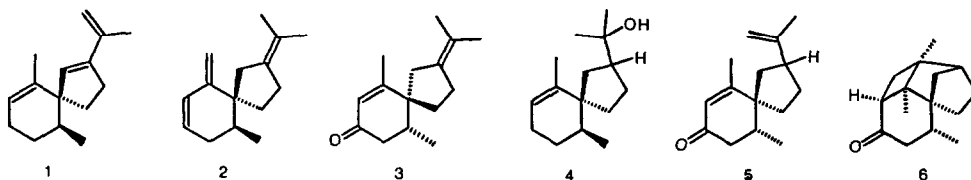


SHORT INTRAMOLECULAR DIELS-ALDER APPROACH
TO FUNCTIONALIZED SPIRO[4.5]DECANES¹

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Summary: The intramolecular Diels-Alder reaction of a (5'-hexynyl)cyclopentadiene provides a 1,2-tetramethylene-bridged norbornadiene which undergoes selective monohydrogenation followed by ozonolysis to provide the title compounds.

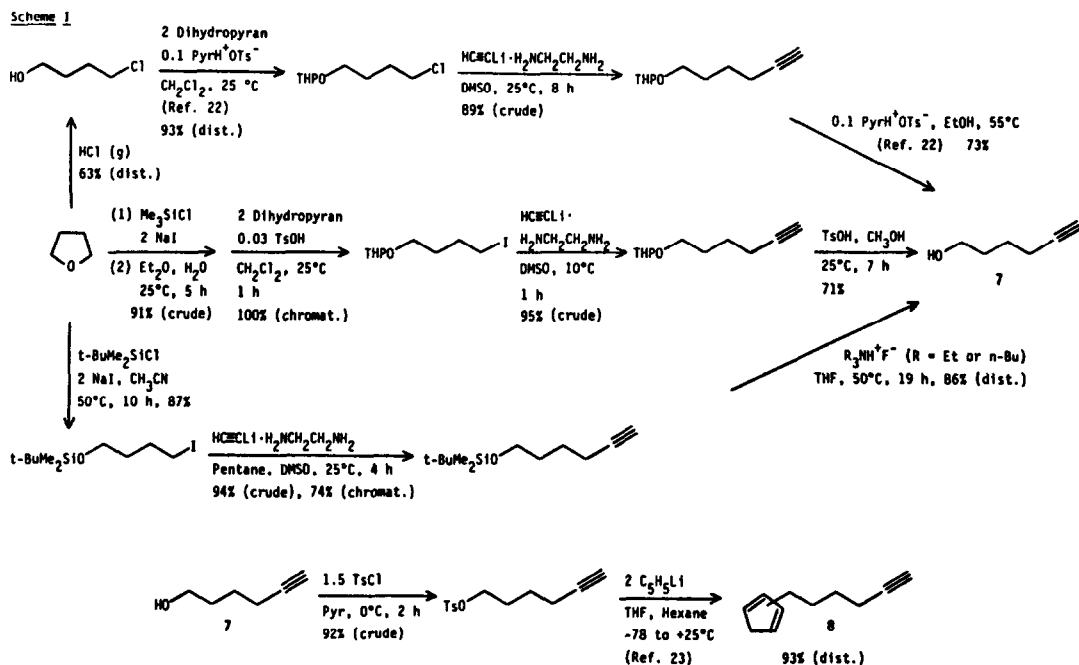
Spirocyclic compounds are of widespread interest. Among the naturally occurring compounds of this type, those having the spiro[4.5]decane ring system are especially prominent.^{3,4} Some specific examples include α -vetispirene (1),⁵ β -vetispirene (2),⁵ β -vetivone (3),⁶ hinesol (4),^{6,7} solavetivone (5),⁸ and solanascone (6).⁸ Also, spirocyclic compounds serve as useful intermediates for the construction of other systems.^{3a}



Several routes have been reported previously for the synthesis of spiro[4.5]decanes.^{3,4} Herein we report an especially direct route based upon an intramolecular Diels-Alder reaction⁹ followed by selective hydrogenation and ozonolysis.

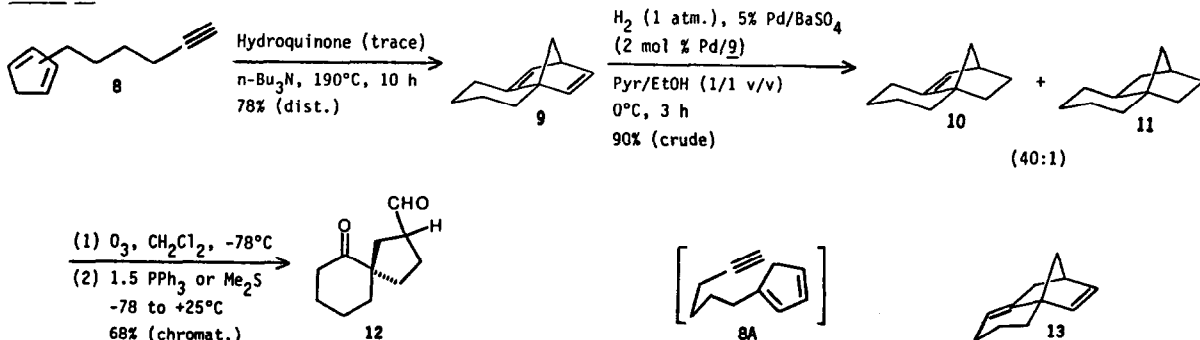
We have prepared our Diels-Alder substrate **8** (1:1 mixture of 1- and 2-substituted cyclopentadienes) by three routes (Scheme I) based upon the cleavage of tetrahydrofuran (THF) and subsequent transformations leading to 5-hexyn-1-ol (**7**).¹⁰ In the first route, cleavage of THF with hydrogen chloride provides 4-chlorobutanol¹¹ as a precursor of **7** whereas in the second route, the cleavage is effected by trimethylsilyl iodide.¹² In the third route, we employ *tert*-butyldimethylsilyl iodide^{13,14} which permits much more direct access to **7**. Trialkylammonium fluorides are conveniently employed for removal of the silyl group.¹⁵

The intramolecular Diels-Alder reaction of **8** proceeds very cleanly at 190 °C with complete conversion of the substrate to give the tetramethylenenorbornadiene derivative **9**. The isolated yield of pure product is 78% after small-scale distillation, but based upon the very clean gas chromatogram of the initially obtained product, the actual yield is probably



higher. The structure of **9** is supported by high-field ^1H and ^{13}C NMR spectra as well as two-dimensional heteronuclear correlation spectra.¹⁶ As expected,^{9e} we have not detected alternative Diels-Alder products obtained from cyclopentadienyl isomers other than **8A**. Also, we have not detected products of ene reactions. However, from some reactions of **8** performed under other conditions (e.g. 220 °C in HMPA), the double bond isomer **13** is obtained as the major product. This compound could conceivably result either from an alkyne/allene equilibration of **8**,¹⁷ perhaps combined with a reversible Diels-Alder reaction, or from direct isomerization of the initial product **9**, perhaps promoted by trace acid impurities. We have observed that when **9** is treated with dilute sulfuric or hydrochloric acid at 25 °C, nearly complete conversion to **13** occurs within a few minutes.

Scheme II



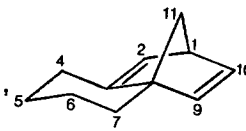
Closely related intramolecular Diels-Alder reactions have been reported by Jäggi,^{18g} Sternbach,^{18j} and others,^{9,18} but their products were employed in quite different applications compared to our present uses. Our product **9** undergoes selective hydrogenation under carefully controlled conditions¹⁹ to give predominantly the desired norbornene derivative **10**.²⁰ Although diimide has been used successfully in a similar system,^{18g} we observe poor double bond selectivity and overreduction when this reagent is employed in the case of **9**. Ozonolysis of **9** under standard conditions followed by reductive work-up provides the spiro[4.5]decane **12**,²¹ the ketone and aldehyde groups of which are expected to provide versatile functionality for further elaboration into substitution patterns of naturally occurring compounds of this series.

In conclusion, the work described in this paper provides a direct entry into the spiro[4.5]decane system with very useful substitution patterns and with complete control over the relative configurations of two key chiral centers. Our ongoing work is concerned with substituted derivatives of the substrate **8** that will permit convenient syntheses of compounds such as **1-6**.

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- (16) **9**: ¹H NMR (300 MHz, CDCl₃) δ 6.68 (dd, J_{9,10} = 5.12 Hz, J_{1,10} = 2.79 Hz, H₁₀), 6.65 (dd, J_{9,10} = 5.12 Hz, J_{1,9} = 1.05 Hz, H₉), 6.07 (br t, J_{1,2} = J_{2,4ax} = 3.0 Hz, H₂), 3.45 (m; 8 lines obsvd, w_{0,1} = 10 Hz, H₁), 2.60 (br d, J_{gem} = 16.3 Hz, H_{4eq}), 2.10 (br d, J_{gem} = 13.1 Hz, H_{7eq}), 1.93 (dd, J_{gem} = 5.60 Hz, J_{1,11} = 1.77 Hz, H₁₁), 1.88 (m, H_{4ax}), 1.72-1.86 (m, H_{5eq}, H_{6eq}), 1.79 (dd, J_{gem} = 5.60 Hz, J_{1,11} = 1.56 Hz, H₁₁), 1.56 (m, H_{7ax}), 1.31-1.48 (m, H_{5ax}, H_{6ax}); ¹³C NMR (75 MHz, CDCl₃) 156.28 (C₂), 145.62 (C₉), 143.80 (C₁₀), 132.12 (C₂), 77.54 (C₁₁), 59.49 (C₈), 48.92 (C₁), 29.97 (C₇), 27.73 (C₄), 24.92 and 24.63 (C₅ and C₆).
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- (20) **10**: ¹H NMR (300 MHz, CDCl₃) δ 5.50 (br t, J_{1,2} = J_{2,4ax} = 2.7 Hz), 2.68 (m, 8 lines obsvd, w_{0,1} = 10 Hz, H₁), 2.34 (br d, J_{gem} = 15 Hz, H_{4eq}), 1.13 (br d, J_{gem} = 8 Hz, one of H₁₁), 1.05 (m, J_{gem} = 8 Hz, one of H₁₁), 1.00-2.10 (m, 13 H, including H₁₁'s); ¹³C NMR (75 MHz, CDCl₃) 146.77 (s, C₂), 126.69 (d, C₉), 53.75 (t, C₁₁), 51.00 (s, C₈), 41.20 (d, C₁), 31.55 (t), 29.75 (t), 29.49 (t), 25.66 (t), 25.33 (t), 23.94 (t).
- (21) **12**: ¹H NMR (300 MHz, CDCl₃) δ 9.13 (d, J = 2.2 Hz, CHO), 2.28 (br quintet, J_{av} = 7 Hz, CHCHO), 1.20-2.05 (m, 12²H), 1.15 (dd, J = 13.48, 9.38 Hz, 1H), 1.07 (dt, J = 12.84, 8.27 Hz, 1H); IR (neat on NaCl plates) 2970 (s), 2900 (m), 1730 (s), 1710 (s), 1450 (m), 1120 (w), 1010 (m) cm⁻¹.
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