

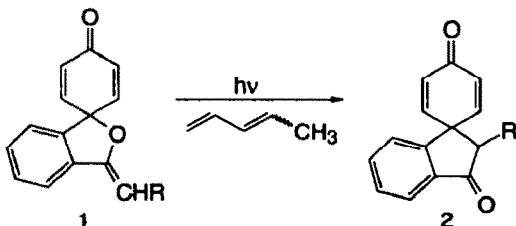
## The Photochemistry of Acetylenic Ethers. A Novel Carbon-Oxygen to Carbon-Carbon Bond Conversion

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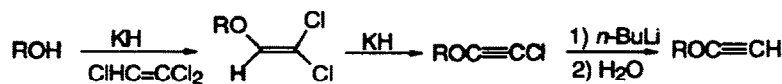
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**Abstract:** Irradiation of acetylenic ethers in methanol gives homologated esters via a formal [1,3]-oxygen-to-carbon migration involving a ketene intermediate.

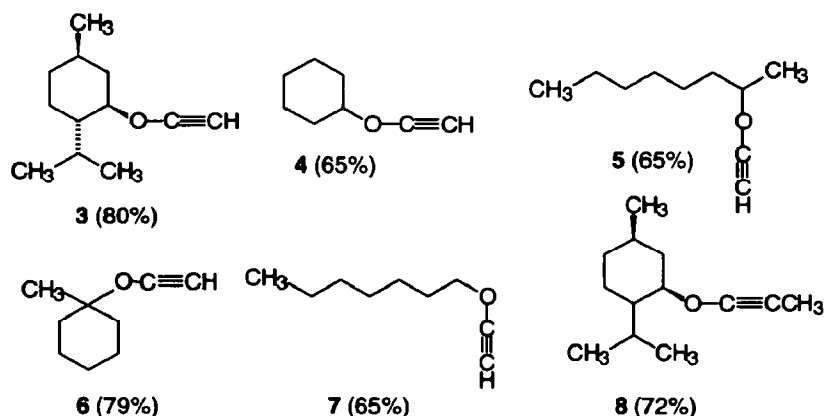
Photochemical [1,3]-oxygen-to-carbon migrations of exocyclic vinyl ethers such as **1** are useful reactions for formation of quaternary carbon-carbon bonds.<sup>1</sup> However, we have not been able to extend this chemistry to simple vinyl ethers. Undoubtedly, the weak carbon-oxygen bond in **1** is important for obtaining high yields in the **1** → **2** transformation. Acetylenic ethers would be expected to be thermodynamically less stable than the corresponding vinyl ether.<sup>2</sup> Thus, there would be more driving force for thermal or photochemical rearrangement and a [1,3]-shift analogous to the **1** → **2** conversion could be more general. We report herein that the photochemical rearrangement of acetylenic ethers<sup>3</sup> in methanol gives carboxylic esters arising from a formal [1,3]-oxygen-to-carbon migration which occurs with a substantial degree of stereospecificity.



The acetylenic ethers used in this work were prepared by the procedure of Greene (see below).<sup>4</sup> Several comments about the preparation are in order. First, if the potassium hydride contained appreciable amounts of potassium,<sup>5</sup> low yields of acetylenic ethers resulted. Second, chromatographic separations were best performed on base-washed silica gel<sup>6</sup> or else partial hydrolysis of the acetylenic ether to the corresponding ester was observed. Since the acetylenic esters were thermally sensitive, we avoided heating the compounds above

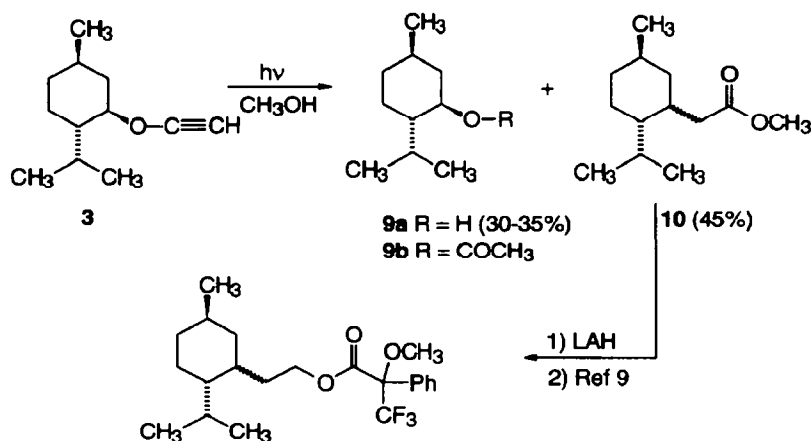


60 °C. When these precautions were observed, the acetylenic ethers could usually be prepared in 65-80% yield (Scheme I). All new compounds in Scheme I showed  $^1\text{H}$  NMR, IR, and exact mass measurements in agreement with the structures.

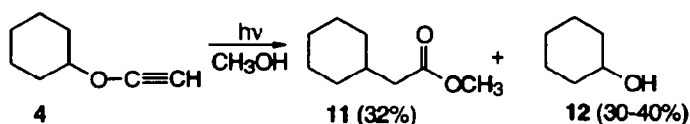


**Scheme I. Acetylenic Ethers Prepared from the Corresponding Alcohols**

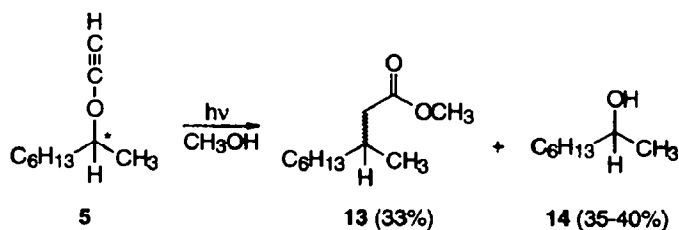
Our initial studies were performed with **3** since its preparation was known and it could be obtained in high purity. Irradiation of **3** through quartz at 253.7 nm<sup>7</sup> in methanol led to a mixture of menthol, **9a**, the acetate of menthol, **9b**, and a product subsequently assigned as **10**. The acetate **9b** undoubtedly arose from addition of water to the acetylenic ether catalyzed by adventitious acid since **9b** is formed in high yield from the acid-catalyzed reaction of water with **3**. When methanol freshly distilled from magnesium/iodine<sup>8</sup> was employed as solvent, the ester **9b** was either totally absent or else a very minor product from the reaction. The mass spectrum of the major product **10** indicated the formula C<sub>13</sub>H<sub>24</sub>O<sub>2</sub>: obsd  $m/z$  212.1769; calcd 212.1776. This compound showed an ester absorption in the IR spectrum at 1741 cm<sup>-1</sup>, and the  $^1\text{H}$  NMR data further supported the presence of a methyl ester:  $\delta$  3.67 (s, 3 H); 2.55 (dd,  $J = 3.8, 14.4$  Hz, 1 H), 2.0-1.9 (m, 2 H), 1.8-1.6 (m, 4 H), 1.35 (m, 1 H), 1.0-0.7 (m, three overlapping doublets at 0.90 ( $J = 7$  Hz), 0.88 ( $J = 7$  Hz), and



0.75 ( $J = 7$  Hz), total area 13H). Although the IR and  $^1\text{H}$  NMR spectra suggested a pure ester and no impurity could be detected by vapor phase chromatography, the  $^{13}\text{C}$  NMR spectrum of **10** showed a minor product having a similar  $^{13}\text{C}$  NMR spectrum. To analyze this mixture, the ester was reduced to the alcohol with lithium aluminum hydride, the alcohol was derivatized to its Moser's ester,<sup>9</sup> and the product mixture was analyzed by  $^{19}\text{F}$  NMR spectroscopy. The  $^{19}\text{F}$  NMR spectrum indicated the product was a 93:7 mixture of two esters. These data suggest that **10** is a difficult-to-separate 93:7 mixture of esters differing at the configuration of the carbon of the original alcohol. The supposition that this was a mixture of diastereomers, rather than two fundamentally different ester photoproducts, was supported by the rearrangement of the cyclohexyl system **4**. Irradiation of the cyclohexyl derivative **4** gave, in addition to cyclohexanol, the ester **11** which showed spectroscopic properties identical to an authentic sample. No second ester product was detected by  $^{13}\text{C}$  NMR spectroscopy.



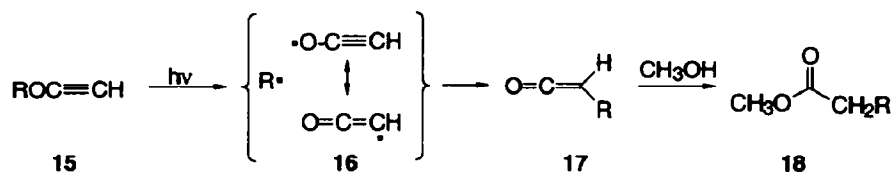
To establish the stereospecificity of the rearrangement, the acetylenic ethers derived from (+) and (-)-2-octanol, **5**, were prepared and irradiated. The esters, **13**, from the rearrangement were reduced to the alcohols and converted to the Moser's esters as described for **10**. Analysis by  $^{19}\text{F}$  NMR showed that in both cases a 4:1 mixture of diastereoisomeric Moser's esters was produced, corresponding to 60% ee. Thus, specificity is associated with the rearrangement of the acetylenic ethers to esters.



The generality of the rearrangement remains to be fully investigated. The acetylenic ethers studied thus far were bonded to  $2^\circ$  centers. Irradiation of the  $3^\circ$  system **6** in methanol afforded the rearranged ester in only 20% yield whereas the  $1^\circ$  system **7** did not give a homologated ester. Finally, irradiation of the methyl-substituted acetylene **8** in methanol gave the rearranged ester as a mixture of diastereomers in 28% yield. It appears that this rearrangement is most facile with  $2^\circ$  systems. However, different reaction conditions were not explored for compounds **6**, **7**, and **8**, and a refinement of reaction conditions could lead to improved yields for these compounds.

The two major photochemical processes for the acetylenic ether linkage are rearrangement to a homologated acid and a cleavage reaction, giving the alcohol. Light is required for the formation of the alcohol since storing **3** dissolved in the irradiation solvent system for several days in the dark did not produce alcohol, **9a**. However, irradiation of this solution afforded the ester **10** together with **9a**. Nucleophilic additions to excited state acetylenes have been proposed and perhaps an exchange reaction involving methanol leads to the alcohol (e.g., **9a**) formed in the reaction.<sup>10</sup> The ester formation is the interesting reaction and could be occurring via a concerted [1,3]-shift in the excited singlet state (**15** excited singlet  $\rightarrow$  **17**) and/or via

a short-lived biradical intermediate (15 excited state  $\rightarrow$  16  $\rightarrow$  17). Both possibilities would give retention of configuration and involve a ketene intermediate. If the reaction was performed in tetrahydrofuran/water, then the corresponding acid was the product. We did investigate reaction conditions for irradiation of 3 in an attempt to maximize the preparative formation of the ester 10. Indeed, irradiation of 3 in a 75:20:5 mixture of dry hexane/xylene/methanol gave on a ca. 1-gram scale the ester 10 (46%) with only a trace of alcohol being detected by vpc.<sup>11</sup> In smaller runs, yields for 10 as high as 60% were recorded.



This chemistry comprises a novel method for a chain extension of an alcohol via its acetylenic ester to a carboxylic acid derivative. Improving the chirality transfer from the acetylenic ether to the carboxylic acid derivative would comprise a useful method for preparation of chiral acid derivatives from readily available optically active alcohols.

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#### References

- (a) Wang, S.; Callinan, A.; Swenton, J.S. *J. Org. Chem.* **1990**, *55*, 2272. (b) Swenton, J.S.; Bradin, D.; Gates, B.D. *J. Org. Chem.* **1991**, *56*, 6156. (c) Swenton, J.S.; Callinan, A.; Wang, S. *J. Org. Chem.* **1992**, *57*, 5568.
- The enthalpy of formation of acetylene is 228.2 kJ/mol whereas that for ethylene is -37.5 kJ/mol. *Handbook of Chemistry and Physics, 71<sup>st</sup> Edition*, CRC Press, 1990, pp 5-11.
- The cycloaddition of acetylenic ethers with aldehydes and ketones has been reported: Bos, H.J. T.; Van Der Bend, H.T.; Boleij, J.S.M.; Everaars, C. J. A.; Polman, H. *Recueil* **1972**, *91*, 65. However, we could find no reports on the intramolecular rearrangements of acetylenic ethers in review articles such as: Coyle, John D. *Organic Photochemistry*; Dekker Publishing: New York, 1985; Chapter I, pp 1-73 or Coyle, J. D. *The Chemistry of the Carbon-Carbon Triple Bond*, Part 2, John Wiley and Sons Publishing: New York, 1978; Chapter 12, pp 523-551. For investigations of the thermal reactions of alkynyl ethers, see: (a) Nieuwenhuis, J.; Arens, J. F. *Recueil*, **1954**, *77*, 761. (b) Vollema, G. Arnes, J. F. *Recueil* **1963**, *82*, 305. (c) Liang, L.; Ramaseshan, M.; MaGee, D. I. *Tetrahedron*, **1992**, *49*, 2159.
- Moyano, A.; Charbonnier, F.; Greene, F., *J. Org. Chem.* **1987**, *52*, 2919.
- Brown, C. A. *J. Org. Chem.* **1974**, *39*, 3913. Sonderquist, J. A.; Rivera, I. *Tetrahedron Lett.* **1988**, *29*, 3195. MacDonald, T. L.; Natalie, K. J. Jr.; Prasad, G.; Sawyer, J. S. *J. Org. Chem.* **1986**, *51*, 1124. The MacDonald procedure was used to purify the potassium hydride used in this work.
- Stern, A. J.; Swenton, J. S. *J. Org. Chem.* **1988**, *53*, 2465.
- Unless otherwise noted, the irradiations were performed at 25-30 °C in quartz tubes using a Rayonet Photochemical Reactor and RPR-2537Å lamps. The ca. 0.1 M solutions of the acetylenic ether in methanol were degassed by bubbling nitrogen through the solution for several minutes before the tubes were sealed and irradiated. The progress of the reaction was monitored by vpc, using a 20" x 0.125" column of 3% OV-17 on Chromosorb G-HP 100/120 mesh column. The yields reported for the ester were actually for the carboxylic acid obtained from potassium hydroxide hydrolysis of the crude reaction mixture. Compound 3 decomposed when heated in methanol at 100 °C for 12 hours, but 10 was not formed.
- Perrin, D. D; Armarego, W. L. F. *Purification of Laboratory Chemicals*, 3<sup>rd</sup> Edition, Pergamon Press, New York, p 217.
- Mosher, H.S.; Dale, J.A.; Dull, D.L., *J. Am. Chem. Soc.* **1969**, *91*, 2543. These derivatives were prepared by reacting the crude alcohol with (R)-(+)- $\alpha$ -methoxy- $\alpha$ -(trifluoromethyl) phenylacetic acid, *N,N*-dicyclohexylcarbodiimide, and *N,N*-dimethylaminopyridine.
- Wan, P.; Culshaw, S.; Yates, K., *J. Am. Chem. Soc.* **1982**, *104*, 2509 and references cited therein.
- For the preparative irradiation, a solution of 3 (930 mg), hexadecane (internal standard, 168 mg), dry hexane (75 mL), xylene (20 mL), and dry methanol (5 mL) was degassed by bubbling nitrogen through the solution for 5 minutes. This solution was irradiated with a 450-watt Hanovia medium-pressure source through Vycor for 26 h. After this time quantitative vpc analysis showed a 46% yield of ester 10 at 92% conversion of 3. The reaction mixture was concentrated in vacuo to about 5 mL and then heated at reflux for 12 h in 1:1 methanol/tetrahydrofuran (100 mL) containing potassium hydroxide (1 g). Workup gave the carboxylic acid (0.41 g, 40%).

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