of tributylphosphine–phenylbromoacetylene, the first term is small, if not negligible; in the three other phosphine–haloalkyne systems, both terms contribute, the first being more important than the second. Equation 9 does not lend itself to facile interpretation of rate data, *e.g.*, activation parameters, element effects, solvent variations, etc. With some plausible, but *ad hoc*, assumptions, we can obtain the more tractable form, eq 10, and refine our rationalizations: the "abnormal"

$$k_{obsd} \simeq k_a + k_c k_d / k_{-c} \quad (10)$$

activation energy and entropy for tributylphosphine–phenylbromoacetylene (Table VII) is associated with a composite rate constant $k_c k_d / k_{-c}$; the element effect and the activation parameters for the reactions of triphenylphosphine and the phenylhaloacetylenes appear to derive from different mixes of the two terms in eq 10 (or eq 9); the rates of formation of **2**, a dipole, and **3**, an ion pair, in eq 2 have different susceptibilities to added methanol, hence the different behavior of the phenylhaloacetylenes (Tables VIII, IX), etc.

In summary, we have suggested that phenylbromoacetylene tends to favor step c of eq 2 and phenylchloroacetylene takes both branches a and c. The methanol scavenging results, the element effect, and perhaps the activation parameters support this approach. Certainly, the rejection of step a by some chemists was premature. It is clear, however, that careful kinetic and product studies over the whole DMF–CH_3OH solvent range will be necessary before eq 8 can be fully exploited and the mechanistic details filled in. Variations on the mechanisms of process 1 appear in the companion paper.[2a]

Registry No.—Phenylbromoacetylene, 932-87-6; phenylchloroacetylene, 1483-82-5; 1-bromo-1-hexyne, 1119-64-8; 1-chloro-1-hexyne, 1119-66-0; ethynyltributylphosphonium chloroplatinate, 34384-16-2; phenylethynyltriphenylphosphonium bromide, 34387-64-9; phenylethynyltriphenylphosphonium chloroplatinate, 34384-17-3; triphenylphosphine oxide, 791-28-6; phenylethynyltriphenylphosphonium tetraphenylboron, 34384-18-4; phenylethynyltributylphosphonium bromide, 34387-65-0; phenylethynyltributylphosphonium chloroplatinate, 34384-20-8; ethynyltriphenylphosphonium chloroplatinate, 34384-19-5; ethynyltriphenylphosphonium tetraphenylboron, 34384-21-9; α-(triphenylphosphonium)-β-(tributylphosphonium)styrene bromide, 34387-66-1; α,β-bis(tributylphosphonium)styrene dibromide, 34387-67-2; triphenylphosphine, 603-35-0; tributylphosphine, 998-40-3; methyl bromide, 74-83-9.

Acknowledgment.—One of the authors, J. I. D., gratefully acknowledges IIT Research Institute for allowing him to use their facilities for part of this work. We thank the Carlisle Chemical Works for the phosphine samples and AIRCO for the ethynyl alcohols.

Nucleophilic Substitution at an Acetylenic Carbon. Kinetics, Mechanism, and Syntheses with Tertiary Amines[1]

JEROME I. DICKSTEIN AND SIDNEY I. MILLER*

Department of Chemistry, Illinois Institute of Technology, Chicago, Illinois 60616

Received December 9, 1971

Haloalkynes cleave one bond at the amine bridgehead to produce ynamines **9** or amides **10**. A number of new substitution products have been obtained with phenylbromo- or phenylchloroacetylene and 1,4-diazobicyclo[2.2.2]octane (Dabco), brucine, dihydrobrucine, quinuclidine, as well as with 2′-(3-chloro-1,1-dimethyl-2-propynyloxy)tetrahydropyran and Dabco. Rate data for the second-order reactions of several halides with Dabco in acetonitrile are ($\Delta H^{\pm}$, kcal/mol; $-\Delta S^{\pm}$, eu; $10^4 k$, M^{-1} sec^{-1} at 60°): $C_6H_5C{\equiv}CBr$ (14.2, 30, 7.95); $C_6H_5C{\equiv}CCl$ (10.7, 40, 10.6); n-C_4H_9Cl (13.8, 34, 1.82). Toward Dabco, the electrophilic order of carbon sites is k (sp) $\geq$ k (sp^2) > k (sp$^{2.5}$). Although Dabco does appear to abstract halogen from the phenylhaloacetylenes, this appears to be far less important than attack on the terminal carbon, which leads to ynamines **2**.

As a part of our interest in nucleophilic displacement reactions at the triple bond, we studied both the synthetic and mechanistic aspects of process 1.[2] When this work was begun, the sp carbon to nitrogen bond system, $-C{\equiv}CN<$, was essentially unknown. In

$$R'C{\equiv}CX + R_3N \longrightarrow (R'C{\equiv}CNR_3{}^+X^-) \quad (1)$$

the meantime, alkynylamines or ynamines have been prepared by several routes and shown to be interesting and useful synthetic intermediates.[3,4] Our present contribution emphasizes the kinetics, mechanism, and some synthetic applications of bridgehead amines in process 1.

Certain complications in reaction 1 are worth attention.[3a] A haloalkyne may form charge transfer complexes, *e.g.*, $C_6H_5C{\equiv}CI \cdot H_2NC_6H_5$.[5] Alternatively, the "positive" halogen may be abstracted by the nu-

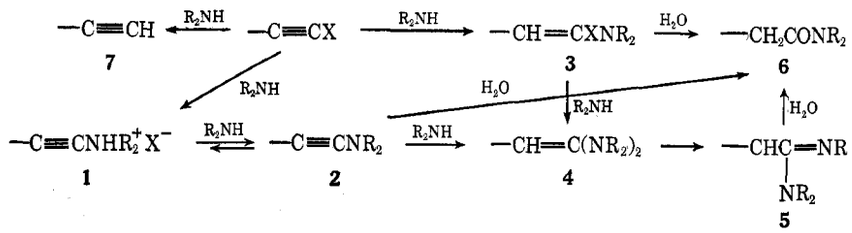
(1) Research supported by National Institutes of Health Grant GM 07021. This work was taken from the Ph.D. thesis of J. I. D., Illinois Institute of Technology, 1970.

(2) (a) J. I. Dickstein and S. I. Miller, *J. Org. Chem.*, **37**, 2168 (1972); (b) H. G. Viehe, S. I. Miller, and J. I. Dickstein, *Angew. Chem., Int. Ed. Engl.*, **3**, 582 (1964); (c) A. Fujii, J. I. Dickstein, and S. I. Miller, *Tetrahedron Lett.*, 3435 (1970); (d) R. Tanaka and S. I. Miller, *J. Org. Chem.*, **36**, 3856 (1971); (e) A. Fujii and S. I. Miller, *J. Amer. Chem. Soc.*, **93**, 3694 (1971); (f) A. K. Kuriakose and S. I. Miller, *Tetrahedron Lett.*, 905 (1962); (g) R. Tanaka, M. Rodgers, R. Simonaitis, and S. I. Miller, *Tetrahedron*, **27**, 2651 (1971).

(3) (a) H. G. Viehe in "Chemistry of Acetylenes," H. G. Viehe, Ed., Marcel Dekker, New York, N. Y., 1969, Chapter 12; (b) S. Y. Delavarenne and H. G. Viehe, Chapter 10; (c) H. G. Viehe, U. S. Patent 3,520,942 (1970); *Chem. Abstr.*, **73**, 98490 (1970); (d) S. Y. Delavarenne and H. G. Viehe, *Chem. Ber.*, **103**, 1198, 1209 (1970); (e) A. Halleux, H. Reimlinger, and H. G. Viehe, *Tetrahedron Lett.*, 3141 (1970).

(4) (a) L. I. Peterson, U. S. Patent 3,499,928 (1970); *Tetrahedron Lett.*, 5357 (1968); (b) T. Sasaki and A. Kojima, *J. Chem. Soc. C*, 476 (1970); (c) J. Freear and A. E. Tipping, *ibid.*, 411 (1969); (d) J. Ficini and C. Barbara, *Bull. Soc. Chim. Fr.*, 2787 (1965); (e) W. G. Galesloot, M. J. A. De Bie, L. Brandsma, and J. F. Arens, *Recl. Trav. Chim. Pays-Bas*, **89**, 575 (1970).

(5) R. H. Baughman, *J. Org. Chem.*, **29**, 964 (1964).



(2)

cleophile to produce an ion pair, which in the presence of a proton source (solvent or nucleophile) may give an acetylenic hydrocarbon, *e.g.*, **7**.[6a-c] Moreover, the substitution process as such may be masked if the amine contains mobile protons: any ynamines formed in these reactions will tautomerize to give nitriles or imines, *e.g.*, **5**; addition–elimination sequences can also intrude and give **4**.[3a,6d,7] Because an ynamine is a weak base, alkyl or hydrogen interchange normally takes place,[2b,6] and the isolation of the initial displacement product, an ethynylammonium salt, is rare.[2d,3a] An additional problem which can prevent the recovery of an ynamine is its facile hydration.[3a,6,7] Thus, the products of reactions of dialkylamines with dichloroacetylene were **3**–**6**,[7a] with phenylbromoacetylene were **4**, **6**, and **7**,[6b] and with 1-bromo-3-methyl-1-pentyn-3-ol were **6**, **7**, and some decomposition products. Some of these problems are alleviated when haloalkynes are treated with alkali metal dialkylamides or trialkylamines in aprotic solvents, and successful replacements have been effected.[2b,d,3a-d]

Experimental Section

Certain analyses, instruments, procedures, compounds, etc., employed here have been described in the accompanying paper.[2a]

Materials.—Anhydrous acetonitrile was distilled from anhydrous sodium carbonate, bp 82° (760 mm), $n^{20}D$ 1.3440 [lit.[8] bp 81–82° (760 mm), $n^{20}D$ 1.3442], no trace of water by infrared spectra (ir), and one peak by gas chromatography (gc). Liquid amines were distilled over KOH and stored under nitrogen. 1,4-Diazobicyclo[2.2.2]octane (Dabco) was recrystallized from methanol–ether (1:1) to mp 155–157° (lit.[9] mp 155–157°); it was water-free, as judged by its ir spectrum. Quinuclidine was distilled under high vacuum at *ca.* 25° into a trap (−78°), taken up in ether, and dried overnight with sodium sulfate. On evaporation of the ether, quinuclidine was recovered, mp 157–158° (lit.[8] mp 158°).

Brucine was recrystallized from acetone–water, mp 176–178°, $[\alpha]^{25}D$ −113° (*c* 0.8520, $CHCl_3$) [lit.[10,11] mp 178°, $[\alpha]^{30}D$ −117° ($CHCl_3$)]. Dihydrobrucine was prepared by the hydrogenation of brucine (5.23 g, 0.0133 mol) in ethanol over platinum(IV) oxide (0.5 g) and recrystallized from ethyl acetate. After drying at 100° (1 mm), it had mp 181–182° and $[\alpha]^{25}D$ 5.2° (*c* 2.3114, $CHCl_3$) [lit.[11] mp 182°, $[\alpha]^{30}D$ 7.6° ($CHCl_3$)].

n-Butyl chloride was fractionally distilled, and had bp 79°, $n^{20}D$ 1.4010, and one gc peak [lit.[10] bp 78.5°, $n^{20}D$ 1.4016].

***N*-Phenylethynyl-*N*-2-(4-aza-1-azoniabicyclo[2.2.2]octane)-ethylpiperazine Bromide.**—Phenylbromoacetylene (18.1 g, 0.1 mol) was mixed with Dabco (22.4 g, 0.2 mol) in ether and left for several days at *ca.* 25°. The quaternary salt which separated was filtered, dissolved in chloroform, and reprecipitated by the addition of ether. This procedure often gave an oil, but after several cycles a solid could be obtained in *ca.* 85% yield: mp 144° dec; ir ($CHCl_3$) 4.51 (C≡C) and 6.07 μ (C=O); nmr ($DCCl_3$) δ 7.3–7.4 (5 ArH) and 2.5–4.0 (24 CH_2, m).

Anal. Calcd for $C_{20}H_{29}BrN_4$: C, 59.25; H, 7.21; Br, 19.71. Calcd for $C_{20}H_{29}BrN_4 \cdot H_2O$: C, 56.73; H, 6.86; Br, 18.87. Found: C, 58.35; H, 7.23; Br, 19.43.

Acidic hydrolysis (25% sulfuric acid) of this compound (10 g, 0.025 mol) gave phenylacetic acid (1 g), mp 76–77°, identical by ir and mixture melting point comparison with an authentic sample.

***N*-Phenylethynyl-*N*-2-(4-aza-1-azoniabicyclo[2.2.2]octane)-ethylpiperazine Chloride.**—This compound was prepared by the procedure described above for the bromide. The chloride was very hygroscopic and the oil which was isolated in *ca.* 70% yield could not be crystallized. The ir spectrum of the oil was identical with that of *N*-phenylethynyl-*N*-2-(4-aza-1-azoniabicyclo-[2.2.2]octane)ethylpiperazine bromide, ir ($CHCl_3$) 4.51 (C≡C) and 6.05 μ (C=O).

Anal. Calcd for $C_{20}H_{29}ClN_4$: Cl, 9.85. Calcd for $C_{20}H_{29}ClN_4 \cdot H_2O$: Cl, 9.38. Found: Cl, 9.52.

Reaction of 2′-(3-Chloro-1,1-dimethyl-2-propynyloxy)tetrahydropyran with Dabco.—The pyranyl ether (10.2 g, 0.05 mol) was heated with Dabco (11.2 g, 0.1 mole) in 250 ml of ether for *ca.* 1 month. The crude product (9.0 g, 40% yield) was removed from the reaction mixture by filtration. The quaternary chloride salt showed an amide band at 6.11 μ and no C≡C absorption in the infrared. This material was dissolved in water and treated with sodium tetraphenylboron to give a quantitative amount of the tetraphenylboron salt. The tetraphenylboron compound was recrystallized in ethanol–water (80:20, v/v) and had mp 65° dec.

Anal. Calcd for $C_{46}H_{61}BO_3N_4$: C, 75.80; H, 8.44. Found: C, 75.58; H, 7.75.

***N*-Phenylethynyl-2-(1-azabicyclo[2.2.2]octane)ethylpiperidine Bromide.**—Phenylbromoacetylene (1.81 g, 0.01 mol) and quinuclidine (2.22 g, 0.02 mol) were dissolved in ether (100 ml) and allowed to stand at *ca.* 25° for 1 week. The insoluble product (2.56 g, 64% yield) was isolated by filtering the reaction mixture. The crude mixture exhibited a C≡C absorption at 4.50 μ and an amide carbonyl band at 6.11 μ. Treatment of this material with water completely removed the C≡C linkage. An nmr proton countr evealed that 1 mol of phenylbromoacetylene had reacted with 2 mol of quinuclidine to form the product. The amide salt was dissolved in water and treated with sodium tetraphenylboron. A quantitative yield of the tetraphenylboron derivative was obtained. This material was recrystallized from ethanol–water (80:20, v/v): mp 77–80° dec; ir (KBr) 6.10 μ (C=O); nmr ($CHCl_3$) δ 6.6–7.4 (25 ArH) and 0.8–4.2 (28 alkyl H).

Anal. Calcd for $C_{46}H_{53}BON_2$: C, 83.61; H, 8.08. Found: C, 83.91; H, 8.04.

18-Bromo-19-(phenylacetyl)-18,19-secobrucine and 20-Bromo-19-(phenylacetyl)-19,20-secobrucine.—Phenylbromoethyne (9.0 g, 0.05 mol) and brucine (13.0 g, 0.033 mol) were dissolved in 200 ml of benzene and left at *ca.* 25° for several days. The products precipitated out of the benzene solution and 18 g (crude yield 92%) was isolated from the reaction mixture by filtration. Fractional crystallization in absolute ethanol resulted in the separation of two isomers. Neither isomer showed C≡C absorption in the ir. Since brucine contains an amide grouping (ring C), the hydration of the phenylethynyl moiety attached to the nitrogen of brucine could not be established by ir. Nmr proton counts indicated that both products resulted from the union of 1 mol of phenylbromoacetylene with 1 mol of brucine.

Isomer A had mp 186° dec, $[\alpha]^{25}D$ +23.62° (*c* 0.7430, $CHCl_3$), nmr ($DCCl_3$) δ 5.5–8.3 (ArH, 7 =CH, broad) and 0.8–5.0 (25 alkyl H, broad).

(6) (a) V. Wolf and W. Block, *Justus Liebigs Ann. Chem.*, **637**, 119 (1960); (b) V. Wolf and F. Kowitz, *ibid.*, **638**, 33 (1960); (c) V. Wolf, W. Block, and H. Piater, *ibid.*, **682**, 112 (1965); (d) V. Wolf and H. Piater, *ibid.*, **696**, 90 (1966).

(7) (a) E. Ott and G. Dittus, *Chem. Ber.*, **76**, 80 (1943); (b) R. Truchet, *Ann. Chim. (Paris)*, **16**, 309 (1931).

(8) "Handbook of Tables for Organic Compound Identification," Z. Rappoport, Ed., Chemical Rubber Co., Cleveland, Ohio, 1967.

(9) S. D. Ross, J. J. Bruno, and R. C. Petersen, *J. Amer. Chem. Soc.*, **85**, 3999 (1963).

(10) I. Heilbron, "Dictionary of Organic Compounds," Oxford University Press, London, 1965.

(11) H. Wieland and W. Munster, *Justus Liebigs Ann. Chem.*, **480**, 39 (1930).

Anal. Calcd for $C_{31}H_{33}O_5N_2Br$: C, 62.73; H, 5.60. Found: C, 62.36; H, 5.84.

Isomer B had mp 216° dec, $[\alpha]^{25}D$ +106.12° (*c* 0.8745, $CHCl_3$), nmr ($DCCl_3$) δ 5.5–8.3 (7 ArH, 1 =CH, broad) and 0.8–5.0 (25 alkyl H, broad).

Anal. Calcd for $C_{31}H_{33}O_5N_2Br$: C, 62.73; H, 5.60. Found: C, 62.31; H, 5.75.

Isomer B (0.77 g, 0.0013 mol) was dissolved in 120 ml of absolute ethanol containing PtO_2 (0.188 g) and hydrogenated. The dihydrobrucine product had mp 215° dec, $[\alpha]^{25}D$ +82.34° (*c* 1.0069, $CHCl_3$).

Anal. Calcd for $C_{31}H_{35}O_5N_2Br$: C, 62.52; H, 5.92. Found: C, 63.22; H, 6.59.

Reaction of Phenylbromoacetylene with Dihydrobrucine.—Dihydrobrucine (1.98 g, 0.005 mol) and phenylbromoacetylene (1.4 g, 0.0075 mol) were heated in benzene (100 ml) for *ca.* 2 days. The crude product (1.76 g, 50% yield) was isolated from the reaction mixture by filtration. This material was recrystallized from ethanol, mp 270° dec, $[\alpha]^{25}D$ +73.7° (*c* 1.4380, $CHCl_3$).

Anal. Calcd for $C_{31}H_{35}O_5N_2Br$: C, 62.52; H, 5.92. Found: C, 62.38; H, 5.76.

18-Chloro-19-(phenylacetyl)-18,19-secobrucine and 20-Chloro-19-(phenylacetyl)-18,19-secobrucine.—Phenylchloroacetylene (4.1 g, 0.03 mol) and brucine (7.5 g, 0.019 mol) were dissolved in benzene (100 ml). The reaction mixture was allowed to stand at *ca.* 25° for 1 week and 6.0 g (58% yield) of the crude products was isolated by filtration. The ir spectrum of this material was identical with that of phenylbromoethyne–brucine crude product. Isomers C and D, obtained by fractional crystallization of crude material in absolute ethanol, are obvious as analogs of compounds A and B. Therefore, we include D, despite a poor analysis.

Isomer C had mp 174–177° dec.

Anal. Calcd for $C_{31}H_{33}O_5N_2Cl$: C, 67.81; H, 6.06. Found: C, 67.34; H, 6.20.

Isomer D had mp 208–210° dec.

Anal. Calcd for $C_{31}H_{33}O_5N_2Cl$: C, 67.81; H, 6.06. Found: C, 66.71; H, 6.04.

Reactions of Phenylbromoacetylene with Trialkyl Amines and Amides.—Phenylbromoethyne (18.1 g, 0.1 mol) and triethylamine (20.2 g, 0.2 mol) in ether or toluene (200 ml) were kept at *ca.* 25°. (Higher temperatures led to lower product yields.) Tetraethylammonium bromide precipitated; this was filtered off and purified by repeated solution in chloroform followed by ether precipitation. The yield was 71%. Identification was made with an authentic sample by ir and elemental analysis. The final work-up of the second product was a short-path distillation of an oil at 50° (10^{-3} mm). This gave *N*,*N*-diethylphenylacetamide (4.1 g, 21%), ir (neat) 6.20 μ (C=O), $n^{22}D$ 1.5323, identical with an authentic sample by ir and elemental analysis.

The general procedure just outlined, except for variations in details, *e.g.*, solvent, temperature, etc., was used with other nitrogen nucleophiles. The haloalkyne and amine or lithium amide in anhydrous ether, toluene, or DMF were kept at ~25° for several days. Work-up of the mixtures yielded salts and intractable tarry residues. As a synthesis of ynamines from phenylbromoacetylene, our experiments were negative; the fact that trimethyl- and tri-*n*-propylamine yielded tetraalkylammonium salts just as with triethylamine indicates that ynamines probably had formed.[3a-c] From secondary amines, *e.g.*, piperidine, di-*n*-butylamine, and di-*tert*-butylamine, the corresponding ammonium hydrobromides were isolated. No isolable products could be obtained with tri-*n*-hexylamine, *N*-methylpyrrolidine, pyridine, quinoline, acridine, lithium piperidide, lithium diethylamide, and lithium dibutylamide, although reaction with ionic halide and tar formation were observed.

Kinetics.—The methods of the companion paper were used.[2a] In each case, the identity of the products and stoichiometry of the reactions (see eq 5) were verified under the conditions used in the rate studies. For the reaction of phenylbromoacetylene with Dabco, rate law 3 was used. Where appropriate, the conductances of the product salts were shown to be linear functions of their concentrations. All of the rate constants have been corrected for the thermal expansion of the solvent (CH_3CN)

$$kt = 2.303(2a - b)^{-1} \log b(a - x)/a(b - 2x) \qquad (3)$$

with the following factors:[12] 1.020 at 39.6°, 1.028 at 45.0°, 1.035 at 49.7°, 1.035 at 49.8°, 1.046 at 57.6°, 1.050 at 60.3°, 1.064 at 70.0°, and 1.066 at 70.3°. Details are given in the thesis;[1b] the rate data are collected in Tables I–IV.

TABLE I

TITRIMETRIC RATE DATA FOR THE REACTION OF 1-PHENYLBROMOACETYLENE WITH DABCO IN ACETONITRILE

Temp, °C	$C_6H_5C{\equiv}CBr$, *M*	Dabco, *M*	$k^a \times 10^4$, M^{-1} sec^{-1}
70.00 ± 0.03	0.02500	0.07523	14.3 ± 0.1
	0.08000	0.2006	14.6 ± 0.2
	0.008108	0.09217	14.3 ± 0.1
	0.06875	0.03134	14.3 ± 0.1
		k_{corr}	15.3 ± 0.1
57.63 ± 0.03	0.02500	0.07523	6.30 ± 0.20
	0.08000	0.02006	6.42 ± 0.17
	0.008108	0.09217	6.47 ± 0.12
	0.06875	0.03134	6.33 ± 0.28
		k_{corr}	6.67 ± 0.20
45.00 ± 0.03	0.02500	0.07523	2.65 ± 0.15
	0.08000	0.02006	2.62 ± 0.06
	0.008108	0.09217	2.72 ± 0.07
	0.06875	0.03134	2.67 ± 0.10
		k_{corr}	2.74 ± 0.10

[a] These are mean values; k_{corr} are final values obtained by correcting the *k*'s for solvent expansion.

TABLE II

CONDUCTOMETRIC RATE DATA FOR THE REACTION OF $C_6H_5C{\equiv}CCl$ WITH DABCO IN CH_3CN

Temp, °C	Dabco, *M*	$k\psi \times 10^4$, sec^{-1}	$k^a \times 10^4$, M^{-1} sec^{-1}
60.30 ± 0.05	0.1613	1.62	10.6
	0.2292	2.30	
	0.4419	4.43	
	0.6193	6.25	
49.80 ± 0.05	0.2131	1.25	6.05
	0.5313	3.12	
	0.7143	4.17	
	0.9938	5.80	
39.00 ± 0.05	0.1582	0.530	3.40
	0.2584	0.870	
	0.4658	1.55	
	0.4715	1.57	

[a] The rate constants are corrected for solvent expansion.

TABLE III

CONDUCTOMETRIC RATE DATA FOR THE REACTION OF *n*-BUTYL CHLORIDE WITH DABCO IN CH_3CN

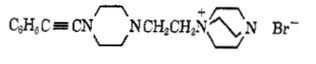
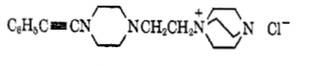
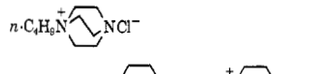
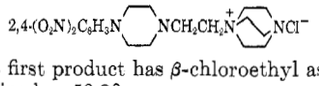
Temp, °C	Dabco, *M*	$k\psi \times 10^5$, sec^{-1}	$k^a \times 10^5$, M^{-1} sec^{-1}
49.70 ± 0.03	0.3026	2.52	8.58
	0.5964	4.95	
	0.9860	8.22	
60.30 ± 0.03	0.1125	2.00	18.2
	0.2987	5.28	
	0.5762	9.77	
	0.8143	13.9	
70.30 ± 0.03	0.2190	7.08	34.3
	0.4100	13.2	
	0.5635	18.8	
	0.7998	25.5	

[a] The rate constants are corrected for solvent expansion.

(12) "International Critical Tables," Vol. 3, E. W. Washburn, Ed., McGraw-Hill, New York, N. Y., 1928, p 28.

TABLE IV

RATE DATA FOR DISPLACEMENT REACTIONS WITH DABCO IN ACETONITRILE AT 60°

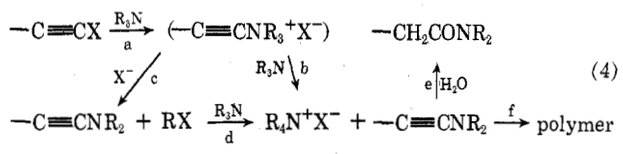
Halide	Product	$k \times 10^4$, M^{-1} sec^{-1}	$\Delta H^{\pm}$, kcal/mol	$\Delta S^{\pm}$, eu
$C_6H_5C{\equiv}CBr$		7.95	14.2 ± 0.5	30 ± 2
$C_6H_5C{\equiv}CCl$		10.6	10.7 ± 0.5	40 ± 2
n-C_4H_9Cl		1.82	13.8 ± 1.0	34 ± 3
2,4-$(O_2N)_2C_6H_3Cl$[a]		1.13[b]		

[a] Reference 9. The predominant first product has β-chloroethyl as the 4-substituent; the chlorine atom is eventually replaced by another Dabco molecule. [b] Determined at 50.8°.

Results and Discussion

Syntheses.—In most areas involving displacement at carbon, there was a firm synthetic base on which to launch mechanism studies. None existed for haloalkynes in the early 1960's, although contributions by several workers have since made them accessible.[3,4] We can, however, report progress with bridgehead nitrogen compounds. Of these, Dabco has proved useful for kinetic and mechanism studies.

Our reactions of trialkylamines with phenylbromoacetylene in aprotic solvents are consistent with eq 4.



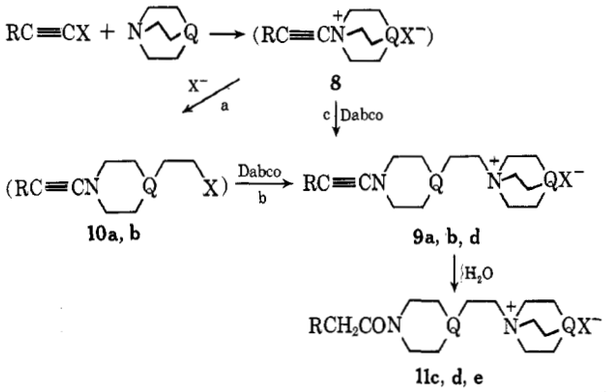
(4)

Although we isolated only *N*,*N*-diethylphenylacetamide and several alkyl quaternary salts, Viehe[3a] has recently given directions for the preparation of dimethylaminophenylacetylene from phenylbromoacetylene and trimethylamine. Since several ethynylammonium salts and the corresponding ynamines have been prepared from other haloalkynes,[2d,3] it would appear that the synthetic problem of preparing ynamines *via* eq 4 has been solved. Nevertheless, the high reactivity of ynamines as electrophiles, nucleophiles, dipolarophiles, etc.,[3,4] provides a rationale for the troublesome diversions e and f in eq 4, and indicate that care in their preparation is essential.

With respect to ethynylammonium salts, several examples in the older literature have been discredited,[13] while several new ones have been reported.[2d,14] *In this study*, at least, the yields (>50%) of quaternary ammonium salts indicate $k_a < k_b$ in eq 4. The presence of the alkyl quaternary salts which turned up routinely is mechanistically significant. Because of the electron-withdrawing character of the ethynyl group, an ynamine is a weaker base than most corresponding alkylamines. Hence the conversion of the ethynylammonium salt either by excess amine or halide is favored thermodynamically. Judging from our mild reaction conditions, *e.g.*, 1–3 days at ~25°, and the low rate constant for reaction between triethylamine and ethyl bromide, *i.e.*, 5.5×10^{-4} M^{-1} sec^{-1} in acetone at 100°,[15] we believe that step b is generally favored over c in eq 4.

(13) F. Klages and E. Drerup, *Justus Liebigs Ann. Chem.*, **547**, 65 (1941).
(14) (a) J. Dumont, *C. R. Acad. Sci.*, **261**, 1710 (1965); (b) B. I. Ionin and A. A. Petrov, *Zh. Obshch. Khim.*, **35**, 2255 (1965).
(15) N. Menschutkin, *Z. Phys. Chem. (Leipzig)*, **5**, 589 (1890); **6**, 41 (1890).

The characteristics of the reactions of trialkylamines show up to some degree with Dabco. The expected salts from phenylbromo- and phenylchloroacetylene form ynamine **9a,b** either by step c or by processes a and b of eq 5. In the latter pathway, excess Dabco



(5)

was used and consequently **10a,b** were not isolated. Ynamines **9a,b** are demonstrably hygroscopic, form amides in water,[2b] and yield phenylacetic acid in concentrated acid. Perhaps because of the long heating period (~1 month), the only product obtained in the reaction of 2′-(3-chloro-1,1-dimethyl-2-propynyloxy)-tetrahydropyran with excess Dabco was the amide **10c**.

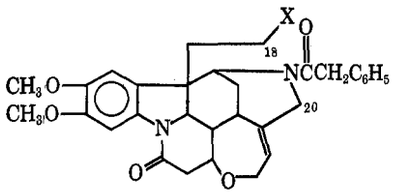
It is interesting that process 5 is closely similar to von Braun's cyanogen bromide reaction with tertiary amines.[16] Furthermore, analogous products have been reported for 2,4-dinitrochlorobenzene and Dabco as well as from 2-iodocyclohepta-2,4,6-trienone and quinuclidine, in which analogs of **8**–**10** were isolated.[17] In all of these examples, the rationale proposed for transalkylation, as in step 5c, or the retro Menschutkin reaction, as in step 5a,[9,17] is analogous to that given for ynamines, namely, that there is a conjugative interaction between the lone pair on nitrogen and the unsaturated system, which stabilizes the base and lowers its base strength.

The action of excess quinuclidine on phenylbromoacetylene gave a mixture of products, **9d** and **11d**.

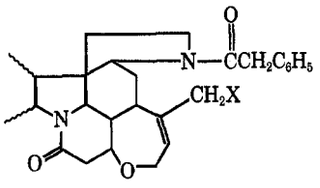
(16) H. A. Hageman, *Org. React.*, **7**, 198 (1953).
(17) F. Pietra and F. D. Cima, *J. Chem Soc. B*, 2224 (1971).

Upon treatment with water, **9d** was easily converted to the amide salt **11d**.

Facile reactions occurred between brucine, which contains a bridgehead nitrogen in ring C, and bromo- and chlorophenylacetylene, which were initially present in excess. Two isomers result from different cleavage modes at the bridgehead: attack by the halide ion at C-18 and C-20 produces 18-halo-19-(phenylacetyl)-18,19-secobrucine (**12**) and 20-halo-19-(phenylacetyl)-18,19-secobrucine (**13**), respectively.



12a, X = Br
b, X = Cl



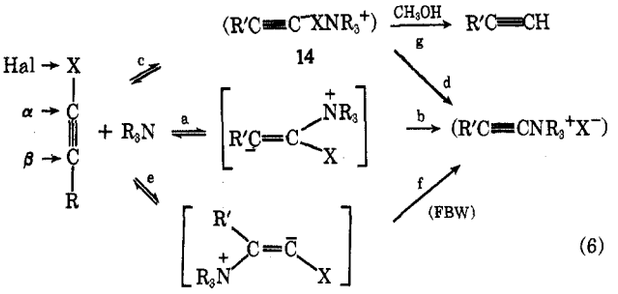
13a, X = Br
b, X = Cl

Although we do not assign structures **12** or **13**, similar scission products have been previously established for strychnine and brucine with cyanogen bromide.[18] In the reaction of dihydrobrucine with cyanogen bromide, it has been demonstrated that bromide ion attacks C-18 exclusively to form a single product. For brucine, SN2 displacement at C-18 appears to compete with the normally more facile allylic cleavage at C-20; in dihydrobrucine, no N–C-20 breakage occurs at all. It has been suggested that this can be taken as a measure of the greater steric accessibility of C-18 over C-20 to the attack of external reagents.[19] Accordingly, the product from the reaction of phenylbromoacetylene with dihydrobrucine is assigned structure **12a**, but without the double bond. An indication of the greater reactivity of C-20 over C-18 in brucine is reflected by the reaction conditions employed for brucine and dihyrobrucine. With brucine and phenylbromoacetylene in benzene, high conversion is obtained at *ca.* 25°, while with dihydrobrucine moderate quantities of product are obtained at 80°.

Kinetics and Mechanism.—The kinetics of the reactions of phenylbromo- and phenylchloroacetylene and *n*-butyl chloride with Dabco in acetonitrile were studied. These systems showed second-order kinetics, first order in Dabco and first order in halide (Tables I–IV). The large negative values for $\Delta S^{\ddagger}$ are in accord with other molecule–molecule reactions in which ion pairs are initially formed.[2d,e] However, the activation parameters for the haloalkynes showed large differences (Table IV): although the rate constants for phenylchloro- and phenylbromoacetylene are similar at 60°, the former is favored by a factor of *ca.* 200 in the energy of activation while the latter is favored by a factor of *ca.* 160 in the entropy of activation. The more negative value of $\Delta S^{\ddagger}$ for the chloro compound is also found in the analogous molecule–molecule reactions of triphenylphosphine with phenylchloro- and phenylbromoacetylene in DMF.[2a] To understand the detailed pattern of activation parameters, we believe that more data are required on solvent and substrate variation in which analogous charge-dispersed but neutral transition states are involved.

Halounsaturates, *e.g.*, vinyl, aryl, and ethynyl, have traditionally been regarded as relatively indifferent to nucleophiles by comparison with haloalkanes. The data in Table IV indicate that phenylchloroacetylene is more reactive than 1-chlorobutane, "standard" for SN2 processes,[20] and is even more reactive than an activated chlorobenzene:[9] k (sp) $\geqslant$ k (sp^3) > k ($sp^{2.5}$). Among unsaturates, a partial rationalization of the high reactivity of the acetylenic carbon towards amines may be attributed to the fact that the sp carbon is more electronegative than aryl or vinyl carbon.

Among the three major mechanisms currently considered for process 1, we favor steps a (slow) and b (fast) of eq 6 for the particular haloalkynes used in this study. Evidence for terminal carbon (α) attack (a, b), halogen abstraction (c, d), and internal carbon



(6)

(β) attack (e) followed by rearrangement has been produced for different systems.[2,3] (Note that "α- and β-attack" are positions relative to halogen.) All can be consistent with second-order kinetics. This means that the generation of any one of the intermediates, *e.g.*, from an alkene, and subsequent isolation of the ynamine is not conclusive as to the mechanism, for any of the intermediates can revert to the starting materials. Thus, there is an inherent uncertainty about any mechanism which can only be settled by specific consideration of actual systems.

With respect to β attack (on the internal carbon) followed by rearrangement, the 1,2-sigmatropic shift of R_2N– is known,[3d] but that of R_3N^+– or alkyl (R′) is forbidden,[21] as well as unprecedented.[22] 1,2-Aryl migrations, however, do occur in the analogous Fritsch–Buttenburg–Weichell (FBW) rearrangement, but the bases used are generally more powerful and the reaction conditions more forcing than those we employed here.[3d,23] For all of these reasons, we believe the FBW sequence e and f in eq 6 to be improbable.

To attempt to find evidence for halogen abstraction

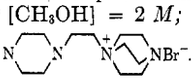
(18) H. G. Boit, *Chem. Ber.*, **86**, 133 (1953).
(19) J. B. Hendrickson in "The Alkaloids," Vol. 6, R. H. F. Manske, Ed., Academic Press, New York, N. Y., 1960, Chapter 6.
(20) A. Streitwieser, *Chem. Rev.*, **56**, 571 (1956).
(21) S. I. Miller, *Advan. Phys. Org. Chem.*, **6**, 185 (1968).
(22) D. V. Banthrope in "The Chemistry of the Amino Group," S. Patai, Ed., Interscience, New York, N. Y., 1968, Chapter 10.
(23) G. Köbrich, *Angew. Chem.*, **79**, 15 (1967).

(c) in eq 6, we used methanol in trapping experiments. Now, both phenylacetylene and ynamine are produced. If one allows for the uncertainties of the product analyses at low conversions, it appears that halogen abstraction is a minor competing process in our systems (Table V). In passing, it is interesting that we observe less

TABLE V

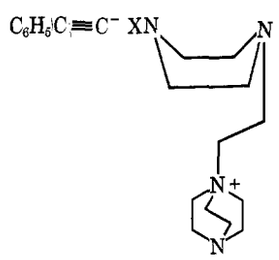
THE REACTION OF DABCO (1 *M*) WITH $C_6H_5C{\equiv}CX$ (0.5 *M*) IN DIMETHYLFORMAMIDE–METHANOL[a]

X	Time, hr	$[C_6H_5C{\equiv}CH]$, *M* (%)	$[X^-]$,[b] *M*	$[X^-]/[C_6H_5C{\equiv}CH]$
Br[c]	0.083	0.0275 (21)	0.1309	4.8
Br[c]	0.5	0.0253 (7)	0.3649	14.4
Br[d]	24	0.0690 (14)	0.4992	7.23
Cl[c]	0.5	0.0102 (2.4)	0.4244	41.6
Cl[c]	19.5	0	0.4995	∞
Cl[d]	24	0	0.4997	∞
e	24	0	0.50	∞

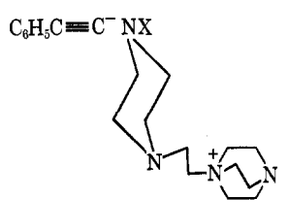
[a] All runs were made in duplicate in separate ampoules. [b] From eq 8a or 8b. [c] $[CH_3OH]$ = 2 *M*; 77°. [d] $[CH_3OH]$ = 12.4 *M*; 70°. [e] X =  .

halogen abstraction with tertiary amine than with tertiary phosphine; *i.e.*, Dabco < $(C_6H_5)_3P$ < $(n\text{-}C_4H_9)_3P$.[2a] This may be attributed to the greater polarizability of the phosphorus atom and to the more energetically favorable P–X bond formation.

Although the production of phenylacetylene is positively diagnostic for step c of eq 6, it provides no information on whether the ynamine is also produced after step c. As a route to the ynamine salt, step d seems plausible on paper, but is, in fact, improbably complex. Consider the ion pairs **14**,**15a**,**b**. The formation of the substitution product *via* step d pre-



15a



15b

sumably requires backside attack of the acetylide ion on nitrogen. In view of the fact that the nitrogen in **14** is a bridgehead atom, such a process cannot take place. Since the bicyclic ring is opened in these reactions, back-side attack could be salvaged by having **15a** rearrange to **15b**, *within* the solvent cage. But in order to form **15a**, Dabco molecules must penetrate the solvent cage in preference to the smaller and more abundant methanol molecules, which seems unlikely. Furthermore, the phenylacetylide ion would presumably move from the original displacement center (N–X) to the new charged site. With all of this relative motion taking place, the acetylide ion is unlikely to survive in the presence of a proton source to give ynamine **9**. All of this suggests that $k_d = 0$, and that the ynamine salt and the acetylene are formed on independent paths in eq 6; halogen abstraction from haloalkynes can occur but it appears to be a dead end, off the route from haloalkyne to ynamine!

We are left with a and b of eq 6 as the dominant sequence for the amine–haloalkyne systems that we studied. However, this mechanism does have real support. The element effect, k (Cl)/k (Br) > 1, is significant in that this is consistent with predominant rate-determining attack on carbon rather than on halogen (Table IV). This order has now been found with the nucleophiles thiolate,[2f] phosphite,[2e] phosphine,[2a] and alkoxide[2g] in process 1; but where nucleophilic attack is on halogen, the order has been shown to be k (Br) ≫ k (Cl).[2c,e,g] There is also product evidence in the reaction of phenylbromoacetylene with diethylamine, which yields β,β-bis(dialkylamino)styrene, presumably *via* the appropriate ynamine.[6a,d] The absence of α-dialkylamino-β-bromostyrene or its derivatives, which were found with alkylhaloalkynes, would also appear to indicate against β attack.[6]

If attack on the terminal carbon is accepted, there is still the problem of obtaining our final product **9**; the alternatives are laid out in eq 5. Our rate constants were determined by following the production of salt by conductance for phenylchloroacetylene and by potentiometric titration for phenylbromoacetylene. If the concentration of the neutral molecule **10** in eq 5 were significant, these methods would not give "constant" rate constants. For 2,4-dinitrochlorobenzene–Dabco, satisfactory kinetic data have been reported for the conditions of amine in large excess over halide; here the concentration of the haloethylpiperazine was negligible.[9] Our rate constants for phenylchloroacetylene were determined by making measurements with the haloalkyne at low concentration and the amine in *ca.* 20–100-fold excess. In fact, for phenylbromoacetylene–Dabco, we obtained identical k values with either reagent in excess. This suggests that step c of eq 5 is relatively fast and there is little or no storage of **10b** during the course of the reaction. This completes our mechanistic proposals for the processes given in eq 5 and 6.

Registry No.—Dabco, 280-57-9; **9a**, 34403-83-3; **9b**, 34403-84-4; **11c** tetraphenylboron derivative, 34459-53-5; **11e**, 34398-84-0; **12a**, 34403-85-5; **12a** dihydro derivative, 34403-86-6; **12b**, 34403-87-7; **13a**, 34403-88-8; **13b**, 34403-89-9; quinuclidine, 100-76-5; brucine, 357-57-3; dihydrobrucine, 34403-90-2; 1-phenylbromoacetylene, 932-87-6; 1-phenylchloroacetylene, 1483-82-5; *n*-butyl chloride, 109-69-3.

Acknowledgment.—We thank Houdry Process Corp. for samples of Dabco.