

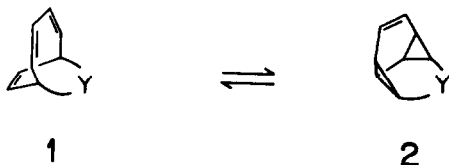
SYNTHESIS OF BICYCLO[4.3.2]UNDECA-2,4,8,10-TETRAEN-7-ONE.
 II. THERMODYNAMIC AND KINETIC CONTROL OF INTRAMOLECULAR CYCLOADDITION

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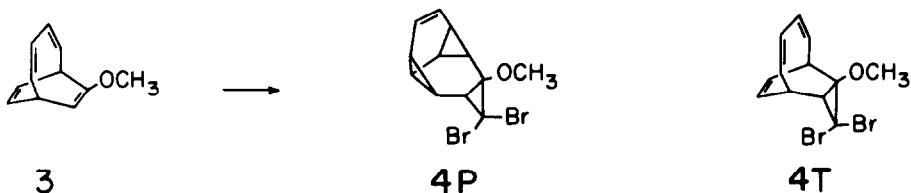
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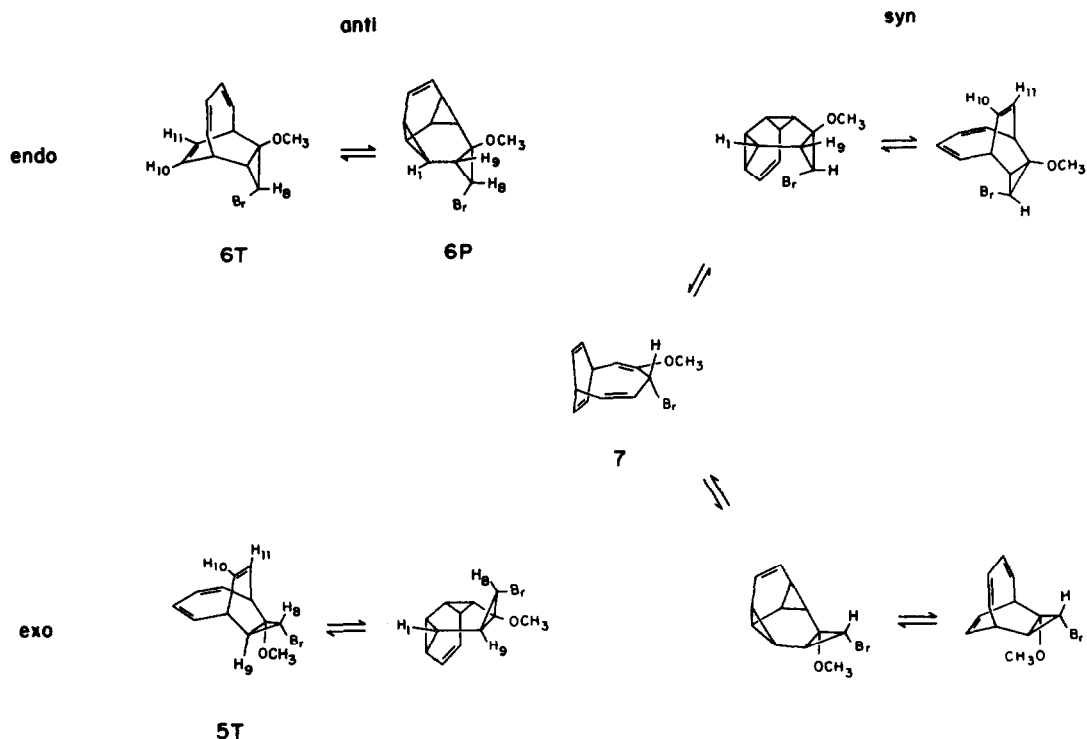
Whenever the two components of a Diels-Alder reaction are joined in a bis-homoconjugative way (1), the cyclopropane strain of the adduct (2, ca. 55 kcal/mol)¹ is expected to overwhelm the otherwise exothermic cycloaddition (e.g., 33 kcal/mole)²; entropy invariably favors dissociation. As a result, such tetracyclic isomers (2) have most often appeared as transient intermediates (Y=R₂C=^{3a}, R₂C=C=^{3b}, HC=^{3c}, O=C=^{3d}, O₂S=^{3e}, -CH=CH-⁴ and its variously substituted derivatives⁵). A few have even been characterized at appropriately low temperatures.^{4b,5}



We were therefore surprised to discover that conventional dibromocyclopropanation of 3⁶ provided the pentacyclic isomer 4P rather than the tricyclic 4T. The expected^{4,5} absence of an appreciable barrier between the two — hence, the unexpected conclusion that 4P is thermodynamically the more stable, was suggested by the behavior of the two epimeric monobromides, both obtained by *n*-Bu₃SnH reduction at 25°.



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Like their precursor, these possess opportunities both for cycloadditive isomerism and for geometric isomerism — syn or anti to the diene bridge of the tricyclics (hence, to the olefin bridge of the pentacyclics). The exo-monobromide (mp 61°, 49%, $\tau_{H8} = 7.02$ ppm⁷, d, $J_{8,9} = 3.8$ Hz) proved to be exclusively tricyclic (5T). The pmr spectrum of the chromatographically homogeneous endo-isomer (mp 46–48°, 42%) revealed a 71:29 mixture* of pentacyclic 6P ($J_{8,9} = 8.5$ Hz) and tricyclic 6T ($\tau_{H8} = 7.20$ ppm⁷, $J_{8,9} = 8.5$ Hz). The uniformly anti-orientation of the cyclopropane ring, an expected consequence of cyclopropanation from the less hindered side⁸ of the methoxyvinyl bridge of 3, was confirmed by the magnitudes of the pentacyclic $J_{1,9}$ (both < 3 Hz), by the high field⁹ tricyclic $\tau_{H10,11}$ (4.41 in 5T, 4.20 in 6T), and by the inconsistency of syn assignments with

(*) Pmr regions (τ), calcd. and obsd. normalized areas: 4.00, 2.58, 2.71 ± 0.18; 4.20, 0.59, 0.58 ± 0.10; 6.38–7.14, 4.29, 4.22 ± 0.16; 7.20, 0.29, 0.37 ± 0.01; 8.08–8.02, 4.53, 4.34 ± 0.12; 8.88, 0.71, 0.77 ± 0.09.

Eu(fod)₃ shifting slopes.*

Such stabilization of a small ring by bromine recalls its analogous effect on the cyclo-octatriene \rightleftharpoons bicyclo[4.2.0]octadiene equilibrium¹⁰. Yet the latter two hydrocarbons differ by only 1.5 kcal/mol. We therefore find it difficult to believe that so subtle an effect could overwhelm the previously estimated enthalpy difference of 22 kcal/mol between P and T isomers. Although part of this discrepancy might be attributed to unanticipated strain in the tricyclic isomer, we think it also possible that the appropriate juxtaposition of three cyclopropane rings — one that corresponds to the trans-trishomobenzenes¹¹ — provides an unexpected stabilizing influence.

Thermodynamic control of the intramolecular Diels-Alder reaction clearly does not extend to the intramolecular homo-Diels-Alder. (Otherwise, the bicyclic isomer (7) should have equilibrated exo and endo epimers; syn isomers should also have been observed.) It is the stereospecificity of the latter reaction which maintains this degree of kinetic control. Whether observed in dienophile addition to cycloheptatrienes¹², in cheletropic loss of CO^{13a}, of SO₂^{13b} and of N₂^{13c}, or in the facile ring opening of cis-trishomobenzenes¹¹, the universally observed stereoselectivity would permit facile equilibration of 7 with its syn isomers but not with its anti.

The importance of the third cyclopropane ring in stabilizing 4P and 6P is further indicated by the silver perchlorate cleavage product of 6 — the originally anticipated bicyclo[4.3.2]undeca-2,4,8,10-tetraen-7-one (1, Y = CH=CH-CO-, mp 26°, 14% overall yield from bicyclo[4.2.1]nona-2,4,7-trien-9-one⁶; ir (CCl₄) 3020, 2920, 1675, 1186, 1039 and 912 cm⁻¹; uv max (isooctane) and ϵ 258 (2500), 267 (2460), 335 (113), 347 (139) and 358 (111) nm; τ (CCl₄) 3.35-3.45 (m, 7.11), 4.75 (t, $J=10.0$ Hz, 0.95), 6.08 (t, $J=9.0$ Hz, 1.02), 6.40 (q, $J=8.0$ Hz, 0.91). The completely analyzed, Pr(fod)₃-shifted, and spin-decoupled pmr spectrum of its (i-Bu)₂AlH-derived alcohol (mp 116°) reveals it also to be bicyclic - homogeneous, and with the alcohol function syn to the diene bridge. Elemental analyses of all compounds agreed with expectation to within $\pm 0.3\%$.

(*). Closely similar stereochemistry is observed in the absence of a methoxyl function. We are most grateful to Prof. G. Schröder for informing us of these results prior to publication.

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