Tetrahedron Letters,Vol.25,No.33,pp 3547-3550,1984 0040-4039/84 $3.00 + .00
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NOVEL INTERMEDIATES FOR THE SYNTHESIS OF CARBOCYCLIC SPIRO COMPOUNDS

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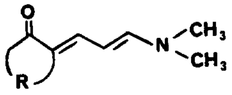
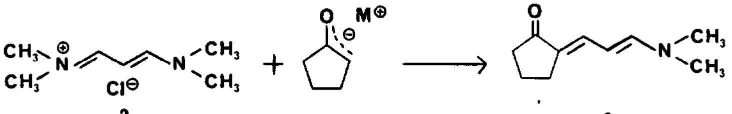
Abstract: Cyclic dienaminones, synthesized from the α-carbon elongation reaction of cyclic ketones with vinamidinium salts, are useful synthetic intermediates to carbocyclic spiro compounds.

The list of naturally occurring carbocyclic spiro compounds continues to grow, and as it does, the need for useful intermediates for their syntheses also grows.[1] This report will show that dienaminones of cyclic ketones 1 may act as synthetic precursors to highly-functionalized spiro compounds *via* thermal or photochemical [4+2] cycloadditions.



1

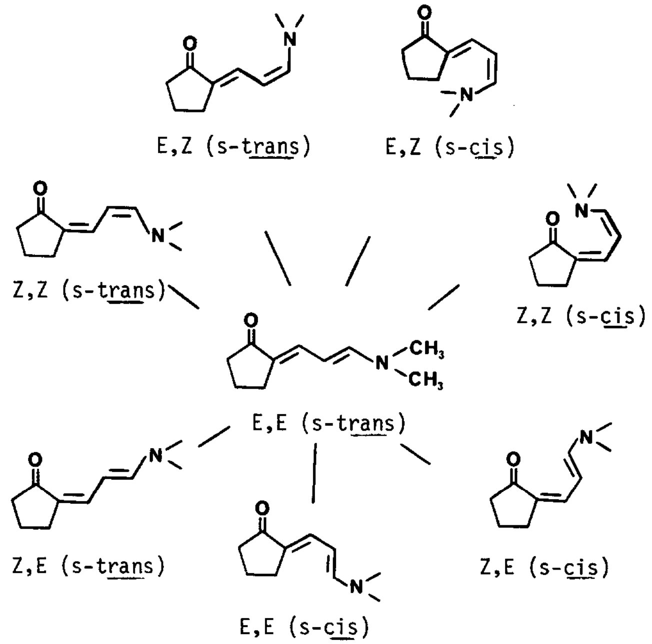
The dienaminones were synthesized by the reaction of 1,1,5,5-tetramethyl-1,5-diazapentadienium chloride 2 with a metal enolate. A wide variety of such dienaminones have been synthesized in our Laboratory.[3-5] An example is the reaction of the metal enolate of cyclopentanone with 2 which gave the dienaminone 3 in ~ 90% isolated yield. The conversion is stereospecific and the sole product is the E,E (s-trans) isomer 3 as evidenced by ^{1}H and ^{13}C NMR data. This was found to be true for all dienaminones formed from cyclic ketones.



2

3

Dienaminone 3 is a push-pull heterosubstituted diene.[6-8] In order for the diene moiety to participate as a 4π-component in Diels-Alder reactions, it is necessary for it to acquire a cisoid conformation. There are eight possible stereoisomers for the dienaminone from cyclopentanone, four of which are cisoid (Scheme 1). ^{1}H NMR evidence from the thermal interconversion of dienaminone 3 at 110°C in DMF-d_7 indicates the presence of another stereoisomer

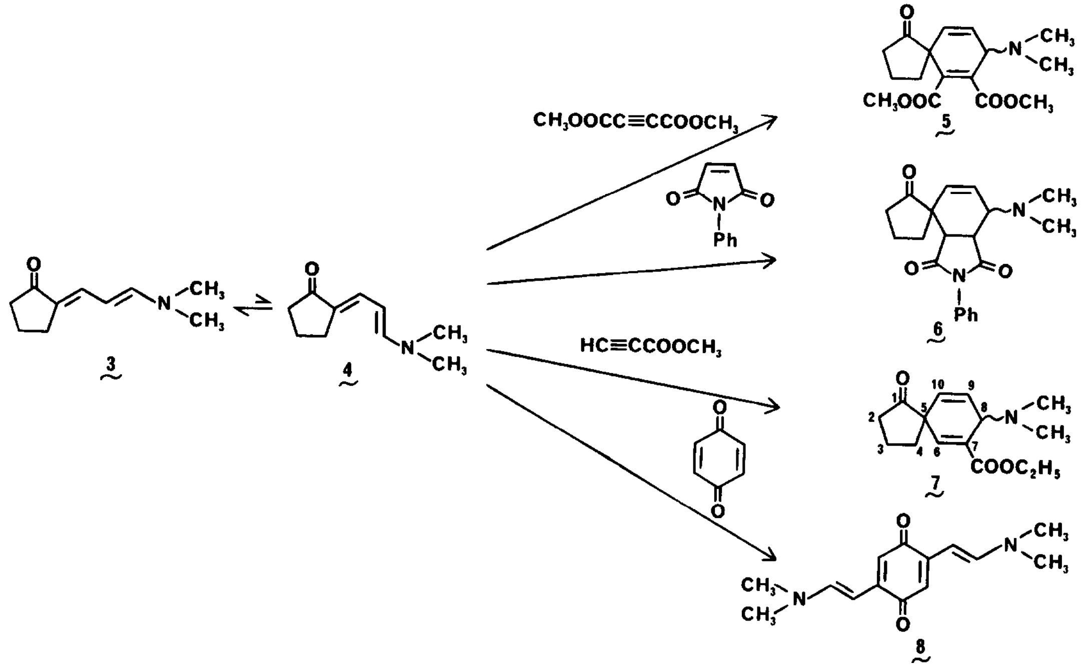


Scheme 1

exhibiting a *trans* coupling and a *cis* coupling for the three protons of the diene moiety.[9] This rules out two of the possible isomerization products, i.e. E,Z (s-*cis*) and Z,Z (s-*cis*). Of the two possibilities remaining [i.e. Z,E (s-*cis*) and E,E (s-*cis*)], differentiation can be made on the basis of the chemical shift of the proton γ to the nitrogen. This proton in the E,E (s-*cis*) isomer is deshielded by the carbonyl group and, based on related simpler systems,[10,11] is expected to show resonance at ~ δ 7.0 ppm. The same proton in the Z,E (s-*cis*) isomer is expected to occur at ~ δ 5.8.[10,11] Observation of a doublet at δ 7.0 (J = 2.4 Hz) for this proton suggested the presence of the E,E (s-*cis*) isomer. The equilibrium favors largely the E,E, (s-*trans*) isomer although an exact ratio could not be calculated from the ^{1}H NMR spectrum due to the presence of overlapping peaks. This isomerization can also be induced photochemically.

When the dienaminone **3** in toluene was treated with dimethylacetylene dicarboxylate under thermal[12] or photochemical conditions,[13] a 90% conversion to the spiro[4,5]deca-6,9-dien-1-one **5**, m.p. 52-53°C, occurred (Scheme 2). The structure of **5** was established by its mass spectrum (307, M$^+$), its UV spectrum in ethanol [λ_{max} 412 nm (ε 2870), 283 nm (ε 33650)], and its high-field ^{1}H and ^{13}C NMR data including delayed-decoupling experiments. Similarly, formation of the spiro compound **6**, m.p. 261-262°C, from the cycloaddition of dienaminone **3** with N-phenylmaleimide was also realized.

The presence of an electron-donating dimethylamino group at one terminus of the dienaminone and an electron-attracting carbonyl group at the other should confer orientational selectivity in its reactions with electron-poor dienophiles. This regiochemistry was established by examination of the thermal cycloaddition with ethyl propiolate. The direction of addition was determined by examination of the coupled and homonuclear decoupled 360 MHz ^1H NMR spectra in $CDCl_3$ of the adduct 7 (25% yield).[14] The NMR data showed H_9 as a doublet of doublets at δ 7.36 ($J_{9,8}$ = 7.7, $J_{9,10}$ = 14.5 Hz), H_8 as a doublet of triplets at δ 7.39 ($J_{8,9}$ = 7.7, $J_{8,10}$ = 2.1, $J_{8,6}$ = 2.1 Hz), and H_6 and H_{10} as an overlapping multiplet. Irradiation of H_8 and H_9 reduced the latter multiplet to a singlet at δ 7.89. The regiospecificity observed in the formation of the spiroadduct 7 is consistent with the polarization in the dienaminone discerned from its ^{13}C NMR data.



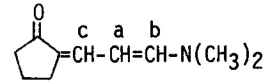
Scheme 2

When the dienaminone (3) was treated with p-benzoquinone under reflux in toluene for 12 h, a red crystalline product 8, m.p. 98-100°C, (25% yield) was isolated after preparative layer chromatography and recrystallization from hexane. A plausible mechanism for the formation of this "2:1" adduct involves two sequential nucleophilic attacks of dienaminone on benzoquinone followed in each case by elimination of α-methylenecyclopentanone. The para substitution pattern of the two vinyl dialkylamino moieties in 7 could be deduced unambiguously from the high-field ^{13}C NMR data.

Finally, as dienaminones may be formed from a great many cyclic ketones, the methodology discussed in this paper may be applicable for the synthesis of a variety of carbocyclic spiro compounds.

Acknowledgments. Support of these investigations by a grant (CHE-8200818) from the National Science Foundation is gratefully acknowledged. The high-field NMR spectrometer (Bruker WM-360) used in this work was purchased in part from funds (CHE-8201836) provided by the National Science Foundation.

References and Notes

1. Krapcho, A.P. *Synthesis* **1978**, 77, and references therein.
2. Desimoni, G.; Tacconi, G.; Barco, A.; Pollini, G.P. "Natural Products Synthesis Through Pericyclic Reactions"; American Chemical Society, Washington, D.C., 1983; Chapter 5.
3. Nair, V.; Cooper, C.S. *Tetrahedron Lett.* **1980**, 3155
4. Nair, V.; Cooper, C.S. *J. Org. Chem.* **1981**, *46*, 4759.
5. Nair, V.; Jahnke, T.S. *Synthesis*, **1984**, In Press.
6. Petrzilka, M.; Grayson, J.I. *Synthesis* **1981**, 753.
7. Gillard, M.; T'Kint, C.; Sonveaux, E.; Ghosez, L. *J. Am. Chem. Soc.* **1979**, *101*, 5837.
8. Danishefsky, S. *Acc. Chem. Res.* **1981**, *14*, 400.
9. 

^1H NMR (DMF-d_7) for new isomer: 5.01 (d,d, J = 12.1, 2.4 Hz, H_a); 6.93 (d, J = 12.1 Hz, H_b); 7.00 (d, J = 2.4 Hz, H_c).
10. Paquette, L.A.; Eizember, R.F. *J. Am. Chem. Soc.* **1967**, *89*, 6205.
11. Crandall, J.K.; Arrington, J.P.; Hen, J. *J. Am. Chem. Soc.* **1967**, *89*, 6208.
12. The dienaminone (2 mmol) and dienophile (20 mmol) in dry toluene (5 mL) were heated to 110°C under N_2 for 28 h. The reaction mixture was taken to dryness under reduced pressure, and the residue was chromatographed on silica gel plates (ethyl acetate).
13. The photochemical cycloaddition was carried out as described in (12) but in a Rayonet photochemical reactor fitted with 3500 Å lamps for 12 h.
14. This isolated yield is probably much lower than the actual yield in this reaction because of considerable decomposition of the product **7** during chromatographic separation.

(Received in USA 22 May 1984)