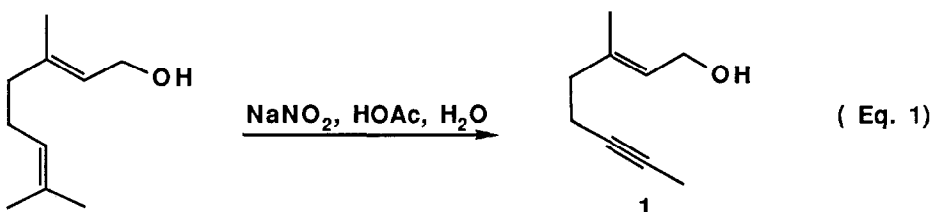


Mechanism of the Nitrous Acid-Induced Dealkylation of Trisubstituted (Terminal Isopropylidene) Olefins to Form Acetylenes

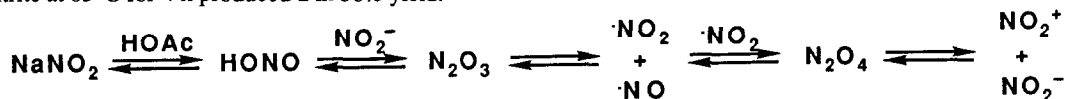
E. J. Corey, William L. Seibel and John C. Kappos
 Department of Chemistry, Harvard University, 12 Oxford St., Cambridge, MA 02138

Summary: Evidence is presented that the conversion of olefins of the type $RCH=C(CH_3)_2$ to acetylenes of structure $RC\equiv CCH_3$ by the action of sodium nitrite in aqueous acetic acid proceeds by a sequence involving two nitrations, Nef conversion of one nitro group to carbonyl, ring closure to an isoxazolone N-oxide and fragmentation to carbon dioxide, NO and the acetylene.

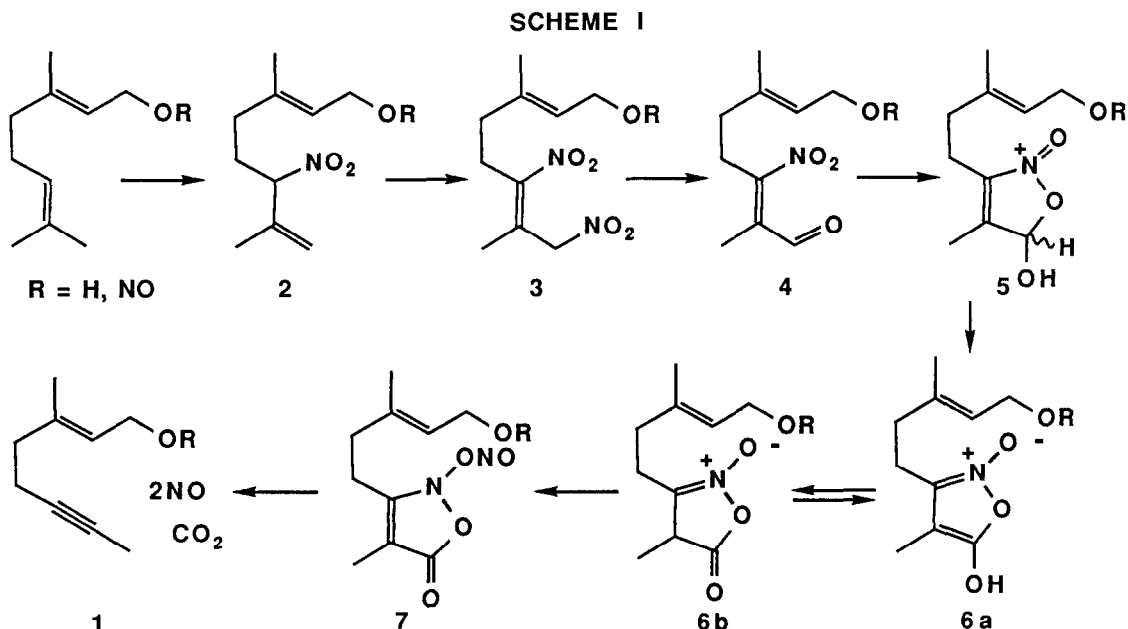
Treatment of various terpenoids containing a terminal isopropylidene unit ($RCH=C(CH_3)_2$) with sodium nitrite in aqueous acetic acid at 60°C has recently been reported to produce 2-alkynes in moderate yield (usually 30-90%).¹ Because of our interest in such acetylenes as synthetic intermediates for the construction of tetrasubstituted exocyclic olefins,² we had occasion to examine this unusual reaction. Our studies have not only confirmed the occurrence of this acetylene-forming transformation in which the elements of methane are formally eliminated from the olefinic substrate, but also have provided mechanistic clarification which we report herein. A typical example of this reaction is the formation of acetylene **1** from geraniol (Eq. 1).



In the case of geraniol the initial step in the transformation was observed to be the nitration of the C-6 position. Treatment of geraniol (7 mmol) in 33 mL of 60% acetic acid at 0° C with 2 equiv of sodium nitrite initially produced the expected nitrite ester of geraniol. Subsequent addition of a large excess of sodium nitrite (25 equiv) at 0° C followed by heating at 60° C for 30 min produced the nitro compound **2** in 85% isolated yield.³ Clearly this arises from reaction of the prenyl unit with NO_2 or NO_2^+ generated from disproportionation⁴ of the various nitrogen oxides present in solution.^{5,6} Subsequent heating of the mixture at 85° C for 4 h resulted in formation of acetylene **1** in 33% yield. Treatment of the isolated nitro compound **2** with 27 equiv of sodium nitrite at 85°C for 4 h produced **1** in 38% yield.



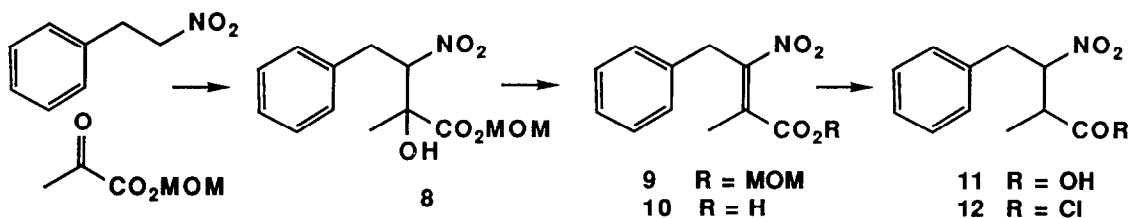
It was determined that the original methyl group is lost as carbon dioxide, isolated by trapping in saturated aqueous barium hydroxide as barium carbonate (89%). Carbon dioxide is not formed in the absence of geraniol. It is also not formed from formaldehyde under the reaction conditions. The facile nitration of **2** and the evolution of carbon dioxide together suggest a mechanism as that shown in Scheme I. A second nitration of intermediate **2** leading to **3** (most likely in the anionic *aci* form) is obviously favorable. Nitrite mediated Nef hydrolysis⁸ of the terminal nitro group gives rise to the aldehyde **4**. The aldehyde thus formed can cyclize via **5** to the isoxazolone N-oxide **6**. Fragmentation of **6** with formation of the acetylene can proceed by a number of plausible pathways, for example, nitrosation to **7** and loss of CO₂ and 2 NO to form **1**.



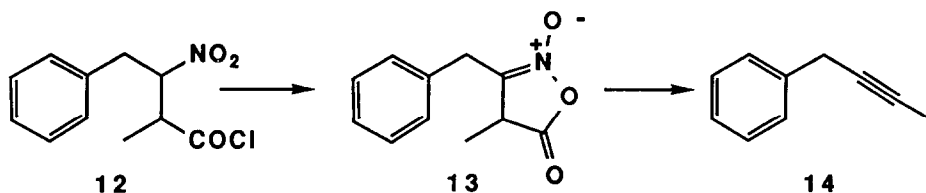
We undertook the preparation of the relevant but unknown isoxazolone N-oxide system⁹ in order to assess the feasibility of this mechanism. As a model, we chose to synthesize 3-benzyl-4-methyl-5-isoxazolone N-oxide (**13**) from the acid **11** which was obtained as shown in Scheme II. Reaction of phenylnitroethane with the methoxymethyl ester of pyruvic acid (10 mol% diisopropylethylamine in CH₂Cl₂ at 23°C for 2 hr) afforded only **8** (41%) and recovered starting materials. Trifluoroacetylation (1.05 equiv trifluoroacetic anhydride, 1.05 equiv diisopropylethylamine in CH₂Cl₂, -50°C, 3 hr) followed by treatment with diazabicyclo[5.4.0]undec-7-ene (1.0 equiv, CH₂Cl₂, -50°C, 1 hr) gave the nitroacrylate ester **9** in 77% yield. Cleavage of the methoxymethyl group in **9** (2 equiv bromotrimethylsilane, trace of methanol in CH₂Cl₂, 23°C, 1.5 hr) gave acid **10** which was treated sequentially with 1.1 equiv of KHCO₃ in dimethoxyethane and 1.5 equiv of sodium borohydride at -10°C for 1.5 hr to give acid **11**.¹⁰ Reaction of **11** with oxalyl chloride (1.1 equiv, 1.1 equiv pyridine in benzene, 23°C,

10 min) afforded the corresponding acid chloride **12** which was purified by Kugelrohr distillation and characterized spectroscopically.

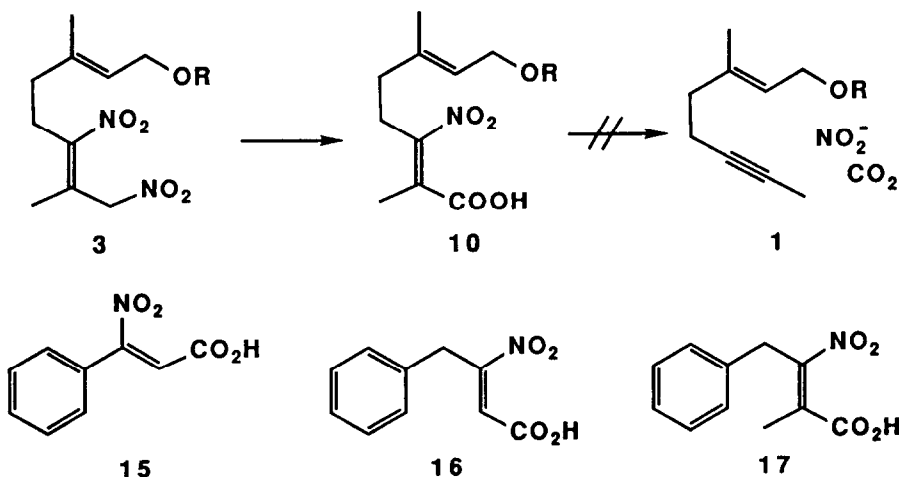
SCHEME II



Treatment of acid chloride **12** with 1.1 equiv of pyridine at -5°C for 30 min in ether generated a new intermediate (infrared analysis) which was too unstable to permit isolation but which is likely the isoxazolone N-oxide **13**. During the reaction of **12** with pyridine, the carbonyl band of **12** at 1785 cm^{-1} is replaced by a new band at 1822 cm^{-1} . When the ethereal solution of this intermediate was added concurrently with aqueous sodium nitrite to aqueous acetic acid at 85°C over 30 min, 1-phenyl-2-butyne (**14**) was produced in 54% yield.¹¹ These results clearly support the mechanism outlined in Scheme I. It should be noted that reaction of nitrous acid with 5-aminoisoxazoles also produces acetylenes in a process clearly related to the conversion of **7** to **1**.¹³

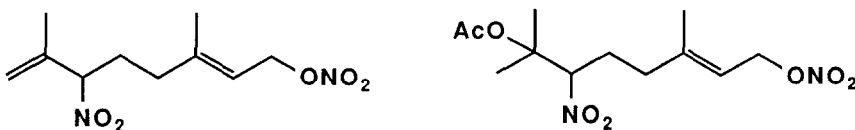


An alternative mechanism in which dinitro compound **3** is converted to nitro acid **10** and thence to **1** by decarboxylative elimination¹⁴ appeared possible. However it was found that **15**, **16** and **17** uniformly produced only products of 1,4-hydration and subsequent retroaldol reaction when subjected to the standard acetylene-forming reaction conditions, a result which argues against the intermediacy of such β -nitroacrylic acids in the formation of **1**.¹⁵

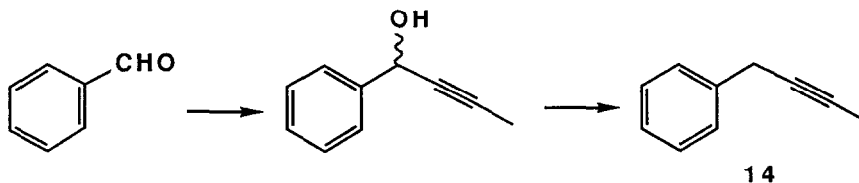


References and Notes

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6. Reaction of geraniol and acetyl nitrate⁷ generates a mixture of the two C-6 nitration products shown.



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9. For benzo derivatives of this ring system see, E. N. Gliben, B. V. Tsukerman, S. S. Tsymbalova, and O. F. Ginzburg, *Zhur. Org. Khim.* **13**, 462 (1977); E. N. Gliben, M. A. Krivtsova, and O. F. Ginzburg, *ibid.* **18**, 386 (1982); A. V. Garabadzhin, E. N. Gliben, *ibid.* **18**, 1243, (1982).
10. Surprisingly, attempts to reduce the nitroacrylate ester **10** with sodium borohydride resulted not in the expected reduction 1,4 to the nitro group (A. Hassner and C. Heathcock, *J. Org. Chem.* **29**, 1350 (1964)) but rather in reduction 1,4 to the carbonyl with consequential elimination of the nitro group.
11. A comparison sample of 1-phenyl-2-butyne was prepared by addition of propynyllithium to benzaldehyde followed by reduction with triethylsilane and trifluoroacetic acid.¹²



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14. See for example: N. Ono, H. Eto, R. Tamara, J. Hayami, and A. Kaji, *Chem. Lett.* 757 (1976); N. Ono, R. Tamara, J. Hayami, and A. Kaji, *Chem. Lett.* 189 (1977).
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