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REGIOSELECTIVE ADDITIONS OF ELECTROPHILES TO OLEFINS REMOTELY PERTURBED. THE CARBONYL GROUP AS A HOMOCONJUGATED ELECTRON DONATING SUBSTITUENT.

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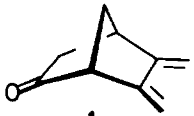
Summary. *Electrophiles attack preferentially at the C(5) position of 2-norborn-5-enone and 2-bicyclo[2.2.2]oct-5-enone whereas the C(6) position is preferred for 2-chloronorborn-5-ene-2-carbonitriles and 2-chlorobicyclo[2.2.2]oct-5-ene-2-carbonitriles.*

The regioselective Diels-Alder additions of 5,6-bis(methylene)-2-norbornanone (1) and 5,6-bis(methylene)-2-bicyclo[2.2.2]octanone (2) suggest that the homoconjugated carbonyl group in these systems can act as an electron donating substituent on the exocyclic dienes of 1 and 2[1]. The hyperconjugative $n(CO)\leftrightarrow\sigma C(1,2)\leftrightarrow\pi C(5,6)$ interaction[2] overrides the withdrawing effect expected for the $\pi^*(CO)\leftrightarrow\pi C(5,6)$ homoconjugative interaction. The CD spectra of optically active 1[4] and 2[5] show an "extra" band between those attributed to the carbonyl and diene chromophores. Similar "charge-transfer" bands were observed in the gas phase CD spectra of 2-norborn-5-enone (3) and 2-bicyclo[2.2.2]oct-5-enone (4)[5]; they were attributed to mixed transitions with a substantial charge-transfer component of the form $n(CO),\sigma\rightarrow\pi^*C(5,6)$[5]. We have now investigated the electrophilic additions of the enones 3 and 4, of the corresponding chlorocarbonitrile derivatives 5 - 8 and of the 2-norborn-5-enone acetals 9 & 10. The results confirm that the homoconjugated carbonyl group in β,γ-unsaturated ketones can play the role of an electron-donating group on the rate and the regioselectivity of the olefin additions to electrophiles[6].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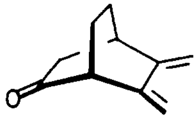
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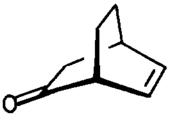
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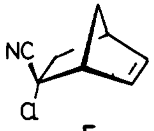
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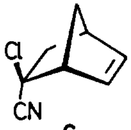
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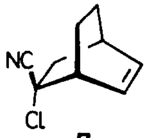
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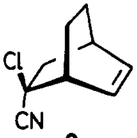
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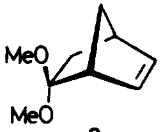
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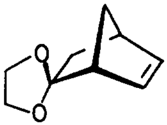
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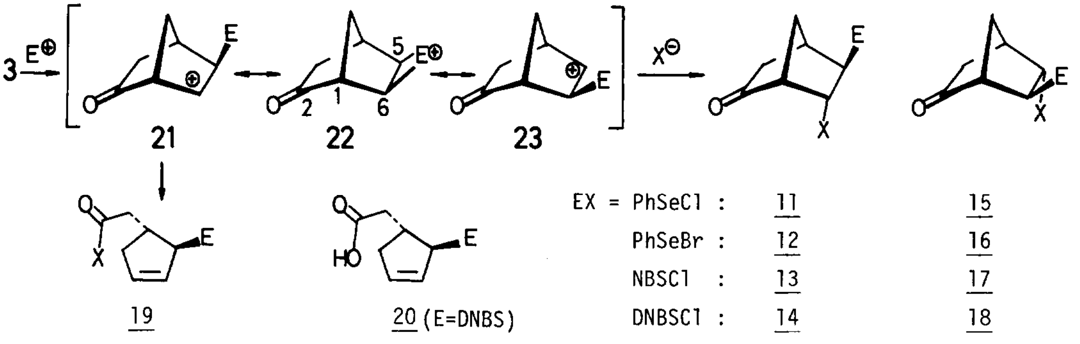
Benzeneselenylchloride (PhSeCl) and bromide (PhSeBr), 2-nitro- (NBSCl) and 2,4-dinitrobenzenesulfenyl chloride (DNBSCl) add to olefins[7,8] and generate bridged seleniranium and sulfeniranium ion intermediates whose stability and reactivity can be influenced by a homoconjugated endocyclic[8,9] or exocyclic double bond[10] and by the medium[8]. With PhSeCl and PhSeBr in $CHCl_3$, CH_3CN or AcOH, 3 gave the adducts 11 (93%) and 12 (95%, isolated), respectively. At 20°, the reactions were instantaneous. At -78° in THF, the addition 3 + PhSeBr gave 12 quantitatively in ca. 2-5 h. The arenesulfenyl chlorides added more slowly ($CHCl_3$, 20°, 12-16 h). With NBSCl only 13 was found (93%, isolated). In CH_3CN or AcOH, the addition of DNBSCl gave 14 (60-70%) together with 19, isolated as the acid 20 (20-30%). In AcOH + 2 eq. of $LiClO_4$, 19 was the major product (80%). No trace of the isomeric adducts 15-18 could be detected (HPLC, ^1H-NMR (360 MHz)) in the mother liquors after crystallization of 11-14[11]. Prolonged heating in CH_3CN (90°, 10 h) of the *a priori* most labile adduct 12[13] led to the slow formation of 16, 3 and polymers, thus confirming that the adducts were formed under kinetic control. The *exo* preference for the electrophile (E^+) attack of 2-norbornenes was expected[14]; the high preference of the *endo*-C(6) vs *endo*-C(5) attack by the counter-ion X^- is most simply attributed to the higher polarizability of the C(6)-E^+ bond rather than of the C(5)-E^+ bond in the cationic intermediate 22; the limiting structure 21 is more stable than 23 because of the hyperconjugative interaction n(CO)$\leftrightarrow\sigma$C(1,2)$\leftrightarrow$pC(6). The carbonyl group behaves as an electron donating group (polarizability) rather than as an electron withdrawing group (-M, -I). The "harder" the electrophile and the stronger the ionizing power of the medium, the more favoured is the n(CO),σC(1,2) participation and the σC(1,2) leakage (frangomeric effect[2]).



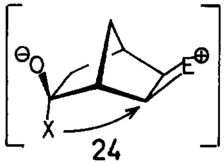
21 22 23

19

20 (E=DNBS)

EX =		
PhSeCl :	11	15
PhSeBr :	12	16
NBSCl :	13	17
DNBSCl :	14	18

Steric hindrance of the quenching of X^- with 22 could be larger at C(5) than C(6) and thus explain the observed regioselectivity. Another hypothesis would be to assume an addition of X^- onto the carbonyl group followed by a simple 1,3-transfer as shown in 24. The additions of PhSeCl and PhSeBr to 2-bicyclo[2.2.2]oct-5-enone (4) gave the adducts 25+26 and 27+28, respectively in high yield[11] (20°, $CHCl_3$ or CH_3CN, 6-12 h). Since the same high regioselecti-



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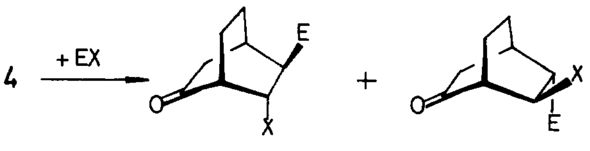
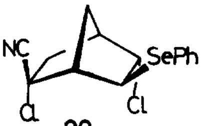


EX =		
PhSeCl :	25 (∿70%)	26 (∿30%)
PhSeBr :	27 (∿70%)	28 (∿30%)

vity was observed for the *endo* and *exo* attacks of the C(5,6) double bond of 4, the two latter hypotheses are not valid, at least not for 4 + PhSeCl → 26 and 4 + PhSeBr → 28.

As expected for olefins perturbed by -I substituents such as CN and Cl, the additions of PhSeCl to the 2-chloronorborn-5-ene-2-carbonitriles 5 and 6 were much slower (48 h, 20°, $CHCl_3$) than those of norbornene and 2-norborn-5-enone (3). They were highly stereo- and regioselective giving the corresponding adducts 29 and 30[11]. Similarly, the 2-chlorobicyclo[2.2.2]oct-5-ene-2-carbonitriles 7 and 8 added PhSeCl very slowly (20% of adducts formed after 72 h at 20°, $CHCl_3$, excess of PhSeCl) giving the adducts 31 and 32, respectively, with the same high regioselectivity (>95%) as 5 → 29 and 6 → 30, but opposite to that observed with the enones 3 and 4.



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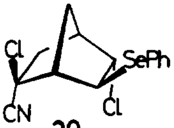

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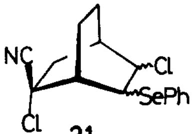

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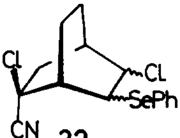

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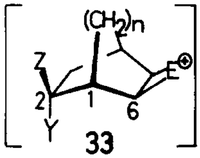

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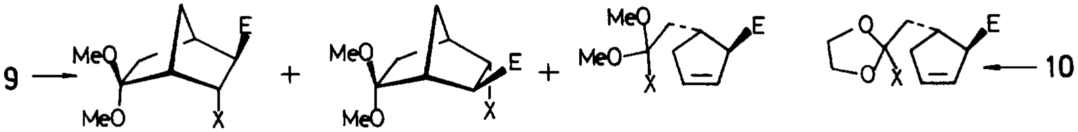
This can be attributed to the field effect of the CN and Cl substituents that makes the C(6)-E^+ bond in the bridged seleniranium ion intermediate 33 less prone to nucleophilic displacement than the C(5)-E^+ bond. The high preference of the *endo*-C(5) vs. *endo*-C(6) attack by X^- could also be attributed to steric hindrance in its approach to the *endo* face of 33.

The dimethylacetal 9 reacted with PhSeCl in $CHCl_3$ much faster (20°, ca. 10 s) than 5 and 6 and gave 34 + 38. Similarly, the adducts 35 + 39 were formed on treatment with PhSeBr ($CDCl_3$, 20°, <10 s). The large rate enhancement of these reactions compared with those of the addition



EX =				
PhSeCl :	34 ($\sim$15%)	38 ($\sim$85%)	-	
PhSeBr :	35 ($\sim$15%)	39 ($\sim$85%)	-	
NBSCl :	36 ($\sim$90%)	40 (< 5%)	42 ($\sim$ 5%)	
DNBSCl :	37 ($\sim$90%)	41 (< 5%)	43 ($\sim$10%)	44

of PhSeCl to 5 and 6 was unexpected for MeO substituents which have a field effect and a bulk analogous to those of Cl and CN. With the "harder" electrophiles NBSCl and DNBSCl (in $CHCl_3$) an opposite regioselectivity was observed, the adducts resulting from the Cl^- attack onto C(5) were not found (40, 41); 42 and 43 were formed in small amounts together with 36 and 37, respectively. As in the case of 22, this suggests that the σC(1,2) bond can participate in stabilizing the cationic intermediates 33 and orienting their reactions. The larger the electronic demand, the more the participation intervenes and competes with the steric effect of the substituent Y at C(2) in directing the quenching of the counter-ion. With +M substituents at C(2), the leakage of the σC(1,2) bond can become a favorable process. This interpretation was confirmed by the addition of DNBSCl (CD$_3$CN) to the ethyleneacetal 10 that gave only the cyclopentenylacetic acid derivative 44. In 10, the n(O) orbitals are forced to stay well aligned with the σC(1,2) bond, thus enhancing the electron donating effect of the $n(O)\leftrightarrow\sigma C(1,2)\leftrightarrow C(6)$ interaction.[2]

The relative fast electrophilic additions of the C(5,6) double bond of 3 and 4 and their high regioselectivity opposite to that of the addition of the corresponding chlorocarbonitrile derivatives 5-8 confirm that the homoconjugated carbonyl group in 3 and 4 can act as an electron donating substituent because of the hyperconjugative $n(CO)\leftrightarrow\sigma C(1,2)\leftrightarrow\pi C(6)$ interaction (the polarizability of the O=C(2)-C(1) bonds overrides the field effect of the carbonyl group).

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References and notes.

1. M. Avenati, P.-A. Carrupt, D. Quarroz & P. Vogel, Helv. Chim. Acta 65, 188 (1982).
2. This hyperconjugative interaction is related to the "frangomeric effect" and to the Grob fragmentation.[3]
3. A. Eschenmoser & A. Frey, Helv. Chim. Acta 35, 1660 (1952); W. Fischer & C. Grob, ibid. 61, 1588 (1978); C.A. Grob, Angew. Chem. 88, 621 (1976); cf. also : R. Hoffmann, Acc. Chem. Res. 4, 1 (1971); R. Hoffmann, A. Imamura & W.J. Hehre, J. Am. Chem. Soc. 90, 1499 (1968); R. Gleiter, Angew. Chem. 86, 770 (1974); E. Heilbronner & A. Schmelzer, Helv. Chim. Acta 58, 936 (1975).
4. J.-M. Sonney & P. Vogel, Helv. Chim. Acta 63, 1034 (1980).
5. P.-A. Carrupt & P. Vogel, Tetrahedron Lett. 22, 4721 (1981).
6. They are several examples of substituents that can be electron withdrawing or electron donating; see e.g. (a) the alkyl substituents : R.W. Taft, M. Taagepera, J.L.M. Abboud, J.F. Wolf, D.J. DeFrees, W.J. Hehre, J.E. Bartness & R.T. McIver, Jr., J. Am. Chem. Soc. 100, 7765 (1978) and ref. therein; (b) the cyano group : P.G. Gassman, K. Saito and J.J. Talley, ibid. 102, 7613 (1980); P.G. Gassman & K. Saito, Tetrahedron Lett. 1981, 1311; (c) the diene-Fe(CO)$_3$ group : C. Barras, L.G. Bell, R. Roulet & P. Vogel, Helv. Chim. Acta 64, 2841 (1981); (d) the α-carbonyl group : X. Creary, J. Am. Chem. Soc. 103, 2463 (1981).
7. G.H. Schmid & D.G. Garratt, The Chemistry of the functional groups. Suppl. A: the chemistry of double-bonded functional groups, S. Pataï, Ed., J. Wiley & Sons, London 1977, pp. 828-854.
8. N.S. Zefirov, N.K. Sadovaja, L.A. Novgorodtseva, R.Sh. Achmedova, S.V. Baranov & I.V. Bodrikov, Tetrahedron 35, 2759 (1979); N.S. Zefirov, A.S. Koz'min & V.V. Zhdankin, Tetrahedron 38, 291 (1982).
9. N.S. Zefirov, N.K. Sadovaja, R.Sh. Achmedova, I.V. Bodrikov, T.C.Morrill, A.M. Nersisyan, V. Rubakov, N.D. Saratseno & Yu. T. Struchkov, Zh. Org. Khim. 16, 580 (1980); Chem. Abstr. 93, 9459z (1980); D.G. Garratt & P.L. Beaulieu, J. org. Chem. 44, 3555 (1979); D.G. Garratt & A. Kabo, Can. J. Chem. 58, 1030 (1980).
10. D. Heissler & J.J. Riehl, Tetrahedron Lett. 1980, 4707, 4711; 1979, 3957; M. Przybylska & D.G. Garratt, Can. J. Chem. 59, 658 (1981).
11. The structure of the adducts were determined by ^{1}H-NMR (360 MHz), with the help of double irradiation experiments and by ^{13}C-NMR. They were confirmed by oxidative-eliminations[12] (NaIO$_4$/NaHCO$_3$ in MeOH/H$_2$O, 20°) that yielded the corresponding substituted olefins. Details will be given in a full paper.
12. J.L. Huguet, Adv. Chem. Ser. 76, 345 (1967); D.N. Jones, D. Mundy & R.D. Whitehouse, J. Chem. Soc. Chem. Commun. 1970, 86; K.B. Sharpless, M.W. Young & R.F. Lauer, Tetrahedron Lett. 1980, 1979; H. Reich, Acc. Chem. Res. 12, 22 (1979).
13. S. Raucher, J. Org. Chem. 42, 2950 (1977).
14. R. Huisgen, Pure Appl. Chem. 53, 171 (1981) and litt. cited.

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