

REACTION OF TOSYLAZOCYCLOHEXENE WITH DIENOPHILES

Wanda Barbieri, Luigi Bernardi and Paolo Masi.

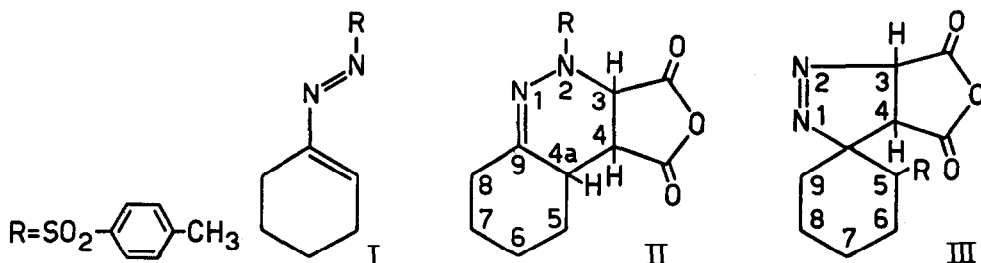
Farmitalia, Istituto Ricerche - Milano - Italy

Luciano Caglioti and Goffredo Rosini^x

Istituto di Chimica Organica e Industriale - Università di Bologna - Italy.

(Received in UK 24 February 1970; accepted for publication 5 March 1970)

We report briefly the peculiar behaviour toward dienophiles of tosylazoalkenes, whose synthesis has been described⁽¹⁾ recently. Treatment of tosylazocyclohexene (I) with maleic anhydride in benzene at room temperature gave, in 70-80 % yield, a compound (m.p. 162°) which was shown by analysis to be a 1:1 adduct. The NMR spectrum of the adduct, however, was not completely consistent with the assumed structure II, since it showed two doublets at δ 6.29 ($J = 9$ cps) and 4.49 ($J = 9$ cps), whereas a doublet and a quadruplet would be expected for protons H_3 and H_4 of formula II. The chemical shifts also could not be explained easily in terms of structure II.

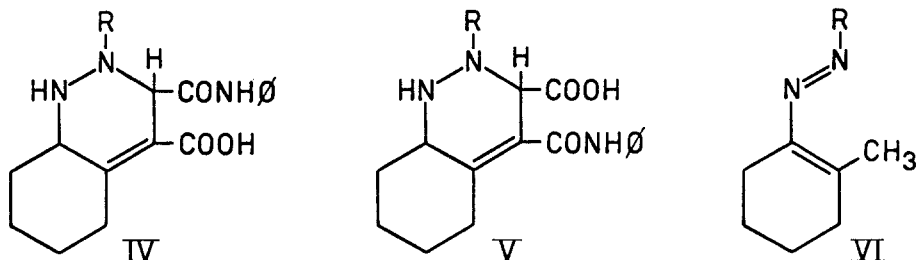


The chemical and physico-chemical data which have allowed us to assign the formula III to the adduct, a formula which has been confirmed by independent X-ray-structure determination described in the following communication, are reported here.

Although the absence of any observed coupling (at 60 and 100 Mcps) between H_4 and H_{4a} (formula II) could still be explained by assuming a diedral angle of 90°, the isolation of two different adducts from I and phenylmaleimide (mp. 195° and 163°), whose spectra did not show, in either case, a quadruplet for H_4 , made this explanation very unlikely. Moreover, these two adducts gave, on treatment with NaOH, followed by acidification, a single compound

^x With financial support of CNR. Contract N° 6900367115621.

(m.p. 214°) which resulted from the addition of one mole of H_2O and a proton shift, since the NMR spectrum no longer showed the downfield signal (see table 2), but only a singlet at δ 5.00. The IR spectrum showed the presence of two NH bands (no NH band was present in the IR spectrum of the adducts), but the compound was not basic. Using these data, structures IV and V were postulated, but neither could explain the UV spectrum which showed a maximum at $\lambda = 291 m\mu$ ($\epsilon = 9.500$ -EtOH).



Likewise, the treatment of the maleic anhydride adduct with NaOH afforded a dicarboxylic acid; the addition of water, however, was accompanied by a prototropic shift as shown by the disappearance of the downfield doublet and the appearance of a UV absorption maximum at $290 m\mu$ ($\epsilon = 10.000$ -EtOH). The ease of rearrangement was even more evident in the case of the acrylonitrile adduct; two compounds were formed as could be seen from the NMR spectrum of the crude product ($CHCN$ signals at 5.62 (dd) and 5.03 (t)), but they could not be obtained in pure form since crystallization resulted in the formation of a new compound having an isolated CH_2 group, an NH group and UV maximum at $\lambda = 286 m\mu$ ($\epsilon = 11.500$ EtOH).

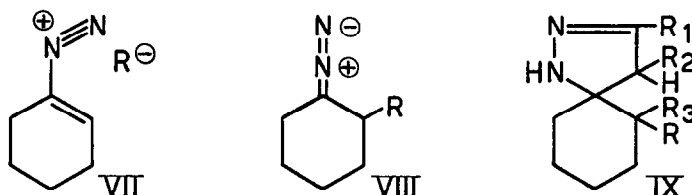
Since it was apparent that these rearrangements greatly hindered the study of the structure of the adducts the synthesis of compounds without the pertinent proton and which, therefore, could not undergo prototropic shift, was undertaken. Addition of maleic anhydride to 2-methyl-1-tosylazocyclohexene (VI) afforded a 1:1 adduct (mp. 180°), which, however, by treatment with NaOH gave a dicarboxylic acid similar to that obtained from the adduct of I with maleic anhydride ($\lambda_{max} = 293 m\mu$) ($\epsilon = 10.200$ -EtOH). This result, although negative, definitely proved that : i) C_2 -cyclohexyl proton (H_{4a} of formula II) was not involved in the rearrangement : ii) structure II, IV and V were excluded.

Addition of methacrylonitrile to I followed by treatment with H_2SO_4 yielded two amides, stable to alkaline and acid treatment and therefore suitable for structure determination. Catalytic reduction (PtO_2 -AcOH) of both these amides afforded a dihydro compound which easily reverted to the starting material by aerial oxidation or, instantaneously, by treatment with $Hg(OAc)_2$.

This result can be explained only by assuming that an azo function is present in the adduct which by hydrogenation yields an unstable hydrazo-derivative and the toluensulphonyl

residue must therefore be bound to carbon and not to nitrogen.

The mechanism of the reaction is under investigation : as a working hypothesis we assume that tosylazocyclohexene (I), possibly by preliminary dissociation into the diazonium tosylsulfinate VII, rearranges to 2-tosyldiazocyclohexane VIII. The latter adds to the activated double bond of the dienophile to give, according to a general reaction of aliphatic diazo-compounds⁽²⁾, Δ^1 -pyrazolines (e.g. formula III), which are in perfect accord with the NMR spectra : the resonance of the allylic, doubly-activated, H_3 is at a low field, whereas H_4 is at a higher field. Furthermore, a double doublet (1 H), in the region of δ 3.8 - 4.2, which is observed in the spectra of all the adducts of I, can be assigned, according to formula III, to the axial $CH-R$, coupled with the vicinal CH_2 ; the absence of these signals in the adducts of VI (CH_3 singlet at δ 1.55) confirms the position of the tosyl residue.



The observed prototropic shifts in alkaline conditions is also easily understood on the basis of formula III, since it is known that Δ^1 -pyrazolines easily rearrange to Δ^2 -pyrazolines (IX)⁽²⁾; the NMR spectrum and particularly the UV spectrum⁽³⁾ are in accord with a Δ^2 -pyrazoline structure.

A complete discussion of the NMR spectra and of the stereochemistry of these compounds will be reported in a later paper. We are at present investigating : 1) the extension of the reaction to different nucleophiles and to other substrates known to react with diazoalkanes; ii) the preparation of novel spiro-cyclopropanes by pyrolysis of the "adducts".

REFERENCES

- 1) L. Caglioti, P. Grasselli, F. Morlacchi and G. Rosini, *Chem. & Ind.* (London), 25 (1968).
- 2) C.H. Jarboe - Pyrazolines and Pyrazolidines; "The Chemistry of Heterocyclic Compounds". (A. Weissberger ed.) Interscience Publishers. New York - p. 195 (1967).
- 3) The UV spectrum⁽⁴⁾ of methyl Δ^2 -pyrazolidine-3-carboxylate presents a maximum at λ = 293 m μ (ϵ = 10.200).
- 4) J.A. Moore, *J. Org. Chem.* 20, 1607 (1955).

TABLE 1

Relevant NMR signals^x of some "adducts" (Δ^1 -pyrazolines).

| Diene | Dienophyle | H ₃ | H ₄ | CH-R |
|-------|-----------------------------|----------------|--|--|
| I | maleic anhydride | 6.29 d J=9 | 4.49 d J=9 | 4.30 dd J _{aa} =12 J _{ae} =4 |
| I | phenylmaleimide | | | |
| | m.p. 195° | 6.19 d J=8.5 | 4.27 d J=8.5 | 4.23 dd J _{aa} =10 J _{ae} =4 |
| | m.p. 163° | 6.19 d J=8.5 | 3.27 d J=8.5 | 4.10 dd J _{aa} =9 J _{ae} =5 |
| I | metacrylamide ^{xx} | | | |
| | m.p. 212°-5° | | 3.33 and 1.47 J _{gem} = 13.5 | 3.80 dd J _{aa} =9 J _{ae} =3.5 |
| | m.p. 194°-5° | | 2.82 and 2.60 J _{gem} = 13.5 | 3.80 dd J _{aa} =10.5 J _{ae} =3.5 |
| VI | maleic anhydride | 6.38 d J=9.5 | 4.33 d J=9.5 | - - |

^x The spectra were obtained on a spectrometer Varian A 60, in DMSO-d₆, using TMS as internal standard; the chemical shifts are expressed as δ and the coupling constants in Hz.

^{xx} In pyridine-d₅.

TABLE 2

Relevant NMR signals^x of some Δ^2 -pyrazolines (VIII).

| R ₁ | R ₂ | R ₃ | H ₄ | CH-R |
|----------------|-----------------------------------|-----------------|--|---|
| COOH | CONHC ₆ H ₅ | H | 5.06 s | 3.64 dd J _{ae} =J _{ee} =6 |
| COOH | COOH | H | 4.97 s | 3.43 dd J _{ae} =J _{ee} =7 |
| CN | H | H | 2.69 d and 3.82 d J _{gem} = 17 | 3.55 dd J _{ae} =J _{ee} =7 |
| COOH | COOH | CH ₃ | 4.83 s | - - |