The Hydrolysis of Vinyl Azides.[1] A Comparison with the Schmidt Reaction

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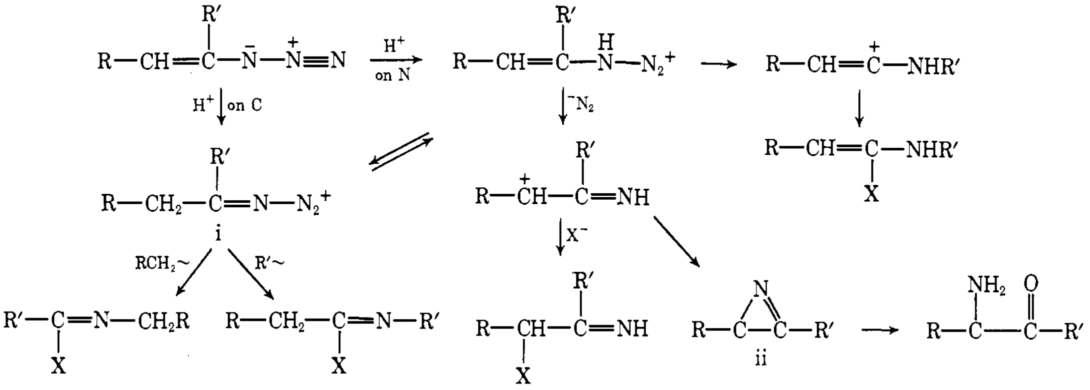
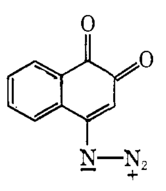
Abstract: The hydrolysis of representative vinyl azides, 1-azido-1-phenylpropene (**3a**), 2-azido-3-phenylpropene (**3b**), and 1-azidoindene (**7**) was studied in 76% sulfuric acid and diethyl ether. Benzene and dioxane were also used as solvents in the hydrolysis of **7**. The products from the hydrolysis were amides and ketones. The same proportion of alkyl and phenyl migration, leading to amides, occurred in the Schmidt reaction of the corresponding ketones under identical conditions, suggesting that the same intermediate is involved in the two reactions.

Reaction of vinyl azides with acids is a potential source of a variety of interesting intermediates involving either N or C protonation followed by rearrangement, ring closure, or trapping (Scheme I). One of the intermediates (i) formed on C protonation or tautomerization following N protonation corresponds to the intermediate postulated in the Schmidt reaction; another is an azirine ring (ii).

Scheme I



Recently, Moore, *et al.*,[2] have reported the ring expansion of 4-azido-1,2-naphthoquinone (**1**), under acidic conditions, to azepinedione (**2**) in good yield. This reaction was found[2] to be analogous to the observed ring expansion of alkyl-1,4-benzo- and 1,4-naphthoquinones to 2,5-azepinediones under Schmidt reaction conditions.[3-6]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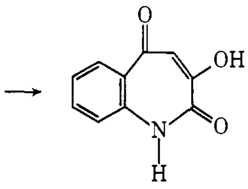
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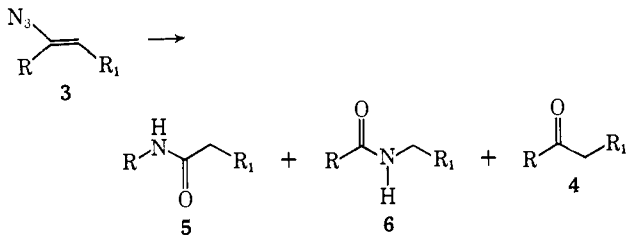
Our recent discovery of a general and convenient synthesis of vinyl azides[7] prompted us to initiate a study of the chemistry of this class of compounds.

In order to establish the analogy between vinyl azide hydrolysis and the Schmidt reaction of ketones with hydrazoic acid, we investigated the hydrolysis of 1-azido-1-phenylpropene (**3a**), 2-azido-3-phenylpropene (**3b**), and 1-azidoindene (**7**) in 76% of sulfuric acid under various conditions and compared it with the Schmidt reaction of propiophenone (**4a**), phenylacetone (**4b**), and 1-indanone (**10**).



a, R = Ph; $R_1 = CH_3$
b, R = $PhCH_2$; R_1 = H

Results

The hydrolysis of 1-azido-1-phenylpropene (**3a**) and 2-azido-3-phenylpropene (**3b**) was carried out in 76% sulfuric acid and ether at room temperature. The only products that were obtained were: N-phenyl propionamide (**5a**), N-ethyl benzamide (**6a**), and propiophenone (**4a**) from **3a**; and N-benzyl acetamide (**5b**), N-methylphenylacetamide (**6b**), and phenylacetone (**4b**) from **3b**. The formulae percentage of products from each hydrolysis was determined from the nmr spectrum of the crude

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[1] Stereochemistry. XLVII. For the previous paper see A. Hassner, R. P. Hoblitt, C. Heathcock, J. E. Kropp, and M. Lorber, *J. Amer. Chem. Soc.*, **92**, 1326 (1970).

[2] H. W. Moore, H. R. Shelden, and W. Weyler, Jr., *Tetrahedron Lett.*, 1243 (1969).

[3] P. A. S. Smith and E. P. Antoniodes, *Tetrahedron*, **9**, 210 (1960).

[4] D. Misrti, H. W. Moore, and K. Folkers, *ibid.*, **22**, 1201 (1966).

[5] H. W. Moore and H. R. Shelden, *J. Org. Chem.*, **32**, 3603 (1967).

[6] R. W. Richards and R. M. Smith, *Tetrahedron Lett.*, 2361 (1966).

[7] A. Hassner and F. W. Fowler, *J. Org. Chem.*, **33**, 2686 (1968).

Table I. Chemical Shifts (τ) of the Methyl and Methylene Groups in **4**–**6**

Compound	$-CH_3$	$-CH_2-$
Propiophenone (**4a**)	8.83 (t)[a]	7.1 (q)
N-Phenyl propionamide (**5a**)	8.83 (t)	7.6 (q)
N-Ethyl benzamide (**6a**)	8.83 (t)	6.4 (m)
Phenyl acetone (**4b**)	7.95 (s)	6.39 (s)
N-Benzyl acetamide (**5b**)	8.11 (s)	5.7 (d)
N-Methyl phenylacetamide (**6b**)	7.39 (d)	6.58 (s)

[a] s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet.

Table II. Product Ratios in the Acid Hydrolysis of Vinyl Azides 1-Azido-1-phenylpropene (**3a**) and 2-Azido-3-phenylpropene (**3b**), and the Schmidt Reaction of Propiophenone (**4a**) and Phenylacetone (**4b**)

Compd	Reaction time, (hr)	% recovery (±4)[a]	% products (±3)[a]		
			5a	**6a**	**4a**
3a	1	76	15	9	76
	3	74	29	19	52
4a	1	98	0	0	100
	3	100	13	6	81
	6	82	18	12	70
			5b	**6b**	**4b**
3b	0.5	78	21	43	36
	1	82	25	50	25
4b	1	96	9	15	76
	2.5–3	87	38	54	8

[a] ±4 and ±3 refers to the deviation from the average percentage recovery and yield, respectively, from a number of runs.

reaction mixture. The methylene protons of **4**, **5**, and **6** in the a or b series all have different chemical shifts (Table I). Since, for a particular reaction, the two amides and the ketone were the only products obtained, the percentage of each component of the reaction mixture was calculated from the ratio of the respective methyl or methylene protons of the products in the nmr spectrum.

The Schmidt reaction was carried out with propiophenone (**4a**) and phenylacetone (**4b**), using 1.1 equiv of sodium azide, under the same conditions as the hydrolysis of the vinyl azides. The identical products were obtained, as was described above, and the yields were calculated in the same manner from the nmr spectrum of the reaction mixture.

The ratios of the amides formed in the acid hydrolysis of the vinyl azides and in the Schmidt reaction were found to be essentially identical, although the total amount of conversion to the amides was greater for the former reaction in a given time (Table II). When the vinyl azides were allowed to react for a longer time, the amount of amides increased but their ratio remained constant.

We then turned to a cyclic analog of **2a**, namely 1-azidoindene (**7**) and carried out its hydrolysis at various temperatures in 76% sulfuric acid using diethyl ether, benzene, or dioxane as a solvent (Table III). In benzene under all reaction conditions that were attempted, the vinyl azide was completely converted to the lactams dihydrocarbostyril (**8**) and dihydroisocarbostyril (**9**) in the ratio 7:3. There was no 1-indanone (**10**) detected in the reaction mixture by thin layer chromatography (tlc) in various solvent systems. When the same reaction was carried out in diethyl ether (heterogeneous medium) at room temperature and at reflux, the only isolable product (85–87%) was 1-indanone (**10**) although trace amounts of the lactams **8** and **9** could be detected by tlc on silica gel (ethyl acetate–hexane 8:2). In dioxane even though the reaction was homogeneous, 1-azidoindene (**7**) was converted only to 1-indanone after 4 hr at 25°; the lactams **8** and **9** could not be detected by tlc.

Table III. Acid Hydrolysis of 1-Azidoindene (**7**)

Solvent	Temp, °C	Reaction time, (hr)	**10**	**8**	**9**	% recovery
Diethyl ether	RT	1	85[a]	Trace	Trace	100
Diethyl ether	RT	4	87[a]	Trace	Trace	100
Diethyl ether	Reflux	1	>80	Trace	Trace	100
Diethyl ether	Reflux	4	>90	Trace	Trace	100
Dioxane	RT	4	100	Not detected by tlc		100
Benzene	60–64	4	0	69	31	70
Benzene	60–64	0.75	0	71	29	80
Benzene	60–64	0.5	0	68	32	94
Benzene	60–64	0.17	0	70	30	100
Benzene	RT	4	0	70	30	94

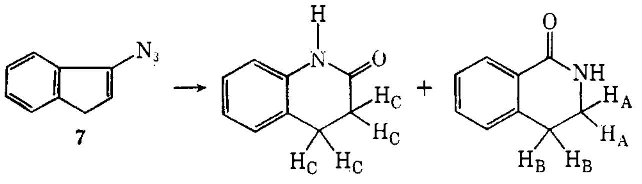
[a] Isolated yields.

Table IV. Schmidt Reaction on 1-Indanone (**10**) using 1.1 Equiv of Sodium Azide

Solvent	Temp, °C	Reaction time, hr	**10**	**8**	**9**	% recovery
Diethyl ether	RT	4	>90	Traces	Traces	100
Diethyl ether	Reflux	1	>90	Traces	Traces	100
Diethyl ether	Reflux	4	>90	Traces	Traces	100
Benzene	60–64	4	0	68	32	100
Benzene	60–64	0.17	0	71	29	100
Benzene	RT	4	0	68	32	100

The Schmidt reaction with 1-indanone (**10**) was carried out under the conditions mentioned for the vinyl azide hydrolysis. Identical results were obtained (Table IV). In benzene, the ketone was converted to the lactams **8** and **9** in the ratio 7:3. Uyeo, *et al.*,[8] have recently reported similar findings. In diethyl ether, there was again virtually no conversion to the lactams both at room temperature or at reflux (Table IV).

The ratios of the lactams **8** and **9**, formed in benzene solution, were calculated from the nmr spectrum of the crude reaction mixture. The methylene protons H_A, α to the nitrogen of lactam **9**, absorb at lower field (τ 6.3–6.6) than the other methylene protons H_B in **9** (τ 6.9–7.3) and the methylene protons H_C of lactam **8** (τ 6.8–7.6). Since no other compounds were formed in the reaction, the percentage of **8** and **9** could easily be calculated from the ratio of these peaks in the spectrum.



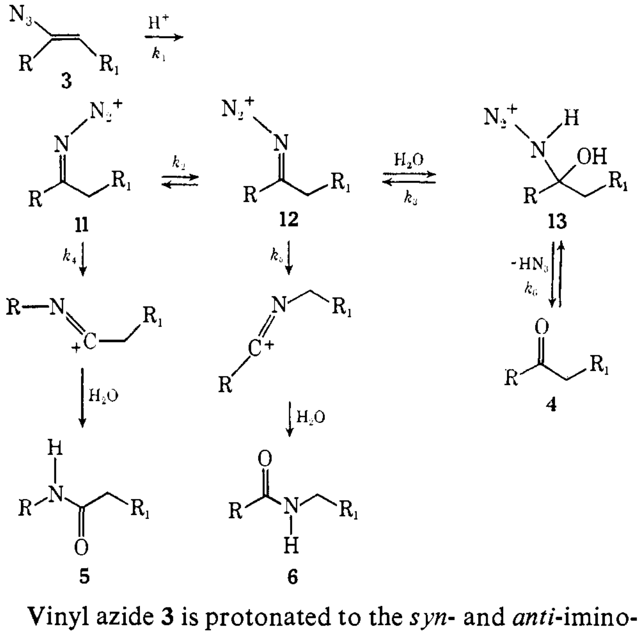
8
H_C τ 6.8–7.6

9
H_A τ 6.3–6.6
H_B τ 6.9–7.3

Discussion

The similarity in the ratios of amides and lactones obtained from the acid hydrolysis of vinyl azides and the Schmidt reaction of the corresponding ketones suggests that the same intermediates are involved in both reactions. A likely pathway for vinyl azide hydrolysis is shown in Scheme II.

Scheme II



Vinyl azide **3** is protonated to the *syn*- and *anti*-iminodiazonium ions **11** and **12** which are in rapid equilibrium. These may rearrange irreversibly and form amides **5** and **6** on solvolysis or add water reversibly to give the hydrated intermediate **13**. The latter in turn may lose hydrazoic acid reversibly to yield ketone **4**. The series of reversible reactions **4** $\rightleftarrows$ **13** $\rightleftarrows$ **12** + **11** $\rightarrow$ **5** + **6** represents in fact the postulated mechanism of the Schmidt reaction.[3] No products resulting from intermediates expected from N-protonation (see Scheme I) were observed.

In the case of the open-chain vinyl azides where a better conversion to amide was observed than in the Schmidt reaction, the lifetime of intermediates **11** and **12** is long enough to permit some rearrangement to amides to take place before the equilibrium **12** + **11** $\rightleftarrows$ **13** $\rightleftarrows$ **4** could be established, that is k_4 and k_5 compete with k_3. For 1-azidoindene, when the same amount of lactam was formed in a given time, as from the Schmidt reaction with 1-indanone, the equilibrium **12** + **11** $\rightleftharpoons$ **13** $\rightleftharpoons$ **4** was established before appreciable rearrangement took place. Hence k_3 and k_6 are much larger than k_4 or k_5. Presumably this difference is due to the larger ring strain involved in the transition state for rearrangement in the cyclic compound.

The ratio of amides and lactams from vinyl azide hydrolysis as well as from the Schmidt reaction is dependent on electronic factors. That is, the migration order of phenyl > alkyl and methyl > benzyl was observed. Such a result cannot always be demonstrated with the Schmidt reaction[9] because the nonmigrating groups affect the mobility of the migrating group, and because sometimes, steric as well as electronic factors are involved.[2] Uyeo, *et al.*,[8] have shown that in the Schmidt reaction with some benzocycloalkenones, alkyl rearrangement increased appreciably when the solvent was changed from benzene–sulfuric acid to molten trichloroacetic acid.

The intermediates **11** and **12** are analogous to oximes in that both *syn* and *anti* isomers are possible. Indeed, the analogy between the Beckmann rearrangement and the Schmidt reaction has been made.[3] However, the oximation of small and medium ring benzocycloalkanones give only the *anti* (to the benzene ring) isomer[10,11] and only one lactam (with phenyl rearrangement) was obtained in the Beckmann rearrangement of the trinitrophenyl ethers.[10,11] The Beckmann rearrangement of the trinitrophenyl ether of 1-indanone oxime was immeasurably slow at 70°[10] and even at elevated temperatures the lactam was obtained in only very low yields.[11] The relatively mild conditions required for lactam formation from 1-azidoindene or 1-indanone and the invariant ratio of rearrangement products suggests two things. First, the activation energy for the transition between **11** and **12** is much lower than for a similar isomerization of the oxime or oxime ether, and k_2 for the equilibrium **11** $\rightleftarrows$ **12** is faster than rearrangement. Second, the leaving group (N_2) is much better than in the Beckmann rearrangement. It is known[12] that the rate for the Beckmann rearrangement increases with the stability of the leaving group.

In diethyl ether the rearrangement to lactams was very slow compared to the same reaction in benzene. It is known that Schmidt reactions do not proceed well in ether.[13] That this is not due to the heterogeneity of the reaction in ether was shown by carrying out the reaction in homogeneous solution in dioxane (see Table

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(8) M. Tomita, S. Minami, and S. Uyeo, *J. Chem. Soc., C,* 183 (1969).

(9) P. A. S. Smith in "Molecular Rearrangements," Vol. 1, Paul de Mayo, Ed., Interscience Publishers, New York, N. Y., pp 470–479.

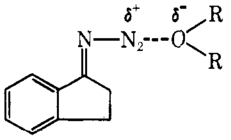
(10) R. Huisgen, J. Witte, and I. Ugi, *Chem. Ber.*, **90**, 1844 (1957).

(11) R. Huisgen, I. Ugi, H. Brade, and E. Ravenbusch, *Ann.*, **586**, 30 (1954).

(12) M. Kuhara, K. Matsumiya, and N. Matsunami, *Mem. Coll. Sci. Univ. Kyoto*, **1**, 105 (1914); M. Kuhara and H. Watanabe, *ibid.*, **1**, 349 (1916); *Chem. Abstr.*, **9**, 1613 (1915); **11**, 579 (1917).

(13) H. Wolff, *Org. Reactions*, **3**, 329 (1946).

III). One possible explanation is that in ether-type solvents the diazonium ion is solvated (see **14**) and therefore relatively stabilized, raising the transition-state energy for rearrangement.



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Experimental Section

The vinyl azides 1-azido-1-phenylpropene (**3a**), 2-azido-3-phenylpropene (**3b**), and 1-azidoindene (**7**) were prepared according to the procedure described by Hassner, *et al.*[7,14] The nmr spectra were taken on a Varian A60-A spectrometer.

An Example of Vinyl Azide Hydrolysis. Diethyl ether (23 ml) was cooled to 0° in an ice–water bath and 76% sulfuric acid (4 ml) was slowly added with stirring. The ice bath was removed and the solution was allowed to come to room temperature. 1-Azido-1-phenylpropene (**3a**) (1 g) in 2 ml of ether was rapidly added with stirring. The reaction mixture was vigorously stirred at room temperature for 1 hour, then quenched by pouring it onto 15 g of potassium carbonate cooled in an ice–water bath. The slurry was diluted with 100 ml of diethyl ether and ice-cold water was slowly added to neutralize the sulfuric acid. The aqueous fraction was separated, diluted with more water, and extracted 4 times with ether. The combined ether fractions were washed once with water, saturated NaCl, and dried over anhydrous $MgSO_4$. The solution was filtered and the solvent was removed *in vacuo*. The nmr spectrum of the crude reaction mixture was then taken in $CDCl_3$. The results of the vinyl azide hydrolysis are tabulated in Tables II and III.

An Example of the Schmidt Reaction with a Ketone. Diethyl ether (23 ml) was cooled to 0° in an ice–water bath and 76% sulfuric acid (4 ml) was slowly added. The ice bath was removed and the solution was allowed to come to room temperature. Propiophenone (1 g) in 2 ml of diethyl ether was rapidly added followed immediately by sodium azide (0.590 g). The mixture was vigorously stirred at room temperature for 1 hr, then poured onto 15 g of potassium carbonate at 0°. The work-up was the same as described in the vinyl azide hydrolysis.

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(14) F. W. Fowler, A. Hassner, and L. A Levy, *J. Amer. Chem. Soc.*, **89**, 2077 (1967).

Rearrangements of Azidoquinones. V.[1] Stereoselective Acid-Catalyzed Rearrangements of Azidoquinones to γ-Cyanoalkylidine- (Cyanoarylidine-) $\Delta^{\alpha,\beta}$-butenolides

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Abstract: Thirteen azido-1,4-benzo- and -1,4-naphthoquinones (**1**) have been shown to rearrange in strong acid to γ-cyanoalkylidine- (or cyanoarylidine-) $\Delta^{\alpha,\beta}$-butenolides (**3**). This rearrangement proceeds by a highly stereoselective, if not stereospecific, process to give the butenolides in which the cyano group on the exocyclic double bond is *trans* to the lactone oxygen. Utilization of the rearrangement as a key step in the total synthesis of a naturally occurring tetronic acid, vulpinic acid (**13**), is described. The mechanism of the rearrangement is discussed in regard to the stereoselectivity of the rearrangement and spectral detection and kinetics of decomposition of the intermediate iminodiazonium ions (**2**).

Very little work has appeared in the literature concerning the chemistry of azidoquinones. This is somewhat surprising in view of their ease of formation, relative stability, and the fact that they are structurally related to vinyl and acyl azides, both of which have received extensive study.[3] A thorough investigation of azidoquinone chemistry has therefore been initiated, and reported here is a general, highly stereoselective acid-catalyzed ring contraction of azido-1,4-quinones (**1**) to the butenolide ring system (**3**).

A general azidoquinone synthesis was reported by Fieser and Hartwell[4] who prepared 2-azido-1,4-napthoquinone by treating the corresponding 2-chloroquinone with azide ion in ethanolic solution. In the same paper, these investigators proposed that azidohydroquinones disproportionate to aminoquinones, a hypothesis which has recently been substantiated experimentally.[5] Mosby and Silva[6] have investigated the reactions of azidonaphthoquinones with phosphines and phosphites and have presented evidence for the intermediacy of a linear phosphazene in these reactions. Van Allen, Priest, Marshall, and Reynolds[7] have shown that the thermal decomposition of azidoquinones follows first-

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(1) A preliminary account of this research has appeared: H. W. Moore and H. R. Shelden, *Tetrahedron Lett.*, 5431 (1968).

(2) (a) Based on the Ph.D. dissertation of Harold Raymond Shelden; (b) NDEA Fellow; (c) NSF Trainee.

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(6) W. L. Mosby and M. L. Silva, *J. Chem. Soc.*, 1003, 2727 (1965).

(7) J. A. Van Allen, W. J. Priest, A. S. Marshall, and G. A. Reynolds, *J. Org. Chem.*, **33**, 1100 (1968).