Partition of Unsaturated Diazotates between Diazoalkenes and Carbonium Ions in Base

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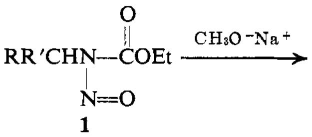
Abstract: Each of eight substituted ethyl allylnitrosocarbamates was converted, with sodium methoxide in methanol, to a mixture of allylic diazo compound and allylic methyl ethers. The products did not interconvert under the reaction conditions. The ratio of "carbonium ion" derived products to diazoalkene was favored by electron-donating substituents and by secondary *vis-á-vis* primary alkenyl groups. Grossly different isomeric mixtures of butenyl methyl ethers were obtained from ethyl *trans*-2-butenylnitrosocarbamate and ethyl 1-methyl-2-propenylnitrosocarbamate; in each case ether derived from the original butenyl structure predominated. Free carbonium ions or ion pairs in which the counter ions have reached an energy minimum are excluded as intermediates. Preferential formation of isomers with unrearranged structures may be due to hydrogen bonding of the solvent with the diazotate ion or diazotic acid.

Alkylnitrosocarbamates (**1**) react with base in protic solvents to give two types of product, diazoalkanes and solvolysis products which can be rationalized from carbonium ion like intermediates. The observations of a number of investigators[2] indicate that the reaction occurs by attack of base on the carbonyl carbon,[3] with the formation of an alkyl diazotate **2** (and dialkyl carbonate). The diazotates can, in the absence of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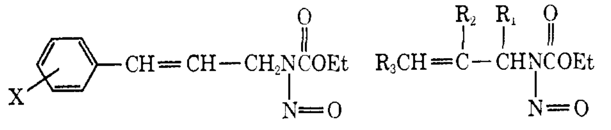
$$\underset{\mathbf{1}}{RR'CHN(N{=}O)\overset{O}{\overset{\|}{C}}OEt} \xrightarrow{CH_3O^-Na^+} \underset{\mathbf{2}}{RR'CHN{=}NO^-Na^+} + CH_3OCO_2Et \qquad (1)$$

$$\mathbf{2} + CH_3OH \longrightarrow \underset{\mathbf{3}}{RR'CHN{=}NOH} + CH_3O^- \qquad (2)$$

$$\underset{\mathbf{4}}{RR'CN_2} \overset{-H_2O}{\rightleftarrows} \mathbf{3} \xrightarrow{-N_2,\ OH^-} \underset{\mathbf{5}}{[RR'CH^+]} \longrightarrow \text{solvolysis products} \qquad (3)$$

protic solvents, be isolated as salts (eq 1).[4] In protic solvents they accept a proton to form the diazotic acid **3** (eq 2) which reacts further to form diazo compound **4** and/or solvolysis products *via* a "carbonium-type" intermediate **5** (eq 3). The diazo compound and solvolysis products (including elimination products) are produced by competitive processes. The partition of **3**[5] between the two paths has been shown to depend on the alkyl structure and on the reaction conditions.[2a,c–e,6] For example, with secondary alkyl groups (R or R′ ≠ H) the solvolysis route was heavily favored, and diazo compounds are favored by methanol compared with water. Further understanding of the factors which influence the partitioning of diazotic acids between the two paths is important because it can increase the synthetic utility of the reaction (especially with regard to preparing diazo compounds) and also because it may clarify the mechanism of amine deamination.

In this paper we focus on these two problems, using alkenylnitrosocarbamates as probes. Four N-cinnamyl-N-nitrosocarbamates (**6**) have been decomposed with base, and the electronic influence of substituents on partition between the diazo and solvolysis paths has been determined. The ratio of isomeric solvolysis products was also established. In addition, four aliphatic N-allyl-N-nitrosocarbamates (**7**) have been decomposed in base. Two of these (**7b** and **7d**) could give the same carbonium ion intermediate, so it was of interest to determine the ratio of isomeric solvolysis products.



6 **7**

X = *m*-NO$_2$, *p*-Cl, H, *p*-CH$_3$

a, $R_1 = R_2 = R_3 = H$
b, $R_1 = CH_3$; $R_2 = R_3 = H$
c, $R_2 = CH_3$; $R_1 = R_3 = H$
d, $R_3 = CH_3$; $R_1 = R_2 = H$

Results

The ethyl alkenylnitrosocarbamates were prepared by nitrosation of the corresponding carbamates with dinitrogen tetroxide or nitrosyl chloride, by established procedures. Solutions of the nitrosocarbamates in

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[1] Michigan State University Graduate Council Fellow, 1965–1966; National Science Foundation Predoctoral Fellow, 1966–1967.

[2] (a) F. W. Bollinger, F. N. Hayes, and S. Siegel, *J. Am. Chem. Soc.*, 72, 5592 (1950); (b) R. Huisgen and J. Reinsertshofer, *Ann.*, **575**, 174 (1952); (c) C. D. Gutsche and H. E. Johnson, *J. Am. Chem. Soc.*, 77, 109 (1955); (d) D. E. Applequist and D. E. McGreer, *ibid.*, **82**, 1965 (1960); (e) R. A. Moss, *J. Org. Chem.*, **31**, 1082 (1966); (f) R. A. Moss and G. H. Temme, III, *Tetrahedron Letters*, 3219 (1968); for related work, see E. R. Stredronsky, J. Gal, R. A. M. O'Ferrall, and S. I. Miller, *J. Am. Chem. Soc.*, **90**, 993 (1968).

[3] With nitrosoureas, however, the site of base attack is apparently the N–H bond: W. Kirmse and G. Wächterhäuser, *Ann.*, **707**, 44 (1967).

[4] For examples, see A. Hantzsch and M. Lehman, *Chem. Ber.*, **35**, 897 (1902); E. Muller, H. Haiss, and W. Rundel, *ibid.*, **93**, 1541 (1960); T. K. Tandy and W. M. Jones, *J. Org. Chem.*, 30, 4257 (1965); R. A. Moss and F. C. Shulman, *Tetrahedron*, 24, 2881 (1968); R. A. Moss, F. C. Shulman, and E. Emery, *J. Am. Chem. Soc.*, **90**, 2731 (1968); H. Hart and J. Brewbaker, *ibid.*, **91**, 706 (1969).

[5] In some circumstances the diazonium ion may be the point of partitioning; see ref 3.

[6] R. A. Moss and S. M. Lane, *J. Am. Chem. Soc.*, **89**, 5655 (1967).

either di-*n*-butyl ether or cyclohexene were treated with a threefold excess of sodium methoxide in methanol, either at room temperature or 4°. The yields of diazoalkenes and methyl alkenyl ethers are given in Tables I and II.

Table I. Products from the Reaction of Ethyl N-Cinnamyl-N-nitrosocarbamates withMethanolic Sodium Methoxide[a]

	Yield, %		
6, X =	$XC_6H_4CH{=}CHCHN_2$	$XC_6H_4CH{=}CHCH_2OCH_3$	$XC_6H_4CH(OCH_3)CH{=}CH_2$
m-NO_2	47	41	7
p-Cl	32	22	10
H	22	56	13
p-CH_3	19	36	15

[a] 10 mmol of nitrosocarbamate in 50 ml of cyclohexene was stirred with 10 ml of 3 *N* methanolic sodium methoxide at 4° for 1.5 to 2.5 hr. The organic layer was washed with 10% aqueous sodium hydroxide, dried (KOH), and allowed to stand in the dark at 25° for 48 hr, then analyzed.

Table II. Products from the Reaction of Ethyl N-Allylic-N-nitrosocarbamates with Methanolic Sodium Methoxide[a]

	Yield, %		
Compd	Diazo compd	Primary ether	Secondary ether
7a	80	13	*b*
7b[c]	10	11	23
7c	65	12	*b*
7d	34	25	7

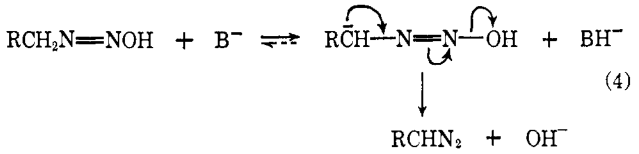
[a] 2.0 mmol of nitrosocarbamate in 10 ml of di-*n*-butyl ether was stirred with 6 mmol of sodium methoxide in 2 ml of methanol in the dark at 25° for 48 hr. [b] Only one methyl ether is possible. [c] Butadiene was also formed, in 26% yield.

The diazoalkenes were not, in fact, thermally stable, and cyclized quantitatively to the isomeric pyrazoles, as discussed in the preceding paper.[7] The reaction solutions were permitted to stand in the dark at room temperature until this reaction was complete, after which time the yield of pyrazole was determined by glpc or spectrophotometrically. The pyrazoles had been previously isolated and identified,[7] and it was assumed that the yield of pyrazole corresponded to the yield of diazoalkene originally produced.

The yields of ethers were determined by glpc, using an internal standard. Ethers derived from **7** and from **6** (X = H) were isolated and purified by glpc, and their identity with authentic samples was established. Ethers from **6** (X = *m*-NO_2, *p*-Cl, *p*-CH_3) were identified by agreement of their ir and nmr spectra with those expected. Butadiene, a product from **7b**, was collected by glpc and identified by ir.

Discussion

Each of the two classes (aromatic and aliphatic) of alkenyl nitrosocarbamates will be treated separately. In the aryl series (Table I) it is clear that electron-withdrawing substituents increase the proportion of diazoalkene relative to solvolysis products (ethers), even though the substituent is quite remote from the reaction site. This suggests that the rate-determining step leading to diazo compound involves proton abstraction from the diazotic acid by the base (eq 4).[2e] The observation[6] that the yield of diazo compound can be raised by increasing the basicity of the reaction medium supports this conclusion.



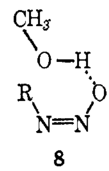
$$RCH_2N{=}NOH + B^- \rightleftharpoons RCH{-}N{=}N{-}OH + BH^- \qquad (4)$$
$$\downarrow$$
$$RCHN_2 + OH^-$$

Regardless of substituent, compounds **6** gave a mixture of unrearranged (cinnamyl) and rearranged (arylvinylcarbinyl) ethers. Unrearranged structures predominated. Although the trend is not entirely clearcut, it appears that a greater proportion of rearranged ether is produced as the electron-donating capacity of the substituents increases (from about 15% to about 30%). If these products are formed *via* a transition state which has carbonium ion like character, it is reasonable that the proportion of nonconjugated product should increase as the electron-donating capacity of the substituent increases.

The data in Table II show several interesting features of the reaction. Once again, the proportion of diazo compound relative to solvolysis product decreases as electron-donating methyl groups are added to the allyl structure. A methyl in the 2 position (**7c**) has only a slight effect, whereas if the methyl is in the 3 position (**7d**) where it may conjugate with any developing charge, the effect is quite large. The only secondary compound (**7b**) gives very little diazo compound, as previously noted in the 2-octyl system.[6]

Compounds **7b** and **7d** would give the same carbonium ion $[CH_3CH\overset{...}{-}CH\overset{...}{-}CH_2]^+$ and therefore the same mixture of ethers if the reaction leading to ethers proceeded through a free cation. This is not the case; the ether corresponding to the original nitrosocarbamate predominates in each case. This result is expected in view of the observation by Moss and coworkers[2f,6] that the 2-octyl and 2-butyl systems give considerable net inversion.

One possible explanation for these results would be that methanol (solvent) is hydrogen bonded to the diazotate ion or diazotic acid, as shown schematically in **8** or **8′**. When the C–N bond breaks, this could favor solvent attack at that carbon, so that in both cases unrearranged ether predominates. Rearranged ethers would then arise from an ion-pair intermediate such as **9**.[8]



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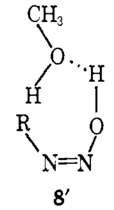

8′

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[7] J. L. Brewbaker and H. Hart, *J. Am. Chem. Soc.*, **91**, 711 (1969).

[8] An SN2′ reaction is also possible, though this seems unlikely because the ratio of rearranged to unrearranged ethers is about the same for **7b** and **7d**. If an SN2′ reaction were involved, one would expect more rearrangement from **7b** than from **7d**, since attack on a $CH_2{=}$ should be favored over attack on a $CH_3CH{=}$ group.

$$[\mathrm{CH_3CH}\overset{\cdots}{-}\mathrm{CH}\overset{\cdots}{-}\mathrm{CH_2}]^+\mathrm{N_2OH}^-$$

9

One additional bit of evidence for the suggested hydrogen bonding of solvent may be the observation that **7b**, where a methyl group would be located near the bound base, gave appreciable amounts of butadiene, whereas **7d** did not.[9]

Experimental Section

Starting Materials. Preparation of the N-nitrosocarbamates used in this work is described in detail in the preceding paper.[7]

Reaction of N-Cinnamyl-N-nitrosocarbamates (6) with Base. A solution of 10 mmol of the nitrosocarbamate in 20 ml of cyclohexene was slowly added to a mixture of 30 ml of cyclohexene and 10 ml of 3 *M* methanolic sodium methoxide. The mixture was stirred in the dark at 4° for 1.5 hr (except for **6**, X = *p*-Cl, where the reaction time was 2.5 hr). After extraction (two 25-ml portions) with cold 10% sodium hydroxide, the red cyclohexene solution was dried briefly at 4° (KOH pellets). The solution was allowed to stand in the dark for 48 hr at room temperature, during which time the red color faded. Aliquots were extracted with 3 *N* hydrochloric acid (four 50-ml portions) and the combined extracts were washed with pentane and analyzed for pyrazole by uv spectroscopy at the known[7] λ_{max} of the particular pyrazole. The yields of diazo compound reported in column 2 of Table I are in fact these pyrazole yields (see text).

The yields of ethers in the cyclohexene phase were determined on aliquots by glpc analysis using internal standards (triphenylmethane for X = *m*-NO_2, fluorene for X = *p*-Cl, pentamethylbenzene for X = H, and hexamethylbenzene for X = *p*-CH_3). The figures in Table I are glpc yields. To identify and characterize the ethers, the cyclohexene was evaporated, and the ethers were isolated by glpc.

Ethers from 6 (X = *m*-NO_2). The ethers were separated by glpc on a 1.5-ft column packed with 20% SE-30 on Chromosorb W at 180° with a helium flow rate of 60 cc/min. The structures are clear from the nmr spectra. **3-Methoxy-3-(*m*-nitrophenyl)propene:** ir (CCl_4) 2930 (s), 1537 (m), 1350 (s), 1095 (s), 995 (m), and 935 (s) cm^{-1}; nmr (CCl_4) τ 6.30 (s, 3), 5.31 (d, 1, *J* = 6.2 Hz), 4.90–4.11 (m, 3), and 2.61–1.80 (m, 4). ***trans*-3-Methoxy-1-(*m*-nitrophenyl)propene:** ir (CCl_4) 2920 (s), 2825 (s), 1660 (w), 1535 (s), 1452 (m), 1350 (vs), 1190 (s), 1120 (vs), 970 (s), and 680 (m) cm^{-1}; nmr (CCl_4) τ 6.32 (s, 3), 5.98 (d, 2, *J* = 4 Hz), 3.97–3.20 (AB q, 2, *J* = 16.4 Hz, with the high-field doublet further split into triplets, *J* = 4.4 Hz), and 2.80–1.88 (m, 4).

Ethers from 6 (X = *p*-Cl). The same glpc column and flow rate were used as in the previous experiment, except at 142°. **3-Methoxy-3-(*p*-chlorophenyl)propene:** ir (CCl_4) 2990 (w), 2930 (m), 2825 (m), 1640 (w), 1494 (s), 1090 (vs), 995 (m), and 930 (s) cm^{-1}; nmr (CCl_4) τ 6.75 (s, 3), 5.50 (d, 1, *J* = 6.2 Hz), 5.00–4.14 (m, 3), and 2.79 (s, 4). ***trans*-3-Methoxy-1-(*p*-chlorophenyl)propene:** ir (CCl_4) 3000 (m), 2925 (s), 2825 (s), 1495 (s), 1660 (w), 1120 (vs), 1090 (vs), and 975 (s) cm^{-1}; nmr (CCl_4) τ 6.66 (s, 3), 6.00 (d, 2, *J* = 4.6 Hz), 4.12–3.29 (AB q, 2, *J* = 16.0 Hz with the high-field doublet further split into triplets, *J* = 4.6 Hz), and 2.75 (s, 4). In addition to the ethers, a small amount of *trans*-3-(*p*-chlorophenyl)-2-propen-1-ol was isolated and identified by comparison of its ir spectrum with that of an authentic sample.

Ethers from 6 (X = H). The ethers were separated on a 5-ft column packed with 20% Carbowax 20M on Chromosorb W, at 200°, helium flow rate 56 cc/min. **3-Methoxy-3-phenylpropene:** ir (CCl_4) 3090 (m), 3030 (m), 2940 (m), 2840 (s), 1642 (w), 1498 (m), 1545 (s), 1100 (vs), 995 (s), 930 (s), and 700 (s) cm^{-1}; nmr (CCl_4) τ 6.76 (s, 3), 5.50 (d, 1 *J* = 6.0 Hz), 5.50–3.83 (m, 3), and 2.79 (s, 5). These spectra were identical with those of a sample of the ether prepared from the sodium salt of 1-phenyl-2-propen-1-ol and methyl iodide. ***trans*-3-Methoxy-1-phenylpropene:** ir (CCl_4) 3050 (m), 3000 (m), 2920 (s), 2820 (s), 1655 (w), 1605 (w), 1498 (m), 1450 (s), 1380 (s), 1190 (s), 1120 (vs), 975 (s), and 675 (s) cm^{-1}; nmr (neat) τ 6.88 (s, 3), 6.15 (d, 2, *J* = 4.5 Hz), 4.18–3.34 (AB q, 2, *J* = 16.0 Hz, with the high-field doublet further split into triplets, *J* = 4.5 Hz), and 2.84 (br s, 5). These spectra were identical with those from a sample of the ether prepared from cinnamyl chloride and sodium methoxide.

Ethers from 6 (X = *p*-CH_3). The ethers were separated on a 5-ft column packed with 20% SE-30 on Chromosorb W, at 190°, helium flow rate 40 cc/min. **3-Methoxy-3-(*p*-tolyl)propene:** ir (CCl_4) 3000 (s), 2930 (s), 1644 (w), 1450 (m), 1420 (m), 1095 (vs), 996 (m), and 930 (s), cm^{-1}; nmr (CCl_4) τ 7.70 (s, 3), 6.78 (s, 3), 5.56 (d, 1 *J* = 6 Hz), 5.09–3.93 (m, 3), and 2.94 (s, 4). ***trans*-3-Methoxy-1-(*p*-tolyl)propene:** ir (CCl_4) 3000 (s), 2930 (s), 1657 (w), 1450 (m), 1380 (m), 1120 (vs), and 975 (s) cm^{-1}; nmr (CCl_4) τ 7.75 (s, 3), 6.76 (s, 3), 6.05 (d, 2, *J* = 5.0 Hz), 4.69–3.35 (AB q, 2, *J* = 15.8 Hz, with the high-field doublet further split into triplets, *J* = 5.0 Hz), and 2.94 (AB q, 4, *J* = 8 Hz).

Reaction of Ethyl N-Allylic-N-nitrosocarbamate (7) with Base. A solution of 20 mmol of the nitrosocarbamate[7] in 100 ml of di-*n*-butyl ether was stirred with 20 ml of 3 *M* methanolic sodium methoxide at room temperature for 48 hr. Saturated salt solution (100 ml) and concentrated hydrochloric acid (10 ml) were added; the crude ethers were separated from the organic phases by distillation, and were purified by glpc using a 10-ft column packed with 20% Carbowax 20M on Chromosorb W, at 75° with a helium flow rate of 20 cc/min. The ethers and butadiene were identified by comparison of their ir and nmr spectra with those of authentic samples. The pyrazoles (extracted by the acid) were identified previously.[7]

In separate experiments run on one-tenth the above scale, the yields of ethers were determined by glpc analysis of the di-*n*-butyl ether layer, using methylcyclohexane as an internal reference, and the same glpc conditions described above. The yields of pyrazoles were determined by basifying the aqueous phase with solid potassium carbonate and analyzing these solutions by glpc on a 5-ft column packed with 10% Carbowax 20M on Fluoropak 80, 215° with a helium flow rate of 20 cc/min. Diethylene glycol was the internal standard. The results of these experiments are given in Table II.

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[9] It is possible, however, that the diazotate oxygen functions as the base for this elimination.