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1,3-DIPOLAR CYCLOADDITIONS OF ALIPHATIC DIAZO COMPOUNDS TO α,β-UNSATURATED CARBOXYLIC ESTERS - SPATIAL AND ELECTRONIC EFFECTS ON THE STERIC COURSE

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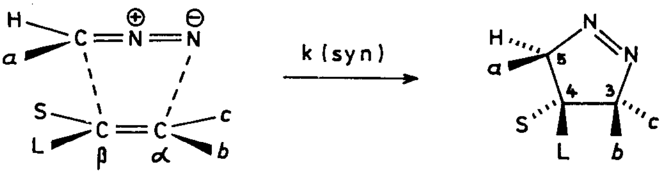
Aliphatic diazo compounds undergo oriented cycloadditions to α,β-unsaturated carboxylic esters such that the diazo carbon atom becomes attached to the β-position of the unsaturated esters; "anomalous" additions have also been observed (1). Information on the steric course of the "normal" addition, i.e. on the nature of the "two-planes" orientation complex of the reactants, can be gained from systems in which the diazo carbon atom and the β-carbon atom of the ester become chiral centers during the cycloaddition. We have treated monosubstituted diazomethanes with olefinic components in which *b* or *c* is an ester group and L and S symbolize large and small substituents.



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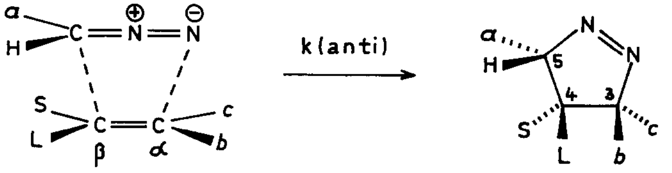

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The steric course is defined as syn when substituent *a* and the large substituent L end up cis in the 4- and 5-positions of the pyrazoline. As pointed out in the preceding communication (1), the interaction of the substituents *a* and L in the syn complex 1 can be of an attractive nature (π-overlap, dipole-dipole interaction) or of a repulsive nature (van der Waals strain). The *anti* cycloaddition takes place *via* the "two-planes" orientation complex **2** and leads to the pyrazoline in which a and L are *trans* to each other.

Although C-α also becomes chiral in the cycloaddition, only two stereoisomeric 1-pyrazolines are formed because the relative configuration of C-α and C-β is retained in the concerted 1,3-dipolar cycloaddition (2). If b or c is hydrogen, a tautomerisation occurs to a 2-pyrazoline, in which the relative configuration at C-4 and C-5 is unaltered. A complication is encountered if substituent a is also an ester group, but the use of different ester units allows one to sort out the pathways as reported (1).

The stereoisomeric 1- or 2-pyrazolines were separated by thick-layer chromatography or fractional crystallization. Their properties and their structural determination by n.m.r. spectra will be published elsewhere. The rate ratios k(syn) / k(anti) shown in the table were obtained by n.m.r. analysis directly on the mixture of cycloadducts.

Table. Pyrazoline Formation from Aliphatic Diazo Compounds and α,β-Olefinic Esters. Ratios of *Syn* and *Anti* 1,3-Dipolar Cycloaddition.

No.	Diazoalkan	α,β-Unsaturated Ester				$\frac{k(syn)}{k(anti)}$
	a	L	S	b	c	
1	CH_3	CO_2CH_3	H	CO_2CH_3	CH_3	0.23
2	CH_3	CO_2CH_3	H	CH_3	CO_2CH_3	0.28
3	CH_3	CO_2CH_3	CH_3	CO_2CH_3	CH_3	0.11
4	CH_3	CO_2CH_3	CH_3	CH_3	CO_2CH_3	0.72
5	C_6H_5	CO_2CH_3	H	CO_2CH_3	CH_3	0.32
6	C_6H_5	CO_2CH_3	H	CH_3	CO_2CH_3	0.85
7	$pCl-C_6H_4$	CO_2CH_3	H	CO_2CH_3	CH_3	0.39
8	CO_2CH_3	C_6H_5	H	H	$CO_2C_2H_5$	1.5
9	CO_2CH_3	C_6H_5	H	H	$CO_2C(CH_3)_3$	2.6
10	CO_2CH_3	C_6H_5	H	CO_2CH_3	H	0.64
11	$CO_2C(CH_3)_3$	C_6H_5	H	H	CO_2CH_3	0.47

The following conclusions can be drawn from the values:

1. In the addition of diazoethane ($a = CH_3$) to citraconic and mesaconic esters

(no. 1,2) the *syn* addition is ca. 4 times slower than *anti* addition. This preference reflects the van der Waals strain between a = CH_3 and L = CO_2CH_3 in the *syn* complex **1** and in its corresponding transition state.

2. Phenyldiazomethane + mesaconic ester (no. 6) shows k(syn) / k(anti) = 0.85. Though substituent a (C_6H_5) is larger than CH_3, the rate ratio increases because the π-overlap between C_6H_5 and CO_2CH_3 overcompensates for the increase of van der Waals strain. In the corresponding interaction of a = CO_2CH_3 and L = C_6H_5 (no. 8, 1.5) k(syn) becomes even larger than k(anti). However, on further increase in the van der Waals strain as illustrated in no. 11 with a = $CO_2C(CH_3)_3$ and L = C_6H_5, the ratio k(syn) / k(anti) drops to 0.47.

3. Dimethyl citraconate, with its *cis* ester groups, is no longer planar. The attractive π-overlap between a = C_6H_5 and L = twisted CO_2CH_3 (no. 5, 0.32) is smaller than in the case of dimethyl mesaconate (no. 6, 0.85). The same phenomenon is illustrated in the additions of methyl diazoacetate to *cis*- and *trans*-cinnamic ester (no. 10, 0.64 *vs.* no. 8, 1.5).

4. The ester groups of 2,3-dimethylmaleic ester are even more tilted than those of methylmaleic ester (citraconic ester). For a = CH_3 k(syn) / k(anti) = 0.11 (no. 3) compared with 0.23 (no. 1).

5. The van der Waals repulsion of bulky *cis* substituents in 3- and 5-position of the 1-pyrazoline (a and b in the *syn*, a and c in the *anti* addition) seems to influence the transition state energy also. For example, k(syn) / k(anti) = 1.5 for methyl diazoacetate + ethyl *trans*-cinnamate (no. 8) is increased to 2.6 when tert.-butyl *trans*-cinnamate (no. 9) is the dipolarophile. A decrease in k(anti) due to the interactions between 3- and 5-substituents may be responsible. The relatively high ratio of 0.72 in the system diazoethane + 2,3-dimethylfumaric ester (no. 4) can also be interpreted in terms of a repression of k(anti).

Thus, the ratio of the two steric courses, *syn* and *anti*, functions as a probe and gives insight into the interplay of steric and electronic substituent effects in the transition state of 1,3-dipolar cycloaddition. The effect of π-overlap and van der Waals strain was also disclosed in the addition of nitrones to styrene (3). Studies of the Diels-Alder reaction (4-6) brought to light similar phenomena that led to the *endo* rule and to the preference for *cis* disubstitution.

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