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# STEREOSPECIFICITY OF DIENOPHILE ADDITION TO CYCLOHEPTATRIENES

M. J. Goldstein, A. H. Gevirtz
Department of Chemistry
Cornell University
Ithaca, New York 14850

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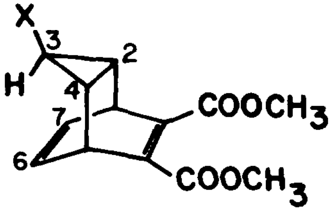
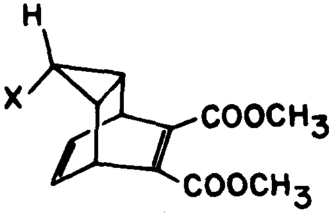
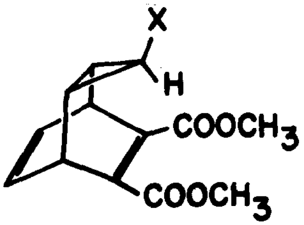
Mono-7-substituted-1,3,5-cycloheptatrienes permit two opportunities for stereospecificity beyond those traditionally envisaged for Diels-Alder addition.(1).



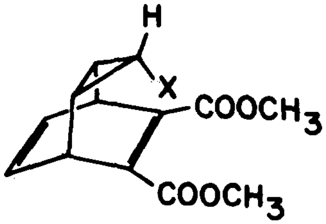
anti-3-exo



anti-3-endo



syn-3-exo



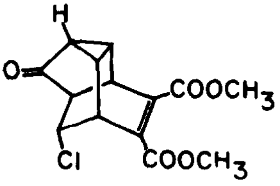
syn-3-endo

The first, a choice of cyclopropane orientation, has prematurely been accepted as the *anti* (2) by virtue only of scattered qualitative estimates of reactivity (3,4). The second, a choice between C-3 epimers, has not hitherto been considered.

We now demonstrate the isolated product of dimethyl acetylenedicarboxylate addition to be that of *anti* configuration when X = H (26%, m.p. 24-25.5°), (5,6,7) that of *anti*-3-*exo* when X = $CH(OCH_3)_2$ (57%, $\underline{n}^{19}D$ 1.5031) or $COOCH_3$ (88%, m.p. 48-50°)(5,8) but, more significantly, to contain both *anti*-3-*exo* and *anti*-3-*endo* isomers when X = CN (9,9a).

In particular, 7-cyano-1,3,5-cycloheptatriene yields 70% of a kinetically controlled 1.1 : 1 mixture of isomers, m.p. 111-113° and 92-94°. Alkaline hydrolysis of either in $D_2O$ affords a common tricarboxylic acid containing deuterium only at C-3. The extent of incorporation, 0.15±0.04 and >0.85 atoms D from higher- and lower-melting adducts under identical conditions implicates the latter as the less stable, therefore, the 3-*endo*, epimer. As expected (10) this also possesses the greater vicinal cyclopropane coupling constants ($J_{2,3} = J_{3,4} = 6.6$ *vs*. 3.1 c.p.s.)(10a).

Its structure is further elaborated as *anti*-3-*endo* from that of its unique product of methanolic HCl treatment, a chloroketone diester (m.p. 143-143.5°), whose spectral properties ($\lambda_{\text{shoulder}}^{CH_3CN}$ 215mμ (ε 7170), $\lambda\lambda_{\text{max}}^{CH_2Cl_2}$ 5.73, 5.80, 6.06μ, $\tau^{CDCl_3}$ 5.69-6.40 and 7.35-8.00 p.p.m. (complex multiplets of relative areas 8.7:4, the former revealing singlets at 6.13 and 6.15 p.p.m.)) are most simply accommodated by the structure I (11).



I

Inpependent support is provided by the consistent variation of proton chemical shift with distance from the deshielding (12) nitrile function. (Table I).

The structures of the remaining adducts then follow both from interconversions with the *anti*-3-*exo* nitrile (Chart I) and from obvious spectral similarities.

TABLE I.

Proton Chemical Shifts ($\tau^{CDCl_3}$, p.p.m.)

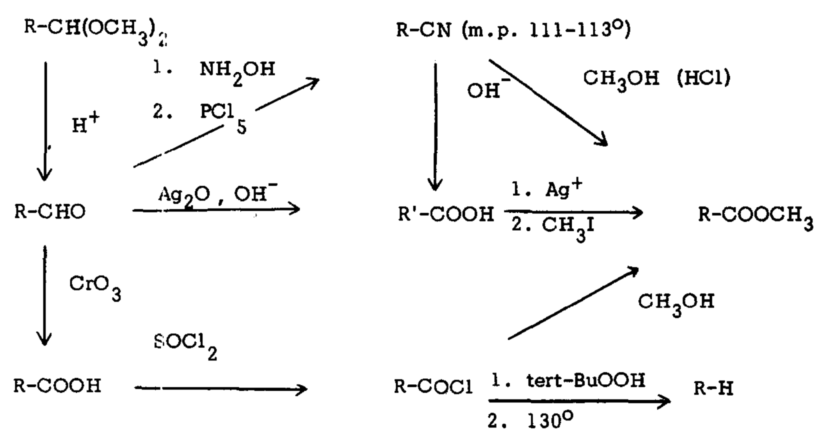
of Dimethyl Acetylenedicarboxylate Adducts

| C-3 Substituents | $H_{6(7)}$ | $H_{2(4)}$ |
|---|---|---|
| H,H | 4.07 | 8.60 |
| H, *exo*-CN | 3.83 | 7.90 |
| H, *endo*-CN | 3.60 | 8.03 |
| CN, CN[a] | 3.50 | 7.22 |

[a] From a spectrum kindly furnished by Dr. E. Ciganek. *Cf.* reference 14.

CHART I.

Interconversions within the anti-3-exo Series.[a]



[a] R = dimethyl 3-tricyclo[3.2.2.$0^{2,4}$]6,8-nonadienyl-6,7-dicarboxylate. R' = 3-tricyclo[3.2.2.$0^{2,4}$]6,8-nonadienyl-6,7dicarboxylic acid.

The apparent absence of syn isomers has now long been both expected and well rationalized within the context of an obligatory norcaradiene intermediate (2,3b). The isolation of the severely hindered anti-3-endo nitrile adduct, and in amount similar to that of its more stable epimer, is more surprising. Several interpretations are possible but we would defer consideration of their relative merit until another time.

We think it nevertheless useful to note the current status of one alternative to the norcaradiene hypothesis, the possibility of 2,5-addition to 1,3,5-cycloheptatriene (13). Originally discounted, in part, because only 1,3-dienes were considered capable of adding dienophiles (15) and, in part, because the norcaradiene hypothesis permitted obvious correlation of the unusual reactivity of 7-carbomethoxy-1,3,5-cycloheptatriene (13) with its (incorrectly) (16) assigned structure, this alternative is now free of both objections and has yet to be excluded.

In any event, the necessary stereochemical consequences to be satisfied by a correct mechanism have now been established.

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4. The corresponding anti configuration of cyclooctatetraene and cyclooctatriene adducts is unambiguously established. R. C. Cookson, J. Hudec, and J. Marsden, Chem. Ind. (London), **21**, (1961); M. Avram, G. Mateescu, and C. Nenitzescu, Ann. Chem., **636**, 174 (1960).
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6. The structure of a second isomeric product is described separately. M. J. Goldstein and A. H. Gevirtz, Tetrahedron Letters, 4413 (1965).
7. Lit. (3b) b.p. 95-100°/0.02 mm.
8. Lit. (3b,19) m.p. 74-75°, 76°. An infrared spectrum kindly furnished by Professor Doering, proved to be quite indistinguishable from that of the material at hand.
9. All adducts were prepared in refluxing toluene. Elemental analyses of isolated compounds agreed with expectation to within ± 0.3%.

9a. We have since learned that the two isomers have been independently isolated by D. W. Wiley, Central Research Dept., E. I. du Pont de Nemours and Company.

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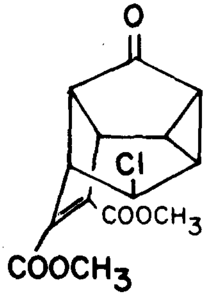
10a. We are grateful to R. G. Pitcher, Spectroscopy Applications Laboratory, Varian Associates, who kindly provided the 3-*endo* adduct spin-decoupled n.m.r. spectra.

11. Spectrally consistent Wagner-Meerwein-related alternatives (*e.g.* Ia) are rendered less plausible by sodium-methoxide (dimethyl sulfoxide) transformation of the chloroketone diester to the *anti*-3-*exo* triester RCOOCH$_3$ of Chart I.



Ia

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