THE REVISED STRUCTURE OF THE THERMAL REARRANGEMENT PRODUCT OF 4-BENZYLIDENEAMINO-3-METHYL-5-STYRYLISOXAZOLE[1]

Andreina Corsico Coda and Giovanni Desimoni

Dipartimento di Chimica Organica, Università di Pavia, Via Taramelli 10, 27100 Pavia, Italy

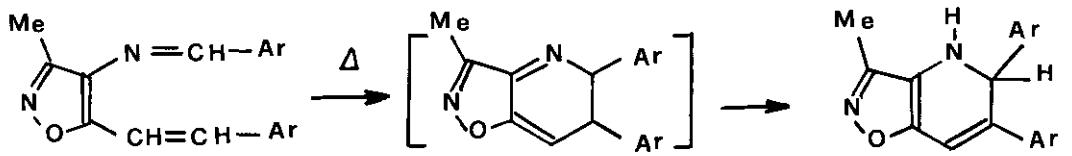
Alessandro Coda

Dipartimento di Genetica - Sezione di Cristallografia -, Università di Pavia, Via Taramelli 16, 27100 Pavia, Italy

Abstract - It had been claimed that the thermal rearrangement of 4-benzylideneamino-3-methyl-5-styrylisoxazole gave an isoxazolo-pyridine. This product was reinvestigated and shown to be 4-cinnamoyl-5-methyl-2-phenylimidazole, confirmed by X-ray analysis. A mechanism of formation is here proposed, involving the cleavage of the isoxazole N-O bond.

A recent paper by an Indian group[2] reported that 4-benzylideneamino-3-methyl-5-styrylisoxazoles undergo a thermal rearrangement to 5,6-diaryl-3-methyl-4,5-dihydroisoxazolo[4,5-b]pyridines through what was claimed to be the first example of electrocyclic ring-closure of an aza-1,3,5-hexatriene derivative (Scheme 1).

Scheme 1



Some of our results on the thermal rearrangement of 4,5-diarylideneaminoisoxazoles[3] suggested that the pathway proposed in Scheme 1 might be wrong since thermal rearrangements involving an isoxazole ring usually take place with the cleavage of its N-O bond.[4-6]

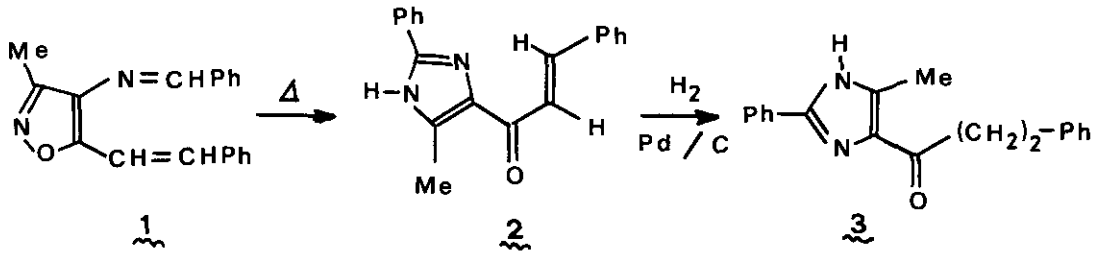
Thus 4-benzylideneamino-3-methyl-5-styrylisoxazole (1) was sinthesized[7] and refluxed either 3 h in diphenyl ether[2] or 7 days in xylene. Under both experimental conditions, the same product 2 was isolated (mp 211°C, ref[2] 212°C) in 60% yield from xylene by simple cooling.

The IR spectrum (KBr), along with NH absorption at 3400 cm^{-1}, showed a strongly

conjugated carbonyl group at 1658 cm^{-1}. The ^{1}H-NMR spectrum ($CDCl_3$) showed a methyl signal at 2.75 δ (3H), a broad NH at 9.5 δ (1H, made to disappear by shaking with deuterium oxide) and 12 protons in the aromatic region. Among these protons an AB system is discernible (2H - 7.81 and 7.88 δ; J=15.8 Hz), which is clearly due to a strong deshielded vinyl group in the trans configuration.

From these data and taking into account that thermal rearrangement of 3-methyl-5-phenyl-4-phenylazoisoxazole gave 4-benzoyl-5-methyl-2-phenyl-1,2,3-triazole,[9] we believe that 2 is 4-cinnamoyl-5-methyl-2-phenylimidazole and not an isoxazolopyridine. This structure was strongly supported by simple catalytic hydrogenation of 2 (C/Pd 10%, EtOH). At room temperature and pressure, within a few minutes, 5-methyl-2-phenyl-4-β-phenylpropionylimidazole (3) was obtained in a quantitative yield[10] (Scheme 2).

Scheme 2



1 2 3

For an unambiguous structural assignment, 2 was subjected to X-ray crystallographic analysis. The crystal data were as follows: Z=4 $[C_{19}H_{16}N_2O]$, MW=288.4, d=1.24 g cm^{-3}, light yellow crystals, space group $P2_1/c$, a=9.738(2), b=16.497(2), c=9.671(2) Å; β=96.63(1)°. The crystal had dimensions of 0.55x0.80x0.80 mm. Intensities for pairs of symmetry-related reflections were collected with a Philips PW 1100 computer-controlled four-circle diffractometer at room temperature using monochromatized MoKα radiation (λ=.7107 Å). Intensities were corrected for Lorentz and polarization factors and an empirical absorption correction in the range 1.0-1.2 was applied.[12] After averaging, out of 2730 independent reflections, collected up to 2Θ=50°, only 1970 with $I \geq 3\sigma(I)$ were processed. The R factor between equivalent intensities was 4.9%. The structure was solved by MULTAN,[13] and anisotropically refined by least-squares, with no weights. All the 16 hydrogen atoms were detected in the final ΔF-Fourier map. The observed coordinates for all hydrogens, taken from ΔF, were inserted and only their isotropic thermal factors refined. The final R was 3.88% (R=5.4% for all reflections). Scattering factors were those listed in the International Tables for X-ray Crystallography.[14] The results of the refinement are shown in the Figure which depicts the 20% probability ellipsoids.[15] Bond lengths and angles are reported in the Table.

The vinyl imidazolyl ketone system is largely planar but both phenyls are significantly twisted. In the solid state the tautomeric form of imidazole is frozen by a nitrogen-nitrogen intermolecular hydrogen bond ($N21^{i}$..H38-N20=2.976(2) Å), as shown in Figure which represents the sequence of hydrogen bonds involved in three units. The crystal structure fully supports our previous assumptions.

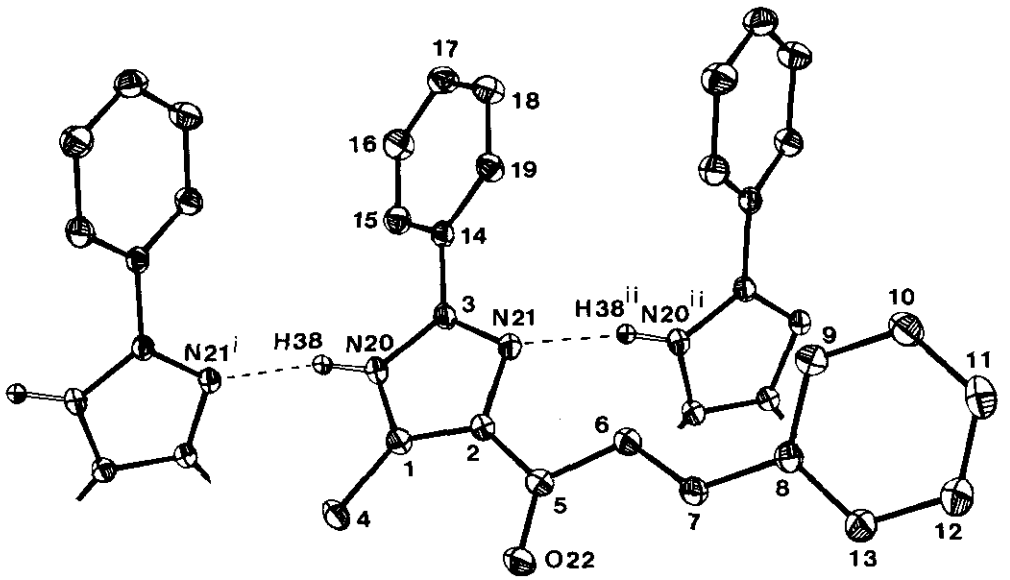


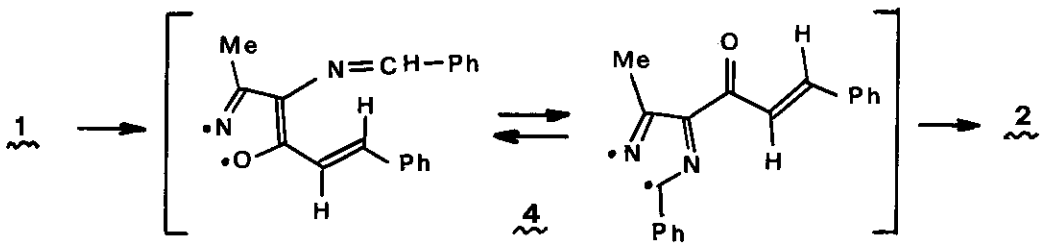
Table - Bond lengths and angles (deviations standard in parentheses).

C1-C2	1.372(2)	C5 -C6	1.474(3)	C14-C15	1.386(3)
C1-C4	1.495(3)	C6 -C7	1.328(2)	C14-C19	1.386(3)
C1-N20	1.373(2)	C7 -C8	1.457(3)	C15-C16	1.389(3)
C2-C5	1.464(3)	C8 -C9	1.393(3)	C16-C17	1.370(3)
C2-N21	1.393(2)	C8 -C13	1.394(3)	C17-C18	1.373(3)
C3-C14	1.472(3)	C9 -C10	1.383(3)	C18-C19	1.381(3)
C3-N20	1.369(2)	C10-C11	1.380(3)	N20-H38	0.993(1)
C3-N21	1.315(2)	C11-C12	1.373(4)		
C5-O22	1.227(2)	C12-C13	1.378(3)		

C4 -C1-N20	122.3(2)	C5 -C6 -C7	121.6(2)	C15-C14-C19	119.0(2)
C2 -C1-N20	105.3(2)	C6 -C7 -C8	127.1(2)	C14-C15-C16	119.8(2)
C2 -C1-C4	132.4(2)	C7 -C8 -C13	118.9(2)	C15-C16-C17	120.5(2)
C5 -C2-N21	121.4(2)	C7 -C8 -C9	122.8(2)	C16-C17-C18	120.0(2)
C1 -C2-N21	110.1(2)	C9 -C8 -C13	118.3(2)	C17-C18-C19	120.0(2)
C1 -C2-C5	128.4(2)	C8 -C9 -C10	120.5(2)	C14-C19-C18	120.6(2)
N20-C3-N21	111.1(2)	C9 -C10-C11	120.1(2)	C1 -N20-C3	107.9(1)
C14-C3-N21	124.3(2)	C10-C11-C12	120.1(2)	C2 -N21-C3	105.5(1)
C2 -C5-O22	121.4(2)	C11-C12-C13	120.1(2)	C1 -N20-H38	123.5(2)
C14-C3-N20	124.4(2)	C8 -C13-C12	120.9(2)	C3 -N20-H38	128.6(2)
C2 -C5-C6	117.0(2)	C3 -C14-C19	117.9(2)		
C6 -C5-O22	121.7(2)	C3 -C14-C15	123.1(2)		

The thermal rearrangement of 1 can be rationalized by a sequence involving homolitic cleavage of the isoxazole N-O bond to produce an intermediate 4 which closes again to 2 (Scheme 3).

Scheme 3



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10. 3: mp 157-8°C from cyclohexane. IR (KBr): 3250 (NH), 1640 cm^{-1} (C=O). ^{1}H-NMR ($CDCl_3$): 2.57δ s (3H, CH_3), 3.18δ m (4H, CH_2-CH_2), 7.0-8.0 δ m (10 H, aromatics), 10δ bb (NH, made to disappear with D_2O). Molecular formula $C_{19}H_{18}N_2O$ by microanalysis and mass spectrum. 4-Acetyl-5-methyl-2-phenylimidazole was shown to have $\nu_{C=O}$ at 1640 cm^{-1} (KBr).[11]
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