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STUDIES ON THE EFFECT OF REMOTE SUBSTITUENTS ON STEREOREACTIVITY. III. INFLUENCE OF DIRECT ELECTRONIC ACTIVATION OF THE DIPOLAROPHILIC DOUBLE-BOND ON THE COURSE OF DIAZOALKANES CYCLOADDITION TO 7 - HALONORBORNADIENES.

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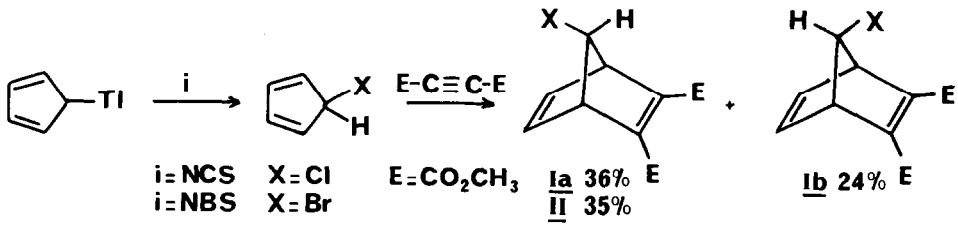
The remarkable endo-anti stereospecificity of diazoalkane cycloadditions to 7-halogenated norbornadienes remains almost unaltered when the reactivity of the anti double bond is strongly enhanced by carbomethoxy substituents.

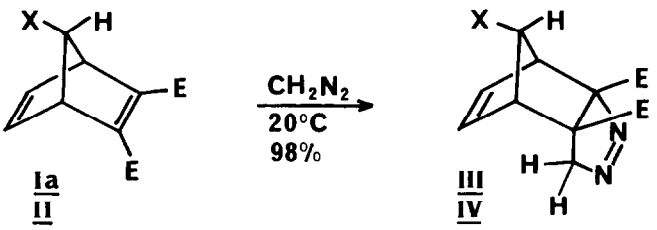
In the preceeding publication (1), the role of the halogen in the seven position and the influence of steric factors on the stereochemistry of the addition of diazoalkanes to 7-halonorbornadienes were highlighted. In relation to WILT's statement on the importance of frontier orbital energy levels (2), we have now investigated the cycloaddition reactions of diazoalkanes with similarly substituted norbornadienes, whose reacting double-bond is however strongly activated by electron withdrawing groups. Substituents such as carbomethoxy groups are well known to enhance the reactivity of multiple carbon-carbon bonds towards diazoalkane attack by lowering the energy levels of the considered frontier orbitals (3). One could now ask if a strong activation of this kind would not perturb the previously observed stereospecificity. All reported diazoalkane additions of unexpected stereoreactivity due to remote substituents were indeed described with relatively slow reacting olefins, activated only by ring strain.

The 7-halo 2,3-dicarbomethoxynorbornadienes necessary for our investigations were unknown compounds, and we had first to synthetize them. This was achieved trough Diels-Alder addition of dimethylacetylene dicarboxylate to the suitable 5-halocyclopentadienes, which were generated in situ from cyclopentadienylthallium (4) suspended in the acetylenic diester (5) :

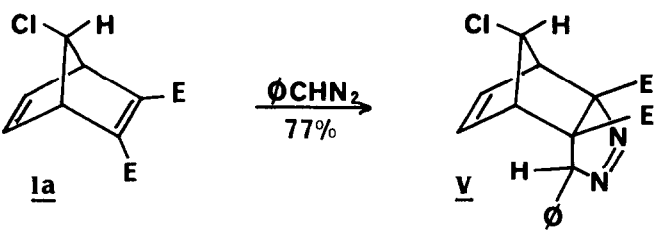


The anti 7-bromonorbornadiene is formed stereospecifically, although with the chlorosubstituted product, the formation of the anti-adduct Ia is accompanied by a lesser amount of the syn-adduct Ib. The structure proof of these Diels-Alder adducts was established by NMR spectroscopy : a coupling constant of 1 Hz between the C-7 proton and the vinylic protons is observed for the compounds Ia and II and not for Ib (6). This is consistent with the well known long-range W coupling typical of this skeleton (7), permitting the attribution of the anti stereochemistry to the first category of adducts.

The cycloaddition of diazomethane to the compounds Ia and II, which is a fast reaction, affords the pyrazolines III and IV in almost quantitative yields (8).

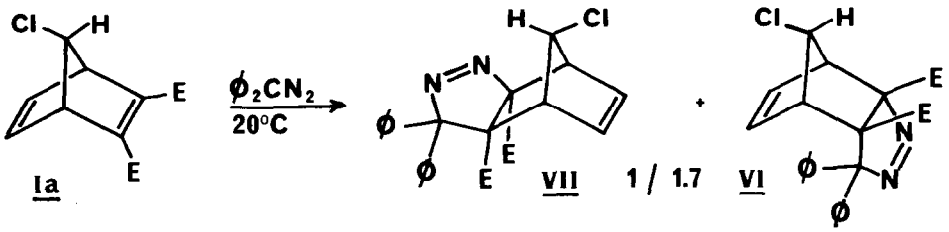


Phenyldiazomethane gave similarly the endo-anti adduct V with the chloronorbornadiene Ia, the sole diester tested in this case.

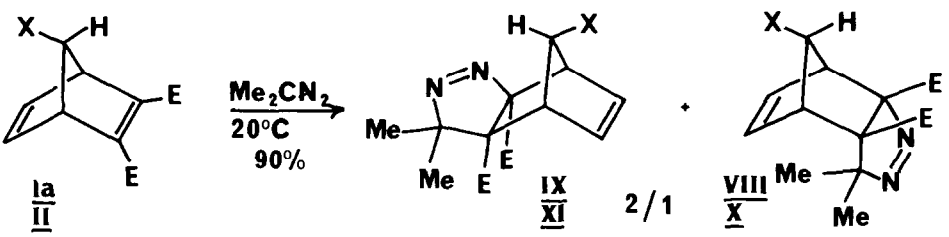


The endo-anti stereospecificity remains consequently unaltered in the case of very reactive substrates such as these electrophilic norbornadienes. The preference for the endo attack is evidently due to the 7-halogen substituent, this preference being in no way cancelled by the direct electronic activation of the reactive double-bond. The cycloaddition of phenyldiazomethane was even shown to be slightly less stereospecific with 7-chloronorbornadiene itself (1). The cycloaddition of this last diene with diphenyldiazomethane is, in turn, only stereoselective in favour of the endo-anti adduct, which was the predominant product (58 %) of the mixture of three isolated components (47 % overall yield (2)). We examined therefore the cycloaddition of this disubstituted diazoalkane with the diester Ia. Again the activation due to the carbomethoxy groups does not seem to be a limiting factor in view of the endo-anti selectivity, since we

observe in our conditions the formation of a mixture of only two adducts besides unreacted Ia, where the major endo-anti adduct VI is at least as predominant as in the case of the reaction with the nonelectrophilic diene (isolated : 35 % Ia, 41 % VI, 24 % VII).



With the more reactive 2-diazopropane the anti 7-chloro- and 7-bromonorbornadienes Ia and II lead to mixtures of anti-endo (VIII, X) and anti-exo adducts (IX, XI) in almost the same ratio of 1/2. This reflects a slightly greater selectivity in favour of the exo addition than the reaction of the 7-chloronorbornadiene itself (I).



These results show that the direct electronic activation of the reactive double-bond does not decrease the magnitude of the orientation effect by remote halogen substituents in the case of small diazoalkane cycloaddition.

This is an important conclusion, since the potential utility of stereoreactivity controlled by remote halogen substituents can now be extended to a wide range of electronically activated dipolarophiles. Further work in this direction is in progress.

References and notes :

1. Part II : M. FRANCK-NEUMANN, M. SEDRATI, preceeding publication in this Journal.

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3. J. GEITTNER, R. HUISGEN, R. SUSTMANN, Tetrahedron Letters, 881 (1977) and references therein.

4. M. SAUNDERS, R. BERGER, A. JAFFE, J.M. McBRIDE, J. O'NEILL, R. BRESLOW, J.M. HOFFMAN Jr. C. PERCHONOCK, E. WASSERMAN, R.S. HUTTON, V.J. KUCK, J. Amer. Chem. Soc., 95, 3017 (1973).

5. No [1.5] H shifts are observed in these conditions.
6. The longe range coupling constant between the bridge hydrogen and the vinyl hydrogens anti to it was measured after double irradiation experiments.
7. E.I. SNYDER, B. FRANZUS, J. Amer. Chem. Soc., 86, 1166 (1964).
8. The identification of the compounds obtained is mainly based on their H^1-NMR spectra ($CDCl_3$/TMS), the IR absorptions (C = O 1740 cm^{-1}, N = N 1560 cm^{-1}) and microanalytical data (C, H, N) being in agreement with the indicated Δ^1-pyrazoline structures. The cycloadditions proceed always on the electrophilic double bond as indicated by the presence of two vinylic protons in all obtained adducts. The chemical shifts of these protons are characteristic of the endo (N = N shielding) or exo stereochemistry and of the substitution pattern of the diazoalkane. The exo adducts clearly show shielded values for the chemical shift of the bridge protons to the halogens in sharp contrast to the endo adducts.

Compound	M. P.	δ H bridge	δ H (C=C)	
III (endo CH_2N_2)	84°C	4.88	6.10	
IV (endo CH_2N_2)	87°C	4.89	6.12	
V (endo ϕCHN_2)	liq.	4.90	5.94	6.24
VI (endo ϕ_2CN_2)	162°C	4.40	4.58	5.70
VII (exo ϕ_2CN_2)	202°C	3.82	5.98	6.67
VIII (endo DAP)	124°C	4.26	6.04	
IX (exo DAP)	154°C	3.37	5.96	6.59
X (endo DAP)	142°C	4.32	6.08	
XI (exo DAP)	139°C	3.39	5.98	6.62

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