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Novel Thermal Tetracyclization by Intramolecular Azine "Criss-Cross" Addition

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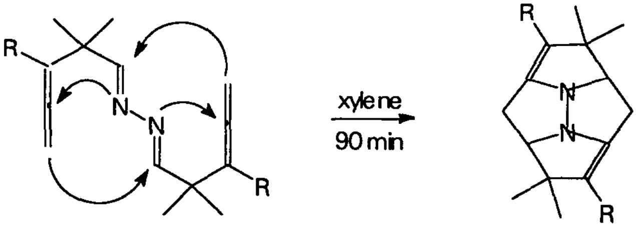
KEY WORDS: addition, azine, criss-cross, intramolecular, tetracyclization

Abstract: An easy, thermally initiated reaction of homoallenylazine **1** affords the new fused heterocyclic system **2** consisting of four five-membered rings in ten-membered carbocycle around the hydrazine moiety.

We report the easy, thermal isomeration of the substituted penta-3,4-dienal azine **1**[1] to the new tetracyclic structure **2**[2] (Figure 1).



1 R: benzyl 2

Figure 1

This new cyclization appears to be an example of the intramolecular "criss-cross" addition of aliphatic azine.

Intermolecular "criss-cross" additions of dienophiles with aryl[3] or trifluoromethyl substituted[4] azines are well documented. Their mechanism has been recognized as a succession of 1,3-dipolar cycloadditions via a nitrilimin intermediate[4,5,6,7].

Our intramolecular "criss-cross" cycloaddition (from **1** to **2**) is the first example involving an aliphatic azine. It is also the first example of such a reaction leading to a "central connection" under formation of four cycles around the central N-N bond.

The only intramolecular "criss-cross" reactions reported[8] till now involve *o*-allyl (or *o*-propargyl) aromatic azines and afford the product of a "lateral" cyclization (Figure 2).

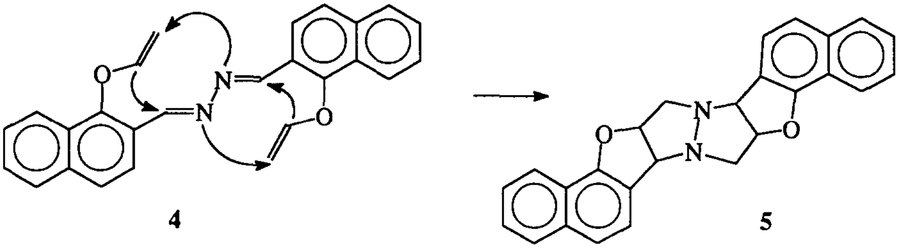


Figure 2

The distance between the azine group and the multiple bond as well as the thermodynamic stability of the cyclic product probably determine whether a "lateral" or a "central" connection is preferred (Figure 3).

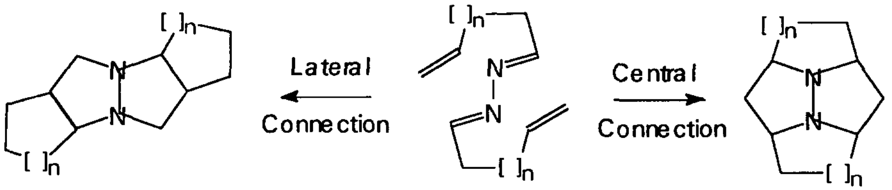


Figure 3

The structure of heterocycle **2** was determined by MS and NMR spectroscopy[2] and X-ray analysis[9]. There are two independent molecules in the asymmetric unit of the crystal with opposite configuration on the chiral centres (*4R*, *9R* and *4S*, *9S*). The hydrogen atoms at C4 and C9 are situated cis.

Future studies will show the scope and limitations of the central tetracyclization through the intramolecular "criss-cross"reaction of azines.

References and Notes

1. 3-Benzyl-2,2-dimethyl-penta-3,4-dienal azine

   Preparation

   Half an equivalent of hydrazine monohydrate is added dropwise to 3-benzyl-2,2-dimethyl-penta-3,4-dienal at room temperature in ether. The azine precipitates. It is filtrated and recrystallized in methanol (96% yield):MS, CI 397; mp 74-75°C;

   IR (KBr, cm^{-1}): 770 (m), 850 (s), 1030, 1040, 1380 (m), 1450 (m), 1495 (m), 1630 (s), 1935 (m), 2910 (s), 2950 (s), 3000 (m), 3350 (m);

   ^1H NMR (200MHz, acetone-d_6, δ) 1.3 (6H, s), 3.3 (2H , t, J=3Hz), 4.7 (2H, t, J=3Hz), 7.2 (5H, s), 7.5 (1H, s);

   ^{13}C NMR(50MHz, acetone-d_6, δ) 25.1, 35.4, 41.0, 78.4, 109.4, 126.7, 128.7, 129.8, 140.7, 167.5, 208.4.

   3-benzyl-2,2-dimethyl-penta-3,4-dienal was prepared according to the method of B. Thompson (U.S. 3,236,869; *Chem.Abst.*, **1966**, 64, 17428).

2. 2,7-dibenzyl-3,3,8,8-tetramethyl-11,12-diazatetracyclo[4.4.2.$0^{4,11}$.$0^{9,12}$]dodeca-1,6-diene.

   Preparation

   The azine is heated in refluxing xylene during 90 minutes. The toluene is evaporated and the resulting solid is recrystallized in methanol (95% yield): MS, CI 397; mp 124-126°C;

   IR (KBr, cm^{-1}): 705 (s), 745 (s), 755 (s,) 975, 1005 (m), 1025 (m), 1070, 1105 (m), 1350 (m), 1380 (m), 1425 (m), 1450 (s), 1465 (m), 1495 (s), 1595 (m), 1685 (m), 2930 (s), 3000 (m), 3040 (m);

   ^1H NMR (400MHz, $CDCl_3$, δ) 0.9 (3H ,s), 1.1 (3H, s), 2.1 (2H, m), 3.3 (2H, m), 3.7 (1H, dd), 7.2 (5H, m,);

   ^{13}C NMR (100MHz, $CDCl_3$, δ) 22.9 (C3a ,C8a), 24.9 (C5, C10), 28.2 (C3b ,C8b), 31.2 (C2a, C7a), 51.8 (C3, C8), 77.0 (C4, C9), 119.4 (C2, C7), 126.0 (C_p-Ar), 128.3 (C-Ar), 128.7 (C-Ar), 140.3 (C_q-Ar), 147.8 (C1, C6);

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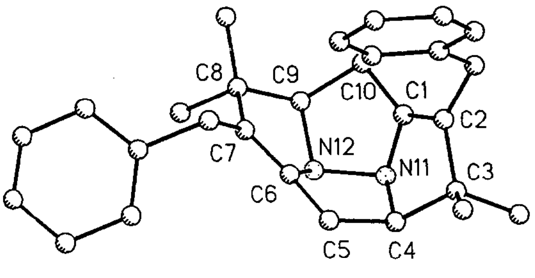
9. Three-dimensional structure of compound **2**:



The data were collected with KUMA KM-4 kappa axis four-circles diffractometer. The structure was solved by direct methods using SHELXS86 (Scheldrick, 1986) and refined by block-diagonal procedure using Syntex XTL system (Syntex AI, 1971). The compound is triclinic with $a=10.621(8)$, $b=10.602(7)$, $c=20.87(1)$ A, $\alpha=100.93(7)$, $\beta=92.89(7)$, $\gamma=90.45(6)°$, $V=2304$ A^3, S. G. P1, $Z=4$, $D_X=1.137$ gcm^{-1}, MoKα=0.71069 A, 7324 rfl. total, $R=0.046$ for 4413 obs. rfl. with $|Fo|>6\sigma(Fo)$. Selected interatomic distances and angles averaged for two independent molecules are: C1-C2 1.320, C2-C3 1.526, C3-C4 1.548, C4-C5 1.554, C5-C6 1.475, C6-C7 1.335, C7-C8 1.516, C8-C9 1.550, C9-C10 1.553, C10-C1 1.491, N11-N12 1.477, N11-C1 1.434, N11-C4 1.488, N12-C6 1.431, N12-C9 1.482 A; C1-C2-C3 108.6, C2-C3-C4 100.0, C3-C4-C5 117.5, C4-C5-C6 103.3, C5-C6-C7 138.0, C5-C6-N12 108.6, C6-C7-C8 108.0, C6-N12-C9 103.2, C7-C8-C9 100.6, C7-C6-N12 112.6, C8-C9-C10 117.9, C9-C10-C1 103.1, C10-C1-C2 138.5, C10-C1-N11 107.9, C2-C1-N11 112.7, C1-N11-N12 103.3, C1-N11-C4 103.0, C4-N11-N12 106.2, C6-N12-N11 103.2, C9-N12-N11 106.5°. The tables of atomic coordinates of all atoms including hydrogens, anisotropic temperature displacement factors and the full list of interatomic distances and angles were deposited and can be obtained upon request from the author ZŽ.

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