

GENERATION AND CYCLOADDITIONS OF HYDROXY(AND TRIMETHYLSILOXY)PHENYLETHYNYLKETENE

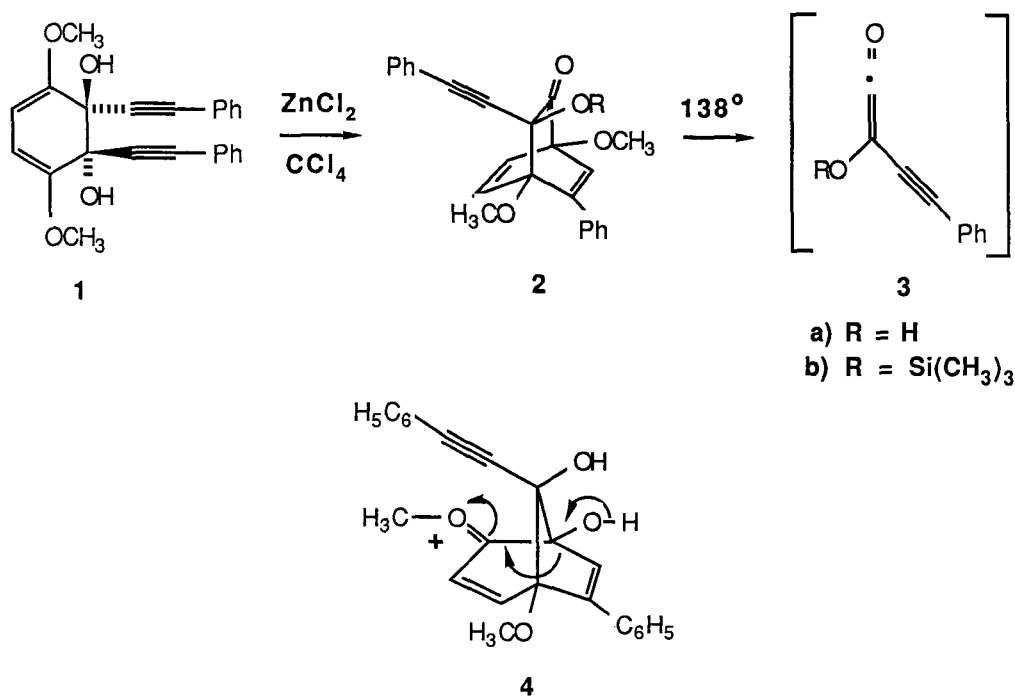
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Abstract: An unusual rearrangement of 5,6-dihydroxy-1,3-dimethoxy-5,6-diphenylethynyl-1,3-cyclohexadiene (**1**) to 7-hydroxy-1,4-dimethoxy-2-phenylethynylbicyclo[2.2.2]octadiene-8-one (**2a**) was observed when **1** was treated with ZnCl_2 in refluxing carbon tetrachloride. The bicyclooctadienones **2a,b** were observed to undergo retro Diels-Alder fragmentation at 138 °C to give hydroxy(or trimethylsiloxy)-phenylethynylketenes **3a,b**, the only examples of alkynylketenes other than alkynylcyanoketenes to appear in the literature.¹ The ketene **3b** cycloadds to a variety of ketenophiles, but most interestingly, it undergoes unusual reactions with diphenylacetylene to give the cyclopentenedione **7** and with ethoxypropyne to yield the highly functionalized benzoquinone **8**.

Cyclohexadiene **1** is available from 3,6-dimethoxy-1,2-benzoquinone upon treatment with excess 1-lithio-2-phenylethyne in THF at -78 °C.² Surprisingly, when a carbon tetrachloride (25 mL) solution of **1** (1.34 mmol) and ZnCl_2 (0.36 mmol) was refluxed for 2 hr bicyclo[2.2.2]octadienone **2a** was realized in 60% yield as a white crystalline solid, mp, 141-142 °C. The structure of **2a** can be assigned on the basis of a detailed analysis of its spectral properties, particularly those from NOE and two-dimensional proton-carbon correlation NMR studies. Furthermore, unambiguous proof of the structure was obtained by single crystal X-ray analysis.³ Details of the rearrangement of **1** to **2a** are yet to be determined, but a reasonable intermediate would be **4**. This is envisaged to arise *via* protonation of one of the alkynyl groups followed by attack of the resulting vinyl cation or its equivalent on the ring alkenyl bond. Subsequent vinyl group migration and proton loss would then give **2a**.

The bicyclooctadienes **2a,b** are of synthetic interest since they proved to be precursors of respectively hydroxyphenylethynylketene **3a** and trimethylsiloxyphenylethynylketene **3b** via retro Diels-Alder reactions.^{4,5} This is noteworthy since alkynylketenes are very rare¹ and the chemistry of hydroxyketenes is virtually unexplored. The ketenes **3a,b** were generated when *p*-xylene solutions of **2a** or **2b** and a ketenophile were refluxed (138 °C) for 8 hr. For example, when

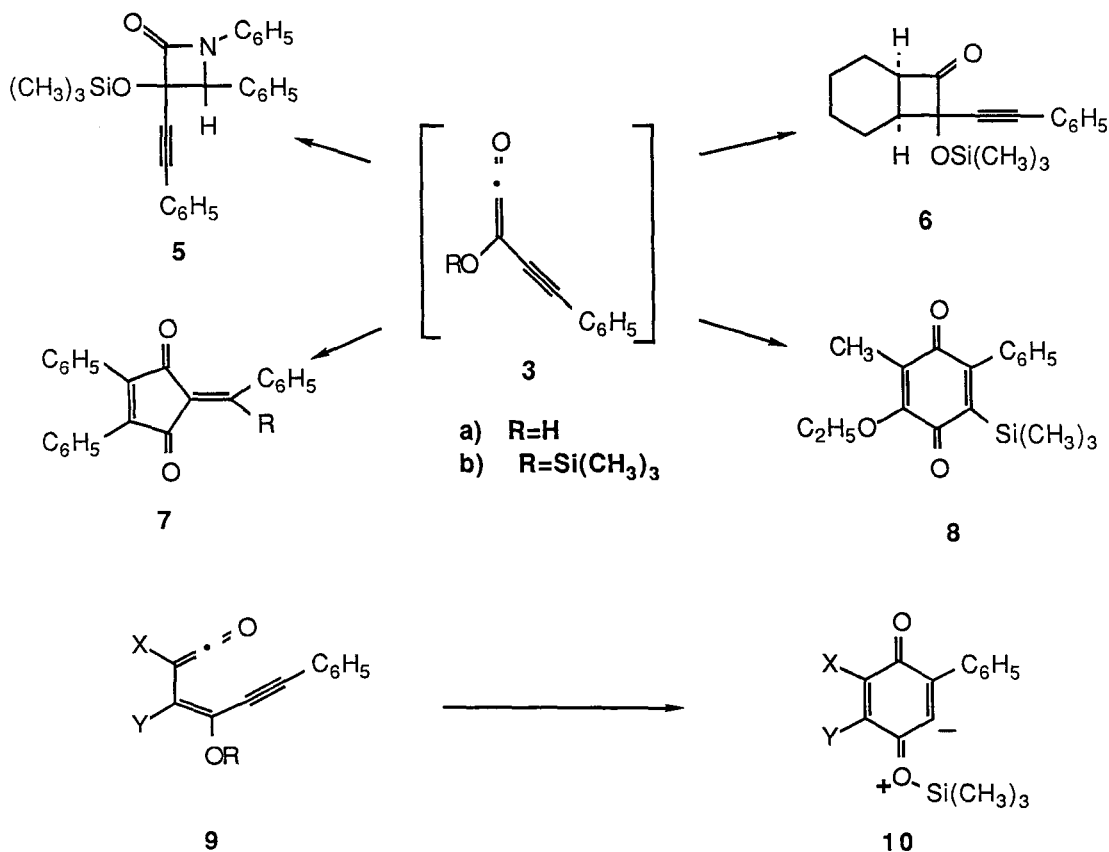
SCHEME 1



1.1 eq. of N-phenylbenzylidenimine was used as the ketenophile the 2-azetidinone **5** was obtained as a single diastereomer in 72% purified yield: mp, 142-143 °C; ir (CHCl₃, cm⁻¹) 2218, 1780; ¹HNMR (CDCl₃) 7.5-7.0 (m, 15H), 5.07 (s, 1H), 0.30 (s, 9H); anal. C, 75.61; H, 5.90. When **3b** was generated in the presence of 44 eq. of cyclohexene the cyclobutanone **6** was obtained in 50% purified yield as a single isomer: mp, 83-84 °C; ir (CHCl₃, cm⁻¹) 1785; ¹HNMR (CDCl₃) 7.45-7.30 (m, 5H), 3.62 (m, 1H), 2.73 (m, 1H), 2.15-1.05 (m, 8H), 0.28 (s, 9H); anal. C, 72.98; H, 7.85.

Cycloadditions of **3a,b** to alkynes gave very unusual results. First of all, when either **3a** or **3b** was generated in the presence of 1 eq. of diphenylacetylene (138 °C, *p*-xylene) the respective cyclopentenones **7a** and **7b** were obtained in 34% and 55% yield: **7a**; mp, 159-160 °C; ir (CHCl₃, cm⁻¹) 1680, 1625; ¹HNMR (CDCl₃) 8.40 (d, J=3.0 Hz, 2H), 7.77 (s, 1H), 7.6-7.2 (m, 13H); anal. C, 85.50; H, 4.49; **7b**; mp, 196-197 °C; ir (CHCl₃, cm⁻¹) 1725, 1690; ¹HNMR 7.45-7.22 (m, 13H), 6.94 (m, Hz, 2H), 0.21 (s, 9H); anal. C, 79.18; H, 5.65. The structures of **7a** and **7b** are based upon the above spectral data as well as upon their ¹³CNMR and mass spectral properties. The formation of **7a,b** presents an interesting mechanistic problem for which there is a precedent.^{6,7} That is, analogous products are observed when 4-phenylethynyl-4-hydroxy(or trimethylsiloxy)-2,3-dimethoxycyclobutenone was thermolyzed at 138 °C in refluxing *p*-xylene. This reaction is envisaged to proceed via the conjugated ketene **9** (X=Y=OCH₃) which undergoes ring closure to a zwitterionic or diradical

SCHEME 2



intermediate. Subsequent migration of R (H or Si(CH₃)₃) then gives the product. In analogy, 7a,b are envisaged to arise from 9 (X=Y=C₆H₅) which, in turn, results from electrocyclic ring opening of the initially formed 2+2 cycloadducts of the ketenes 3a,b with diphenylacetylene, i.e. the corresponding cyclobutenones. To our knowledge, the cycloaddition of 3a to diphenylacetylene constitutes the first example of a hydroxyketene cycloaddition.

Finally, we report the formation of the benzoquinone 8 (45% isolated yield) when 3b was generated in the presence of 10 eq of ethoxypropyne: yellow oil; ir (CHCl₃, cm⁻¹) 1650; ¹H NMR (CDCl₃) 7.41-7.35 (m, 3H), 7.15-7.09 (m, 2H) 4.30 (q, J=7.0 Hz, 2H), 1.96 (s, 3H) 1.39 (t, J=7.0 Hz, 3H), -0.09 (s, 9H); exact mass, 314.1314.⁸ Here again, an analogy helps explain this unusual transformation. Specifically, similar ring expansions have recently been reported for the thermolysis of some 4-alkynyl-4-trimethylsiloxy cyclobutenones.^{6,7} Here, the ring opened conjugated ketene proceeds to a zwitterionic intermediate and subsequently to the quinone products upon transfer of the trimethylsilyl group. In the case at hand, the ketene 9 (X=CH₃, Y=OC₂H₅) proceeds to 10 followed by trimethylsilyl migration to give 8. This mechanism was

further documented when the cyclobutenone precursor of **9** was independently prepared by sequential treatment of 3-ethoxy-4-methylcyclobutenone with 1-lithio-2-phenylethyne (-78°) and chlorotrimethylsilane and subjected to thermolysis in refluxing *p*-xylene (138°C) for 0.5 hr. This gave the same reaction products as were formed in the cycloaddition itself.⁸

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REFERENCES AND NOTES

1. Moore, H. W.; Chow, K.; Nguyen, N. V. *J. Org. Chem.* **1987**, *52*, 1315.
2. West, K. F.; Wriede, U.; Fernandez, M.; Chow, K.; Moore, H. W. *J. Org. Chem.* **1987**, *52*, 2537.
3. We are grateful to Drs. Shoumo Chang and Joseph Ziller for respectively NMR and X-ray analyses studies.
4. Compound **2b** was readily obtained as a colorless oil (60%) from **2a** upon treatment with butyllithium in THF at -78° followed by the addition of 2.8 eq of TMSCl. Its spectral and analytical properties are in agreement with its structure.
5. For a review of the synthetic use of the retro Diels-Alder reaction see: Desimoni, G.; Tacconi, G.; Barco, A.; Pollini, G. P. *Natural Products Synthesis Through Pericyclic Reactions* ACS Monograph 180, **1983**, American Chemical Society, Washington D.C.
6. Karlsson, J. O.; Nguyen, N. V.; Foland, L. D.; Moore, H. W. *J. Am. Chem. Soc.* **1985**, *107*, 3392.
7. Perri, S. T.; Foland, L. D.; Decker, O. H. W.; Moore, H. W. *J. Org. Chem.* **1986**, *51*, 3067.
8. Another product is also formed and is believed to be the corresponding cyclopentendione analogous to **7**. The ratio of the quinone to this product in the crude reaction mixture is 3:2 and together they constitute a 47% yield. These products in an identical relative ratio are also realized in the cyclobutenone thermolysis. Here, the relative ratio of the two products remained constant and their combined yield was 58% after 0.5 h and 72% after 19 h.

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