# Solvent Effects and Nucleophile Competition in Reactions of 3-Chloro-3-methyl-1-butyne[1]

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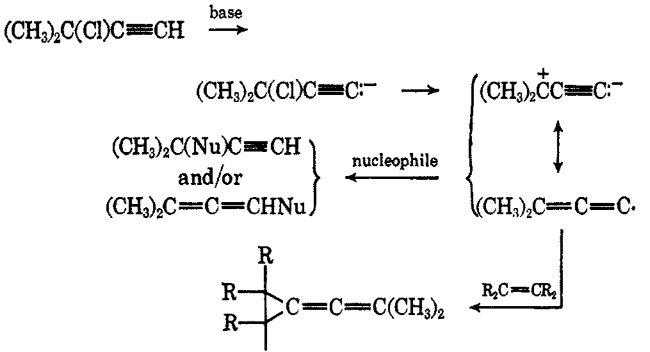
The title compound reacts at 25° with (aqueous) alcohols in the presence of base *via* second-order kinetics (first order each in halide and base) and with rates related to the dielectric constant (water content) of the solvent but only slightly affected by ordinary salt effects or by the nature of the alcohol used. The reactions produce *t*-propargylic ethers in satisfactory yield from methanol and ethanol. Use of aqueous isopropyl or *t*-butyl alcohol results in hydrolysis, elimination, and rearrangement to the carbinol, enyne, and chloroallene, respectively. Relative rates of ether formation from alcohols follow (approximate): methyl (standard), 100; ethyl, 45; isopropyl, 4; *t*-butyl, 0. Unlike alcohols, amines of all types are excellent nucleophiles and lead to amino products in good yield. The reactions with amines are catalyzed by traces of either copper powder or cuprous chloride and are notably insensitive to steric factors.

Aliphatic *t*-propargylic chlorides (and bromides), *e.g.*, 3-chloro-3-methyl-1-butyne (I) and homologs, successfully alkylate methanol, ethanol, ammonia, and amines of virtually all types to produce the corresponding propargylic ethers and amines.[3] All of these reactions proceed under very mild conditions in alkaline, partially aqueous media[4] and generally give good yields. The novelty and notable utility of these processes arise from the fact that they achieve nucleophilic substitution at tertiary aliphatic carbon, a reaction which is ordinarily unsatisfactory.

It is now generally accepted[3,5,6] that the successful *t*-propargylic halide reactions involve an intermediate (neutral) zwitterion–allenecarbene which is rather stable to proton elimination and notably electrophilic at the tertiary carbon. Nucleophiles employed in these reactions include not only solvents such as alcohols (alkoxide ions?), and many amines as mentioned above, but also sodioacetoacetic ester,[7] sodiodiethyl malonate[8] and diethyl methylmalonate,[9] and thiophenoxide.[5c] It is obvious that the zwitterion–allenecarbene should be an ambident electrophile, capable of yielding both propargylic and allenic products as has been observed in particular cases.[3g,5c,9] Good evidence for the validity of the mechanism pictured above arises not only from kinetic studies[3a,3c,5,6] and reaction products, but also from the fact that the unique allenecarbene has been trapped by stereospecific reaction with olefins in the manner typical of ordinary carbenes.[10]



There remain, however, a variety of observations not readily reconcilable with the general zwitterion–allenecarbene mechanism. Methanol and ethanol give good yields of the propargylic ethers[3e] and the alkaline aqueous alcohols containing up to 40–50 mol % water produce much more ether than carbinol. The reactions follow second-order kinetics (first order each in *t*-propargylic halide and base) and the significance of this has already been discussed in considerable detail.[5,6] *t*-Butyl alcohol, however, gives no ether product,[3e] despite the fact that steric inhibition of *t*-butyl allenyl ether formation should not be serious. This is in sharp contrast to the reactions with *t*-alkyl and other sterically crowded amines which afford N-*t*-propargylic amines in reasonably good yields.[3d,3f,11] Furthermore, trialkylamines react typically and lead to *both* propargylic and allenic quaternary ammonium salts.[3g] It is also not clear why all of the reactions with amines are markedly catalyzed by trace amounts of cuprous salts.[3d] In our hands some good nucleophiles give no substitution products even though steric effects cannot explain the failure. Thus, for example, reaction of I with excess potassium cyanide in aqueous methanol yields only the solvent derived methyl ether (no nitriles). On the other hand, similar use of diethyl malonate and diethyl methylmalonate leads to the desired propargylic and/or allenic products[8,9] despite the seemingly unfavorable steric features of the reaction. Also significant is the fact that reaction with phenoxide[3e] results in competitive O and ring C alkylation. Enamines derived from cyclopentanone and cyclohexanone lead to C-*t*-propargylic derivatives, again despite anticipated steric difficulties.[12] In conclusion, no satisfactory correlation now exists between the basicity, nucleophilicity, polarizability, steric features of the nucleophilic reagent, solvent employed, and success, failure, or outcome of

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[1] Paper No. 87 on substituted acetylenes; previous paper, G. F. Hennion and J. E. Reardon, *J. Org. Chem.*, **32**, 2819 (1967).

[2] Eli Lilly Co. Fellow, 1964–1967. Abstracted from a portion of the Ph.D. dissertation of J. F. M.

[3] (a) G. F. Hennion, *et al.*, *J. Amer. Chem. Soc.*, **73**, 4735 (1951); (b) *ibid.*, **75**, 1653 (1953); (c) *ibid.*, **79**, 2142 (1957); (d) *ibid.*, **82**, 4908 (1960); (e) G. F. Hennion, *et al.*, *J. Org. Chem.*, **26**, 2677 (1961); (f) *ibid.*, **30**, 2645 (1965); (g) *ibid.*, **31**, 1977 (1966); also references cited.

[4] Except in the case of ammonia where anhydrous liquid ammonia is needed.[3b,c,f]

[5] (a) V. J. Shiner, *et al.*, *J. Amer. Chem. Soc.*, **84**, 2402 (1962); (b) *ibid.*, **84**, 2408 (1962); (c) *ibid.*, **89**, 622 (1967).

[6] W. J. le Noble, *ibid.*, **87**, 2434 (1965).

[7] L. Crombie and K. Mackenzie, *J. Chem. Soc.*, 4417 (1958).

[8] N. R. Easton and R. D. Dillard, *J. Org. Chem.*, **27**, 3602 (1962).

[9] A. F. Bramwell, L. Crombie, and M. H. Knight, *Chem. Ind.* (London), 1265 (1965).

[10] (a) H. D. Hartzler, *J. Amer. Chem. Soc.*, **81**, 2024 (1959); (b) *ibid.*, **83**, 4990, 4997 (1961); (c) *ibid.*, **88**, 3155 (1966); (d) H. D. Hartzler, *J. Org. Chem.*, **29**, 1311 (1964).

[11] N. R. Easton, R. D. Dillard, W. J. Doran, M. Livezey, and D. W. Morrison, *ibid.*, **26**, 3772 (1961).

[12] Unpublished work with F. X. Quinn in progress.

the alkylation reaction. It must be noted, however, that all of the known reactions recited above occur in strongly basic media. 3-Chloro-3-methyl-1-butyne does not react with potassium acetate in acetic acid at temperatures up to 60°; use of silver acetate, however, leads to a mixture of propargylic and allenic esters.[13]

**Kinetics.**—We report now the results of a preliminary study of nucleophilic solvent variation, with respect to both kinetics and products formed, and nucleophile competition experiments. The findings are summarized in Tables I–IV. Most of the reactions showed clean second-order kinetics and the rates varied relatively little (only by a factor of about 7; Table I, entries 1 and 12). Rates in various alcohol mixtures were similar to those in individual alcohols so long as other solvent features were comparable (Table II). Increase in solvent dielectric constant resulting from increase in water concentration resulted in rate acceleration as expected.[14]

Table I

Second-Order Rate Constants for Reaction of 3-Chloro-3-methyl-1-butyne (I) with Alcohols and KOH[a] at 25.0°

| Entry | Solvent | | Added salt (equiv) | $k_2$[b] |
|---|---|---|---|---|
| | Alcohol | $H_2O$, % (v/v) | | |
| 1 | EtOH | 5 | None[c] | 0.48, 0.48 |
| 2 | EtOH | 10 | None[c] | 0.71, 0.70 |
| 3 | EtOH | 15 | None[c] | 0.96, 0.94 |
| 4 | EtOH | 20 | None | 1.35, 1.35[d] |
| 5 | EtOH | 20 | KCl (1)[c] | 1.47 |
| 6 | EtOH | 20 | KBr (1) | 1.42 |
| 7 | EtOH | 20 | KI (1) | 0.9 → 0.7 |
| 8 | EtOH | 20 | $KNO_3$ (1)[e] | 1.41 |
| 9 | EtOH | 25 | None | 2.02, 1.98 |
| 10 | EtOH | 30 | None | 2.31, 2.30 |
| 11 | EtOH | 35 | None | 2.95 |
| 12 | EtOH | 40 | None | 3.64, 3.60 |
| 13 | *i*-PrOH | 25 | None[c] | 2.19 |
| 14 | *i*-PrOH | 30 | None | 2.66 |
| 15 | *i*-PrOH | 35 | None | 3.03 |
| 16 | *i*-PrOH | 40 | None | 3.37 |
| 17 | *t*-BuOH | 35 | None | 1.99 |
| 18 | *t*-BuOH | 45 | None | 2.61 |

[a] $c_0(I) = c_0(KOH) = 0.1\ M$. [b] In l. mol$^{-1}$ hr$^{-1}$; multiple entries are for duplicate runs. [c] KCl crystallizes as the reaction proceeds. [d] Previously reported to be 1.40 (ref 3a) and 1.27 (ref 3c) using NaOH. [e] Only partially soluble.

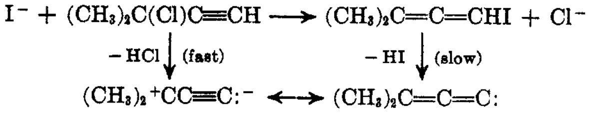
Table II

Second-Order Rate Constants for the Reaction of 3-Chloro-3-methyl-1-butyne (I) with Mixed Alcohols and KOH[a] at 25.0°

| Entry | Solvent, 20% water (v/v) | | $k_2$[b] |
|---|---|---|---|
| | ROH (%) | R′OH (%) | |
| 1 | EtOH (60) | MeOH(20) | 0.78 |
| 2 | EtOH (40) | MeOH (40) | 0.62 |
| 3 | EtOH (20) | MeOH (60) | 0.47 |
| 4 | EtOH (60) | *i*-PrOH (20) | 1.55 |
| 5 | EtOH (40) | *i*-PrOH (40) | 1.80 |
| 6 | EtOH (20) | *i*-PrOH (60) | 2.12 |
| 7 | EtOH (60) | *t*-BuOH (20) | 1.62 |
| 8 | EtOH (40) | *t*-BuOH (40) | 1.77 |

[a] $c_0(I) = c_0(KOH) = 0.1\ M$. [b] In l. mol$^{-1}$ hr$^{-1}$

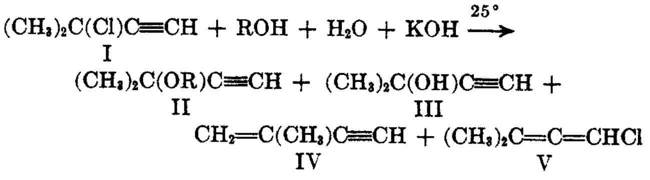
**Salt Effects.**—Except for potassium iodide, the effect of salts in concentrations (0.1 *M*) equivalent to substrate halide (Table I, entries 4–8) appeared too small to assess with confidence. The limited solubility of potassium salts in our solvent systems (potassium hydroxide used as base) did not permit a critical study of the type Shiner and Wilson reported[5a] for 3-bromo-3-methyl-1-butyne, using sodium hydroxide as the base along with various sodium salts. These investigators noted large rate depressions (40% in the presence of 0.22 *M* NaBr and 18% for either $NaNO_3$ or $NaClO_4$) using 80% ethanol as the solvent. Our findings suggest that rate enhancement (in the case of the *t*-chloride) arises both from increase in dielectric constant of the solvent medium and (slightly) from increase in ionic strength of the solution. We interpret the observed iodide effect (Table I, entry 7; rate depression with drifting rate constant) as indicative of a competing $S_N2'$ reaction leading to the allenyl iodide[15] which then forms the zwitterion–allenecarbene at a slower rate.



$$\begin{array}{ccc} \mathrm{I^- + (CH_3)_2C(Cl)C{\equiv}CH} & \longrightarrow & \mathrm{(CH_3)_2C{=}C{=}CHI + Cl^-} \\ {\scriptstyle -\mathrm{HCl}}\big\downarrow{\scriptstyle \mathrm{(fast)}} & & {\scriptstyle -\mathrm{HI}}\big\downarrow{\scriptstyle \mathrm{(slow)}} \\ \mathrm{(CH_3)_2{}^+CC{\equiv}C{:}^-} & \longleftrightarrow & \mathrm{(CH_3)_2C{=}C{=}C{:}} \end{array}$$

**Reaction Products.**—The reaction of halide I with aqueous alcohols in the presence of base takes the course given in Scheme I with respect to the major products. The relative amounts of these varied widely even though the reaction rates did not. The previous report[3e] that isopropyl ethers form only in low yield while *t*-butyl ethers cannot be made in this way was confirmed. Whether or not this relates to steric features or to the acidity ($k_a$) of the alcohol used remains obscure. It may well be that both aspects are critical so that ethers arise only from sterically suitable lyate ions and not from alcohols *per se*. While the rates of ether formation (as distinct from other products) have not been determined, Table III provides information for the estimation of relative rates. Thus entries 1 and 2 show $k_{\mathrm{ROMe}}/k_{\mathrm{ROEt}} \approx 2.3$; from entry 4, $k_{\mathrm{ROMe}}/k_{\mathrm{RO\text{-}}i\text{-}\mathrm{Pr}} \approx 24$; from entries 7 and 8 $k_{\mathrm{ROEt}}/k_{\mathrm{RO\text{-}}i\text{-}\mathrm{Pr}} \approx 11.4$. The latter figure is in fair agreement with the expected ratio 10.4 (=24/2.3).[16] The yields listed in Table III account for 65–85% of the *t*-chloride used. Competitive formation of carbinol III was established

Scheme I



$$\begin{array}{l} \underset{\mathrm{I}}{\mathrm{(CH_3)_2C(Cl)C{\equiv}CH}} + \mathrm{ROH + H_2O + KOH} \xrightarrow{25°} \\ \quad \underset{\mathrm{II}}{\mathrm{(CH_3)_2C(OR)C{\equiv}CH}} + \underset{\mathrm{III}}{\mathrm{(CH_3)_2C(OH)C{\equiv}CH}} + \\ \qquad \underset{\mathrm{IV}}{\mathrm{CH_2{=}C(CH_3)C{\equiv}CH}} + \underset{\mathrm{V}}{\mathrm{(CH_3)_2C{=}C{=}CHCl}} \end{array}$$

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[13] A. I. Zakharova, *J. Gen. Chem. USSR*, **15**, 429 (1945); *Chem. Abstr.*, **40**, 4654 (1946). See also ref 5a, p 2405.

[14] Analysis of the solvent effect data presented in Table I, entries 1–4 and 9–12, and earlier solvolysis data[3a] in the manner of J. G. Kirkwood [*J. Chem. Phys.*, **2**, 351 (1934)] and E. Grunwald and S. Winstein [*J. Amer. Chem. Soc.*, **70**, 846 (1948)] results in typical straight-line plots, except for low water concentrations. The Grunwald–Winstein substrate susceptibility constant in ethanol, $m_{\mathrm{EtOH}}$, was found to be about 0.66 for $S_N1$ ionization of I and 0.52 for reaction in the presence of base.

[15] T. L. Jacobs and W. L. Petty, *J. Org. Chem.*, **28**, 1360 (1963).

[16] It was established experimentally that the ethers do not react with alcohols, water, or other nucleophiles present under the reaction conditions and are therefore products of kinetic control. The relative reactivities of the alcohols used are therefore approximately as follows: methyl, 100; ethyl, 45; isopropyl, 4; *t*-butyl, 0.

TABLE III

PRODUCTS FROM REACTION OF 3-CHLORO-3-METHYL-1-BUTYNE (50 mmol) WITH MIXED AQUEOUS ALCOHOLS AND KOH (55 mmol) AT 25°

| | Solvent, 20% water (v/v) | | | Yields of products, % | | | |
|---|---|---|---|---|---|---|---|
| | Alcohols (mmol) | | Water, | Ethers[a] | | | |
| Entry | ROH | R'OH | mol % | R | R' | Enyne | Isomer[b] |
| 1 | Me(247) | Et (171) | 40 | 55.0 | 15.9 | 12.9 | 0 |
| 2 | Me (124) | Et (257) | 42 | 38.4 | 37.2 | 13.3 | 0 |
| 3 | Me (247) | *i*-Pr (131) | 42 | 57.0 | 0.5 | 19.8 | 0 |
| 4 | Me (124) | *i*-Pr (196) | 47 | 54.3 | 3.6 | 22.9 | 0 |
| 5 | Me (371) | *t*-Bu (50) | 40 | 67.6 | 0 | 14.3 | 0 |
| 6[c] | Me (124) | *t*-Bu (150) | 50 | 43.8 | 0 | 24.8 | 6.0 |
| 7 | Et (171) | *i*-Pr (131) | 48 | 55.1 | 3.9 | 19.1 | 0 |
| 8 | Et (86) | *i*-Pr (196) | 50 | 49.9 | 9.4 | 23.6 | 0 |
| 9 | Et (257) | *t*-Bu (50) | 48 | 55.9 | 0 | 17.4 | 0 |
| 10 | Et (171) | *t*-Bu (100) | 51 | 52.6 | 0 | 25.8 | 5.7 |
| 11[c] | Et (86) | *t*-Bu (150) | 54 | 41.6 | 0 | 29.6 | 6.3 |
| 12[c] | *i*-Pr (196) | *t*-Bu (50) | 53 | 18.6 | 0 | 34.1 | 9.4 |
| 13[c] | *i*-Pr (131) | *t*-Bu (100) | 55 | 15.4 | 0 | 38.5 | 11.1 |

[a] Ether refers to 3-alkoxy-3-methyl-1-butyne. [b] 1-Chloro-3-methyl-1,2-butadiene. [c] Yields are corrected for unreacted 3-chloro-3-methyl-1-butyne (5%).

TABLE IV

REACTION OF 3-CHLORO-3-METHYL-1-BUTYNE (0.50 mol) WITH KOH (0.55 mol) IN ALCOHOL–AMINE SOLVENTS AT 25°

| | Solvent | | Yields of reaction products, % | | | |
|---|---|---|---|---|---|---|
| Entry | Alcohol[a] | Amine[a] | Ether[b] | Amine[c] | Enyne | Isomer[d] |
| 1 | MeOH | $t\text{-BuNH}_2$ | 24.1 | 36.7 | 16.1 | 9.5 |
| 2 | EtOH | $\text{EtNH}_2$ | 12.1 | 52.3 | 14.8 | 8.6 |
| 3 | *i*-PrOH | $\text{MeNH}_2$ | 2.6 | 60.1 | 12.9 | 12.1 |
| 4 | EtOH | $\text{PhNH}_2$ | 52.4 | 2.7 | 15.1 | 9.1 |
| 5 | | $\text{HOCH}_2\text{CH}_2\text{NH}_2$[e] | 9.5 | 33.4 | Nd[f] | Nd |
| 6 | | $\text{HOCH}_2\text{CH}_2\text{NH}_2$[e,g] | 0.0 | 58.3 | Nd | Nd |
| 7[h] | MeOH[i] | $i\text{-PrNH}_2$[g] | 4.8 | 59.8 | Nd | Nd |

[a] 0.75 mol used, except for entries 5 and 6 as noted. [b] Ether refers to 3-alkoxy-3-methyl-1-butyne. [c] Amine refers to 3-alkylamino-3-methyl-1-butyne. [d] 1-Chloro-3-methyl-1,2-butadiene. [e] Total amount of ethanolamine used was 2.0 mol. [f] Not determined. [g] Reaction catalyzed with copper (0.1 g); KOH was not used. [h] Only 0.25 mol of 3-chloro-3-methyl-1-butyne used. [i] 1.0 mol of MeOH used.

only qualitatively. Analyses for III could not be achieved satisfactorily due to its polarity, water solubility, and unfavorable glpc response in columns suitable for mixtures of I, II, IV, and V.[17]

Isopropenylacetylene (IV) was always a reaction product although relatively large amounts were formed only when ether formation was suppressed due to lack of sufficiently high methanol and/or ethanol concentrations in the solvent medium. It is particularly noteworthy that the allenyl chloride (V), isomeric with I, appears when solvent composition deters ether formation (Table III, entries 6 and 10–13). Since S$_N$1 ionization of I is extremely slow,[3a,3c] V probably arises from external return.

Table IV, entries 1, 2, 3, and 5, show that highly basic amines are better nucleophiles than alcohols, even when the amine is sterically handicapped and the alcohol is not. The product ratios observed are understandable if ether formation results only from alkoxide ion, present in low concentration, competing with amine in high concentration. Entry 4 of Table IV shows, however, that only highly basic amines are sufficiently nucleophilic to react preferentially in competition with alcohols. Entries 5 and 6 both refer to use of ethanolamine as the nucleophile but under very different conditions. In the presence of potassium hydroxide (entry 5) N alkylation predominates (3.5:1) over ether formation much as expected. In the absence of hydroxide, using copper powder as a catalyst (entry 6) only N alkylation occurred. This supports the view that ethers arise only from alkoxide ion. It was thus expected that in competition between methanol and isopropylamine, using copper powder as a catalyst and in the absence of hydroxide (entry 7), no methyl ether would be produced. A low yield (4.8%) was realized, however, suggesting that the solution was near the borderline of basicity required for ether formation. In all of these experiments (Table IV) solvent components were not in notably high concentration and so formation of some enyne (III) and allenyl chloride (V) was observed as expected.

Formation of allenyl products other than V was never encountered although trace amounts may have escaped detection. It appears from other studies[3g,10c,18] that allenyl amines and ethers form only when steric effects strongly disfavor the propargylic isomer.

Correlation of the present findings with the literature cited emphasizes that second-order rate constants, such as reported here, measure only rates of the intermediate zwitterion–allenecarbene formation, loss of halide ion being rate determining, and bear no significant relation to the reaction end products. Clearly the dipolar ion–carbene is a discriminating electrophile often

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[17] Reaction products were extracted into pentane and III was removed by washing with water. The dried pentane solutions were analyzed by glpc.

[18] T. L. Jacobs and S. Hoff, *J. Org. Chem.* **33**, 2986 (1968).

uniquely useful in synthetic work and deserving of further study.

## Experimental Section

**3-Chloro-3-methyl-1-butyne** (I), triply distilled, bp 75.3–75.4°, $n^{25}\mathrm{D}$ 1.4142, was prepared from the carbinol as previously reported.[3c,19]

***t*-Propargylic ethers, $(CH_3)_2C(OR)C{\equiv}CH$,[3e] isopropenylacetylene,[20] and 1-chloro-3-methyl-1,2-butadiene,[19]** needed as pure standards for glpc, ir, and nmr comparison with reaction products, were prepared by literature methods cited.

Reaction rate measurements were made as previously described[3a,c] except that the rate constants were calculated from the integrated second-order rate expression on the University of Notre Dame UNIVAC 1107 computer.

**Alcohol Competition Reactions.**—In a typical experiment 4.6 g (55 mmol) of potassium hydroxide (86% assay) was dissolved in 5.0 ml of distilled water and the appropriate amounts of the respective alcohols (Table III). Then 5.12 g (50 mmol) of I was added dropwise over the period of 1 hr while the temperature was maintained at 25 ± 3°. After 48 hr at room temperature, the reaction mixture was chilled and filtered to remove potassium chloride. Two 10-ml portions of pentane were used to wash the residue and were combined with the filtrate. The layers were separated. The aqueous layer was extracted with two 7-ml portions of pentane. The combined pentane extracts were washed with two 20-ml portions of water and dried over calcium chloride. The filtered pentane solutions were analyzed by glpc using a 10-ft stainless steel column packed with 20% Octoil-S on firebrick employing isothermal operation at 78° with a He flow of 60 cc/min. The actual presence of 1-chloro-3-methyl-1,2-butadiene (V) in some cases was further established by preparative glpc isolation and comparison of the ir and nmr spectra with those of an authentic sample.

**Reaction of I with Ethanolamine—Copper Catalysis.**—To a mixture of 48.8 g (0.8 mol) of ethanolamine, 12.3 g of water (80% amine solution), and *ca.* 0.1 g of copper powder was added dropwise with vigorous stirring 20.5 g (0.2 mol) of I while the temperature was maintained at 25 ± 5°. After 6 hr of stirring at 30°, the reaction mixture was allowed to stand overnight at room temperature. The dark syrupy mixture was diluted with 50 ml of saturated brine and extracted thrice with 50-ml portions of benzene and once with 50 ml of ether. The combined organic extracts were washed thrice with 50-ml portions of saturated brine. The organic layer was then treated with 100 ml of 4 *N* HCl. The acidic layer was separated and extracted twice with 25 ml of ether (discarded). The aqueous solution was adjusted to pH 12 with 40% sodium hydroxide, saturated with sodium chloride, and then extracted with three 50-ml portions of benzene. Distillation through a 20-cm Vigreaux column yielded 14.8 g (58.3%) of 3-(2-hydroxyethylamino)-3-methyl-1-butyne: bp 82.0–82.8° (4.1 mm); $n^{25}\mathrm{D}$ 1.4633; ir (neat) 3.05 $\mu$ ($\equiv$CH), 3.12 (associated –NH and –OH), 4.8 (C$\equiv$C), 7.28 (doublet, $CeM_2$). The hydrochloride salt had mp 101–103° (lit.[21] mp 84–86°).

*Anal.* Calcd for $C_7H_{14}ClNO$: C, 51.37; H, 8.62; Cl, 21.67; N, 8.56. Found: C, 51.37; H, 8.83; Cl, 21.60; N, 8.56.

**Reaction of I with Ethanolamine and Potassium Hydroxide.**—To 122 g (2.0 mol) of ethanolamine was added with stirring one-half of a 120-ml solution of 97.9 g (1.5 mol) of potassium hydroxide (86% assay) in 75 ml of water. At 5 ± 5°, 51.3 g (0.5 mol) of I and the remaining 60 ml of the base solution were added dropwise (simultaneously) to the amine solution over a period of 3 hr. After the yellow syrupy mixture (KCl precipitate) had been stirred for 3 more hr at 5 ± 5°, the mixture warmed to room temperature overnight and was then stirred vigorously with 100 ml of ether plus 100 ml of water for 1 hr. After separation, the aqueous layer was extracted twice with 100-ml portions of ether. The combined ether extracts were washed with three 50-ml portions of saturated brine. The aqueous layer from above, together with the brine washes, was extracted thrice with 100-ml portions of benzene. The combined organic extracts (ether plus benzene) were stripped of solvents at reduced pressure. Distillation of the residue through a micro spinning band column gave two distinct fractions. The lower boiling hygroscopic liquid, 3-(2-aminoethoxy)-3-methyl-1-butyne, was recoverd in 9.5% yield: bp 57–58° (14.5 mm); $n^{25}\mathrm{D}$ 1.4433; ir (neat) 3.05 $\mu$ ($\equiv$CH), 3.18 ($NH_2$), 3.40 ($-CH_2$), 3.45 ($-CH_3$), 4.8 (C$\equiv$C), 7.25 (doublet, $CMe_2$), and 9.70 (COC); nmr ($CDCl_3$) $\delta$ 1.45 (s, 6, $CMe_2$), 1.62 (s, 2, $NH_2$), 2.42 (s, 1, $\equiv$CH), 2.84 (t, 2, $CH_2N$), 3.48 (t, 2, $CH_2O$).

*Anal.* Calcd for $C_7H_{13}NO$ + 3% $H_2O$: C, 64.12; H, 10.30. Found: C, 64.38; H, 10.42.

The hydrochloride salt had mp 123–125° after four crystallizations from ethanol plus ethyl acetate.

*Anal.* Calcd for $C_7H_{14}ClNO$ + 4.1% $HOCH_2CH_2NH_2 \cdot HCl$: C, 50.24; H, 8.60; N, 8.79. Found: C, 50.24; H, 8.51; N, 8.64.

The higher boiling liquid, 3-(2-hydroxyethylamino)-3-methyl-1-butyne, produced in 33.4% yield, had bp 79° (3.2 mm), $n^{25}\mathrm{D}$ 1.4628, and gave a hydrochloride, mp 101–103°, not depressed by mixture with the sample described above.

**Nucleophile Competition between *t*-Butylamine and Methanol.**—To a stirred solution of 54.9 g (0.75 mol) of *t*-butylamine and 24.0 g (0.75 mol) of methanol was added with stirring 51.3 g (0.50 mol) of I. No indication of reaction was apparent. The temperature was adjusted to 25° and 35.9 g (0.55 mol) of potassium hydroxide dissolved in 35.9 g of water was added dropwise over a period of 2 hr. The temperature was maintained at 25 ± 3°. After the addition, the mixture was stirred for 6 more hr at 25° and then was allowed to stand overnight at room temperature.

The reaction mixture was transferred to a separatory funnel containing 100 ml of ether. The layers were separated and the aqueous layer was extracted with an additional 100-ml portion of ether. The combined ether extracts were washed four times with 100-ml portions of water (discarded), and then treated with a 100-ml portion of 4 *N* HCl. The acidic aqueous layer was saved and combined with an additional 50-ml portion of water used to wash the ether layer. The ether layer was dried over calcium chloride. Analysis by glpc showed 3.3 g (10.1% yield) of isopropenylacetylene and 11.6 g (24.1% yield) of 3-methoxy-3-methyl-1-butyne.

The acidic aqueous layer was adjusted to pH 12 by the addition of 40% potassium hydroxide solution and then extracted with two 75-ml portions of ether. The combined ether extracts were washed with 100 ml of saturated brine solution and dried over potassium carbonate. Distillation through a small Vigreaux column yielded 25.3 g (36% yield) of 3-*t*-butylamino-3-methyl-1-butyne: bp 131–135°; $n^{25}\mathrm{D}$ 1.4285 (lit.[22] bp 135–136°; $n^{25}\mathrm{D}$ 1.4292).

**Nucleophile Competition between Isopropylamine and Methanol *via* Copper Catalysis.**—To a stirred mixture of 29.5 g (0.5 mol) of isopropylamine, 32.0 g (1.0 mol) of methanol, and 0.1 g of copper powder was added dropwise with cooling 25.6 g (0.25 mol) of I. The temperature was maintained at 25 ± 3° over the 2 hr required for the addition. After standing overnight, the reaction mixture was cooled and added to 150 ml of cold 3 *N* HCl with vigorous stirring. The chilled acidic mixture was extracted with two 50-ml portions of ether. The combined ether extracts were washed four times with water and then dried over calcium chloride. Analysis by glpc as described above showed 1.18 g (4.8% yield) of 3-methoxy-3-methyl-1-butyne. The acidic aqueous layer was adjusted to pH 12 by the addition of 40% KOH solution and then extracted with two 50-ml portions of ether. The combined ether extract was washed with three 50-ml portions of water and then dried over anhydrous potassium carbonate. Distillation yielded 19.3 g (59.8% yield) of 3-isopropylamino-3-methyl-1-butyne: bp 113–118°; $n^{25}\mathrm{D}$ 1.4172 (lit.[22] bp 117°; $n^{25}\mathrm{D}$ 1.4179).

**Registry No.**—I, 1111-97-3; 3-(2-hydroxyethylamino)-3-methyl-1-butyne, 4067-36-1; 3-(2-aminoethoxy)-3-methyl-1-butyne, 19766-40-6; 3-(2-aminoethoxy)-3-methyl-1-butyne (HCl salt), 19766-41-7.

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# Halogenation of Diazopropane with *t*-Butyl Hypobromite. Evidence for the Formation of α-Bromopropylidene[1]

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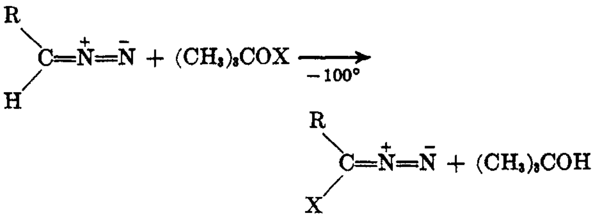
Reaction of diazopropane and *t*-butyl hypobromite at −100° and subsequent warming of the reaction mixture to room temperature leads to the formation of *cis*- and *trans*-1-bromopropene, 1-bromopropane, 1,1-dibromopropane, 1,1-dibromopropene, and *cis*- and *trans*-3-bromo-3-hexene. The effect of reaction conditions on the product distribution and other observations have been interpreted on the basis of the formation of α-bromodiazopropane and its thermal or photochemical decomposition to give α-bromopropylidene.

The syntheses of α-bromo- and α-chlorodiazomethane (1, R = H; X = Br or Cl) by reaction of the corresponding *t*-butyl hypohalite with diazomethane (eq 1)



(1)

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have permitted a comparison of the reactivities of the free α-halomethylenes arising from compounds **1** with unsubstituted methylene and the formally analogous halocarbenoid species.[3] The results indicate that halogen substitution increases the selectivity of methylene,[4] but that the free halomethylene intermediates are significantly more reactive than chloromethylene transfer reagents generated by α-elimination reactions.[3,5]

Methylene and α-halomethylenes are restricted to intermolecular reactions such as C–H insertion, addition to multiple bonds, and reaction with the diazo precursor to produce the corresponding dimeric ethylenes.[5] However, alkyl-substituted methylenes (alkylidenes) react virtually exclusively by intramolecular rearrangements giving olefins and cyclopropanes.[5] For example, diazopropane (2) yields propylene and cyclo-

$$\underset{\mathbf{2}}{CH_3CH_2CHN_2} \xrightarrow{-N_2} CH_3CH_2CH\!: \longrightarrow CH_3CH{=}CH_2 + c\text{-}C_3H_6 \quad (2)$$

propane in the ratio of approximately 9:1 (reaction 2).[6] Studies have been carried out to determine the effect of varying β and γ substitution, and α-alkyl or α-aryl substitution, on the reactivity of such alkylidenes,[5-7] but no information is available concerning α-halogen substitution. The available data for α-halomethylenes[3] suggest that α halogenation of alkylidenes would increase their stability and possibly enable them to participate in intermolecular reactions.

The particular haloalkylidene precursor chosen for study was α-bromodiazopropane (**3**) and the products which were anticipated from intramolecular reactions of the intermediate α-bromopropylidene were *cis*- and *trans*-1-bromopropene (**4** and **5**) and bromocyclopropane (**6**). In view of the 9:1 propylene/cyclopropane ratio

$$\underset{\mathbf{3}}{CH_3CH_2CBrN_2} \longrightarrow CH_3CH_2\ddot{C}Br \longrightarrow \underset{\mathbf{4,\,5}}{CH_3CH{=}CHBr} + \underset{\mathbf{6}}{c\text{-}C_3H_5Br} \quad (3)$$

found from the intramolecular reactions of propylidene (eq 2), an increased selectivity due to α halogenation would lead to the prediction of a larger ratio for (**4** + **5**)/**6**. The low-temperature halogenation of diazopropane with *t*-butyl hypobromite was investigated as the potential source of α-bromodiazopropane.

This study has proven to be complex; however, evidence will be presented to support the formation of α-bromodiazopropane, and the thermal and photochemical decomposition of this diazo compound to yield α-bromopropylidene.

## Results

Slow addition of trichlorofluoromethane (Freon 11) solutions of *t*-butyl hypobromite (*ca.* 0.5–0.6 *M*) to cold (−100°), stirred, pentane solutions containing *ca.* 40 mol % excess diazopropane (*ca.* 0.1 *M*) in the absence of light led to gas evolution and the formation of maroon solutions. Gas evolution was monitored in one experiment and it appeared that about 30–40% of the theoretical nitrogen yield (based on *t*-BuOBr) occurred during mixing of the reagents at −100°. The solutions underwent no subsequent gas evolution or further color change under the same conditions for periods up to 5 hr. However, on warming to −30° in the absence of

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