The Cyclic Addition of Hetero Radicals. III. Cyclic Addition of Alkoxy Radicals in Alkynes[1]

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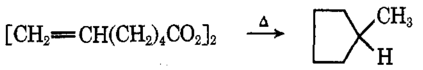
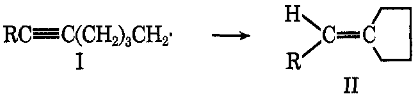
4-Pentynyl nitrite ester was photolyzed to study the cyclic addition of the resulting alkoxy radical to the carbon–carbon triple bond. The photolysis was carried out in a poor hydrogen atom donating solvent, a good hydrogen atom donating solvent, and in the presence of a good radical trap. In none of the above-mentioned reactions were any cyclic addition products observed. The reasons for the failure of this alkoxy radical to undergo cyclic addition are discussed.

The intermolecular addition of free radicals to olefins has received considerable attention in recent years and invariably the additions go in such a direction as to produce the most stable radicals.[2] However, many recent free-radical cyclic addition reactions have been found to violate this principle. Lamb and coworkers[3] found that the pyrolysis of 6-heptenoyl peroxide resulted in methylcyclopentane instead of the expected cyclohexane (eq 1). Numerous other examples have appeared in recent years reporting cyclic additions of carbon radicals which proceed *via* the five-membered ring addition product.[4,5] The cyclic addition is thought to be controlled by entropy factors giving the kinetically controlled product rather than the thermodynamically preferred six-membered ring product. Julia[6,7] has made a careful study of the cyclic addition of the 5-hexenyl radical; he found that the addition becomes reversible if radical stabilizing groups are added to the primary carbon. In this case, the observed product is the six-membered ring product.



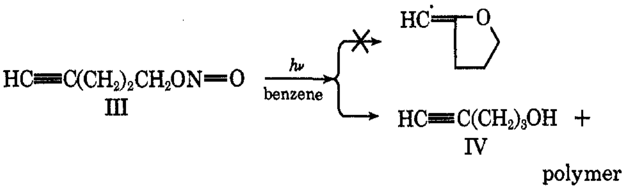
(1)

We have been investigating the cyclic addition of alkoxy radicals,[8,9] and in this paper we would like to report some of our observations regarding the cyclic additions of alkoxy radicals in alkynes. Crandall and Keyton[10] have studied the cyclic addition of the acetylenic alkyl radical I and found that the addition yields the five-membered ring product II in high yields. Julia[11] has also reported the cyclic additions of alkyl acetylenic radicals to yield five-membered ring products in high yields. However, no attempts have been reported on the cyclic addition of alkoxy radicals in alkynes.

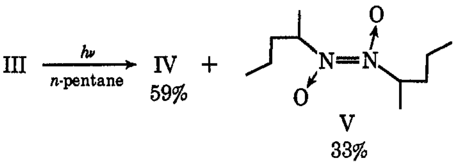


Results and Discussion

We have found that a convenient source of alkoxy radicals is the photolysis of the corresponding nitrite ester.[8,9] 4-Pentynyl nitrite (III) was irradiated with a 450-W, medium-pressure Hanovia mercury lamp with a Pyrex filter. The solutions were purged with a stream of vanadate-scrubbed nitrogen prior to photolysis to remove all oxygen. When III was photolyzed with benzene as the solvent, there was no sign of any cyclic addition products in the reaction mixture. The only product isolated was a 20% yield of 4-pentynol (IV). The rest of the material was highly colored and very polar. This material could not be gas chromatographed and would only move on thin layer plates or chromatography columns with highly polar solvents. The observed 4-pentynol apparently arose by proton abstraction of the solvent or from starting material. The rest of the material apparently was polymeric material.



When III was photolyzed in *n*-pentane, a much better hydrogen donor than benzene, a substantially higher yield of IV (59%) was observed along with 33% of 2-pentyl nitroso dimer V. However, there was no sign again of any cyclic addition products.



The high yields of IV are easily explained considering the fact that *n*-pentane is a reasonably good hydrogen atom donating solvent. The resulting 2-pentyl radical then combined with the NO to give the 2-pentyl nitroso monomer, which dimerized to give V. The exclusive formation of the 2-pentyl derivative is apparently consistent with other results in the literature. Kabasakalian,[12] in a study on the photolysis of *n*-octyl nitrite in *n*-heptane, observed only 2-heptyl nitroso dimer. He rationalized his results by assuming that *n*-heptane existed in a folded conformation which rendered the in-

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[1] For part II of this series, see R. D. Rieke and N. A. Moore, *J. Org. Chem* , in press.

[2] W. A. Pryor, "Introduction to Free Radical Chemistry," Prentice Hall, Englewood Cliffs, N. J., 1966.

[3] R. C. Lamb, P. W. Ayers, and M. K. Toney, *J. Amer. Chem. Soc.*, **85**, 3483 (1963).

[4] C. Walling and M. S. Pearson, *ibid.*, **86**, 2263 (1964).

[5] N. O. Brice, *ibid.*, **86**, 524 (1964); N. O. Brice, *J. Org. Chem.*, **31**, 2879 (1966); N. O. Brice, *J. Chem. Soc.*, **32**, 2711 (1967).

[6] M. Julia, M. Maumy, and L. Mion, *Bull. Soc. Chim. Fr.*, 2641 (1967); M. Julia and M. Maumy, *ibid.*, 2427 (1969).

[7] M. Julia, *Pure Appl. Chem.*, **15**, 167 (1967).

[8] R. D. Rieke and N. A. Moore, *Tetrahedron Lett.*, 2035 (1969).

[9] R. D. Rieke and N. A. Moore, submitted for publication in *J. Amer. Chem. Soc.*

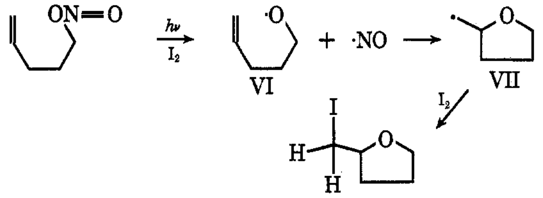
[10] J. K. Crandall and D. J. Keyton, *Tetrahedron Lett.*, 1653 (1969).

[11] M. Julia, *Rec. Chem. Progr.*, **25**, 3 (1964).

[12] P. Kabasakalian and E. R. Townley, *J. Amer. Chem. Soc.*, **84**, 2711 (1962).

terior methylene protons sterically inaccessible. Evidently, similar arguments are valid for *n*-pentane.

Compound III was then photolyzed in the presence of a large excess of a very efficient radical trap, iodine. It was felt that the lack of cyclic addition products might be a result of an inability of the NO to trap the vinyl radical, either because of the high reactivity of the vinyl radical or because of some conformational factor. In the cyclic addition of the 4-pentenyl alkoxy radical (VI), the resulting primary carbon radical (VIII) can be very efficiently trapped with an excess of iodine.[8,9]



However, when III was photolyzed in the presence of an excess of iodine in benzene, no cyclic addition products were observed. In this particular experiment, the excess iodine was removed with aqueous sodium thiosulfate. Among the volatile products found were 4-pentynol (10%) and 4-pentynal (4%). In addition, three other volatile products in low yield were observed. We were not able to fully characterize these compounds, but from ir, nmr, and mass spectral data they definitely all had a carbon–carbon triple bond and aromatic hydrogens. These minor products evidently arise by attack of the 4-pentynyloxy radical on the solvent, benzene. One possible source of the 4-pentynol is from a disproportionation reaction. However, the fact that this was not observed in any of the previous experiments made this seem doubtful. When the experiment was repeated and the reaction was worked up without the removal of excess iodine with aqueous sodium thiosulfate, no 4-pentynal was found. Also, no 4-pentynol was found in this reaction mixture. This suggests that in the presence of iodine in a benzene solution, a significant portion of the 4-pentynyloxy radical is trapped as the hypoiodite. The hypoiodite upon work-up with aqueous sodium thiosulfate undergoes hydrolysis to 4-pentynol and a base-catalyzed elimination of HI to give 4-pentynal. Base-catalyzed eliminations of HX from hypohalites to produce ketones have been reported.[13]

The lack of any cyclic addition products from the 4-pentynyloxy radical under a variety of conditions is surprising. This is especially so in view of the fact that the corresponding carbon radical analog cyclizes in high yield.

Molecular models of the 4-pentenyloxy radical and the 4-pentynyloxy radical show little difference in the distance of the double or triple bond to the alkoxy radical site. Thus, it would appear that the vast difference in chemistry of the two alkoxy radicals cannot be attributed to a difference in strain energy of the two transition states. One possible explanation is that in the transition state for cyclic addition of the 4-pentynyloxy radical there are additional electron–electron repulsion interactions between the electrons of the π cloud of the triple bond and the electron-rich oxygen atom over that of the 4-pentenyloxy radical. Whatever the reason, the lack of cyclic addition of the 4-pentynyloxy radical represents a striking anomaly in a large number of radical cyclic addition reactions.

Experimental Section

4-Pentynol, bp 65–66° (16 mm) [lit.[14] bp 64–65° (16 mm)], was prepared from tetrahydrofurfuryl chloride[15] according to the procedure of Eglinton, Jones, and Whiting.[14]

Preparation of 4-Pentynyl Nitrite.—To a foil-wrapped flask fitted with a condenser and magnetic stirrer was added 10.97 g (0.120 mol) of 4-pentynol, 12.4 g (0.180 mol) of $NaNO_2$, and 60 ml of water. The mixture was cooled to ice-bath temperature and 15 ml of concentrated HCl was added with stirring in three portions over a 1-hr period. Stirring was continued for an additional 30 min. The mixture was then extracted with several portions of CH_2Cl_2. The organic layers were combined, and the solvent was removed at reduced pressure, yielding 13.82 g (0.116 mol, 97% crude yield) of 4-pentynyl nitrite: bp 51° (97 mm); ir ν (neat) 3310, 2965, 1645, 1607, 800 cm^{-1}; nmr τ (ppm, TMS, CCl_4) 5.7 (t, $J = 7$ cps, 2 H) and 7.8–8.2 (complex m, 4–5 H).

Photolysis of 4-Pentynyl Nitrite in Benzene.—A solution containing 2.562 g (21.5 mmol) of nitrite ester and 300 ml of freshly distilled benzene ([RONO] = 0.715 *M*) was purged with N_2 for 45 min and photolyzed using a Hanovia 450-W lamp (with a Pyrex filter). The photolysis was followed by monitoring the disappearance of the band at 357 mμ in the uv and carried to 86% completion. Gas evolution was noted during the photolysis. Removal of the solvent at reduced pressure yielded 1.89 g of a red oil. Gc analysis showed the presence of 0.204 g (0.17 mmol) of nitrite ester, 0.312 g (3.7 mmol, 20% yield) of 4-pentynol, and eight minor components, each in less than 1% yield. Attempts to resolve the product mixture using elution chromatography were unsuccessful.

Thermolysis of the crude product at 54° resulted in the formation of no new volatile components detectable by gc analysis.

Photolysis of 4-Pentynyl Nitrite in Pentane.—A solution containing 1.078 g (9.05 mmol) of nitrite ester in 300 ml of pentane was degassed and photolyzed in the manner described above. After 20 min, the uv spectrum showed no maxima between 320 and 370 mμ, and a new maxima at 294 mμ. Removal of solvent at reduced pressure resulted in the isolation of 0.873 g of yellow liquid. Analysis using gc showed the presence of 500 mg (5.4 mmol, 59% yield) of 4-pentynol, identified on the basis of its ir spectrum and gc retention time. Two other products were detected in minor (2–3%) amounts and were not characterized. A total of 298 mg (1.47 mmol) of crude 2-pentyl nitroso dimer, identified on the basis of its ir spectrum {(ν_{max} (CCl_4) 1197 (s) and 1100 (m) cm^{-1} [lit.[16] ν_{max} 1193 cm^{-1} (ε 900) and 1096 (100)]}, was isolated using elution chromatography (silca gel, pentane, and pentane–ether mixtures).

A sample consisting of 189 mg of crude 2-pentyl nitroso dimer was heated on a steam bath for 10 hr in a stoppered flask. Analysis using gc showed the presence of three products in 2:96:2 ratios. A sample of the major product was collected using preparative gc and yielded an ir spectrum identical with that of authentic 2-pentanone oxime, prepared from 2-pentanone in the usual manner.

Photolysis of 4-Pentynyl Nitrite in Benzene in the Presence of Iodine.—A solution containing 1.201 g (10.03 mmol) of nitrite, 1.907 g (7.5 mmol) of I_2, and 300 ml of benzene was degassed and photolyzed in the above manner. The photolysis was monitored by periodically withdrawing samples from the reaction mixture, reducing the I_2 with 10% $Na_2S_2O_3$, and monitoring the disappearance of the band at 357 mμ using uv spectrometry. After 9.5 hr, it was found that the photolysis was 90% complete. An identical solution was stored in the dark for 9.5 hr and analyzed for nitrite ester, with the following results: per cent nitrite remaining, 80 (uv); 82 (gc).

The photolysis solution was washed with 10% $Na_2S_2O_3$ solution and analyzed using gc. This resulted in the detection of nitrite

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[13] P. R. Story and S. R. Fahrenholz, *J. Amer. Chem. Soc.*, **86**, 1290 (1964).

[14] G. Eglinton, E. R. H. Jones, and M. C. Whiting, *J. Chem. Soc.*, 2873 (1952).

[15] "Organic Syntheses," Collect. Vol. III, Wiley, New York, N. Y., 1955, p 698.

[16] B. G. Gowenlock, H. Spedding, J. Trotman, and D. H. Whiffen, *J. Chem. Soc.*, 3928 (1957).

ester in 10–11% yield. Solvent and nitrite ester were removed at reduced pressure, resulting in the isolation of 661 mg of red oil.

Analysis of the red oil using gc showed the presence of seven products, samples of which were isolated using preparative gc and characterized spectrally. A total of 79 mg (0.94 mmol, 10% yield) of 4-pentynol, characterized by comparison of its ir and nmr spectra with that of an authentic sample, was detected by this method. The following products, in order of their elution from the gc, were also detected.

4-Pentynal: ir ν_{max} (CCl_4) 3312 (s), 2820 (m), 2720 (m), 2120 (w), 1720 (s) cm^{-1}; nmr τ (ppm, TMS, CCl_4) 0.07 (1 H), 7.45 (3–4 H), 8.17 (2 H); 28 mg (0.34 mmol; 4% yield).

Component A: ir ν_{max} (CCl_4) 3320 (s), 3070 (w), 1720 (s), 1570 (m), 993 (s), 680 (s), 650 (s), 625 (s) cm^{-1}; nmr (ppm, TMS, CCl_4) 2.35 (d), 2.84 (t), 7.75, 8.20, 8.65; mass spectrum *m/e* 205, 204 (C_6H_4I + H), 128 (HI), 127 (I), 106, 105 (C_6H_4CO), 79–74 (phenyl ring), 66, 51, 50, 43, 39 ($CH{\equiv}CCH_2$); 0.43 mmol detected (*ca.* 5% yield).

Component B: ir ν_{max} (CCl_4) 3312, 3075, 2952, 1520, 1340, 848 cm^{-1}; mass spectrum *m/e* 204 ($CH{\equiv}C(CH_2)_3OC_6H_4NO_2$ − 1), 139 ($OC_6H_4NO_2$ + H), 123 ($C_6H_5NO_2$), 105, 93 (C_6H_5O), 84, 83 [$CH{\equiv}C(CH_2)_3O$], 78, 77, 66, 65, 55, 53, 51, 46 (NO_2), 39 ($CH{\equiv}CCH_2$), 30 (NO); 0.21 mmol detected (*ca.* 2–3% yield).

Component C: ir ν_{max} (CCl_4) 3312, 3235 (br), 3080 (w), 1610, 1586, 1527, 1470, 1450, 1320, 1245 cm^{-1}; mass spectrum *m/e* 139, 122, 109 (OC_6H_4OH), 93 (C_6H_5O), 81, 65, 64, 53, 39; 0.31 mmol detected (*ca.* 3–4% yield).

In a similar manner, 1.907 g (10.0 mmol) of nitrite, 1.907 g (7.5 mmol) of I_2, and 300 ml of benzene were photolyzed for 7.5 hr (77% completion; uv analysis). A total of 250 mg of insoluble polymer precipitated from the solution after 8 hr. Excess I_2 was not reduced with 10% thiosulfate solution. The solution was concentrated to 10 ml and analyzed using gc. No 4-pentyn-1-ol or 4-pentynal was detected.

Registry No.—III, 30428-24-1; IV, 5390-04-5; V, 30428-26-3.

Acknowledgment.—Financial support of this investigation by the University of North Carolina Research Center under Contract SD-100 with the Advanced Research Projects Agency and by a University of North Carolina Research Grant is gratefully acknowledged.

Heterocyclic Studies. 34. Toluenesulfonyl Derivatives of 2,3-Dihydro-5-methyl-6-phenyl-1,2-diazepin-4-one. Rearrangement to a 1,4-Dihydropyridazine[1]

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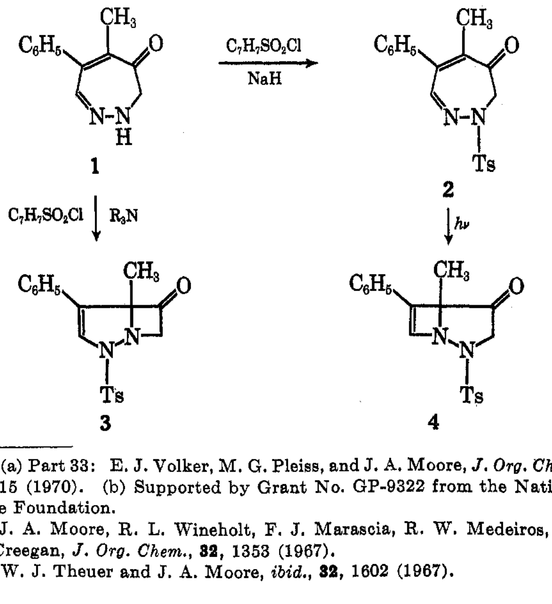
The 2-tosyldiazepinone **2** undergoes rearrangment in the presence of triethylamine to the 2-tosylamido-3-hydroxypyridine **5**. With sodium alkoxides, **2** rearranges with loss of $ArSO_2H$ to give the dihydropyridazine esters **11**; a bicyclo[4.1.0] intermediate is suggested. The 2-tosylbicyclo[3.2.0] ketone **3** undergoes ring opening in methanol and rearrangement to the 1-tosylamidopyridinium ylide **18** in strong acid. In base, **3** gives the 6-tosylamido-3-hydroxypyridine **17**.

In a continuation of work on the diazepinone **1**, sulfonyl derivatives were of interest for comparison of some reactions with those of acyl counterparts.[2] Acylation of the diazepinone **1** can be directed by choice of conditions to give either seven-membered or bicyclic derivatives.[3] Similarly, the reaction of **1** with tosyl chloride and tertiary amines gave the bicyclic sulfonamide **3**, whereas, in the presence of sodium hydride, attack of tosyl chloride on the N-2 anion of **1** led to **2**.



2-Tosyldiazepinone (2).—The yellow 2-tosyl ketone **2** showed an ir carbonyl band (1680 cm^{-1}) and uv spectrum typical of other 2,3-dihydrodiazepinones in this series. Irradiation (sunlight) converted **2** cleanly to the photoisomer **4**, also obtained by tosylation of the photoisomer of **1**.[1a]

Our principal interest in the chemistry of **2** lay in its reactions in base. Deuterium exchange of the C-3 methylene protons occurred rapidly in DMSO–D_2O containing triethylamine. On heating a solution of **2** in benzene containing triethylamine, a colorless isomer was obtained in 60% yield. This product was recognized from its properties as the 2-tosylamidopyridine **5**; the structure was confirmed by further tosylation to the *O,N*-ditosyl derivative **6** and comparison with a sample prepared by vigorous treatment of the aminopyridine **7** with toluenesulfonyl chloride. Unexpectedly, the initial monotosylation product of **7** was the *O*-tosylate **8** rather than the sulfonamide **5**. Parallel behavior was observed on tosylation of 2-amino-3-hydroxypyridine (**9a**) and also the 3-hydroxy-6-aminopyridine **19a**; the *O*-tosyl esters were obtained with excess tosyl chloride and triethylamine or pyridine at room temperature. Treatment of **9a** with 1 equiv of benzoyl chloride similarly gave the ester **9c** (Chart I).

The transformation of **2** to the pyridine **5** presumably occurs by an enolization–valence isomerization sequence *via* the bicyclo[4.1.0] system **10**, as proposed

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[1] (a) Part 33: E. J. Volker, M. G. Pleiss, and J. A. Moore, *J. Org. Chem.*, **35**, 3615 (1970). (b) Supported by Grant No. GP-9322 from the National Science Foundation.

[2] J. A. Moore, R. L. Wineholt, F. J. Marascia, R. W. Medeiros, and F. J. Creegan, *J. Org. Chem.*, **32**, 1353 (1967).

[3] W. J. Theuer and J. A. Moore, *ibid.*, **32**, 1602 (1967).