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THE DIENOPHILIC REACTIVITY OF 7-SUBSTITUTED NORBORNADIENES. KINETIC ACTIVATION OF ENDO,SYN-CYCLOADDITION BY OXYGEN SUBSTITUENTS

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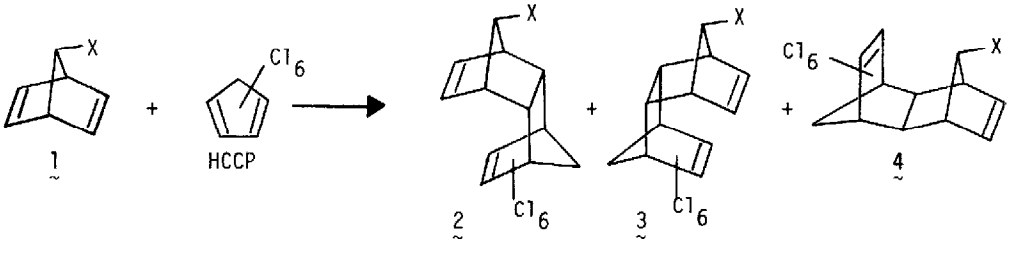
When employed as dienophiles norbornene and its anti-7-substituted derivatives react exclusively by exo-cycloaddition. Similar stereospecificity might have been anticipated for norbornadiene (1a) and its 7-substituted derivatives (1b-e); however, as recently reported by two groups of workers,[1,2] surprisingly significant amounts of cycloaddition occur from the endo-face of both the syn- and anti-double bonds. In fact, if an oxygen containing substituent is located at the bridge position, e.g. 1b-1d, endo-adduction out weighs exo-adduction by a factor of 2.5-3.0:1.0 (see Table I).



1 + HCCP → 2 + 3 + 4

a, X=H; b, X=OAc; c, X=OCOPh; d, X=Ot-Bu; e, X=Me

Our interest in these cycloadditions stems from an earlier independent examination of the products from the reaction of HCCP with 7-norbornadienyl benzoate (1c).[3] We were particularly intrigued by the fact that endo,syn-adduction occurred to at least as great, if not greater, extent than endo,anti-adduction despite an increase in non-bonded interactions between the 7-substituent (benzoyloxy) and the C-4a, C-8a hydrogens in the transition state for formation of adduct 2c. Subsequent n.m.r. or glpc determination of the product ratios 2:3:4 for the reaction of HCCP with 1c,[3] 7-t-butoxynorbornadiene (1d)[1,3] and 7-norbornadienyl acetate (1b)[2]

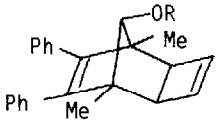
TABLE I - PRODUCT DISTRIBUTION IN THE REACTION OF HCCP WITH SOME 7-SUBSTITUTED NORBORNADIENES

Norbornadiene	Rel. %[a]			
	2	3	4	Ref.
1a		5.6(4)	94.4(96)	b(2)
1b	47	28	25	2
1c	40.3	35.4	24.4	b
1d	57.7(61)	27.4(23)	14.9(16)	b(1)
1e	4(?)[c]	9	87	2

a) The values in parentheses are those from the similarly indicated literature citation; b) This work; see footnote 3b; c) Not identified.

(see Table I) clearly established the strong preference for endo,syn-addition in these 7-oxy derivatives. By contrast 7-methynorbornadiene (1e) was found[2] to react "normally" with HCCP to afford primarily (87%) the exo-adduct 4e followed by the endo,anti-adduct 3e (9%).

If the product distribution from 7-methylnorbornadiene is taken to reflect the stereoselectivity of HCCP addition to 7-substituted norbornadienes on purely steric grounds, then the enhanced endo mode of addition to the 7-oxynorbornadienes 1b, 1c and 1d, especially syn to the oxygen substituent, would appear to require an alternative explanation based on electronic considerations. One such explanation, offered as early as 1967 to explain the preference for endo, syn-attack by phenyl azide on 1d,[4] is that the proximity of the electron rich oxygen atom activates the syn-double bond towards electrophilic addition by essentially a through-space interaction. While there has been no kinetic data to support this contention in the norbornadiene series Warrener and Paddon-Row have reported kinetic data for the related lone-pair activation of cycloaddition reactions of the exo-tricyclo [4.2.1.$0^{2,5}$]nona-3,6-dien-9-ol derivatives 5-OH and 5-OMe.[5] The latter of these authors has also provided a theoretical interpretation of their observations.[6]



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We now wish to report the first kinetic evidence for cycloadductive activation of the syn-double bond of 7-oxy substituted norbornadienes. Employing a 20:1 molar ratio of HCCP to diene we have determined the pseudo first rate constants at 120.0° ± 0.1° for the disappearance of norbornadiene (1a) and 7-t-butoxynorbornadiene (1d).[7] These rate constants are, for 1a,

TABLE II - PARTIAL RATE FACTORS FOR ADDITION OF HCCP TO NORBORNADIENES 1a, 1c and 1d at 120°

Norbornadiene	Cycloaddition Site[a]			
	endo-syn	endo-anti	exo-anti	exo-syn
1a	1.0		16.9(24)	
1d	1.65(2.3)	0.78(1.1)	0.42(0.59)	0.0
1c	0.32(0.45)	0.28(0.39)	0.20(0.28)	0.0

a) The partial rate factors in parentheses are those calculated using the product distribution (aldrin/isodrin) for norbornadiene (1a) cited in Ref. 2.

$3.98\pm0.05 \times 10^{-4}$ sec^{-1}, for 1d, $3.17\pm0.10 \times 10^{-5}$ sec^{-1}, and represent the total rate of cycloaddition to HCCP in the endo and exo mode. As perhaps expected on the basis of the strong inductive effect of the 7-OtBu substituent, 1d is ca. a factor of 10 less reactive than 1a. Combination of the product data in Table I with the above kinetic data permits calculation of the partial rate factors for exo and endo (syn or anti) cycloaddition of HCCP to 1a and 1d, the endo addition rate per double bond of norbornadiene (1a) serving as standard (see Table II). The partial rate factors for the related cycloadditions of HCCP to benzoate 1c at 120° are similarly obtained from the psuedo first order rate constant, $k_{\psi}=8.8\pm0.5 \times 10^{-6}$ sec^{-1}, and the product distributions in Table I.

The 40 fold decrease in the partial rate factor for exo-anti-adduction of 1d is strikingly consistent with a similarly determined (HCCP, 120°) relative rate factor of ca. 40 for norbornene/anti-7-norbornenyl acetate.[8] In light of the observed product ratio for the 7-methyl derivative 1e with HCCP (Table 1) one is led to the conclusion that the rate-retarding effect on exo-anti adduction by the 7-OtBu in 1d is largely inductive in origin. Since, in the absence of other factors, the endo adduction modes for 1d should experience a similar rate retarding inductive effect the endo-syn and endo-anti pathways are actually accelerated by factors of ca. 65-90 and 30-45, respectively. Furthermore, the apparent endo-syn acceleration is at best a minimum estimate since the unfavorable steric factors for this pathway, compared to endo-anti cycloaddition, have yet to be properly assessed.

Comparison of the partial rate factors for 1d with those for benzoate 1c reveals relative rate decrease factors of 2, 3, and 5 for exo-anti, endo-anti, and endo-syn cycloaddition to 1c, respectively. Since of the three possible cycloaddition modes endo-syn should be the most sensitive to net electron density on the oxygen bound to C-7, these relative rate differences

are in good accord, qualitatively, with the expected electronic effect of replacing a t-butyl group by a benzoyl group. For both 1c and 1d the intermediate reactivity of the anti-double bond in the endo-mode is presumably a result of favorable secondary orbital interactions in the transition state for [4+2] cycloaddition.

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References and Footnotes

1. K. B. Astin and K. Mackenzie, JCS Perkin II, 1004 (1975).

2. L. T. Byrne, A. R. Rye and D. Wege, Aust. J. Chem., 27, 1961 (1974).

3. (a) See footnote to first paragraph in Ref. 1; (b) Product ratios in this work (Table I) were obtained by detailed nmr analysis of the kinetic solutions at 120° (vide infra) and represent average values for several independent runs. These ratios (2:3:4) appear to be essentially invariant in the 40-80% reaction range, although in the case of 1a and 1c appreciable diadduct formation is noted after 3-4 halflives.

4. G. W. Klumpp, A. H. Veefkind, W. L. DeGraaf, and F. Bickelhaupt, Ann., 706, 47 (1967); cf. B. Halton and A. D. Woolhouse, Aust. J. Chem., 26, 619 (1973) and M. Franck-Neuman and M. Sadrati, Angew. Chem. Internat. Edn., 13, 606 (1974).

5. M. N. Paddon-Row and R. N. Warrener, Tetrahedron Lett., 1405 (1972); cf. I. W. McCay, M. N. Paddon-Row, and R. N. Warrener, ibid., 1401 (1972).

6. M. N. Paddon-Row, ibid., 1409 (1972).

7. Accurately determined (by wt.) binary solutions of HCCP and 1a, 1d, or 1c were sealed in nmr tubes and heated at 120.0° ± 0.1° for varying time integrals. Integration of the vinyl proton region allowed calculation of the mole fraction of starting dienophile to product olefins as a function of time. Good first order plots were obtained up to at least 3 halflives. The integral ratios for the remainder of the proton signals indicated negligible decomposition or polymerization of the dienophile within the stated error limits.

8. Norbornene (HCCP, 120°), $k_{\psi} = 2.6 \times 10^{-4}$ sec^{-1}; anti-7-norbornenyl acetate(HCCP, 130°), $k_{\psi} = 1.3 \times 10^{-5}$ sec^{-1}.