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SIMPLE DERIVATIVES OF TETRACYCLO[4.3.0.0^{2,9}0^{5,7}]NON-3-ENE: GENERATION AND TRANSFORMATIONS

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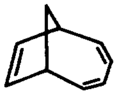
The mechanism of the thermal transformation of bicyclo[4.2.1] nona-2,4,7-triene 1 into cis-9,10-dihydroindene has received considerable mechanistic attention.[1] While there is some uncertainty concerning the detailed reaction mechanism, there seems to be general agreement that the dihydroindene is ultimately formed from the tetracyclic olefin 2 produced in low equilibrium concentration via intramolecular Diels-Alder cycloaddition. The suggested instability of 2 seemed reasonable based on the considerable structural strain coupled with the fact that the carbon skeleton of the cycloadduct is that of a bridged derivative of cis-bis-homobenzene, a material of known thermal lability.[2]



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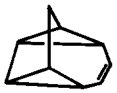

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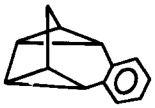

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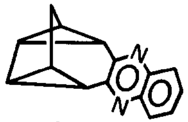

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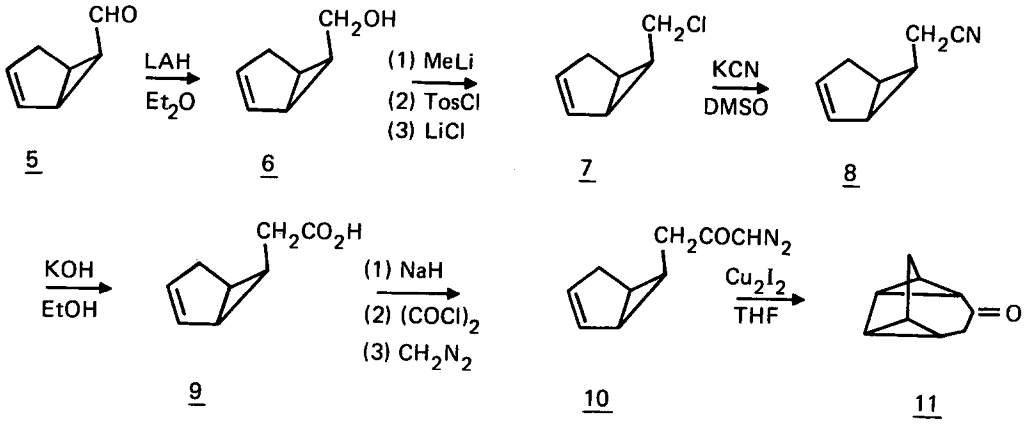
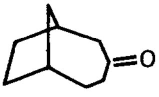
We[3a] and others[3b] have recently described the preparation of the first derivatives, 3 and 4, containing the basic tetracyclo[4.3.0.0^{2,9}0^{5,7}] nonene carbon skeleton. The considerable thermal stability imparted by the aromatic substitution in 3 and 4 however makes them poor models for predicting the relative stability of the hydrocarbon 2 itself. For this reason, we initiated efforts to prepare simple derivatives of 2 containing the same basic carbon skeleton but without stabilizing aromatic substituents.

A successful synthetic route to functionalized tetracyclo[4.3.0.0^{2,9}0^{5,7}]nonane derivatives is shown below. The ketone 11 generated in an overall yield of 30% from the readily available aldehyde[4] is the key intermediate and the first reactively functionalized derivative containing the desired carbon skeleton. The structure of 11 rests firmly on spectral and analytical data:[5] ir(neat) C=O, 1675cm^{-1}; ^{1}H$_{nmr}$(CCl$_4$) τ 7.4-8.1(m,5H), 8.1-8.6(m,4H) and 8.82(m,1H). Further structural conformation was obtained by catalytic hydrogenation of 11 (PtO$_2$,EtOH) to the known[6] bicyclo[4.2.1]nonan-3-one 12.

The ketone itself was relatively unstable and rearranged upon heating (110°, 4hr) to produce the α,β-unsaturated derivative 13a in quantitative yield: ir(neat) 1645cm^{-1}; ^{1}H$_{nmr}$(ØD$_6$) τ 3.92(d,d,J=11,8Hz,1H), 4.39(d,J=11Hz,1H), 4.6(m,2H), 7.38-7.88(m,4H), 8.10-8.43(m,1H) and 8.58(d,J=10Hz,1H); UV(EtOH) 321nm(ε=60) and 230nm(ε=6660).



All attempts to directly convert the ketone 11 into 2 failed due to its lability under various reaction conditions. In an effort to introduce appropriate functionality for elimination to 2 under mild conditions, the ketone was reduced with LAH to generate the corresponding exo alcohol 14a. This material was subsequently characterized by conversion to the more stable acetate 14b or methyl ether 14c.[7] The alcohol 14a was quite sensitive to acid conditions and rearranged quantitatively to 15a even upon standing over magnesium sulfate. The sensitivity of the basic carbon skeleton of 14a to ring opening prevented reactive functionalization and attempts resulted in rearrangement to derivatives of 15. A representative example is the formation of 15b in quantitative yield upon treatment of 14a with thionyl chloride-pyridine. Similar rearrangements were encountered in attempts to prepare the corresponding tosylate or mesylate even under very mild reaction conditions. The lability of derivatives of 14a apparently results from strain relief upon ionization coupled with anchimeric assistance provided by the favorable disposed cyclopropane bond.[8]



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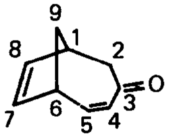
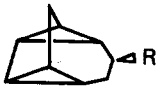


13a

b - 7,8-Dihydro



14a R = OH

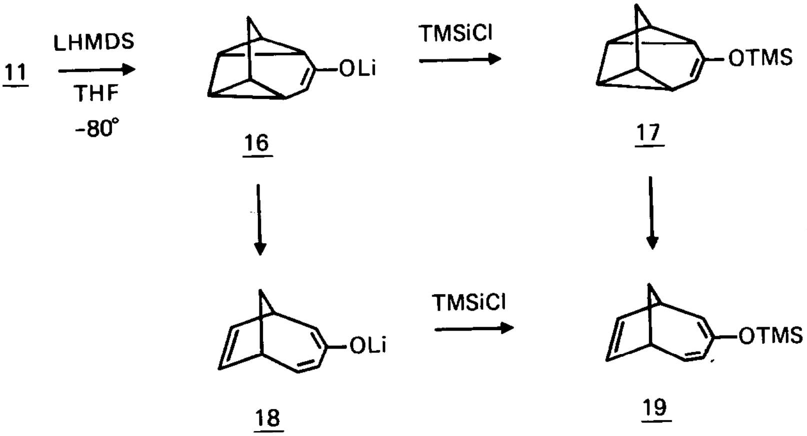
b = OAc

c = OMe

15a R = OH

b = Cl

In hopes circumventing unwanted skeletal rearrangements, the direct enolization of 11 was investigated as a route to oxygenated derivatives of 2. Initial experiments utilizing LDA (-40°) in an attempt to produce the corresponding enolate of 11 resulted in the isolation of the rearranged ketone 13a. The use of ND_4Cl-D_2O as the quenching reagent produced 13a which was 83%d_1. In an effort to determine whether 16 is actually produced upon enolization of 11 at low temperatures, a solution of 11 in THF-d_8 was reacted for 1 hr (-80°) with excess lithium hexamethyldisilamide (LHMDS) in the same solvent. The resulting homogeneous pale yellow solution was quenched at -80° with trimethylsilyl chloride and filtered rapidly (-80°) into an nmr tube. The resulting colorless solution showed a single proton resonance in the olefin region at τ 5.07 as a doublet (J=6Hz) due to coupling with an upfield cyclopropane hydrogen, as well as the high field absorptions characteristic of the tetracyclonane skeleton. This material was extremely unstable and rapidly rearranged ($t_{1/2}^{-52°}$ <8 min) to produce 3-trimethylsiloxybicyclo[4.2.1.]nona-2,4,7-triene 19 as the only detectable product: $^1H_{nmr}(CCl_4)\tau$ 3.9(d,d,J=11,7Hz,1H), 4.29(d,d,J=11,2Hz,1H), 4.55(d,J=7Hz,1H), 4.73(brs,2H), 6.95(m,2H), 7.95(m,1H), 8.47(d,J=11Hz,1H), and 9.78(s,9H); mass spectroscopic molecular weight 206. The same product 19 was produced by the direct enolization of 13a and subsequent quenching with trimethylsilyl chloride. On the basis of this data it seems likely that the unstable intermediate formed upon quenching the enolate of 11 with trimethylsilyl chloride is 17.



To eliminate the unlikely possibility that it is the unusual charge polarization of vinyl ethers (i.e., increased electron density β to the ether oxygen) which destabilizes 17 and not the basic carbon skeleton itself, the lithium enolate 16 was prepared at -80° and observed by nmr. The nmr spectrum of 16 prepared directly from the ketone 11 showed a single vinyl resonance at τ 5.34 which appeared as a broadened doublet (J=7Hz). The upfield shift of this proton relative to the comparable resonance in 17 is consistent with the predicted increased charge density at the β carbon atom. Quenching of 16 (-80°) with trimethylsilyl chloride produced 17 which rapidly rearranged to 19 upon warming. When the solution of 16 was allowed to stand at -52° it rearranged to the thermodynamically[10] more stable enolate 18 which ultimately produced 19 upon treatment with trimethylsilyl chloride. Consistently the same anion 18 could be generated directly from the unsaturated ketone 13. The half-life for the rearrangement of 16 to 18 was 23 minutes (-52°) indicating that increased anionic character at the β ring carbon of the tetracyclononane skeleton actually seems to stabilize it toward rearrangement. It therefore seems likely that 16 and 17 are reasonable models for 2 and that the hydrocarbon itself will be similarly unstable.

REFERENCES

1. (a) J. A. Berson, R. R. Boettcher and J. J. Vollmer, J. Am. Chem. Soc. 96, 1540 (1971); (b) R. C. DeSelms, J. Am. Chem. Soc. 96, 967 (1974); (c) For rearrangement of a related system see T. S. Cantrell and H. Schechter, J. Am. Chem. Soc. 89, 5868 (1967).
2. (a) K. Menke and H. Hopf, Angew. Chem. Int. Ed. 15, 165 (1976); (b) G. Kaupp and K. Rosch, Angew, Chem. Int. Ed. 15, (1976).
3. (a) R. D. Miller and D. L. Dolce, Tet. Lett., 1059 (1976); (b) H. D. Martin, S. Kagabu and H. J. Schiwek, Tet. Lett., 3311 (1975).
4. J. Meinwald, S. S. Labana and M. S. Chadha, J. Am. Chem. Soc. 85, 582 (1963).
5. Spectral data in accord with all structures were obtained. Complete data on any of the compounds described will be provided upon request.
6. C. W. Jefford, V. Burger and F. Delay, Helv. Chim. Acta. 56, 1083 (1973). We thank Professor Jefford for providing copies of pertinent spectral data for comparison.
7. Preliminary thermal stability studies on 14b,c indicate that the lability previously observed for 11 is not a result of a strain relieving concerted 1,5-sigmatropic rearrangement of the bis-homocyclohexadiene moiety unless the carbonyl in 11 is exerting a strong substituent effect. For example, neat 14c is stable for prolonged periods at 180° (17 hr) and under forcing conditions (350°, gas phase) produces only the triene _.
8. In this respect, the p-nitrobenzoate of 14a solvolyzed with a rate (k^{75°=3x10^{-4}sec^{-1}, 80% acetone-water) considerably faster than expected for a geometrically rigid monocyclopropyl carbinyl derivative.[9] The only product from this reaction was the exo alcohol 15a.
9. "Carbonium Ions," Vol. III, C. A. Olah and R. von R. Schleyer, Wiley-Interscience, New York, N.Y., 1972, p. 1295ff.
10. In addition to the obvious strain relief attending the ring openings, the possibility of anion stabilization via bis-homoconjugated interaction of the Π systems should be considered. Preliminary nmr comparisons of 18 with the corresponding anion derived from the dihydro model compound 13b where no homoconjugative interaction is possible indicates no significant interaction between the Π systems in 18.