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# HETERODIENE SYNTHESES—XIII[1]

## THE STEREOCHEMICAL CONSEQUENCES OF ELECTRONIC AND STERIC INTERACTIONS IN THE TRANSITION STATE OF THE CYCLOADDITION BETWEEN 4-ARYLIDENE-5-PYRAZOLONES AND VINYLETHERS

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**Abstract**—The competition between *exo* and *endo* transition states in the cycloaddition of 4-arylidene-5-pyrazolones and vinylethers is rationalized in terms of steric and electronic interactions.

The steric interactions depend mainly upon the requirements of the substituent in position 3 of the starting pyrazolone.

The electronic factors are rationalized in terms of secondary non-bonding interactions between the HOMO of the vinylether which acts as donor and the LUMO of the pyrazolone which acts as acceptor.

An E configuration of the pyrazolone is suggested as "reacting" species.

In a recent paper in this series[2] we investigated the reaction of various 3-phenyl-4-arylidene-5-pyrazolones and -isoxazolones with *cis* and *trans* 1-methyl-2-n-propoxyethylene. The stereochemistry of the starting ether is retained in the adduct and a *trans*[3,4]configuration of the substituents is always preferred.

As an *exo* vs *endo* approach cannot rationalize this preference, we have suggested a concerted model for the cycloaddition and Fig 1 shows the different possibilities for the arrangement of the transition state.

The B transition state should be strongly unfavoured by three to two *gauche* interactions and by the steric hindrance between the Me group of the ether and the phenyl group of the heterocycle, hence a *trans*[3,4]isomer is predominant.

On the basis of previous work, a few considerations can be made: (a) the steric hindrance between increasingly bulky groups in position 3 on the heterocyclic ring and the Me group of the ether (R/Me interaction) should stabilize the *cis*[3,4]-isomer; (b) increased *gauche* interactions should favour a *trans*[3,4]isomer; (c) as 3-methyl and 3-phenyl-4-arylidene-5-pyrazolones have the Z configuration, whereas the 3-hydrogen derivatives have an E configuration,[3] is the configuration of the ground state retained during the cycloaddition or can isomerization occur?

In order to investigate these questions we have performed the reaction between *cis* and *trans* 1-methyl-2-n-propoxyethylene and various pyrazolones with both E and Z configuration and with different substituents in position 3 (Scheme 1).

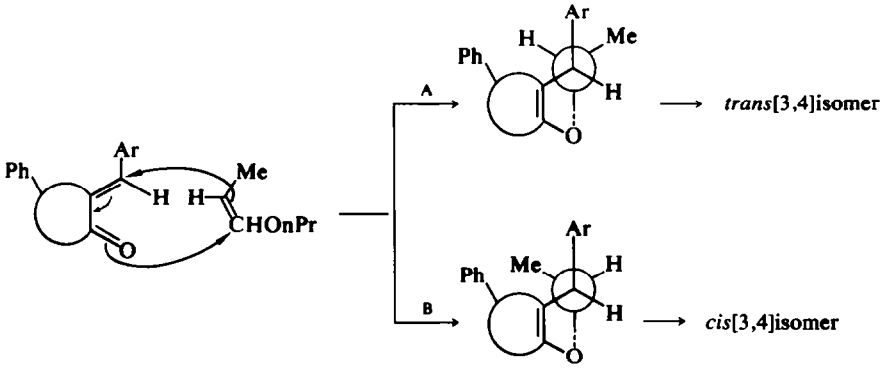
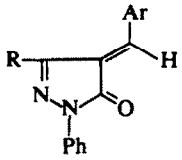
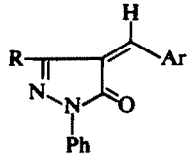



Fig 1.



**1a**: R = H Ar = *p*-$NO_2$Ph
**1b**: R = H Ar = Ph
**1c**: R = H Ar = *p*-OMePh
**1j**: R = H Ar = Mesityl
**1k**: R = Me Ar = Mesityl
**1m**: R = Ph Ar = Mesityl



**1d**: R = Me Ar = *p*-$NO_2$Ph
**1e**: R = Me Ar = Ph
**1f**: R = Me Ar = *p*-MeOPh
**1g**: R = Ph Ar = *p*-$NO_2$Ph
**1h**: R = Ph Ar = Ph
**1i**: R = Ph Ar = *p*-MeOPh
**1l**: R = Me Ar = Mesityl

SCHEME 1

The different substituents in the *para* position of the arylidene group should show if the configurational control is steric alone or electronic too.

*Reaction of benzal,* p-$NO_2$ *and* p-OMe *benzalpyrazolones*

We considered first the reactions of **1a–g** and the results, together with those of **1h** and **1i** previously reported,[2] are summarized in Scheme 2. The composition of the reaction mixtures was monitored by their NMR spectra, usually in the region of the anomeric protons and for **1d–f** from the signal of the pyrazole Me group. The yields are reported in Table 1.

Table 1

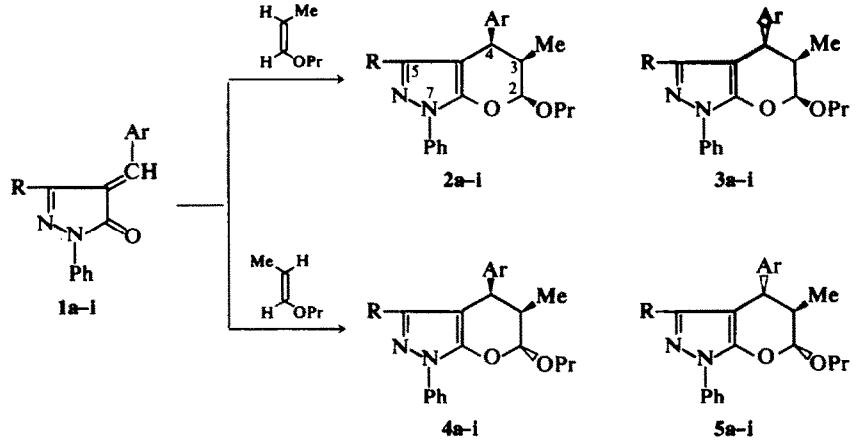
| 1 | 2% | 3% | 4% | 5% |
|---|---|---|---|---|
| *a* | 90 | 10 | 11 | 89 |
| *b* | 85 | 15 | 16 | 84 |
| *c* | 77 | 23 | 19 | 81 |
| *d* | 14 | 86 | 12 | 88 |
| *e* | 18 | 82 | 11 | 89 |
| *f* | 25 | 75 | 15 | 85 |
| *g* | 5 | 95 | < 3 | > 97 |
| *h* | 7 | 93 | — | ~ 100 |
| *i* | 10 | 90 | 3 | 97 |

Note: all yields are ± 3%.

The configuration of the pure isomers can be determined easily with the aid of the coupling constant values from the NMR spectra,[4] (Table 2), if one remembers that two forces govern the conformational equilibrium;[5] *i.e.* the anomeric effect and the conformational preference of the 4-aryl group for the *pseudo*-equatorial position, partially counterbalanced by the steric interaction with the pyrazole substituent $R^1$.

This interpretation rationalizes some couplings unusual for a *trans* isomer as $J_{23}$ values of **4** which lie in the range 2·2–4·0 Hz. The net preference for conformation (i) (Scheme 3) can be easily explained as both the above reported forces stabilize it, therefore an equatorial/equatorial character for the *trans* coupling is conceivable.

Inspection of the relative yields is interesting because even though the arylidene substituent has only a small effect on the isomer ratio the substitution of R = phenyl with a methyl group causes a small but nevertheless significant increase of the *cis*[3,4] isomers **2** and **4**. This trend is increased if

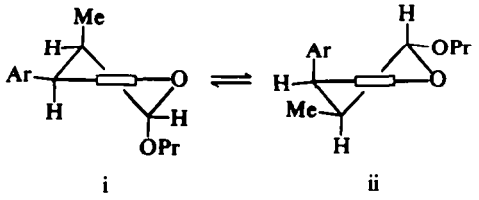


SCHEME 2

Table 2

| | Dihydropyrane substituents | | | | | | | | | | Propoxy group | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | Dihydropyrane protons | | | | | Methyl | | | | | O—$CH_2$— | | | | | —$CH_3$ | |
| Compd. | $\delta H_2$ (D) | $\delta H_3$ (M) | $\delta H_4$ (D) | $J_{23}$ | $J_{34}$ | δMe (D) | $J_{Me,H_3}$ | δR (S) | Aromatic protons | δX (S) | $\delta H_a$ | $\delta H_b$ | $-J_{gem}$ | $J_{vic}$ | —$CH_2$— (M) | δMe (T) | $J_{vic}$ |
| **2a** | 5·29 | 2·5 | 4·25 | 2·0 | 6·7 | 0·86 | 7 | 7·28 | 7·2–8·3 | — | 3·85 | 3·48 | 9·5 | 6·5 | 1·5 | 0·80 | 6·5 |
| **3a** | 5·31 | 2·1 | 3·86 | 2·1 | 10·35 | 0·93 | 7 | 7·00 | 6·9–8·3 | — | 3·89 | 3·56 | 9·5 | 6·5 | 1·6 | 0·87 | 6·5 |
| **4a** | 5·26 | 2·3 | 4·54 | 2·2 | 5·45 | 0·91 | 7 | 7·26 | 7·3–8·4 | — | 3·80 | 3·58 | 9·5 | 6·5 | 1·6 | 0·73 | 7·0 |
| **5a** | 5·09 | 2·2 | 3·76 | 6·3 | 7·4 | 1·04 | 7 | 7·11 | 7·2–8·3 | — | 3·89 | 3·53 | 9·5 | 6·5 | 1·5 | 0·83 | 7·0 |
| **2b** | 5·28 | 2·3 | 4·20 | 1·9 | 6·2 | 0·75 | 7 | 7·31 | 7·2–8·0 | — | 3·87 | 3·49 | 9·5 | 6·5 | 1·5 | 0·85 | 6·7 |
| **3b** | 5·26 | 2·1 | 3·72 | 2·1 | 10·1 | 0·95 | 7 | 7·05 | 7·1–8·1 | — | 3·81 | 3·61 | 9·5 | 6·5 | 1·5 | 0·89 | 6·7 |
| **4b** | 5·25 | 2·3 | 4·43 | 2·2 | 5·4 | 0·73 | 7 | about 7·3* | 7·1–8·0 | — | 3·87 | 3·62 | 9·5 | 6·5 | 1·6 | 0·73 | 6·7 |
| **5b** | 5·06 | 2·1 | 3·57 | 7·8 | 9·2 | 0·98 | 7 | 7·07 | 7·1–8·0 | — | 3·89 | 3·56 | 9·5 | 6·5 | 1·6 | 0·92 | 6·7 |
| **2c** | 5·27 | 2·4 | 4·16 | 1·85 | 6·2 | 0·91 | 7 | 7·28 | 6·6–7·8 | 3·75 | 3·89 | 3·51 | 9·5 | 6·5 | 1·5 | 0·82 | 6·7 |
| **3c** | 5·24 | 1·9 | about 3·7† | 2·2 | ⩾ 9·6† | 0·95 | 7 | 7·04 | 6·7–8·0 | 3·77 | 3·83 | 3·56 | 9·5 | 6·5 | 1·6 | 0·84 | 6·7 |
| **4c** | 5·19 | 2·1 | 4·35 | 2·2 | 5·35 | 0·93 | 7 | about 7·3* | 6·7–8·0 | 3·80 | (†) | (†) | 9·5 | 6·5 | 1·6 | 0·74 | 6·7 |
| **5c** | 5·03 | 2·1 | 3·50 | 7·9 | 9·45 | 0·96 | 7 | about 7·05* | 6·6–8·0 | 3·77 | 3·95 | 3·58 | 9·5 | 6·5 | 1·6 | 0·90 | 6·7 |
| **2d** | 5·23 | 2·4 | 4·06 | 2·2 | 6·9 | 0·92 | 7 | 1·82 | 7·1–8·2 | — | 3·81 | 3·42 | 9·5 | 6·5 | 1·5 | 0·87 | 7·0 |
| **3d** | 5·26 | 2·0 | 3·84 | 2·15 | 10·0 | 0·91 | 7 | 1·62 | 7·1–8·3 | — | 3·81 | 3·60 | 9·5 | 6·5 | 1·6 | 0·87 | 6·5 |
| **4d** | 5·18 | 2·2 | 4·43 | 3·3 | 5·8 | 0·73 | 7 | 1·85 | 7·1–8·3 | — | 3·82 | 3·60 | 9·5 | 6·5 | 1·7 | 0·85 | 7·0 |
| **5d** | 5·06 | 2·3 | 3·72 | 5·35 | 6·6 | 1·08 | 7 | 1·75 | 7·0–8·3 | — | 3·84 | 3·48 | 9·5 | 6·5 | 1·5 | 0·79 | 6·5 |
| **2e** | 5·22 | 2·3 | 4·00 | 2·1 | 6·75 | 0·85 | 7 | 1·80 | 7·1–8·0 | — | 3·80 | 3·42 | 9·5 | 6·5 | 1·5 | 0·79 | 7·0 |
| **3e** | 5·25 | 2·1 | 3·69 | 2·15 | 9·9 | 0·94 | 7 | 1·64 | 7·1–8·1 | — | 3·85 | 3·59 | 9·5 | 6·5 | 1·6 | 0·87 | 6·5 |
| **4e** | 5·17 | 2·2 | 4·25 | 3·85 | 5·85 | 0·74 | 7 | 1·85 | 7·0–8·0 | — | 3·83 | 3·58 | 9·5 | 6·5 | 1·6 | 0·85 | 6·7 |
| **5e** | 4·99 | 2·1 | 3·51 | 7·4 | 8·35 | 1·00 | 7 | 1·65 | 7·1–8·0 | — | 3·93 | 3·54 | 9·5 | 6·5 | 1·6 | 0·90 | 6·5 |
| **2f** | 5·20 | 2·3 | 3·96 | 2·2 | 6·65 | 0·87 | 7 | 1·83 | 6·6–8·0 | 3·78 | 3·82 | 3·45 | 9·5 | 6·5 | 1·5 | 0·87 | 6·5 |
| **3f** | 5·22 | 2·1 | about 3·7† | 2·0 | about 10·0† | 0·85 | 7 | 1·64 | 6·6–8·0 | 3·78 | 3·78 | 3·62 | 9·5 | 6·5 | 1·6 | 0·85 | 7·0 |
| **4f** | 5·14 | 2·2 | 4·18 | 3·9 | 5·7 | 0·76 | 7 | 1·87 | 6·7–8·0 | 3·81 | 3·80 | 3·58 | 9·5 | 6·5 | 1·6 | 0·86 | 7·0 |
| **5f** | 5·00 | 2·1 | 3·47 | 7·5 | 8·5 | 0·97 | 7 | 1·68 | 6·7–8·0 | 3·78 | 3·91 | 3·60 | 9·5 | 6·5 | 1·6 | 0·94 | 7·0 |
| **2g** | 5·22 | 2·6 | 4·31 | 2·1 | 6·8 | 0·93 | 7 | Arom | 7·0–8·2 | — | 3·85 | 3·54 | 9·5 | 6·5 | 1·5 | 0·72 | 6·5 |
| **3g** | 5·29 | 2·5 | 4·14 | 2·05 | 9·1 | 1·03 | 7 | Arom | 7·0–8·1 | — | 3·87 | 3·56 | 9·5 | 6·5 | 1·6 | 0·91 | 6·5 |
| **4g** | 5·22 | 2·4 | 4·68 | 4·0 | 5·8 | 0·93 | 7 | Arom | 7·0–8·1 | — | 3·89 | 3·61 | 9·5 | 6·5 | 1·6 | 0·67 | 6·5 |
| **5g** | 5·19 | 2·4 | 4·12 | 4·0 | 4·3 | 1·17 | 7 | Arom | 7·0–8·2 | — | 3·83 | 3·40 | 9·5 | 6·5 | 1·5 | 0·73 | 6·5 |

*Partly overlapped by aromatic protons.
†Partly overlapped by OMe signal.



i ii

SCHEME 3

the substituent R is hydrogen, smoothly for **4** but dramatically for **2** which becomes the main product of the reaction (about 80–90% yield).

This result cannot be explained in terms of diminished steric repulsion (R/Me interaction) only; some attractive force must be involved and the overwhelming factor could be an *endo* interaction involving the lone pairs of the oxygen atom.[6]

If one assumes for **1d–i** that the reacting species has the configuration of the ground state, *i.e.* Z, the preferred configuration of the adducts requires the reported transition states (Fig 2).

Clearly both transition states from *cis* and *trans* ethers have the unfavourable Me/R interaction and sometimes the *endo*, sometimes the *exo* interaction predominates. However the approach of the vinyl ether to a Z pyrazolone for a 1,4-cycloaddition must cause severe steric interactions and, in addition to this, the above reported rationalization in terms of random preferences must be regarded as meaningless.

On the contrary, the stereoselectivity shown by **1a–c** can be reasonably explained (Fig 3).

The steric interaction between Me and R is considerably lowered if R = H and therefore *endo* stabilization predominates. In the light of the above reported results we believe that an overall rationalization must involve an isomerization of the Z into the E species when Z is the configuration of the ground state. Even if a single arylidene-5-pyrazo-

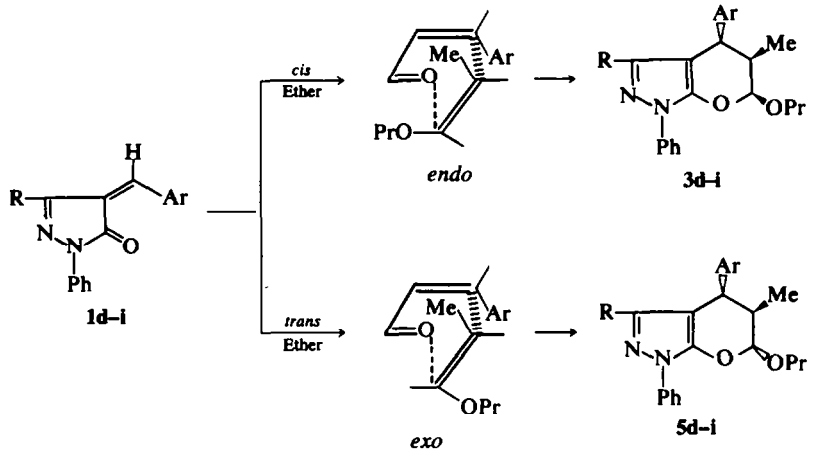



Fig 2.

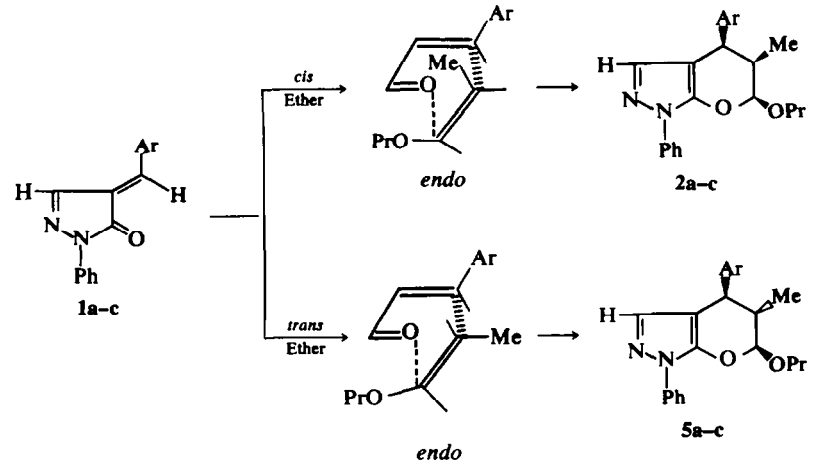



Fig 3.

lone isomer is usually isolated,[3,7] an equilibrium seems likely and has been suggested[8] in order to rationalize the non-stereospecific addition of benzonitrileoxide to **1e** in protic polar solvents. The faster reactivity of E, due to easier approach, would displace the equilibrium in its favour (Fig 4).

The choice between the different transition states is governed by electronic (*endo* stabilization) and steric interactions (R/Me destabilization); when both are favourable, the stereoselectivity is marked, when they are opposite, the intensity of the interactions causes the selection.

In order to test the assumption that E is the largely predominant reacting isomer, we have performed the cycloaddition with mesityl derivatives (**1j–m**).

*Reaction with mesityliden-pyrazolones*

As expected, the reaction becomes more difficult owing to the electron donating character of the mesityl group in addition to the obvious increased steric hindrance. The *cis* ether requires 30–40 days at 80° and the *trans* ether 5–7 days at the same temperature.

Fortunately, under the experienced conditions **1k** Z does not isomerize and, after the same reaction period and under the identical conditions used for **1k** E, this isomer is recovered unchanged in 95% yield, both from *cis* and *trans* ether.

We believe this can be regarded as a strong point in favour of the proposed mechanism and therefore it seems reasonable to state that the Z configuration of pyrazolones does not favour the 1,4-cycloaddition.

The overall reaction is reported in Scheme 4.

The reaction with E mesityl derivatives (**1j–m**) is stereospecific both with *cis* and *trans* ether, the configuration of the ether is still retained in the adduct and the $C_3/C_4$ junction is totally *trans*. The parameters of the NMR spectra are reported in Table 3.

The strict stereospecificity cannot be assigned to an increased *endo* selectivity, as the transition states leading to **3** and **5** require opposite interactions. A possible explanation in terms of *gauche* interactions could be ruled out as the size of the mesityl group should be strongly unfavourable to the approach of the ether Me group from the pyrazole side whatever the nature of R and the eventual *endo* stabilization.

The bulkiness of the mesityl group makes the molecule rigid (*ortho* methyl groups and *meta* protons of the mesityl ring are magnetically non-equivalent) and the overwhelming factor in the conformational equilibrium becomes the preference of this group for the *pseudo*-equatorial position. Hence both $J_{34}$ and $J_{23}$ (when *trans*) always have an axial/axial character.

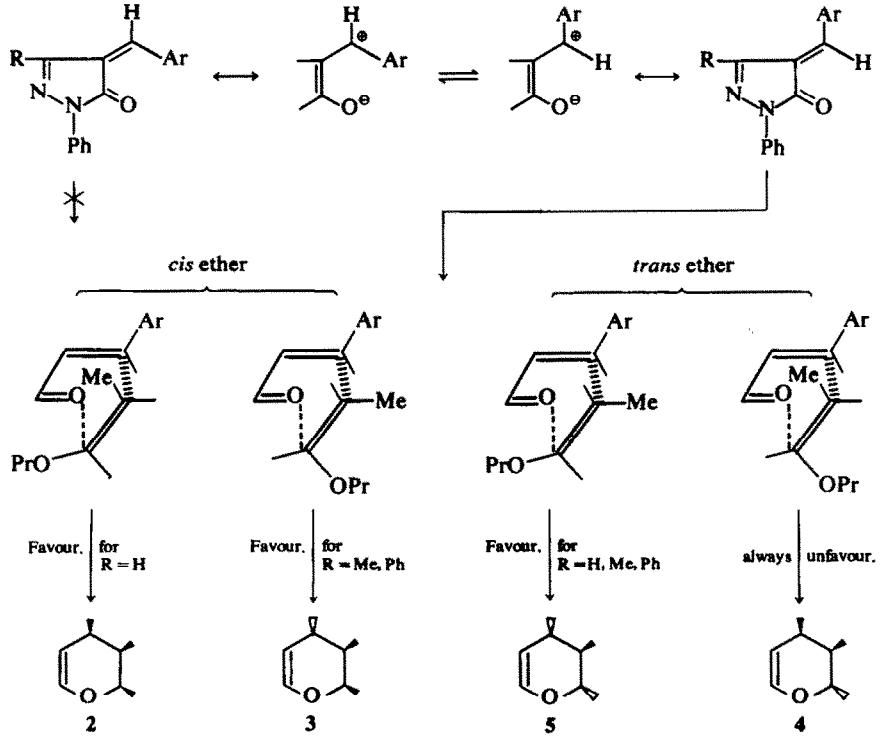
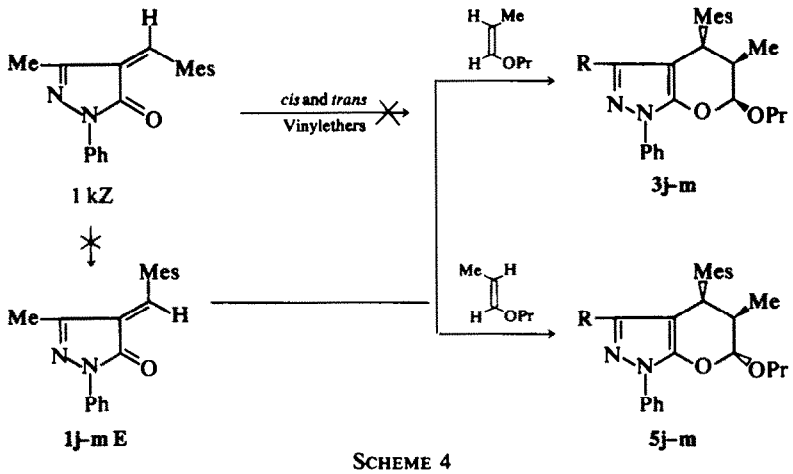



Fig 4.

Table 3

| | Dihydropyrane substituents | | | | | | | | | Mesityl group | | | | | Propoxy group | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | Dihydropyrane protons | | | | | Methyl | | | | | | | | | O—$CH_2$— | | | | | —$CH_3$ | |
| Compd. | $\delta H_2$ (D) | $\delta H_3$ (M) | $\delta H_4$ (D) | $J_{23}$ | $J_{34}$ | $\delta$Me (D) | $J_{Me,H_3}$ | $\delta$R (S) | Aromatic protons | $\delta Me_o$ (S) | $\delta H_m$ (BS) | $\delta Me_p$ (S) | $\delta H_{m'}$ (BS) | $\delta Me_{o'}$ (S) | $\delta H_a$ | $\delta H_b$ | $-J_{gem}$ | $J_{vic}$ | —$CH_2$— (M) | $\delta$Me (T) | $J_{vic}$ |
| **3j** | 5·34 | 2·5 | 4·42 | 2·15 | 11·15 | 0·90 | 6·7 | 7·06 | 7·2–8·0 | 2·05 | 6·84 | 2·45 | 7·06 | 2·29 | 3·91 | 3·60 | 9·5 | 6·5 | 1·65 | 0·95 | 6·7 |
| **5j** | 5·05 | 2·4 | 4·20 | 8·45 | 10·9 | 0·95 | 6·5 | 7·00 | 7·2–8·0 | 2·01 | 6·81 | 2·38 | 6·88 | 2·26 | 4·03 | 3·63 | 9·5 | 6·5 | 1·7 | 1·00 | 6·7 |
| **3k** | 5·57 | 2·5 | 4·31 | 2·3 | 11·1 | 0·91 | 6·7 | 1·57 | 7·1–8·0 | 1·99 | 6·79 | 2·38 | 6·87 | 2·23 | 3·75 | 3·59 | 9·5 | 6·5 | 1·6 | 0·85 | 6·7 |
| **5k** | 5·00 | 2·4 | 4·15 | 8·35 | 10·45 | 0·98 | 6·5 | 1·58 | 7·1–8·0 | 2·02 | 6·79 | 2·39 | 6·87 | 2·26 | 4·03 | 3·61 | 9·5 | 6·5 | 1·7 | 1·00 | 6·7 |
| **3m** | 5·29 | 2·5 | 4·51 | 2·3 | 10·65 | 0·97 | 6·7 | Arom | 6·9–8·1 | 1·87 | 6·70 | 2·41 | 6·45 | 2·08 | 3·83 | 3·59 | 9·5 | 6·5 | 1·6 | 0·87 | 6·7 |
| **5m** | 5·10 | 2·4 | 4·31 | 8·3 | 9·85 | 1·01 | 6·5 | Arom | 6·9–8·1 | 1·90 | 6·70 | 2·34 | 6·51 | 2·09 | 4·03 | 3·61 | 9·5 | 6·5 | 1·7 | 0·99 | 6·7 |




SCHEME 4

*Nature of the ENDO interaction*

The nature of the Diels-Alder transition state has been a well studied point since Alder first enunciated his *endo* rule[9] and Hoffman and Woodward rationalized it in terms of secondary non-bonding interactions;[10] however the concept of the different importance of the HOMO/LUMO or LUMO/HOMO interactions, first emphatized by Fukui,[11] has only recently been developed in various papers[12–14] where different stabilizing interactions have been suggested in *normal* and *inverse*[15] reactions *i.e.* in electron poor dienophiles/electron rich dienes (i) and in the opposite reaction (ii) (Scheme 5).

It is clear that the dominant interaction in the *normal* reaction occurs between $LUMO_{Dienophile}$ and $HOMO_{Diene}$, whereas the *inverse* has a greater control from the interaction between $HOMO_{Dienophile}$ and $LUMO_{Diene}$; this follows from the general assumption that the lower the separation of the interacting orbitals the better stabilization results. In both cases the relevant interaction occurs between $LUMO_{Acceptor}$ and $HOMO_{Donor}$.[14]

A simple and schematic representation of interactions between frontier orbitals of α,β-unsaturated carbonyl compounds[16] and vinylethers is given in Fig 5.

The dominant interaction (if this is regarded as an inverse Diels-Alder reaction) occurs between the HOMO of the donor (vinylether) and the LUMO of the acceptor (α,β-unsaturated carbonyl derivative) and therefore stabilizes the *endo* t.s., whereas the opposite interaction should lead to an *exo* t.s.

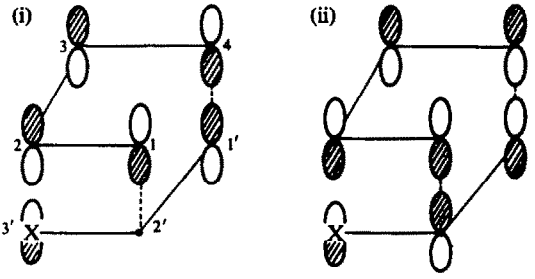
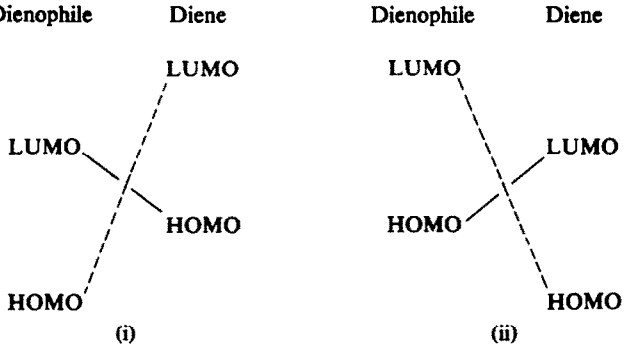



Fig 5. $LUMO_{Diene}/HOMO_{Dienophile}$ interaction (i) and $HOMO_{Diene}/LUMO_{Dienophile}$ interaction (ii). Diagrams are schematic: *e.g.* due to the asymmetry of the wave function of vinylether, the nodal point in (i) does not coincide with the nuclear position 2′ which therefore should become bonding from nonbonding.




SCHEME 5. HOMO/LUMO interactions in *normal* (i) and *inverse* (ii) Diels-Alder reactions. Solid arrows show predominant interactions. Diagrams are schematic.

Table 4

| Compd. | React. time at 80° | Type of separation | m.p. (solvent) | Physical state | Elemental analysis |
|---|---|---|---|---|---|
| **4a** | 15 hr | Fract. Cry + Col. Chrom. Cy/AcOEt 9:1 | 152·5–3·5° (EtOH) | light yellow small prisms | Found: C, 66·86; H, 5·89; N, 10·14 |
| **5a** | 15 hr | Fract. Cryst. EtOH/AcOEt | 185–6° (EtOH) | light yellow needles | Found: C, 66·99; H, 5·91; N, 10·96 for $C_{22}H_{23}N_3O_4$ Calc.: C, 67·16; H, 5·89; N, 10·68% |
| **2b** | 60 hr | Fract. Cryst. (Pet. Eth.) | 104–5° (Pet. Eth) | soft white needles | Found: C, 76·15; H, 7·10; N, 8·06 |
| **3b** | 60 hr | id. id + Col. Chrom. Cy/AcOEt 9:1 | 94–5° (dil EtOH) | white needles | Found: C, 75·70; H, 6·94; N, 8·19 |
| **4b** | 30 hr | Fract. Cry + Col. Chrom. Cy/AcOEt 9:1 | 69–70° (dil EtOH) | white needles | Found: C, 75·81; H, 7·02; N, 8·23 |
| **5b** | 30 hr | Fract. Cryst. dIPE | 110–1° (dIPE) | soft white needles | Found: C, 75·84; H, 7·01; N, 8·04 for $C_{22}H_{24}N_2O_2$ Calc.: C, 75·83; H, 6·94; N, 8·04% |
| **2c** | 8 days | Fract. Cryst. EtOH | 95–6° (EtOH) | whitish prisms | Found: C, 73·07; H, 6·91; N, 7·63 |
| **3c** | 8 days | id. id + Col. Chrom. Cy/AcOEt 9:1 | 146–7° (dIPE) | colourless prisms | Found: C, 72·99; H, 7·08; N, 7·70 |
| **4c** | 5 days | Fract. Cry + Col. Chrom. Cy/AcOEt 9:1 | 109–10° (EtOH) | white crystals | Found: C, 72·62; H, 6·98; N, 7·45 |
| **5c** | 5 days | Fract. Cryst. EtOH | 143–4° (EtOH) | soft white needles | Found: C, 73·31; H, 6·96; N, 7·54 for $C_{23}H_{26}N_2O_3$ Calc.: C, 72·99; H, 6·93; N, 7·40% |
| **2d** | 40 hr | Fract. Cry + Col. Chrom. Cy/AcOEt 8:2 | 149–50° (dIPE) | yellowish needles | Found: C, 67·67; H, 6·27; N, 10·51 |
| **3d** | 40 hr | Fract. Cryst. EtOH | 125–6° (EtOH) | light yellow bright prisms | Found: C, 67·47; H, 6·32; N, 10·51 |
| **4d** | 15 hr | Fract. Cry + Col. Chrom. Cy/AcOEt 9:1 | 107–8° (PE/AcOEt) | yellowish small prisms | Found: C, 67·90; H, 6·32; N, 10·25 |
| **5d** | 15 hr | Fract. Cryst. EtOH | 133–4° (EtOH) | small white crystals | Found: C, 67·53; H, 6·18; N, 10·32 for $C_{23}H_{25}N_3O_4$ Calc.: C, 67·79; H, 6·18; N, 10·31% |
| **2e** | 90 hr | Fract. Cry + Col. Chrom. Cy/AcOEt 9:1 | 92–3° (dil EtOH) | white prisms | Found: C, 75·97; H, 7·43; N, 7·71 |
| **3e** | 90 hr | Fract. Cryst. dIPE | 74–5° (dIPE) | small white crystals | Found: C, 76·52; H, 7·63; N, 7·77 |
| **4e** | 48 hr | Fract. Cry + Col. Chrom. Cy/AcOEt 85:15 | 186–7° (dil EtOH) | white crystals | Found: C, 76·43; H, 6·97; N, 7·45 |
| **5e** | 48 hr | Fract. Cryst. EtOH | 163–4° (EtOH) | small white needles | Found: C, 75·97; H, 7·43; N, 7·71 for $C_{23}H_{26}N_2O_2$ Calc.: C, 76·21; H, 7·23; N, 7·73% |
| **2f** | 6 days | Fract. Cry + Col. Chrom Cy/AcOEt 95:5 | 104–5° (EtOH) | small white crystals | Found: C, 73·68; H, 7·24; N, 5·52 |
| **3f** | 6 days | Fract. Cryst. EtOH | 110–1° (EtOH) | white needles | Found: C, 73·53; H, 7·26; N, 7·31 |
| **4f** | 5 days | Fract. Cry + Col. Chrom. Cy/AcOEt 95:5 | 104–5° (dIPE) | whitish prisms | Found: C, 73·60; H, 7·08; N, 7·16 |

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|---|---|---|---|---|---|---|
| **5f** | 5 days | Fract. Cryst. EtOH | 124–5° (EtOH) | small white needles | for $C_{24}H_{28}N_2O_3$ | Found: C, 73·42; H, 7·09; N, 7·38 Calc.: C, 73·44; H, 7·19; N, 7·26% |
| **2g** | 12 hr | Fract. Cry + Col. Chrom. Cy/AcOEt 9:1 | 130–1° (PE/AcOEt) | yellowish crystals | | Found: C, 71·97; H, 5·43; N, 8·71 |
| **3g** | 12 hr | Fract. Cryst. EtOH | 168–9° (EtOH) | white-yellowish needles | | Found: C, 71·54; H, 5·84; N, 8·98 |
| **4g** | 6 hr | Fract. Cryst. MeOH | 241–2° (MeOH) | large colourless prisms | | Found: C, 71·31; H, 5·60; N, 9·03 |
| **5g** | 6 hr | Fract. Cryst. EtOH | 221–2° (EtOH) | white needles | for $C_{28}H_{27}N_3O_4$ | Found: C, 71·59; H, 5·80; N, 9·17 Calc.: C, 71·62; H, 5·80; N, 8·95% |
| **3j** | 30 days | — | colourless oil purified by column chromatography | | | Found: C, 76·53; H, 7·80; N, 7·23 |
| **5j** | 8 days | — | 128–9° (dIPE/PE) | small colourless prisms | for $C_{25}H_{30}N_2O_2$ | Found: C, 76·90; H, 7·79; N, 7·33 Calc.: C, 76·89; H, 7·74; N, 7·17% |
| **3k** | 35 days | — | 124–5° (EtOH) | colourless crystals | | Found: C, 77·50; H, 7·85; N, 7·01 |
| **5k** | 70 hr | — | 145–6° (EtOH) | colourless prisms | for $C_{26}H_{32}N_2O_2$ | Found: C, 77·63; H, 8·06; N, 7·04 Calc.: C, 77·19; H, 7·97; N, 6·93% |
| **3m** | 40 days | — | 145–6° (dIPE) | light yellow prisms | | Found: C, 80·17; H, 7·24; N, 6·12 |
| **5m** | 7 days | — | 177–8° (EtOH) | colourless needles | for $C_{31}H_{34}N_2O_2$ | Found: C, 79·58; H, 7·32; N, 6·14 Calc.: C, 79·79; H, 7·35; N, 6·00% |

We believe that this is the first evidence for the stereochemical consequences of the different importance of orbital interactions as in previously considered examples both LUMO/HOMO and HOMO/LUMO interactions give rise to the same *endo* stabilization.[10,17]

Since an electron attracting substituent on 4-aryl group lowers both HOMO and LUMO, it should further stabilize the *endo* t.s. (*e.g.* the *endo* selectivity is increased in the normal Diels-Alder reaction between cinnamic acid derivatives and cyclopentadiene[18]). E pyrazolones seem to support this assumption, but we believe that this effect will be more evident on rate constants.

## EXPERIMENTAL

M.ps are uncorrected. NMR spectra ($CDCl_3$ as solvent and TMS as internal standard) were run on a Perkin-Elmer R12 A spectrometer by Dr. A. Invernizzi Gamba; GLC were run by Dr. M. De Bernardi and microanalyses were performed by Dr. L. Dacrema Maggi.

*Materials. cis* and *trans* 1-Methyl-2-n-propoxyethylene was prepared according to ref 19 and separated as described in ref 2; for 4-arylidene-5-pyrazolones see ref 3.

cis[2,3] cis[3,4] (**2a**) *and* cis[2,3] trans[3,4] (**3a**) *2-n-propoxy-3-methyl-4-p-nitrophenyl-7 phenyl-2,3-dihydropyran* [2,3-c] *pyrazoles.* A mixture of *cis* 1-methyl-2-n-propoxyethylene (2·0 ml) and **1a** (1·00 g) was heated in a sealed tube at 80° for about 30 hr. The brick-red starting colour disappeared and the light yellow soln was evaporated. An homogeneous sample of the solid residue (about 50 mg) was monitored by NMR and the region of the anomeric proton proved it to be a mixture of **2a** and **3a** in the ratio 90:10. This mixture was chromatographed over kieselgel Merck with cyclohexane/AcOEt 9:1 as eluant. *cis*[2,3] *cis*[3,4] (**2a**) isomer was eluted first and crystallized from EtOH as small light yellow prisms, m.p. 102–3° (Found: C, 66·98; H, 5·92; N, 10·84. Calc. for $C_{22}H_{23}N_3O_4$: C, 67·16; H, 5·89; N, 10·68%.) The *cis*[2,3]*trans*[3,4] isomer (**3a**) was isolated as light yellow crystals, m.p. 158–9° from EtOH (Found: C, 66·91; H, 5·81; N, 10·84. Calc. for $C_{22}H_{23}N_3O_4$: C, 67·16; H, 5·89; N, 10·68%).

*Reaction of Z 1-phenyl-3-methyl-4-mesityliden-5-pyrazolone* (**1k** *Z*) *with* cis *and* trans *1-methyl-2-n-propoxyethylene.* (a) A mixture of **1k** Z (1·00 g) and *cis* ether (1·0 ml) was heated at 80° in a sealed tube for 35 days. From the cold suspension 0·95 g of the starting product was recovered and its identity was confirmed by IR. (b) A mixture of **1k** Z (0·91 g) and *trans* ether (1·0 ml) was heated at 80° for 70 hr. Unchanged material was recovered (0·87 g, 96%). After 35 days the yield of unreacted starting product was ⩾ 90%.

*Reaction of 4-arylidene-5-pyrazolones* (**1b–m**) *with* cis *and* trans *1-methyl-2-n-propoxyethylene.* In accordance with the method described for the reaction of **1a**, the adducts reported in Table 4 were obtained.

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