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ISOXAZOLE RING CLEAVAGE BY MEANS OF BIS(TRIMETHYLSILYL)MERCURY; PREPARATION OF SUBSTITUTED 1,5-HEXADIENES

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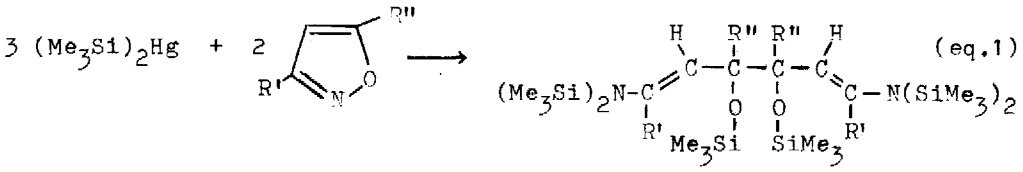
Pyridine and many derivatives thereof react with bis(trimethylsilyl)-mercury (I); the product of these reactions is generally an N,N'-bis(trimethylsilyl)tetrahydro-4,4'- or 2,2'-bipyridyl. The bipyridyls dissociate on warming to give stable N-trimethylsilylpyridinyl free radicals[1].

It seemed to us likely that other nitrogen heterocycles would react in an analogous manner; in the course of our investigations we observed a completely different type of reaction between (I) and isoxazole, on which we wish to report here. We find that isoxazole (and methyl-substituted isoxazoles) react with (I) in refluxing benzene (or on irradiation with a daylight lamp) in a molar ratio isoxazole : (I) of 2 : 3. The N - O bond of the isoxazole ring is cleaved, and the product is a highly-substituted 1,5-hexadiene (IV).



(IV)

Reaction times for the thermal reaction are typically 2-3 h; after separation of the mercury and removal of volatile materials at the water pump, products (IVa - IVc) can be distilled without decomposition as pale yellow viscous oils. Product (IVd) is isolated as colourless crystals; physical properties of compounds (IVa - IVd) are given in Table I. In each case the yield is almost quantitative.

The proposed structure is supported by a) osmometrically-determined molecular weight values; b) mass spectrometric studies (at 16 and 70 eV the base peak corresponds in each case to $(M/2)^+$); c) IR spectra ($\nu_{C=C}$ 1635 - 1640 cm^{-1}; cf. 1,5-hexadiene 1640 cm^{-1}); d) ^1H and ^{13}C NMR data (see Table). Since mixtures of the dl- and meso-forms of (IV) are obtained, each type of carbon atom in the hexadiene chain can give rise to two resonances; in most cases these are clearly resolved, as can be seen from the Table. The corresponding proton resonances are only resolved in the case of (IVc).

Table 1. Physical Properties of 1,6-bis bis(trimethylsilyl)amino -3,4-bis(trimethylsilyloxy)-1,5-hexadienes (IV)

IV	R'	R"	b.p. (°C/mm Hg)	MW [a]	^1H - NMR [b]	^{13}C - NMR [c]
a	H	H	$125\text{-}128/10^{-2}$	569 (576)	0.20(Me_3Si) 4.10(R") 5.08(H) 6.22(R')	136.2, 136.6(C-1, C-6) 115.6, 116.0(C-2, C-5) 77.9, 79.2 (C-3, C-4)
b	CH_3	H	$150/10^{-2}$	609 (604)	0.20, 0.23(Me_3Si) 1.77(R') 4.39(R") 5.23(H)	141.4, 142.5(C-1, C-6) 124.3 (C-2, C-5) 74.2, 75.1 (C-3, C-4) 22.7, 23.1 (CH_3)
c	H	CH_3	$145\text{-}150/10^{-2}$	605 (604)	0.22(Me_3Si) 1.40(R") 5.18(H) [d] 6.26(R')[d]	133.8, 134.3(C-1, C-6) 120.0 (C-2, C-5) 81.6, 81.8 (C-3, C-4) 22.9, 23.1 (CH_3)
d	CH_3	CH_3	[e]	632 (632)	0.20, 0.26(Me_3Si) 1.50(R") 1.94(R') 5.03(H)	[f]

[a] Molecular weight, determined osmometrically. Theoretical values in parentheses

[b] δ - Values, ppm, in C_6D_6 at 37°C, δ(TMS) = 0

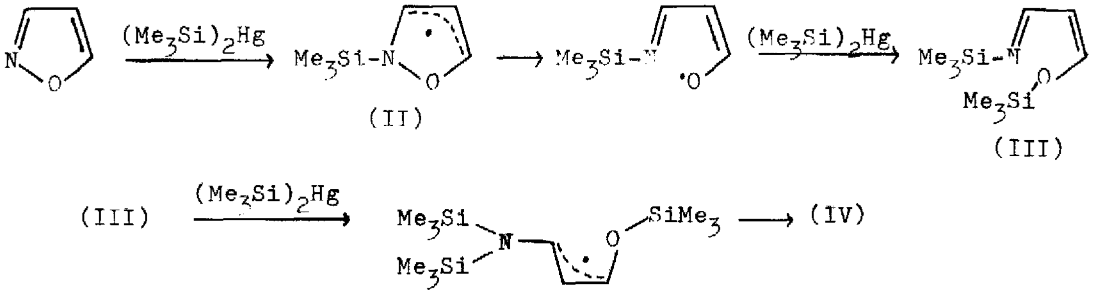
[c] δ - Values, ppm, at 45°C with C_6D_6 as internal lock or solvent. Shifts for Me_3Si - carbons not given. δ(TMS) = 0

d ^3J(H - H) 14.3 Hz; two smaller doublets with the same J - value are observed at δ - 5.21, 6.32. The intensity of these is ca. 30% of that of the larger doublets.

e m.p. 125-128°

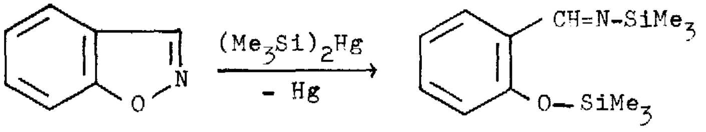
f Not measured

Scheme I shows the proposed reaction mechanism:



S C H E M E I

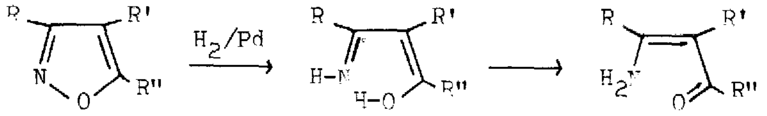
Radicals of type (II) have been observed during the reactions of (I) with isoxazole itself and with benz[d]isoxazole (indoxazene, V): in the latter case, the corresponding product of type (III) is the end product of the reaction, and has been isolated and characterised.



(V)

(eq. 2)

Products of type (III) could not be observed during the reactions of isoxazole and the methylisoxazoles. However, related products are known to be formed when isoxazoles are treated with other reducing agents. For example, Grignard reagents give magnesium analogues of (III) [2], while catalytic hydrogenation of isoxazoles leads via iminoalcohols to their stable tautomers, aminoketones (eq. 3) [3]. The latter reaction is of particular interest as it has recently been used in the total synthesis of nickel(II) octamethylcorphin [4].



(eq. 3)

Isothiazole reacts exothermically with (I): although the ^1H - NMR spectra indicated the formation of a substituted 1,5-hexadiene, attempted distillation of the product mixture in vacuo apparently lead to polymerisation, as only tarry residues were obtained.

We have tested the reactivity of the isoxazole system towards a number of other organometallic reagents, and find that $(Me_3Si)_2Hg$ occupies a unique position. No reaction occurs with di-tert.-butylmercury, $(Et_3Ge)_2Hg$, triethyltin hydride, trimethylchlorosilane/lithium or triethylsilane/di-tert.-butylperoxide.

Further investigations on the reactions of other nitrogen heterocycles with $(Me_3Si)_2Hg$ are in progress.

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