked differences of opinion,[1, 2, 17] and since many parts of reaction Scheme 2 have not been investigated previously, we examine the primary processes of our system in the context of Scheme 12.

Does the substitution product **2** form by alkoxide attack on the terminal carbon? With high probability, yes. That is, we favor the sequence **1** → **20** → **2** in Scheme 12, because nucleophilic additions to alkynes involve intermediates such as **20**[16, 18] base-promoted proton-deuterium exchange or *syn*-eliminations of haloalkenes involve intermediates such as **20**,[19] and the element rate effect $k_{1'2}$ (Cl)/$k_{12}$ (Br) is consistent with it.

The rate of growth of **2** (Figs. 1, 2; Table 4) exceeds that of **3**, **4a** or **5a** (**5'a**) so that paths to **2** *via* these components are not significant. Although the rate of growth of **2** is less than that of **4'a** the chloroether is sufficiently stable so that it cannot be a




(12)

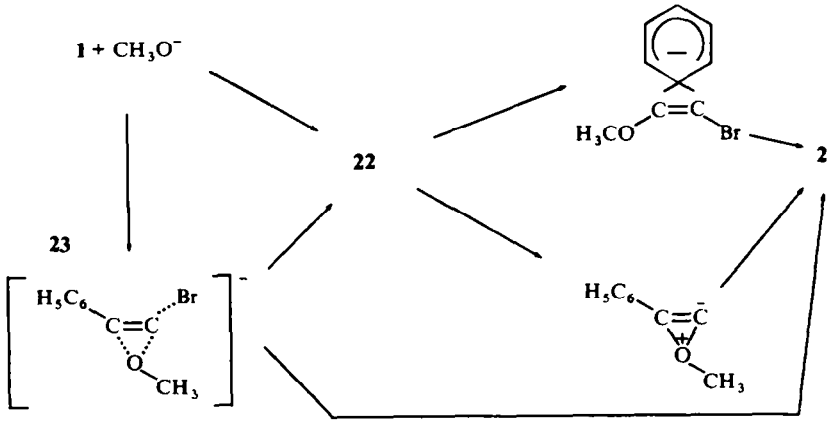
precursor to **2**.

Although **2** does not arise from **3**, **4a**, or **5a**, does it derive from the intermediates leading to them? The sequence, **1** → **21** → **2**, has been advocated as a substitution route.[1, 20] Certainly, the ion pair intermediate **21** would be plausible in eq 12, 5 and 6. In fact, the small amount of phenylacetylene found in our reactions must arise from the formation of **21** and its reaction with methanol. However, rearrangement within

the ion pair **21** so that acetylide can displace halide from oxygen is open to question. Although acetylide can attack "positive" sulfur[3a] and halogen,[2,6] analogous reactions at oxygen are not known to us. In fact, sodium phenylacetylide attacks the chlorine in ethyl hypochlorite to give **1'** and not ethyl phenylethynyl ether.[21] Since phenylacetylide abstracts protons from proton solvents ($k \simeq 10^8$ $M^{-1}$ $sec^{-1}$ at 25° in water[22]) or halogen from hypohalite ($OX^-$) ($k(Cl) = 2{\cdot}3 \times 10^{-4}$ $M^{-2}$ $sec^{-1}$ at 25° in water[23]) at relatively high rates, the possibility that **21** can both rearrange and collapse in methanol to give **2** must be small.

Recently, a new mechanism for process **1** has been proposed.[2,24] In the present context, it involves steps **1** → **22** → **2**. Were it possible, the conversion in strong base **5a** → **22** → **2** would be an example of the Fritsch-Buttenberg-Wiechell (FBW) rearrangement.[25]

An attempted check of this mechanism was made by subjecting **5a** and **5b** in methanol to the reaction conditions 2M sodium methoxide at reflux, or 4M sodium methoxide at 155°. In both cases, no **2**, **6**, **8**, or **12** were observed in the products; **5a** and **5b** were recovered intact. Other work has shown that related alkenes would form vinylic carbanions under these conditions.[19,25-27] Likewise, a typical example of this FBW reaction is found in 1-halo-2,2-diphenylethylene, in which proton exchange is > 100 times faster than elimination with potassium t-butoxide in t-butanol.[27] Such a mechanism is, therefore, unlikely here for several reasons: the formation of **22** would probably lead to **5**; transition state **23**, which is not on a least motion

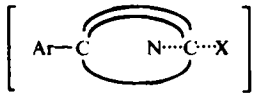



(13)

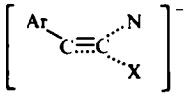
path,[22] involves an improbable merged process of addition–substitution–rearrangement.[29] Therefore, we conclude that a substitution path *via* **23** is improbable in general and that a path *via* **22**, as in Scheme 13, is ruled out for our system.

There is one additional mechanism of substitution, namely a concerted process at the terminal carbon, which we must discredit. By analogy with SN2 processes which involve strong interaction between highest occupied molecular orbital (HOMO) of the nucleophile and the lowest unoccupied orbital (LUMO) of the electrophile,[30] we consider the interaction of the nucleophile (HOMO) with $\sigma^*_{C-X}$ in **24** and $\pi^*_{C-C-X}$ in **25**. By pressing the analogy of the Walden inversion to its extreme, we have the

patently absurd transition state **24**. In order that **25** may be a transition state, the principle of microscopic reversibility requires that it should be symmetrical when N and X are identical.[31] Experimental and theoretical evidence indicate that the vinyl anion, of which **25** is an example, should be a relatively stable, unsymmetrical (bent)



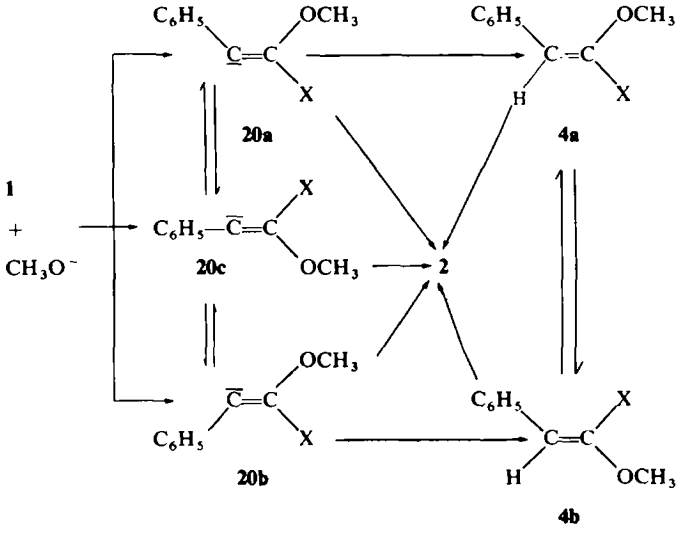
**24**



**25**

intermediate.[19,26] In fact, we know of no authentic example of nucleophilic attack at an unsaturated center, carbonyl, aromatic, vinylic, etc, which proceeds in a single step. In the interest of parsimony, intermediate **20**, which is already a necessary intermediate on the path to **4a**, can also serve as an intermediate for **2**.

Finally, we shall argue that the observed element effect (Table 4) is inconsistent with a concerted process. It will be recalled that for CX generally $k$ (Cl) $\ll$ $k$ (Br), when carbon–halogen bond-breaking *is* involved, and often $k$ (Cl) $>$ $k$ (Br), when carbon–halogen *is not* involved in the rate-determining step. Displacement processes at unsaturated sites, e.g. aromatic, vinyl, and ethynyl, provide examples of the second type.[1,32] In our systems, the halogen abstraction step $k_{13}$ belongs to the concerted type and the terminal carbon attack $k_{12} + k_{14}$ belongs to the step-wise type.



(14)

Before sequence **1** → **20** → **2** in eq 12 is accepted as the probable mechanism, we make some additional points. Concerning eq 14, paths to **2** *via* **4a** are excluded, but firm evidence on the other alternatives is lacking. The barrier to isomerization of an arylvinyl carbanion, eq **20a**, **b**, has been variously estimated at $<$ 20 kcal/mole and $>$ 9 kcal/mole.[26] The activation energy for proton capture by the carbanion will obviously be $<$ 9 kcal. We believe that the loss of halide will also be fast. It has

been shown that the dehydrobromination of *cis*-β-bromostyrene by methoxide in methanol at 30°, has a $k = 7{\cdot}2 \times 10^{-5}\ M^{-1}\ sec^{-1}$,[33] and that the same reaction in isopropyl alcohol is accompanied by little D-exchange (6%) in deuterated solvent.[34] Evidently, the elimination is either E2 or has a carbanion which sheds halide easily. Thus, any one of the ions (**20**) appears fully formed on the generally descending portion of the reaction coordinates for ethynyl or vinyl ether formation, even though they originated in **1**.

Compound **4b** has never been prepared and its reactivity towards methoxide could not be tested. We consider that precedent renders the *syn* addition, **1** → **20b** → **4b**, highly improbable.[18] Nevertheless, this process has really not been rejected by this work. Indeed, the fact that *syn* elimination from alkenes to alkynes are known[28] (independent of other paths in eq 14) suggests that *syn* additions are not impossible. In summary, steps through **20a** in eq 14 probably constitute the most favorable path from **1** to **2**.

*Miscellaneous phenylbromoacetylene-alkoxide reactions.* With extensive information on the nature of system 1 in hand, we considered the possibility of a practical synthesis of **2**. Several variations in our reaction conditions were tried. **1** was refluxed in *t*-butanol saturated with sodium methoxide, but there was little change in the nature of the reaction from that in methanol. Compound **1** and a saturated solution of sodium methoxide in dimethylsulfoxide (DMSO) reacted completely at 0–15°: **3** was the dominant product, amounting to more than 10 times that of **8**. When **1** was refluxed in a solution of potassium t-butoxide in t-butanol, the only significant product extracted in ether was **3**; there was no evidence for the presence of products related to phenylacetic acid.

From the preceding experience it was clear that reaction of alkoxides in an aprotic solvent was "fast". To reduce halogen abstraction we used phenylchloroacetylene. In this way, we were able to overcome the problems of alcohol addition and attack on halogen. Several examples of phenylalkoxyacetylenes will be reported in a separate communication.[1b]

*The halomethoxystyrenes.* In clarifying scheme 2, we had to investigate the properties of a number of related compounds and their reactions. This centered on the haloethers and their structure. In the course of this work we were able to extend known pmr correlations and utilize them for structural assignments. These will be given in the last section.

Of the six possible bromomethoxystyrenes, **19a** and **19b** were encountered only on a path to **2**, Eq. 4, which was clearly unconnected (under our conditions) with the chemistry of Eq. 2 and 3. The structures of **19** were tentatively assigned on the basis of their PMR spectra (see below).

The bromoethers, **5a** and **5b**, were prepared as in Eq. 3. The major isomer (75%) from **14** in Eq. 3 and the sole isomer from **1** in Eq. 2 was assigned the *seq-cis* structure (**5a**). Stereoselectivity arguments and PMR spectral assignments support this choice. A key product in scheme 3 is α-bromoacetophenone (**13**) which can arise under various conditions from **11**, **17** and **5**. Because of its ease of formation, we treated it with sodium methoxide in refluxing methanol. None of the terminal products of Scheme 2, i.e. **5a**, **6**, **8**, or sodium phenylacetate, were found. Instead, two completely different compounds, **15** and **16**, were identified; such products have their analogies in the reactions of other haloketones with alkoxides.[11] Since the bromoethers **5** did

not react with sodium methoxide even under forcing conditions, we can say that the conversions of Scheme 3 are essentially separate from those of Scheme 2.

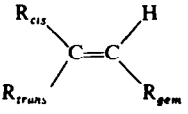
Analogous to the bromo compounds, the chloroethers were prepared and assigned to structures **5'a** and **5'b**. It was established that the major ether product from **1'** was neither one of these and that at most traces ( $< 1\%$) of **5'a** were formed.

One remaining haloether was found in the products and assigned the *seq-cis* structure **4a** (and **4'a**). In the absence of **4b**, this assignment must be regarded as plausible rather than compelling. The formation of **4a** and **4'a** is consistent with known *anti* additions to alkynes, and its relative stability to base is indicative of a *cis* disposition of hydrogen and bromine; judging from the reactivity of related β-halostyrenes, **4b** would not long survive in sodium methoxide-methanol at 78°.[33, 34] Although **4'a** is more stable towards sodium methoxide than **4a**, it is eventually converted to the terminal products **6**. **8**. and **12**.

*PMR correlation with alkene structure.* Recently, an empirical method of determining the geometry of substituted ethylenes based on substituent chemical shifts has

$$\delta_{calc} = 5{\cdot}25 + Z_{gem} + Z_{cis} + Z_{trans} \qquad (15)$$

been developed.[35, 36] The additive relation 15 holds with a standard deviation in $|\delta_{calc} - \delta_{obs}| \simeq 0{\cdot}17$ ppm for over 4000 examples of the structure,




Certain "problem" substituents, e.g. alkoxy or acyl, give rise to larger deviations. Although such deviations are interesting and certain corrections may be anticipated, we shall limit ourselves here to structural assignments of the haloethers and some checks on Eq. 15 with new alkenes (bottom of Table 1). Equation 15 is indeed useful: except for one *cis-trans* pair, we could differentiate numerous styrenes with confidence, if not with absolute certainty.

## REFERENCES


[1] Previous papers on this subject:
[a] A. Fujii, J. I. Dickstein and S. I. Miller, *Tetrahedron Letters* 3435 (1970);
[b] R. Tanaka and S. I. Miller, *Ibid.* in press

[2] S. Y. Delavarenne and H. G. Viehe, *The Chemistry of Acetylenes*, (Edited by H. G. Viehe) Chap. 10. Marcel Dekker, New York, N.Y. (1969)

[3] [a] L. Brandsma, H. J. T. Bos, and J. F. Arens, *The Chemistry of Acetylenes* (Edited by H. G. Viehe) Chap. 11. Marcel Dekker, New York, N.Y. (1969);
[b] J. F. Arens, *Advan. Org. Chem.* **2**, 117 (1960)

[4] H. G. Viehe, *Angew. Chem.* **75**, 638 (1963)

[5] V. Grignard and H. Perrichon, *Ann. Chim. Paris* [10] **5**, 5 (1926)

[6] R. Truchet, *Ibid.* [10] **16**, 325 (1931)

[7] J. U. Nef, *Liebigs. Ann.* **308**, 264 (1899)

[8] T. L. Jacobs and W. R. Scott, Jr., *J. Am. Chem. Soc.* **75**, 5500 (1953)

[9] T. L. Jacobs and W. R. Scott, Jr., *Ibid.* **75**, 5497 (1953)

[10] V. A. Mikhalev, M. I. Dorokhova, N. E. Smolina, A. M. Zhelokhovtseva, O. Ya. Tikhonova, A. P. Skolidinov, A. P. Arendaruk, D. D. Smolin, T. V. Golovkina, and L. A. Slonova, *Antibiotiki* **4**, 21 (1959); *Chem. Abstr.* **54**, 5545 (1960)

[11] [a] J. G. Aston and R. B. Greenberg, *J. Am. Chem. Soc.* **62**, 2590 (1940);
[b] T. I. Temnikova, A. K. Petryaeva, and S. S. Skorokhodov, *Zh. Obshch. Khim.* **25**, 1575 (1955); *Ibid.* **23**, 1338, 1498 (1953); *Ibid.* **19**, 1917 (1949);
[c] J. A. Berson, *J. Am. Chem. Soc.* **74**, 5175 (1952)
[12] K. Meinel, *Liebigs. Ann.* **516**, 238 (1935)
[13] [a] E. L. Jackson, *J. Am. Chem. Soc.* **48**, 2166 (1926);
[b] D. M. Alpatov, *Acta Univ. Voronegiensis* **9**, 172 (1937); *Chem. Abstr.* **32**, 7024 (1938)
[14] J. König and V. Wolf, *Tetrahedron Letters* 1629 (1970)
[15] T. Mukaiyama, *Yuki Gosei Kagaku Kyokai Shi* **19**, 29 (1961); *Chem. Abstr.* **55**, 7267 (1961)
[16] [a] S. I. Miller, *J. Am. Chem. Soc.* **78**, 6091 (1956);
[b] S. I. Miller and G. Shkapenko, *Ibid.* **77**, 5038 (1955)
[17] G. R. Ziegler, C. A. Welch, C. E. Orzech, S. Kikkawa, and S. I. Miller, *Ibid.* **85**, 1648 (1963)
[18] S. I. Miller and R. Tanaka, *Selective Organic Transformations* (Edited by B. S. Thyagarajan) p 143. Wiley: Interscience, New York, N.Y. (1970).
[19] [a] S. I. Miller and W. G. Lee, *J. Am. Chem. Soc.* **81**, 6313 (1959);
[b] W. K. Kwok, W. G. Lee and S. I. Miller, *Ibid.* **91**, 468 (1969)
[20] J. F. Arens, *Rec. Trav. Chim.* **82**, 183 (1963)
[21] M. M. Mousseron and P. Froger, *Bull. Soc. Chim. Fr.* [5] **12**, 69 (1945)
[22] E. A. Halevi and F. A. Long, *J. Am. Chem. Soc.* **83**, 2809 (1961)
[23] R. R. Lii and S. I. Miller, *Ibid.* **91**, 7524 (1969)
[24] S. Y. Delavarenne and H. G. Viehe, *Chem. Ber.* **103**, 1216 (1970)
[25] [a] G. Köbrich, *Angew. Chem.* **79**, 15 (1967);
[b] G. Köbrich and P. Buck, *The Chemistry of Acetylenes* (Edited by H. G. Viehe), Marcel Dekker, New York, N.Y., 1969 (p. 132)
[26] [a] J. M. Lehn and B. Munsch, *Theoret. Chim. Acta* **18**, 143 (1970);
[b] J. M. Lehn, B. Munsch and Ph. Millie, *Ibid.* **16**, 351 (1970)
[27] J. G. Pritchard and A. A. Bothner-By, *J. Phys. Chem.* **64**, 1271 (1960)
[28] S. I. Miller, *Advan. Phys. Org. Chem.* **6**, 185 (1968)
[29] J. N. Murrell and K. J. Laidler, *Trans. Faraday Soc.* **64**, 371 (1968)
[30] K. Fukui, *Fortschritte Chem. Forsch.* **15**, 1 (1970)
[31] R. L. Burwell, Jr., and R. G. Pearson, *J. Phys. Chem.* **70**, 300 (1966)
[32] Z. Rappoport, *Advan. Phys. Org. Chem.* **7**, 1 (1969)
[33] G. Marchese, F. Naso, N. Tangari and G. Modena, *J. Chem. Soc. B* 1196 (1970)
[34] S. J. Cristol and C. A. Whittemore, *J. Org. Chem.* **34**, 705 (1969)
[35] U. E. Matter, C. Pascual, E. Pretsch, A. Pross, W. Simon and S. Sternhell, *Tetrahedron* **25**, 691 (1969)
[36] S. W. Tobey, *J. Org. Chem.* **34**, 1281 (1969)