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Stereoselectivity in the Kinetically Controlled Cycloadditions of N-tosyl-trihalomethyl-imines with Cyclopenta- and Cyclohexa-1,3-dienes

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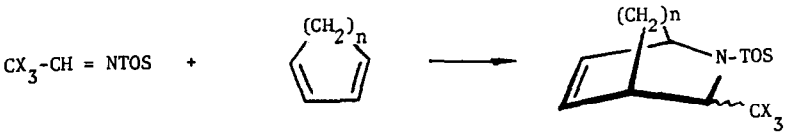
One of the synthetically useful aspects of the Diels-Alder reaction is an often remarkable stereospecificity.[1] Although numerous studies have been concerned with the stereochemical outcome of carbocyclic syntheses, little is known about the stereochemical course of hetero-dienophilic additions to dienes.[2] We here report our results for the reactions of trihalomethyl-N-tosylimines with cyclopenta- and cyclohexa-1,3-diene.

N-p-toluenesulfonyltrifluoromethylimine[3] $\underset{\sim}{1}$ and cyclopentadiene reacted immediately in benzene-d_6, as monitored by F^{19}-nmr, to quantitatively afford $\underset{\sim}{3}$. The stereochemical result of the reaction as determined from the relative areas for the protons adjacent to trifluoromethyl (Table I) was preferential formation of the exo-CF_3 adduct (57% exo). Crystallization of the mixture $\underset{\sim}{3}$ from 95:5 heptane/ethanol afforded crystalline solid (crop 1) mp 124-125°, found to be enriched in the endo-CF_3 isomer (68% endo) and a second solid (crop 2) mp 77-79°, enriched in the exo-CF_3 isomer (75% exo). The original 57% exo rich mixture after one week at ambient temperature became further enriched in the exo-CF_3 isomer (71% exo). Careful monitoring of this change by integration of the F^{19} resonances indicated that preferential decomposition of the endo-CF_3 isomer to several new unidentified species having complex fluorine resonance patterns was occurring. Continued heating of $\underset{\sim}{3}$ in d_6-benzene for three days resulted in virtually complete elimination of the endo isomer (1-2%), retention of a portion of the exo isomer (21%) and formation of other fluorine containing species (77-78%).

Similarly, reaction of trichloromethylimine[3] $\underset{\sim}{2}$ with cyclopentadiene afforded after two hours at 30° adduct $\underset{\sim}{4}$, shown by nmr integration (Table I) of the protons adjacent to CCl_3 to be enriched in the endo-CCl_3 isomer (78% endo). Crystallization from 95:5 heptane/ethanol afforded crystals, mp 118-119°, of the endo-CCl_3 isomer only. When the original reaction mixture was heated to 80° in benzene-d_6 for 17 hrs, the ratio of isomers $\underset{\sim}{4}$ changed in favor

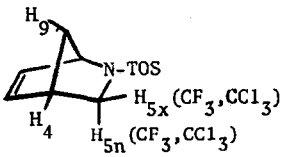


1. X = F
2. X = Cl

3. X = F n=1
4. X = F n=2
5. X = Cl n=1

Table I

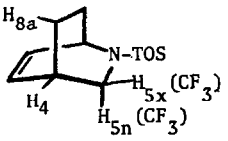
Major features of the 100 MHz proton nmr spectrum of 3 and 4 (benzene-d_6)



Adduct	Proton	endo-trifluoromethyl Shift (δ)	Description	Proton	exo-trifluoromethyl Shift (δ)	Description
3	H_{5x}	4.05	qd($J_{4,5x}$=3.25 Hz $J_{F,5x}$=6.6 Hz)	H_{5n}	3.56	$J_{5n,9}$ < 0.5 Hz; $J_{F,5n}$ = 7.3 Hz; $J_{4,5n}$ = 0 Hz
4	H_{5x}	4.78	d($J_{4,5x}$=3.8 Hz)	H_{5n}	4.18	s

Table II

Major features of the 100 MHz proton nmr spectrum of 5 (acetone-d_6)



Proton	endo-trifluoromethyl Shift (δ)	Description	Proton	exo-trifluoromethyl Shift (δ)	Description
H_{5x}	4.38	$J_{5x,F}$ = 6.5 Hz; $J_{4,5x}$ = 2.5 Hz	H_{5n}	3.86	$J_{5n,F}$ = 6.95 Hz; $J_{5n,4}$ = 3.0 Hz; $J_{5n,8a}$ = 1.3 Hz

of the exo-CCl_3 isomer (90% exo). On the basis of material balance as determined by nmr integration some of the exo-CCl_3 adduct must have been formed by isomerization of the endo adduct. This likely occurred via a cleavage-recombination process, since extended reflux in benzene for three days resulted in decomposition of 4 with formation of major amounts of imine 2 and cyclopentadiene dimer.

Cyclohexa-1,3-diene and imine 1 in benzene-d_6 quantitatively reacted after two hours at reflux temperature to form 5, which by nmr integration of the protons adjacent to CF_3 (Table II) indicated a preference for the endo-CF_3 isomer (56% endo). Crystallization from 80:20 heptane/ethanol afforded a white solid, mp 95-97°, of an equimolar exo-endo-CF_3 mixture of 5. Reflux in benzene for eight days resulted in a slight change in the isomer ratio to 52% endo-CF_3. Careful monitoring of the fluorine resonances indicated that this change was the result of preferential decomposition of the exo-CF_3 isomer.

Variable temperature nmr observation of imines 1 and 2 from +40 to -60° indicated no line broadening of imine proton resonances. On the basis of literature precedent on imine barriers[5] a low barrier to configurational inversion is likely rather than a single imine configuration.

A possible explanation for the observed kinetic stereochemical preferences (Table III) in the formation of bicyclic adducts involves cycloaddition of the diene with an E-imine

Table III

Stereochemical Results of Trihalomethylimine Additions

Diene	Imine	Kinetic Preference	Thermodynamic Stability[a]
	1	exo (57%)	exo
"	2	endo (78%)	exo
	1	endo (56%)	endo

[a]One of the isomers preferentially decomposes thermally. Equilibrium positions were not determined.

in which trifluoromethyl and tosyl compete in the transition state for the endo position.[6] However, the present data do not allow definitive statements to be made concerning the role of Z-imines, or the orienting ability of the nitrogen lone-pair.[2d] Of special interest is the change in stereopreference of the CF_3 group from exo to endo in the reactions of 1 with cyclopentadiene and cyclohexa-1,3-diene (Table III). The paucity of data on additions of trans-olefins with cyclohexa-1,3-diene precludes present evaluation of this result.

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6. See Ref. 1a, p.551, Table 8.