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A CASE OF NON-ELECTROSELECTIVE AND π-FACIAL NON-STEREOSELECTIVE ADDITION TO NORBORNADIENE

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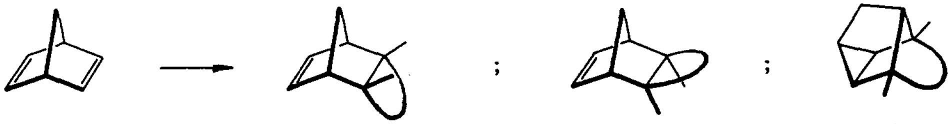
2-(4-Chlorophenylimino)-1-phenylethanone **5** or its adduct **6** with methanol add to norbornadiene **1** under BF_3 or SO_2 catalysis with low degree of electroselectivity and π-facial stereoselectivity giving **7**, **8**, **9**, and **10**. A reaction mechanism is proposed.

Three modes of concerted cycloaddition to norbornadiene **1** are documented: non-homo _endo_, non-homo _exo_, and homo, with respective formation of the adducts **2**, **3**, and **4**, although with reagents of widely different electronic request, _i.e._ a reagent behaves toward **1** electroselectively either as a diene,

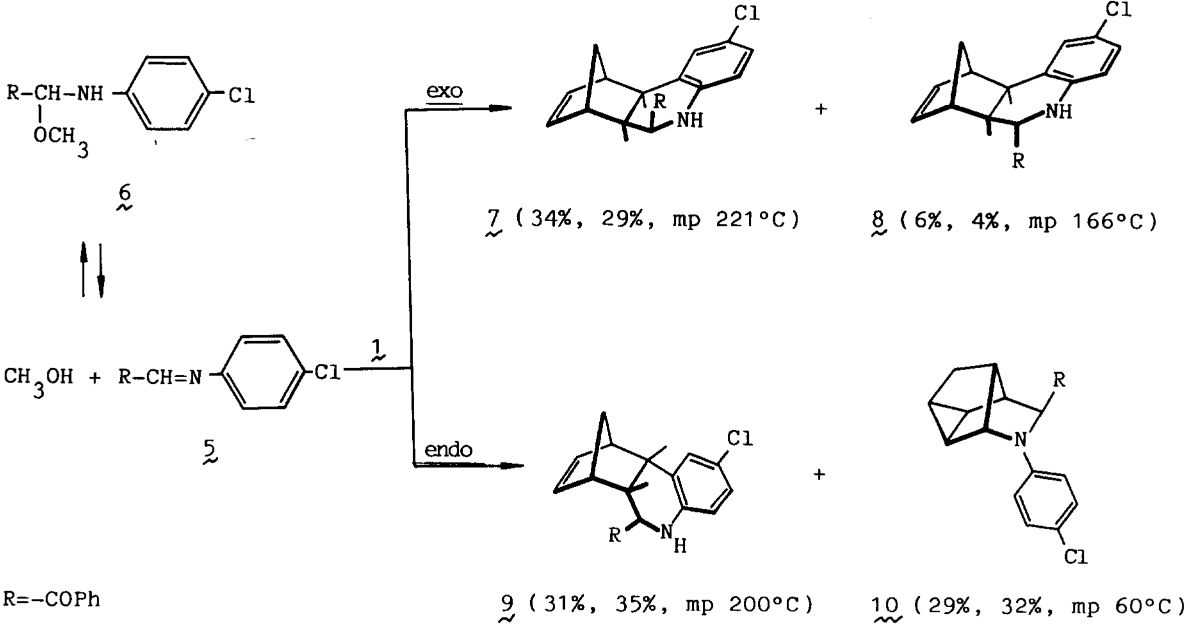


1 2 3 4

giving non-homo addition, or as a dienophile, with formation of the adduct **4**. Reagents capable of concerted addition to either side of the norbornadiene molecule are very uncommon, the only unambigous example being offered by halocarbenes.[1,2] As for as the non-homo addition is concerned, the vast majority of enophiles add with exclusive _exo_ π-facial stereoselectivity (the "_exo_ rule" of Alder and Stein). _Endo_ addition may be forced by substitution at the 7-position,[5] but the non-substituted norbornadiene can give an appreciable ratio of _exo_ and _endo_ adducts with halocarbenes[1] and with some 1,3-dipoles[6] only.

A promising substrate which can add to **1** with low selectivity is the phenylglyoxal anil **5**. We have in fact recently shown[7] that **5** can behave as "amphoteric" Diels-Alder reagent, in the sense that it can react as a diene (making use of the C=N double bond and of the conjugated Kekulè double bond of the aniline ring), and as a dienophile, depending on the nature of the reaction partner. The reactions proceed quickly at room temperature only under Lewis acid catalysis (etherated BF_3 in CH_2Cl_2 or liquid SO_2, acting as catalyst and as solvent); the adduct **6** of **5** with methanol, in equilibrium with **5**,[8] can be alternatively and more conveniently used.

"Amphoteric" Diels-Alder reagents are not uncommon, but their electroselectivity is generally more marked. As an example, N-sulphinylamine behaves preferentially as a dienophile and can adapt to react as a diene only when in the presence of a non-conjugated double bond.[9] From this point of view, the behaviour of **5** depends on more subtle properties of the reaction partner. With butadienes the preference seems to be dictated by the substitution pattern,[10] whereas with norbornadiene **1** the reaction, catalyzed by BF_3 or SO_2,[11] affords quantitatively the primary adducts given in the Scheme, together with the percent yields (from BF_3 and SO_2 catalysis in the order) as determined from integration of selected resonances in the n.m.r. spectrum of the reaction mixture; the product ratios do not change in the time under the reaction conditions.



7 (34%, 29%, mp 221°C)

8 (6%, 4%, mp 166°C)

9 (31%, 35%, mp 200°C)

10 (29%, 32%, mp 60°C)

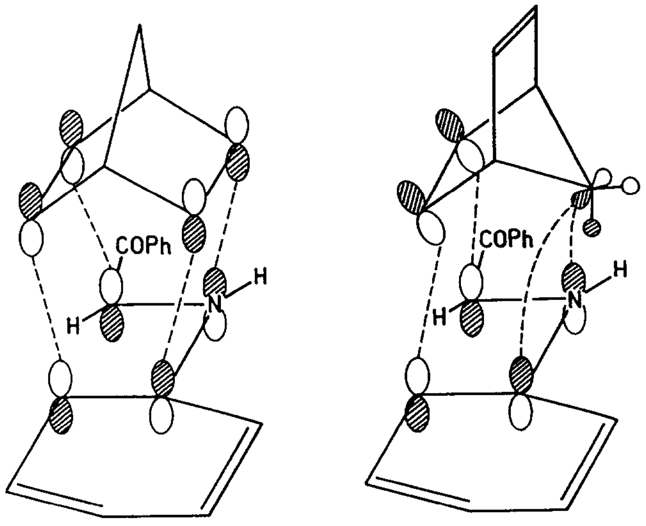
The adducts have been fractionated by flash chromatography. Their stereochemistry was firmly ascertained through measurement of the nuclear Overhauser effects (n.O.e.) with the aid of differential n.m.r. spectroscopy.[12]

It should be noticed that the <u>exo</u> addition of **5** is obviously electrospecific but not stereospecific, (yielding both β-benzoilic **7** and α-benzoylic **8** isomers), while both dienic and homodienophilic endo additions occur, however with stereospecific formation of the β-benzoylic 9 and β-benzoylic 10 isomers. The steric course of these additions cannot be invoked as a proof for a concerted mechanism. Nevertheless the various degrees of stereoselectivity in the exo and endo additions are fairly accounted for by the consideration of a concerted addition with secondary orbital interaction. Preliminary to this discussion is the determination of the conformation of 5 in the solution state. N.O.e. measurements , carried out in $CDCl_3$ or in SO_2,[12] have established the trans conformation for the free anil 5 as well as for the anil which separates from the adduct 6 in solution.

It can be reasonably presumed that the Lewis acid operates on the anil 5 with the consequence of a FMO energy lowering, so that the dienophilic addition of 5 to 1 is a case of normal Diels-Alder reaction, while the dienic addition is a Diels-Alder reaction with reverse electronic demand. In any case the relevant interaction is between the HOMO of norbornadiene 1 and the LUMO of the anil 5. The nodal properties of the FMO have been estimated with ab-initio computations at the STO-3G level,[13] carried out on norbornadienes and on the model molecule N-protonated N-phenylimine.

Even at this low sofistication level the ab-initio method shows a significant antisymmetric mixing, in the norbornadiene HOMO, of the CH_2 orbital of π symmetry and of the π_- orbital.[14]

The interaction between the relevant FMO in the case of an endo transition state shows a total phase concordance for the endo approach. It should be noticed that essentially the same interaction diagram explains the stereospecificities which accompany the formation of both the non-homo endo adduct 9 and the homo endo adduct 10.



Endo approach

Exo approach

As for the *exo* approach, the stabilizing secondary orbital interaction is between the π system of the anyl and the π_{CH_2} contribution to the norbornadiene HOMO. Since this contribution is not so great, the β-benzoylic stereoselectivity is expected to be, as it is, smaller.

Either as a concerted or non concerted reaction, the addition of **5** to norbornadiene **1** presents two major points of novelty: (a) the anil **5** represents the first example of a diene with no π-facial stereoselectivity toward norbornadiene. The only other dienes which add non exclusively *exo* to the unsubstituted norbornadiene are hexachlorocyclopentadiene,[15] tetrachloro-o-benzoquinone,[16] and o-benzoquinone diimine,[17] which are however much more selective; (b) it is the only Diels-Alder reagents so far which adds to the *endo* face of **1** with essentially no electroselective preference.

1. Jefford, C.W.; Mareda, J.; Geheret, J.-C.E.; Kabengele, nT.; Graham, W.D.; Burger, U. *J. Amer. Chem. Soc.* **1976**, *98*, 2585, and papers cited therein.
2. Another not-so-clear example may be offered by SO$_2$,[3,4] which gives chelotropic addition to the homodienic system of **1** and may undergo 2+2 cycloreversion from the intermediate proposed for the SO$_2$ catalized conversion of quadricyclane to **1**
3. De Lucchi, O.; Lucchini, V. *J. Chem. Soc., Chem. Commun.* **1982**, 1105.
4. De Lucchi, O.; Lucchini, V. *J. Chem. Soc., Chem. Commun.* **1982**, 464.
5. Mazzocchi, P.H.; Stahly, B.; Dodd, J.; Rondan, N.G.; Domelsmith, L.N.; Rozeboom, M.D.; Caramella, P.; Houk, K.N. *J. Amer. Chem. Soc.* **1980**, *102*, 6842, and papers cited therein.
6. Taniguchi, H.; Ikeda, T.; Imoto, E. *Bull Chem. Soc. Japan*, **1978**, *51*, 1495, and papers cited therein.
7. Lucchini, V.; Prato, M.; Quintily, U.; Scorrano, G. *J. Chem. Soc., Chem. Commun.* **1984**, 48.
8. Prato, M.; Quintily, U.; Scorrano, G. *Gazz. Chim. Ital.* **1984**, *114*, 0000
9. Kresze G.; Wucherpfenning, W. *Angew. Chem., Int. Edn. Engl.* **1967**, *6*, 149
10. With methyl substituents at the 2 and 3 positions, butadienes react as dienes, with formation of tetrahydropyridine derivatives; unsubstituted butadiene and alkyl- substituted butadienes at the peripheral 1 and 4 positions, behave as dienophiles, giving tetrahydroquinoline derivatives. The reason for this electroselective behaviour is not clear and is currently under investigation.
11. The reaction is istantaneous, so that the addition of SO$_2$ to norbornadiene **1**, which was reported to be rather slow,[3] does not interfere.
12. Details will be given in the full paper.
13. Csizmadia, I.G.; Peterson, M.R.; Poirier, R.A. "Program MONSTERGAUSS", University of Toronto, Ontario, Canada, **1981**
14. This fact has already been pointed out by Mazzocchi, Houk, *et.al.*[5] (note however that the phase alternance of the HOMO is reported uncorrectly).
15. Battiste, M.A.; Timberlake, J.F.; Malkus, H. *Tetrahedron Lett.* **1976**, 2529
16. Friedrichsen, W.; Epbinder, R. *Tetrahedron Lett.* **1973**, 2059.
17. Friedrichsen, W.; Schmidt, R. *Liebigs Ann. Chem.* **1978**, 1129.

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