Tetrahedron Letters,Vol.28,No.28,pp 3201-3204,1987 0040-4039/87 $3.00 + .00
Printed in Great Britain Pergamon Journals Ltd.

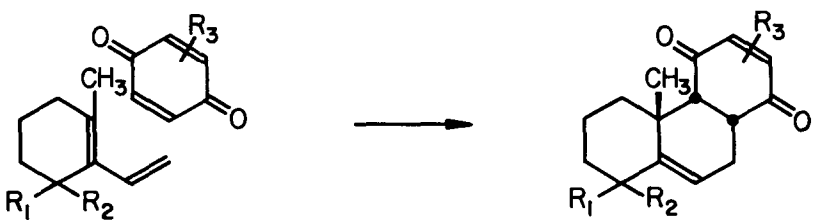
DIELS-ALDER REACTIONS OF VINYLBICYCLO[4.1.0]HEPTENES

Makoto Sakaino and Jerrold Meinwald*

Department of Chemistry, Cornell University
Ithaca, New York 14853-1301

Abstract: Efficient syntheses of 1,3-dimethyl-2-vinylbicyclo[4.1.0]hept-2-ene (**1**) and 2,2-ethylenedioxy-4,6-dimethyl-5-vinylbicyclo[4.1.0]hept-4-ene (**2**) are described. These dienes, which undergo Diels-Alder reactions with p-benzoquinones readily, may serve as versatile intermediates for terpenoid synthesis.

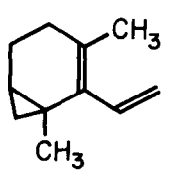
The Diels-Alder addition of a vinylcyclohexene to a p-benzoquinone represents a simple approach to the synthesis of a variety of diterpenoids (eq. 1). The substituents (CH_3,R_1,R_2)



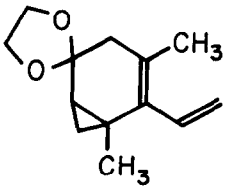
(1)

in such dienes, however, can make it difficult for the conjugated double bonds to attain coplanarity, and in addition, they hinder approach of the dienophile. Our exploratory experiments have confirmed that 1,3,3-trimethyl-2-vinylcyclohexene reacts only reluctantly with quinones,[1] and a recent publication has shown that even at high pressure, long reaction times are required to obtain the quinone adduct of this diene in good yield.[2]

In an attempt to design more reactive vinylcyclohexenes useful for terpenoid synthesis, we have prepared the novel dienes 1,3-dimethyl-2-vinylbicyclo[4.1.0]hept-2-ene (**1**)[3] and 2,2-ethylenedioxy-4,6-dimethyl-5-vinylbicyclo[4.1.0]hept-4-ene (**2**).[4] In these compounds, the



1



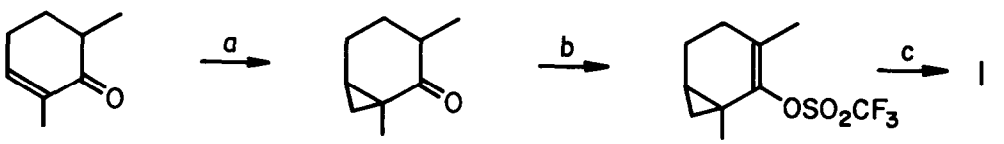
2

cyclopropane ring can serve both as a potential methyl group and as a source of additional ring-A functionality. Molecular models suggest that **1** and **2** are less hindered than 1,3,3-trimethyl-2-vinylcyclohexene, and we anticipated that they would react with a variety of dienophiles under conditions mild enough to permit the retention of some relatively sensitive functional groups. We anticipated further that the resultant adducts might serve as

versatile intermediates for the regio- and stereo- controlled synthesis of a variety of natural products. We now report the preparation of these dienes, and their conversion to Diels-Alder adducts (**5-8**) using two model p-benzoquinones (**3** and **4**).

Chart I summarizes the preparation of **1**, obtained in good overall yield in three steps from 2,6-dimethylcyclohex-2-ene-1-one.[5] An efficient, four step synthesis of **2** from 2,6-dimethyl-p-benzoquinone is outlined in Chart II.[6]

CHART I

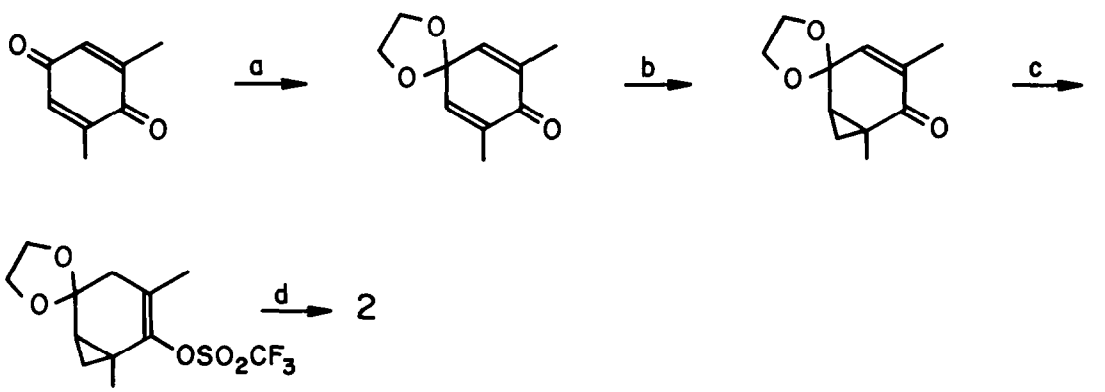


a: $(CH_3)_2S(O)CH_2^-$ Na^+

b: LDA; Tf_2NPh

c: $(C_2H_3)_2CuCN(MgBr)_2$

CHART II



a: $HOCH_2CH_2OH$, p-TSA, $HC(OCH_3)_3$

b: $(CH_3)_2S(O)CH_2^-$ Na^+

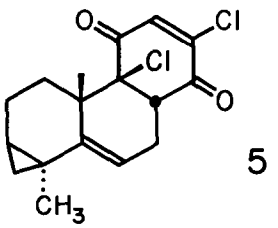
c: L-Selectride; Tf_2NPh

d: $(C_2H_3)_2CuCN(MgBr)_2$

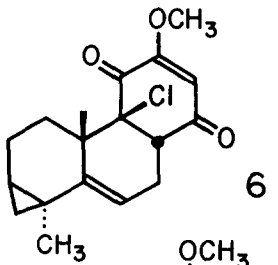
Additions of 2,5-dichloro-p-benzoquinone (**3**) and 2-chloro-6-methoxy-p-benzoquinone (**4**)[7] to **1** and **2** proceeded smoothly in 1:1 CH_2Cl_2/propylene oxide at 60°C, in a sealed tube, giving essentially complete reaction in 1-1.5 days for **1** and 2-7 days for **2**. These reactions each gave only a single adduct.

In the simplest case, the crystalline adduct **5**,[8] m.p. 163°, resulting from the reaction of **1** and **3**, was shown to have the anticipated structure and stereochemistry by a detailed analysis of its ^1H and ^{13}C NMR spectra, including difference NOE studies. The coupling

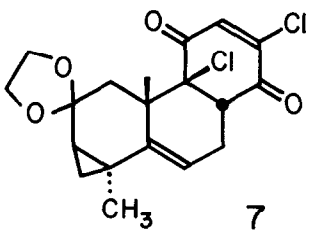
pattern of the single bridgehead proton α to the carbonyl group (δ 3.92, t, J=9.3 Hz) establishes the regiochemistry of the addition process. The strong NOE effects observed between the angular methyl group and this α-proton, as well as with the syn-cyclopropane proton, indicate that **5** is the endo adduct formed by approach of the quinone to the diene from the side opposite that occupied by the cyclopropane ring.



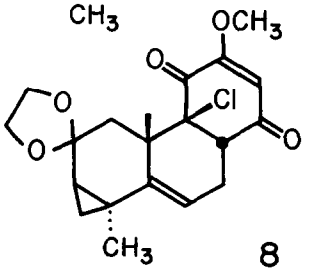
5



6



7



8

Similarly, adducts **6**, **7** and **8** were each obtained as crystalline products whose structures and stereochemistry were readily determined as in the case of **5** itself. We have also defined conditions for the transformation of compounds such as these into products in which the cyclopropane ring has been opened to give a methyl group,[1] and we hope to report the details of those results elsewhere.

Acknowledgements: We are grateful to the Oji Paper Co. for generous support to M.S., and to the NIH for partial support of this research via grant no. AI-12020. Kevin McCormick's participation in this project is acknowledged with pleasure.

References and Notes:

1. M. Sakaino, Ph.D. Thesis, Cornell University (1986).
2. T.A. Engler and S. Naganathan, Tetrahedron Lett., 1986, 27, 1015.
3. **IR**(film): 3080, 3050, 1627, 1592, 985, 897 cm^{-1}; **^{1}H NMR**: δ(400 MHz, $CDCl_3$) 0.29(t, 1H, J=4.2 Hz), 0.78(dd, 1H, J=8.1, 3.7 Hz), 0.86(m, 1H), 1.09(m, 1H), 1.13(s, 3H), 1.66(dt, 1H, J=15.6, 4.0 Hz), 1.76(s, 3H), 2.10(m, 1H), 2.22(br. t, 1H, J=14 Hz), 5.05(dd, 1H, J=11.1, 2.0 Hz), 5.29(dd, 1H, J=17.5, 2.0 Hz), 6.62 (dd, 1H, J=17.5, 11.1 Hz)ppm; **^{13}C NMR**: δ(100 MHz, $CDCl_3$), 15.30(s), 19.21(d), 19.88(q), 24.50(q), 25.14(t), 26.42(t), 31.47(t), 112.86(t), 132.57(d), 133.66(s), 135.47(s) ppm; **UV**(cyclohexane): 239 (ε=529), 245(531), 251(521), 256(459), 266 (430)nm; **CIMS**: m/z 149(100%); **EIMS**: m/z 148(66), 133(100), 120(65), 105(98), 91(66%).
4. **IR**(film): 3075, 2940, 2868, 1628, 1591, 1440, 1378, 1367, 1225, 1042, 983, 965, 940, 898, 855 cm^{-1}; **^{1}H NMR**: δ(300 MHz,$CDCl_3$) 0.72(t, 1H, J=4.8 Hz), 0.82(dd, 1H, J=8.6, 4.3 Hz), 1.09(dd, 1H, 8.6. 5.5 Hz), 1.19 (s, 3H), 1.77 (s, 3H), 1.97(br. d, 1H, J=15.7 Hz),

3.85-4.05(m, 4H), 5.14(dd, 1H, J=11.1, 1.9 Hz), 5.26(dd, 1H, J=17.6, 1.9 Hz), 6.52 (dd, 1H, J=17.6, 11.1 Hz)ppm; **^{13}C NMR**: δ(100 MHz, $CDCl_3$) 19.06(s), 20.12(t), 20.20(q), 23.38(q), 27.72(d), 40.93(t), 63.74(t), 64.08(t), 108.65(s), 114.87(t), 129.23(s), 132.35(d), 132.92(s) ppm; **UV**(cyclohexane): 204(ε=344), 223(515), 241(518), 244(520), 247(533), 249(528), 252(534), 256(528), 259(497), 264(465), 287 (158)nm; **CIMS**: m/z 207(100), 145(23%); **EIMS**: m/z 206(69), 191(20), 178(12), 135(15), 134(23), 133(100), 120(46), 119(84), 117(12), 105(45), 99(16),93(15), 91(39), 84(14), 79(14), 77(16), 73(14), 55(11), 53(11), 49(17), 41(14), 38(12%).

5. A.S. Kende, P. Fludzinski, J.H. Hill, W. Swenson, and J. Clardy, J. Am. Chem. Soc., 1984, 106, 3551.

6. 2,6-Dimethylbenzoquinone was prepared in 90% yield using the procedure described by J. Cason in "Organic Reactions" R. Adams, ed., Vol. 4, 325(1948) for the preparation of 2,3,6-trimethylbenzoquinone from 2,3,6-trimethylphenol.

7. This quinone was prepared from vanillin as described by L.C. Raiford and J.G. Lichty, J.Am. Chem. Soc., 1930, 52, 4576 and L. Asp and B. Lindberg, Acta Chem. Scand., 1950, 4, 60.

8. **IR**($CHCl_3$): 3016, 2978, 2940, 2858, 2828, 1703, 1638, 1590, 1457, 1445, 1373, 1305, 1294, 1170, 1022, 894, 825 cm^{-1}; **^{1}H NMR**: δ(300 MHz, $CDCl_3$) 0.51(t, 1H, J=4.9 Hz), 0.72(dd, 1H, J=8.6, 4.6 Hz), 1.11(s, 3H), 1.11(m, 1H), 1.22(s, 3H), 1.34(dt, 1H, J=13.3, 5.6 Hz), 1.55(m, 1H), 2,22(ddd, 1H, J=19.2, 9.4, 4.6 Hz),2.3-2.4 (m, 1H), 2.39 (td, 1H, J=9.7, 5.8 Hz), 2.66 (ddd, 1H, J=19.2, 9.3, 3.3 Hz), 3.92(t, 1H, J=9.3 Hz), 5.40(t, 1H, J=3.8 Hz), 6.86(s, 1H) ppm; **^{13}C NMR**: δ(100 MHz, $CDCl_3$) 19.02(s), 20.74(t), 22.11(t), 23.18(d), 25.42(q), 26.29(q), 27.80(t), 28.38(t), 40.24(s), 52.30(d), 79.08(s), 116.21(d), 135.89(d), 143.08(s), 147.00(s), 188.23(s), 189.73(s) ppm; **CIMS**: m/z 329(6), 328(7), 327(26), 326(16), 325(48), 324(11), 297(27), 291(30), 290(22), 289(94), 287(40), 148(25), 147(100, bp), 59(27), 49(52%); **EIMS**: m/z 328(2), 327(2), 326(10), 325(4), 324(14), 311(10), 309(15), 289(20), 273(21), 147(100, bp), 146(37), 133(83), 131(29), 126(23), 119(48), 115(25), 105(34%).

(Received in USA 2 April 1987)