Reaction of *N*-Isopropylallenimine with Organic Azides[1]

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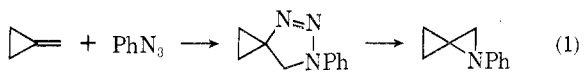
The reaction of *N*-isopropylallenimine (1) with several organic azides has been examined. Phenyl azide gives a mixture of triazole 3 and amidine 7. *p*-Toluenesulfonyl azide reacts with 1 to give only amidine 11; likewise *tert*-butyl and ethyl azidoformate give 12 and 13, respectively. Reaction of 12 with dry HCl gives *N*-isopropyl-β-lactamimide (14). The formation of the amidines and triazole 3 is rationalized in terms of triazoline intermediates.

We have recently reported on the highly strained 1-azaspiropentane structure.[2,3] This novel heterocyclic system was obtained by photochemical decomposition of triazoline precursors derived from thermal cycloaddition of phenyl azide to methylenecyclopropanes (see eq 1). We now report on our attempts to extend this synthetic sequence to allenimine 1 in hopes of effecting conversion to a 1,4-diazaspiropentane (2).



(1)

N-Isopropylallenimine (1) reacts slowly with phenyl azide to yield 1-phenyl-5-(*N*-isopropylaminomethyl)-1,2,3-triazole (3) as the major product. The NMR of 3 shows, among other features, a sharp singlet for the aliphatic methylene group and a one-proton singlet at δ 7.66 for the triazole ring proton. The uv spectrum of 3 displays a maximum at 228 nm, supporting assignment as a 5-substituted 1-phenyl-1,2,3-triazole. Substitution at the 4 position of the triazole ring is known to shift the uv maximum of the parent 1-phenyl-1,2,3-triazole (4) (248 nm) to longer wavelength, whereas substitution at the 5 position causes a shift to shorter wavelength.[4] ^{13}C NMR confirms the 5-substituted 1-phenyl-1,2,3-triazole structure for 3; the chemical shifts of the triazole and phenyl carbons of 3 and 4 are listed in Table I. The C-5 carbon of the triazole ring in 3 is shifted downfield 14.5 ppm relative to 4, indicating substitution at that position, whereas the C-4 carbon experiences only a slight upfield shift. An important indicator of substitution at the 5 position of 3 is the ca. 4.5-ppm downfield shift of the phenyl ortho carbons relative to 4. This is an effect seen in 5-substituted triazoles,[5] presumably resulting from steric interaction between the substituents.

Table I
^{13}C Spectra of Triazoles[a]

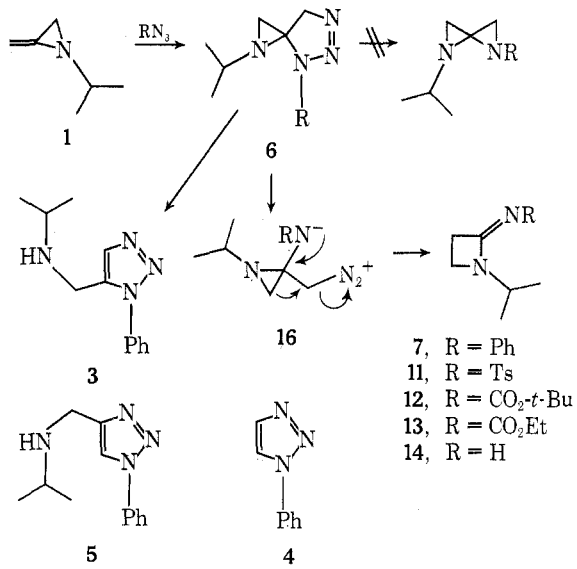
Compd	C-4	C-5	*N*-Ph	*o*-Ph	*m*-Ph	*p*-Ph
3	133.3	136.3	136.6	124.7	129.3	129.3
4	134.0	121.7	136.6	120.2	129.4	128.4

[a] Chemical shifts in parts per million relative to internal Me_4Si.

An authentic sample of 3 was obtained by independent synthesis. Phenyl azide reacts with *N*-isopropylpropargylamine to yield a 60:40 mixture of 4- and 5-(*N*-isopropylaminomethyl)-1-phenyl-1,2,3-triazole (5 and 3). Each of the NMR signals of the major isomer appears at lower field than the corresponding one of the minor isomer. The triazole ring protons are particularly characteristic of this, appearing at δ 7.85 for 5 and δ 7.66 for 3. A sample of pure 3 was obtained by column chromatography and shown to be identical with the product obtained from the reaction of 1 with phenyl azide.

The formation of 3 is rationalized by the addition of phenyl azide to 1 to give triazoline 6 as shown in Scheme I.

Scheme I

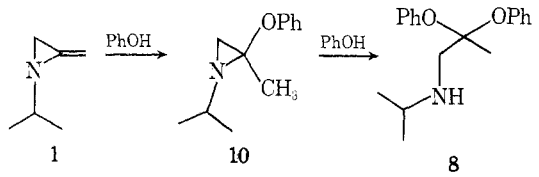


Azides ordinarily react with double bonds so that the substituted nitrogen atom of the azide bonds with the olefinic carbon best able to bear a positive charge;[7] this is the exclusive mode of addition for enamines.[8] The triazoline thus formed is unstable to the reaction conditions and isomerizes to the aromatic triazole 3 with the concomitant relief of strain inherent in the three-membered ring.

A second product isolated from the reaction of 1 with phenyl azide was identified as *N*-isopropyl-*N'*-phenyl-β-lactamimide (7), the first example of this small-ring heterocyclic system. Amidine 7 is a pale yellow oil, surprisingly stable to a variety of reaction conditions, e.g., acid, base, pyrolysis, photolysis, and chemical reduction. The ir spectrum of 7 shows a characteristic 6.0-μ imine band, while the pertinent features of the NMR spectrum consist of a pair of two-proton triplets in the aliphatic region. The mass spectrum of 7 shows a prominent peak at *m/e* 117 corresponding to the ketenimine fragment arising from retro-cycloaddition of the four-membered ring. This places the phenyl substituent on the imine nitrogen, fixing the assigned structure.

Yields of triazole 3 and amidine 7 from the reaction of 1 with phenyl azide varied erratically, and, in some cases, a third product was formed in the reaction. This latter product was isolated and identified as 1-*N*-isopropylamino-2-propanone diphenyl ketal (8) on the basis of its spectral properties and its reaction with ethereal HCl to yield phenol and the hydrochloride salt of 1-*N*-isopropylamino-2-propanone (9).

An authentic sample of 8 was rapidly and smoothly obtained from the reaction of 1 with excess phenol at 25°. This reaction probably proceeds by Markovnikov addition of phenol to the exocyclic double bond of 1 to yield 10,



1 10 8

which subsequently adds a second phenol in the expected manner to give **8**. The origin of **8** in the reaction of **1** with phenyl azide was baffling until it was ascertained that phenol was present as an impurity in the phenyl azide. (In a subsequent experiment, purified phenyl azide reacted with **1** to yield a 65:35 mixture of **3** and **7**; no **8** was observed.)

Reaction of **1** with *p*-toluenesulfonyl azide yielded amidine **11** as the only product. *N*-Isopropyl-*N'*-*p*-toluenesulfonyl-β-lactamimide (**11**) is a pale yellow solid possessing a characteristic 6.11-μ imine band in the ir. Basic hydrolysis of **11** yields *p*-toluenesulfonamide and *N*-isopropyl-β-aminoproprionic acid (isolated and identified as the ethyl ester.[9])

In a similar fashion, **1** reacted with *tert*-butyl and ethyl azidoformate to give the corresponding lactamimides **12** and **13**. The ester function of **12** is readily cleaved in ethereal HCl to yield the parent *N*-isopropyl-β-lactamimide (**14**). Amidine **14** shows significant bands at 3.1, 5.97, and 13.3 μ in the ir spectrum. The NMR includes a pair of triplets in the aliphatic region and a broad singlet at δ 4.07 attributed to the imine hydrogen. The mass spectrum of **14** displays a peak at *m/e* 84 (and the appropriate metastable) corresponding to the carbodiimide fragment from retrocycloaddition of the four-membered ring.

The ^{13}C chemical shifts for the ring carbons of amidines **7**, **11**, **13**, and **14** are listed in Table II, along with *N*-isopropyl-β-lactam (**15**) for comparison. Each of the three ring carbons of amidine **14** shows a higher field resonance than the corresponding carbon of lactam **15**. This can be rationalized in terms of higher electronic charge on the carbons in the amidine owing to the smaller polarization of the C=N bond relative to the C=O function. There are also significant differences among the ring-carbon resonances of the substituted amidines, but again the chemical shifts increase with the electron-withdrawing ability of the imide substituents.

Table II
^{13}C Spectra of Amidines[a]

Compd	C_2	C_3	C_4
7	158.8	29.3	39.2
11	167.3	32.1	42.3
13	162.1	32.0	41.6
14	165.4	31.0	37.9
15	166.4	35.3	43.3

[a] Chemical shifts in parts per million relative to internal Me_4Si.

The formation of the amidine products can be rationalized readily by the pathway shown in Scheme I. Triazoline **6** can open to betaine **16**, which, upon extrusion of molecular nitrogen and rearrangement, leads to the corresponding amidine. The presence of strong electron-withdrawing functions on the azides favors formation of betaine **16** and the ultimate predominance of amidine products.[10]

Experimental Section

General. NMR spectra were recorded for $CDCl_3$ solutions on a Varian HR-220 spectrometer. Ir spectra were obtained on neat samples or $CHCl_3$ solutions using a Perkin-Elmer 137 Infracord. Carbon-13 spectra were obtained on $CHCl_3$ solutions with a Varian XL-100-15 NMR spectrometer operating in the Fourier-transform mode; chemical shifts are given in parts per million relative to internal Me_4Si. Mass spectra (70 eV) were obtained on Varian MAT CH-7 and AEI MS-9 spectrometers. Gas chromatography (GLC) was performed on an Aerograph A-700 preparative instrument. Analyses were run by Midwest Microlab, Inc. Anhydrous $MgSO_4$ was routinely used as a drying agent.

Reaction of 1 with Phenyl Azide. A mixture of 1 g of **1**[11] and 2.5 g of phenyl azide was heated at 90° for 4 days under a nitrogen atmosphere. NMR examination of the crude reaction mixture showed a 16:37:32:15 mixture of **1**, **3**, **7**, and **8**. Separation of the products was accomplished by column chromatography on silica gel. Ketal **8** showed bp 115° (0.1 mm); ir 6.26, 6.71, 7.24, 8.2, 9.2, 11.2, 13.3, and 14.4 μ; NMR δ 0.86 (br s, 1), 0.92 (d, 6, *J* = 7 Hz), 1.76 (s, 3), 2.55 (septet, 1, *J* = 7 Hz), 2.84 (s, 2), 6.94 (t, 2, *J* = 6 Hz), and 7.12 (m, 8); ^{13}C NMR δ 22.9, 48.8, 52.8, 58.1, 106.6, 121.1, 123.1, 129.1, and 150.9; mass spectrum *m/e* (rel intensity) 285 (0.01), 213 (40), 192 (100), 176 (27), 134 (15), 133 (13), 105 (11), 99 (69), 94 (63), 84 (44), 83 (20), 82 (10), 77 (33), 72 (57), 65 (16), 56 (35), 43 (76), and 30 (37).

Anal. Calcd for $C_{18}H_{23}NO_2$: C, 75.76; H, 8.12; N, 4.91. Found: C, 76.0; H, 8.1; N, 5.1.

Amidine **7** showed bp 130° (0.1 mm); ir 6.0, 7.2, 8.0, 8.32, 11.2, 12.8, and 14.7 μ; NMR δ 1.16 (d, 6, *J* = 7 Hz), 2.76 (t, 2, *J* = 4 Hz), 3.31 (t, 2, *J* = 4 Hz), 3.90 (septet, 1, *J* = 7 Hz), 6.63 (d, 2, *J* = 6 Hz), 6.74 (t, 1, *J* = 6 Hz), and 7.02 (t, 2, *J* = 6 Hz); ^{13}C NMR δ 19.7, 29.3, 39.2, 43.7, 121.9, 122.2, 128.6, 149.0, and 158.8; mass spectrum *m/e* (rel intensity) 188 (27), 118 (83), 117 (25), 97 (14), 91 (10), 77 (33), 56 (20), and 51 (15).

Anal. Calcd for $C_{12}H_{16}N_2$: C, 76.56; H, 8.57; N, 14.87. Found: C, 76.2; H, 8.2; N, 15.0.

Distillation of crude **3** at 130° (0.1 mm) gave a pure sample: mp 46–47.5°; ir 3.05, 6.9, 8.55, 10.3, 13.2, and 14.5 μ; uv (ethanol) λ_{max} 227 nm (log ε 4.12); NMR δ 0.99 (d, 6, *J* = 7 Hz), 1.89 (br s, 1), 2.77 (septet, 1, *J* = 7 Hz), 3.80 (s, 2), 7.45 (m, 3), 7.55 (m, 2), and 7.66 (s, 1); ^{13}C NMR δ 22.7, 39.9, 48.2, 124.7, 129.3, 133.3, 136.3, and 136.6; mass spectrum *m/e* (rel intensity) 217 (2), 216 (0.3), 201 (2), 173 (19), 130 (44), 118 (19), 117 (37), 96 (48), 77 (58), 72 (100), and 51 (25).

Anal. Calcd for $C_{12}H_{16}N_4$: C, 66.64; H, 7.46; N, 25.90. Found: C, 66.4; H, 7.5; N, 26.1.

Similar reactions were run on a number of occasions. In general, triazole **3** was the major constituent (50% or greater) of the product mixture with either **7** or **8** as a second component in an erratic manner depending upon the source and age of the reactants, among other variables.

A mixture of 2.5 g of phenyl azide (purified by base extraction and redistillation) and 1 g of **1** was stirred at 90° for 5 days under a nitrogen atmosphere. NMR examination of the crude material showed a 9:59:32 ratio of **1**, **3** and **7**.

1-Phenyl-5-(*N*-isopropylaminomethyl)-1,2,3-triazole (3). A mixture of 1.5 g of *N*-isopropylpropargylamine and 1.8 g of phenyl azide in 25 ml of toluene was heated on a steam bath for 28 hr. The toluene was removed by distillation and the residue was washed with pentane. NMR examination of the oily precipitate showed a 60:40 mixture of 4- and 5-(*N*-isopropylaminomethyl)-1-phenyl-1,2,3-triazole (**5** and **3**). Compound **5** showed NMR δ 1.11 (d, 6, *J* = 7 Hz), 2.88 (septet, 1, *J* = 8 Hz), 3.93 (s, 2), 7.25–7.60 (m, 5), and 7.85 (s, 1). A pure sample of **3** was obtained by column chromatography on silica gel. Triazole **3** obtained by this method was spectroscopically identical with the material from the reaction of **1** with phenyl azide.

Attempted Reaction of 7. A. A 71-mg sample of **7** was stirred with 0.5 ml of 10% HCl in 1 ml of THF for 17 hr at 70°. The mixture was poured into water, adjusted to pH 10 with 10% NaOH, and extracted with ether. The ether layer was washed with water, dried, and concentrated. Ir examination of the residue showed only **7**.

B. A 30-μl sample of **7** was refluxed for 2 hr in 250 μl of methanol with 10 mg of NaOH. The reaction mixture was diluted with water and extracted with ether. After drying and solvent removal, NMR examination showed only **7**.

C. A 33-mg sample of **7** was vacuum transferred (0.01 mm) through a 15 × 1 cm quartz tube packed with quartz chips at 500°. The transferred material was trapped in methanol cooled to −78°. Solvent removal gave 32 mg of unchanged **7**.

D. A 100-mg sample of **7** in 10 ml of benzene was irradiated for 6 hr through quartz with a 450-W high-pressure mercury lamp. After solvent removal, ir and TLC examination showed only **7**.

E. A 61-mg sample of **7** (0.3 mmol) was stirred and refluxed for 2 hr in 2 ml of dry THF with 10 mg (0.3 mmol) of $LiAlH_4$. The reac-

tion mixture was hydrolyzed with water and extracted with ether. After drying and solvent removal, ir showed only **7**.

Reaction of 8 with HCl. A 112-mg sample of **8** was dissolved in 2 ml of ether and 5 ml of ethereal HCl was added. Solvent removal and recrystallization from acetone gave 25 mg of **9** as white needles: mp 179–180°; ir 5.75 μ; NMR δ 1.19 (d, 6, J = 7 Hz), 2.27 (s, 3), 3.45 (septet, 1, J = 7 Hz), and 3.95 (s, 2); mass spectrum m/e (rel intensity) 115 (2), 100 (4), 72 (65), 57 (6), 43 (16), and 30 (100).

The mother liquors from the recrystallization were concentrated to yield 55 mg of phenol.

1-*N*-Isopropylamino-2-propanonone Diphenyl Ketal (8). Crystalline phenol (3 g) was combined with 1 g of **1** and the resulting solution was stirred for 10 min at 25° with cooling in a water bath (exothermic reaction). NMR examination of the crude mixture showed only **8** and phenol. A pure sample of **8** was obtained by column chromatography on silica gel and shown to be spectroscopically identical with **8** from the reaction of **1** with phenyl azide.

Reaction of 1 with *p*-Toluenesulfonyl Azide. A 0.5-g sample of **1** was combined with 1 g of *p*-toluenesulfonyl azide and heated slowly to 45°, at which point gas evolution commenced. After stirring at 45° for 3.5 hr, the dark red mixture was cooled and allowed to stand overnight. The resulting crystalline material (1.35 g) was washed with hexane. Pure **11** was obtained as light yellow plates by column chromatography on neutral alumina: mp 92.5–93.5°; ir 6.11, 8.70, 9.15, and 11.1 μ; NMR δ 1.11 (d, 6, J = 7 Hz), 2.35 (s, 3), 3.18 (t, 2, J = 3 Hz), 3.51 (t, 2, J = 3 Hz), 3.93 (septet, 1, J = 7 Hz), 7.20 (d, 2, J = 8 Hz), and 7.70 (d, 2, J = 8 Hz); ^{13}C NMR δ 19.6, 21.4, 32.1, 42.3, 45.0, 126.2, 129.1, 140.2, 142.1, and 167.3; mass spectrum m/e (rel intensity) 266 (9), 251 (6), 155 (64), 111 (20), 91 (100), 83 (5), and 65 (20).

Anal. Calcd for $C_{13}H_{18}N_2O_2S$: C, 58.60; H, 6.82; N, 10.52. Found: C, 58.4; H, 6.7; N, 10.5.

Hydrolysis of 11. A 132-mg (0.5 mmol) sample of **11** was heated at 60° for 12 hr with 2 ml of 10% NaOH. The reaction mixture was cooled, diluted with water, and acidified with 10% HCl. The water layer was extracted with ether and the ether extract was dried and concentrated to give 54 mg of *p*-toluenesulfonamide. The water layer was concentrated to dryness on a rotary evaporator. The residual solids were dissolved in 2 ml of anhydrous ethanol containing 1 drop of concentrated H_2SO_4 and heated at 60° for 24 hr. The reaction mixture was cooled, diluted with 10% $NaHCO_3$ solution, and extracted with ether. The ether was washed with saturated NaCl solution and dried. Solvent removal gave 44 mg of a 50:50 mixture of *p*-toluenesulfonamide (76 mg total, 90%) and ethyl *N*-isopropyl-3-aminoproprionate (22 mg, 28%) which was spectroscopically identical with authentic material.[9]

Reaction of 1 with Ethyl Azidoformate. A mixture of 5.0 g of allenimine **1** and 5.75 g of ethyl azidoformate was stirred at 75° for 36 hr, at which time the ir spectrum showed little remaining azide. The resulting red-brown product was distilled under vacuum to give 5.6 g (60%) of pure **13**: bp 99–102° (1 mm); ir 5.96, 6.15, 6.93, 7.93, 8.05, 8.34, 9.17, and 9.53 μ; NMR δ 1.16 (d, 6, J = 6.5 Hz), 1.27 (t, 3, J = 7 Hz), 3.23 (t, 2, J = 3.5 Hz), 3.56 (t, 2, J = 3.5 Hz), 4.08 (q, 2, J = 7 Hz), and 4.12 (septet, 1, J = 6.5 Hz); ^{13}C NMR δ 13.8, 19.0, 32.0, 41.6, 43.6, 60.0, 162.1, and 171.0; mass spectrum m/e (rel intensity) 184 (54), 169 (10), 156 (10), 142 (4), 139 (92), 113 (4), 112 (12), 97 (100), 84 (11), 83 (11), 71 (13), 70 (32), 69 (62), 68 (13), 56 (71), and 43 (75).

Anal. Calcd for $C_9H_{16}N_2O_2$: C, 58.65; H, 8.76; N, 15.21. Found: C, 58.4; H, 8.7; N, 15.5.

Reaction of 1 with *tert*-Butyl Azidoformate. A mixture of **1** (2.00 g) and *tert*-butyl azidoformate (2.88 g) was stirred for 24 hr at 85°. Ir examination showed only **12** and a trace of the starting azide. Pure **12** obtained by sublimation at 90° (2 mm) showed mp 68.5–70°; ir 5.95, 6.12, 8.0, 8.23, 8.62, 9.4, and 9.8 μ; NMR δ 1.09 (d, 6, J = 6.5 Hz), 1.47 (s, 9), 3.23 (t, 2, J = 4 Hz), 3.53 (t, 2, J = 4 Hz), and 4.16 (septet, 1, J = 6.5 Hz); mass spectrum m/e (rel intensity) 212 (2), 157 (4), 156 (6), 139 (11), 97 (10), 59 (50), 57 (100), and 41 (43).

Anal. Calcd for $C_{11}H_{20}N_2O_2$: C, 62.21; H, 9.50; N, 13.20. Found: C, 62.3; H, 9.7; N, 13.4.

Hydrolysis of 12. An 835-mg sample of crude **12** was stirred with ether saturated with HCl at 50° for 20 hr. The yellow supernatant ether layer was decanted and the oily red residue (522 mg) was taken up in water and carefully neutralized to pH 7 with 10% NaOH. The water layer was extracted with $CHCl_3$; the $CHCl_3$ was dried and concentrated to give 90 mg of a red tar, ir 5.85 μ. The water layer was then adjusted to pH 10 and reextracted with $CHCl_3$. The solvent was dried and removed to yield 200 mg (85%) of **14**: ir 3.1, 5.97, 8.0, and 13.3 μ; NMR δ 1.12 (d, 6, J = 6.5 Hz), 2.71 (t, 2, J = 4.5 Hz), 3.30 (t, 2, J = 4.5 Hz), 3.78 (septet, 1, J = 6.5 Hz), and 4.07 (br s, 1); ^{13}C NMR 19.6, 31.0, 37.9, 43.4, and 165.4; mass spectrum m/e (rel intensity) 112 (55), 97 (54), 85 (48), 84 (18), 83 (84), 70 (23), 69 (75), 56 (100), 54 (19), 43 (81), 42 (44), and 41 (55).

Exact mass. Calcd for $C_6H_{12}N_2$: 112.1001. Found: 112.098.

Registry No.—**1**, 55268-35-4; **3**, 55268-36-5; **5**, 55268-37-6; **7**, 55268-38-7; **8**, 55268-39-8; **9**, 55268-40-1; **11**, 55268-41-2; **12**, 55268-42-3; **13**, 55268-43-4; **14**, 55268-44-5; phenyl azide, 622-37-7; *N*-isopropylpropargylamine, 6943-48-2; hydrochloric acid, 7647-01-0; *p*-tolunesulfonyl azide, 941-55-9; ethyl azidoformate, 817-87-8; *tert*-butyl azidoformate, 1070-19-5.

References and Notes

(1) Support of this work by a grant from the National Science Foundation is gratefully acknowledged.
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