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ORIENTATION IN THE 1,3-DIPOLAR CYCLOADDITION OF DIAZOMETHANE WITH ALKYLETHYLENES

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ABSTRACT The regiochemistry of diazomethane cycloadditions with simple alkylethylenes, heretofore not reported, was investigated in the simplest case, diazomethane and propene. The products were 3- and 4-methylpyrazolines in 7.4/1 ratio, in accord with the diradical mechanism. This mechanism also accounts for the abnormal orientation in intramolecular cases and with bridgehead olefins

The purpose of this article is to show that the orientation in the 1,3-dipolar cycloaddition of diazomethane with alkylethylenes is that predicted by the diradical mechanism[1] The better diradical is $\underline{1}$, and therefore the predominant regioisomer should be the 3-substituted pyrazoline $\underline{3}$ and not the 4-isomer $\underline{4}$.
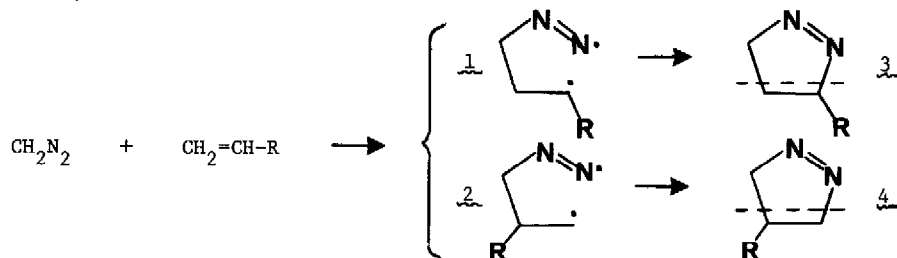
Attention was focussed on the problem by Padwa and Ku[2], who recently reported an intramolecular cycloaddition giving $\underline{5}$, which corresponds to regioisomer $\underline{4}$, incorrect for diradicals In an earlier study, Kirmse and Grassmann also obtained the 4-isomer $\underline{6}$ from an intramolecular cycloaddition[3]


Whether these orientations were normal or abnormal could not be decided because the literature contained no example of the regiochemistry of diazomethane with simple monoalkylethylenes[4-9] Therefore the simplest possible case, diazomethane and propylene, was investigated

To 2 ml liquefied propylene was added 27 ml diazomethane in ether (from nitrosomethylurea and 40% KOH; 0 78 M if 100% yield). The mixture was sealed into a stout 50 ml Teflon-lined screw-cap vial and kept for 6 days at room temperature in the dark. There was plenty of diazomethane color left at the end Analysis by GC-MS of the crude reaction mixture (8' x 3mm SP 2401 column at 100°, injector heater off) showed only two closely spaced peaks after solvent, ratio ca. 10·0, and no

others. Both had essentially the same mass spectrum (84, M^+, 69, M^+-CH_3, 56, M^+-N_2), showing that the sole volatile products were 3 and 4 (R = CH_3). To preserve the product ratio, volatiles were removed very carefully, the bulk through a 5" helix-packed column (heating bath not above 47°, residue ca. 1-2 ml), and last traces slowly at low vacuum (27 mm) without heat to constant weight, 0 99 g ($\geq$56% yield) Proton NMR (300 MHz, $CLCl_3$) showed a mixture of 3 and 4 (R = CH_3) in a 7 4/1 ratio, based on the methyl peak heights NMR of 3, δ 1.47 d, J = 7 Hz, CH_3, 4 63 m, $NCHCH_3$; 4 44 m, 4 26 m, CH_2N 1 86 m, 1 09 m, CCH_2C NMR of 4 0 90 d, J = 7 HZ, CH_3, 2 18 m, C_2CHCH_3 Suitable decoupling experiments established the connections in 4 ^{13}C NMR (with off-resonance) confirmed 3 as the principal isomer (ppm, multiplicity) C-3, 82 7, d, C-5, 75 8, t, C-4, 24 8, t, CH_3, 18 4, q Finally, the Raman spectrum showed N=N stretch at 1550 cm^{-1}

Thus the 3-substituted pyrazoline 3 is established as the normally favored regioisomer[10]. Simple alkyl is therefore like alkoxy[11] as an electron-donating dipolarophile substituent that orients correctly for the diradical mechanism In the present case, however, unlike the former one[11], PMO calculations[12] for the concerted mechanism predict that neither isomer will be greatly favored over the other

The kinetic advantage $\Delta\Delta G^*$ of 1 over 2, 1 22 Kcal/mole at 25°, is less than the difference in stabilization energy between secondary and primary alkyl radicals, 3 Kcal/mole[13], because both steric and electronic[1,11,14] factors produce a higher ratio of extended to cyclo diradicals in 1 than 2. Thus in 1, group R sterically interferes more with the cyclo form above than with the extended form, while the reverse is true for 2. Electronically also, the electron-releasing alkyl group destabilizes cyclo 1 vis-a-vis extended 1 by creating apposed like partial charges, cf 1 below, and also structure V in ref 11. These effects, undoubtedly small, seem quite appropriate in magnitude to account for 1 8 Kcal/mole in $\Delta\Delta G^*$


1 extended   2 extended   1
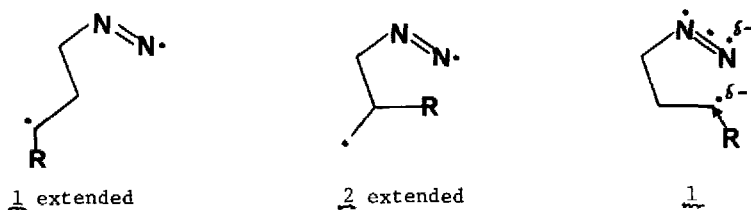
The question then arises, why do the intramolecular cycloadditions[2,3] lead to abnormal orientations? The simplest answer is that, in the formation of the first bond creating the diradical, closure to 7, a 5-membered ring (5-exo-trig)[15] enjoys a kinetic advantage over 8, a 6-ring (6-endo trig) This kinetic advantage need not be large, only $\geq$3 Kcal/mole (vide supra) It is indeed well known


9   8   7   5
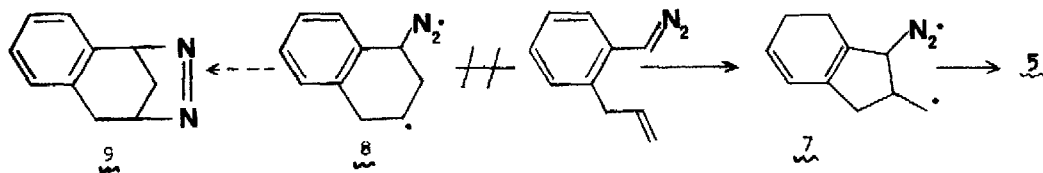
that in the cyclization of 5-hexenyl radicals, the kinetic product is the cyclopentylmethyl radical although the thermodynamic one is the cyclohexyl radical, only under the influence of powerful radical-stabilizing groups can the cyclohexyl radical be made the kinetically favored one[16]

The failure to obtain the more strained product 9 cannot obviously be ascribed to the preliminary appearance of product strain in a concerted transition state, because in a series of stereochemically similar intramolecular nitrone cycloadditions, both (3,2,1) and (3,3,0) bicyclic products were obtained[17], with control depending solely on the position of radical-stabilizing groups[1,14]

Another recent article reported the predominant regioisomers 10-14[18] The interesting feature

10	11	12	13	14
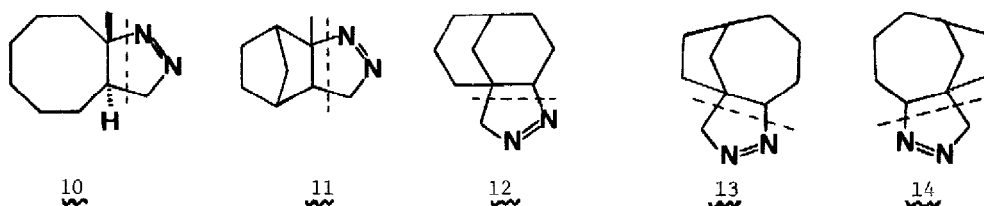
is that the strained trisubstituted olefins gave normal orientation except for the anti-Bredt olefins, which gave abnormal orientations The explanation for the reversal with bridgehead olefins is that e g diradical 15, which would normally be favored over its regioisomer 16 by only 3 Kcal/mole (the difference in stabilization energy between secondard and tertiary alkyl radicals)[13], is disfavored
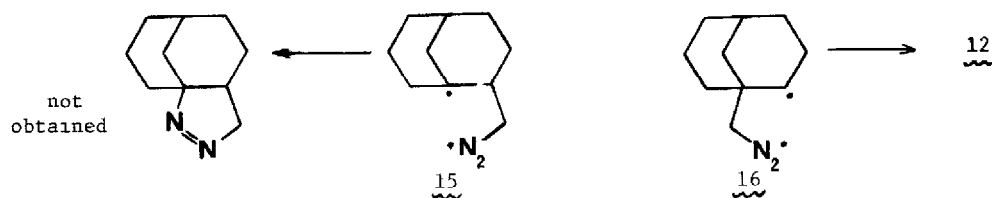

because small bridgehead radicals are destabilized[19], being constrained too far from planarity[20] Therefore the secondary diradical 16 is formed preferentially, leading to 12 as the major product; and similarly for 13 and 14 It is noteworthy that phenyl azide also orients normally with non-bridgehead olefins, and abnormally with bridgehead olefins[18]

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Footnotes and References

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, CH_2XCH_2Ph (X = 0, S)[7], CH_2Ph[9]
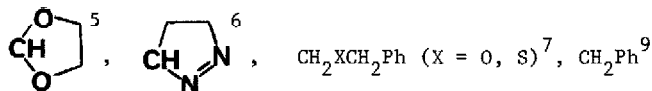
Cf the intramolecular analog which, like 5 and 6, gives reversed orientation
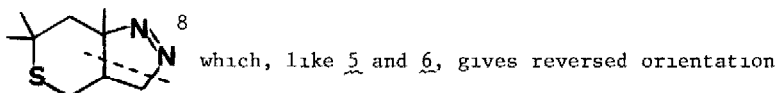
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