Pentacyclic Cage Formation in the Intramolecular [3 + 2]Addition of Tricyclic Nitrones

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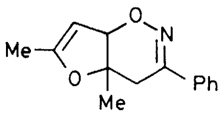
Despite their *anti*-configurations three tricyclic nitrones, on heating in toluene, undergo high-yield [3 + 2] intramolecular addition to give the corresponding pentacyclic cages; a co-product from heating two of the nitrones in tetrachloroethylene is the pyridyl ketone.

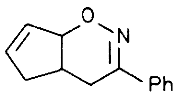
In the preceding communication[1] we showed that α-nitrosostyrene adds in a [1,3] fashion to the imino-group of the bicyclic oxazines (**1**) and (**2**) to give the tricyclic nitrones (**3**) and (**5**), respectively, a new type of reaction for nitrosoalkenes. We describe here reactions of these, in particular their isomerization to a highly heterosubstituted pentacyclic system.

Refluxing of (3) in toluene (15 h) gave an isomer (80%), m.p. 182.5—183 °C. Its i.r. spectrum had no absorption, other than for C–H, above 1500 cm^{-1}, and the most significant change in its ^{1}H n.m.r. spectrum was the absence of vinylic protons. These observations were indicative of a saturated structure, obtained by intramolecular reaction of the unsaturated ends of (3), and a surprising result in view of the *cis–anti–cis* configuration of (3). Accordingly we carried out an *X*-ray analysis and found the isomer to be the pentacyclic trioxadiaza-cage compound (**6**).

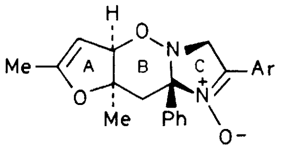
The *p*-nitronitrosostyrene adduct (**4**) cyclized similarly to give (**7**). The cyclopentadiene-derived system (**5**) was even more reactive, the dioxadiaza-cage compound (**8**), m.p. 149 °C, being quantitatively formed in 2 h.



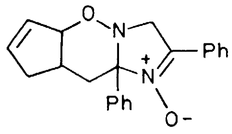
(**1**)



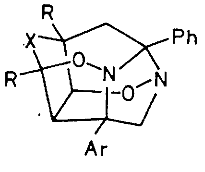
(**2**)



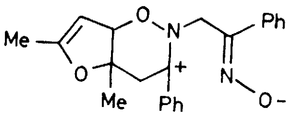
(**3**) Ar = Ph
(**4**) Ar = $p-NO_2C_6H_4$



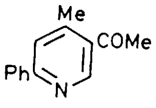
(**5**)



(**6**) R = Me , Ar = Ph , X = O
(**7**) R = Me , Ar = $p-NO_2C_6H_4$, X = O
(**8**) R = H , Ar = Ph , X = CH_2



(**9**)



(**10**)

The isomerization (**3**) → (**6**) requires in effect an *anti* → *syn* isomerization at the B/C ring junction, followed by the [2 + 3] dipolar addition of the enol ether double bond of ring A to the nitrone of ring C. The stereochemical change may involve opening of (3) to the stabilized dipole (**9**), which can epimerize at nitrogen and re-cyclize.† Though intramolecular additions of alkenes to nitrones are well known,[2] and of current importance in the synthesis of natural products,[3] this is the first example we are aware of involving an intramolecular reaction of a cyclic 'ene' with a cyclic nitrone.

When (**3**) was heated in tetrachloroethylene, rather than toluene, the yield of (**6**) dropped to 40% and was accompanied by a comparable yield of the ketone (**10**), m.p. 96 °C, corresponding to the loss of nitrosostyrene and water. Its formation was inhibited by the presence of Na_2CO_3, but traces of acid did not improve the yield. Its structure follows unequivocally from the following observations. Oxidation to the carboxylic acid and decarboxylation gave 2-phenyl-4-methylpyridine,[4] identical with the major product of phenylation of γ-picoline with benzoyl peroxide.[5] This identifies the phenyl and methyl positions. That of the acetyl group is established from the ^{1}H n.m.r. spectrum in which the only observed pyridine ring coupling of 0.9 Hz must be that of α,β' protons,[6] and from the off-resonance decoupled ^{13}C n.m.r. spectrum which showed a low field (α) carbon doublet.[7]

Since the oxygen in (**10**) must be that of ring A in (**3**) the separation of the Me groups in (**10**) represents a contraction by one atom of the carbon skeleton in the original dimethylfuran. We have no explanation for such a profound reorganization of the framework of (**3**), but we have determined that (**10**) does not come from the cage compound (**6**), nor from (**1**) [thus ruling out the sequence (**3**) → (**1**) → (**10**)], and that the phenyl group is that of ring B, since heating of (**4**) in tetrachloroethylene gave (**10**) as the only ketone.

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† If an equilibrium exists between the *anti* and *syn* forms, the amount of the latter must be very small since the ^{1}H n.m.r. spectrum of (3) is unchanged at 120 °C (tetrachloroethylene).