Tetrahedron. Vol. 26, pp. 4963 to 4968. Pergamon Press 1970 Printed in Great Britain

ACYL MIGRATION TO N-OXIDE OXYGEN

MECHANISM OF THE THERMAL DECOMPOSITION OF β-PHENYLAZOXY TOSYLATE

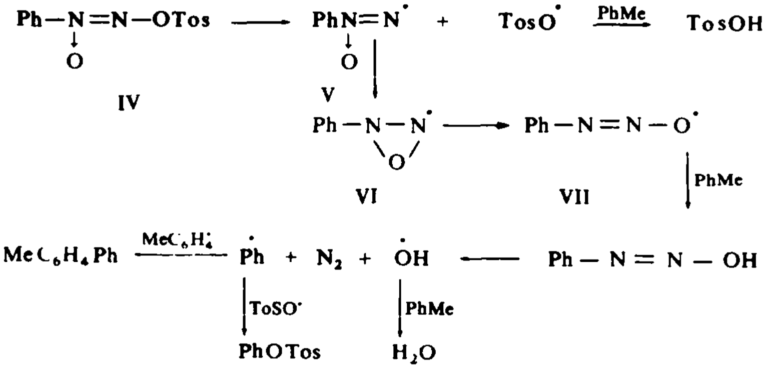
L. A. NEIMAN, V. S. SMOLYAKOV, YU. S. NEKRASOV and M. M. SHEMYAKIN
Institute for Chemistry of Natural Products, USSR Academy of Sciences, Moscow, USSR

(*Received in the UK* 17 *March* 1970; *Accepted for publication* 11 *May* 1970)

Abstract—Tosyl migration to N-oxide oxygen in the thermal decomposition of β-phenylazoxy tosylate has been demonstrated with the aid of ^{18}O. The structure of β-phenylazoxy tosylate has been confirmed also using ^{18}O and ^{15}N tracer techniques.

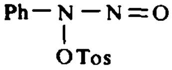
EARLIER we showed by means of ^{18}O that acetoxylation of aldonitrones $R{-}CH{=}N(\rightarrow O)R'$ is accompanied by O,O′ migration of the acetyl residue, yielding the corresponding N-acyloxyamides $RCON(OAc)R'$.[1] These findings were interpreted as evidence of the intermediate formation of the compounds $RC(OAc){=}N(\rightarrow O)R'$ (I) which are converted to the end products by acyl migration. However, the recently discovered ability of nitrones to add acetoxy radicals with the formation of nitroxide radicals of the type $RCH(OAc){-}N(-\dot{O})R'$ (II)[2] showed that one had to take into account a possible alternate mechanism whereby acyl migration occurs in radical II, rather than in compound I. Although such an assumption was less probable than the former, it could not be dismissed off hand and in this connection our attention was attracted to the nitrogeneous analogs of acetoxynitrones (I), namely azoxy esters of the type $RN(\rightarrow O){=}N{-}OAcyl$ (III) because in this case one could also expect migration of the acyl residue to the N-oxide oxygen. As a rule, azoxy esters (III) are unstable,[3] the only exception being azoxy tosylates (III, Acyl = Tos),[4] which are

SCHEME I

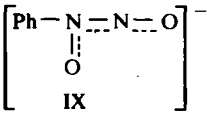


thermally stable up to 110°, when they decompose largely to the tosylates ROTos.[5] The azoxy tosylates were interesting the more so that the proposed decomposition mechanism of β-phenylazoxy tosylate (IV)* in boiling toluene[5] (see Scheme 1) involves the intermediate formation of an oxadiaziridinyl radical (VI), in other words, migration of the azoxy oxygen takes place from one N atom to the other. However, by analogy with C-acetoxynitrones we considered it more likely that the first stage of the thermal decomposition of azoxy ester (IV) should be migration of the tosyl residue to the more negative oxygen of the N-oxide grouping with the formation of N-nitroso-O-tosyl-N-phenylhydroxylamine (VIII).

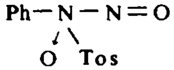
But before attempting an experimental test of this assumption it was desirable to provide a more convincing proof of the structure of azoxy tosylate (IV) than that given by Stevens.[4-6] In fact the product of the reaction of *p*-toluenesulfonyl chloride with the ambident N-nitrosophenylhydroxylamine anion (IX) could *a priori* possess any of the following four structures—azoxy ester (IV), N-nitroso-O-tosyl-N-phenylhydroxylamine (VIII), N-nitrosamide-N-oxide (X) and N,N'-dioxide (XI). Formation of the azoxy compound PhN(→O)=NR (XII)[4] on reaction with Grignard reagent excludes structures X and XI. However, contrary to Stevens' opinion, this is still insufficient for choosing between structures IV and VIII. Leaving for the time being detailed discussion of the radical mechanism he proposed for the reaction with RMgX, we shall only mention that in the homolytic rupture of the N—O bond in the case of the azoxy ester (IV), the ambident radical V will be formed and in case of the N-nitroso ester (VIII), the ambident radical VII will be formed. Their interconversion is quite possible via the oxadiaziridinyl radical (VI)† and Stevens himself assumes the rearrangement V → VI → VII to take place in the thermal decomposition of β-azoxy tosylate (see Scheme 1). However, the reverse course VII → VI → V is just as possible and attack of (V) by Ph· would yield the azoxy compound (XII). Hence their formation cannot serve as criterium for choosing between structures IV and VIII.


$\mathrm{Ph{-}N(OTos){-}N{=}O}$

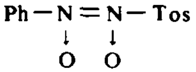
VIII


$[\mathrm{Ph{-}N(\overset{\cdot\cdot}{=}O)\cdots N\cdots O}]^-$

IX


$\mathrm{Ph{-}N(\to O)(Tos){-}N{=}O}$

X


$\mathrm{Ph{-}N(\to O){=}N(\to O){-}Tos}$

XI

The following new proof of the azoxy ester structure IV for the product of the reaction between TosCl and the ammonium salt of N-nitrosophenylhydroxylamine (cupferron) has been obtained by us with the aid of ^{15}N and ^{18}O. This product synthesized from Ph^{15}NHOH (55 at % ^{15}N)‡ could have either structure XIII or XIV. The choice between the two was made from a comparison of the IR spectrum of the labelled compound with that of its unlabelled counterpart. The peak intensity of the 1295 cm^{-1} absorption decreases by *ca* 1/2 and a new maximum appears at 1268 cm^{-1} (isotopic shift = 27 cm^{-1}), while the spectra of the two compounds are identical

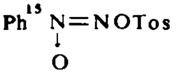
---

* Stevens[4-6] named this compound N-phenyl-N'-tosyloxidiimide-N-oxide, whereas according to Woodward and Wintner's nomenclature[7] it is tosyloxazonylbenzene. Our name is more convenient since it properly refers these substances to the class of azoxy compounds.

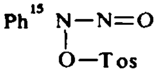
† It should be mentioned that rearrangement of azoxy compounds to oxadiaziridines[8] occurs on irradiation by UV, i.e. under conditions highly favourable for radical formation.

‡ This synthesis was carried out under the conditions and with the yield reported by Stevens[4] for the unlabelled compound.

in all other regions. The shift of this peak establishes the presence of an azoxy group (stretching frequency region 1250–1310 cm^{-1}) in the compound in question, whereas if formula XIV were correct one should have expected an isotopic shift characteristic of N—N (the N—N frequency for nitrosamines lies in the region 1050 cm^{-1}) and of NO bonds (absorption region of the N—O ester bond 800–900 cm^{-1}). These data were supplemented by results with ^{18}O. The starting compound in this case was PhNH^{18}OH.[9] containing 22 at % ^{18}O and converted into cupferron-^{18}O (XV).*

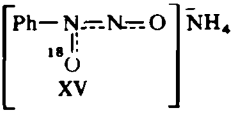

$\mathrm{Ph}\underset{\substack{\downarrow\\ \mathrm{O}}}{^{15}\mathrm{N}}{=}\mathrm{NOTos}$

XIII

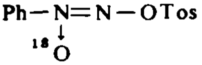

$\mathrm{Ph}\underset{\substack{|\\ \mathrm{O{-}Tos}}}{^{15}\mathrm{N}}{-}\mathrm{N{=}O}$

XIV

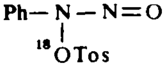
Two formulas XVI and XVII are possible for the reaction product of XV with TosCl, the choice between them being made from the results of the reaction of this product with 1 mole PhMgBr (in methylene chloride—abs ether mixture without subsequent treatment with water). Under these conditions the main reaction product (yield over 50 %) turned out to be PhOTos, not containing excess ^{18}O. From this it follows that, firstly, the compound in question does have an O-tosyl group (and this is further argument against formulas X and XI), and secondly, the tosyl residue is attached to the unlabelled O atom, hence excluding structure XVII and unambiguously proving the validity of the azoxy ester structure XVI.


$\left[\mathrm{Ph{-}}\underset{\substack{\vdots\\ ^{18}\mathrm{O}}}{\mathrm{N}}\mathrm{{\cdots}N{\cdots}O}\right]^{-}\mathrm{NH_4}$

XV


$\mathrm{Ph{-}}\underset{\substack{\downarrow\\ ^{18}\mathrm{O}}}{\mathrm{N}}\mathrm{{=}N{-}OTos}$

XVI


$\mathrm{Ph{-}}\underset{\substack{|\\ ^{18}\mathrm{OTos}}}{\mathrm{N}}\mathrm{{-}N{=}O}$

XVII

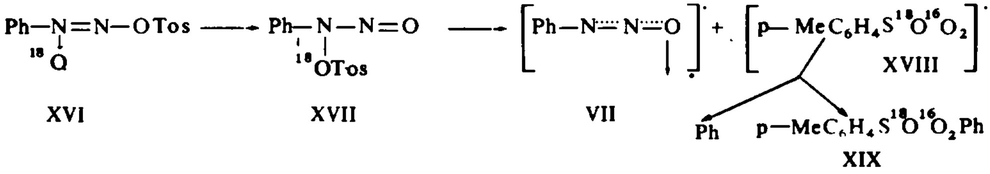
The azoxy-^{18}O ester XVI (22 ± 1 at % ^{18}O) was used to study the thermal decomposition mechanism. Refluxing of this compound in toluene afforded the phenyl tosylate XIX (see Scheme 2) containing 21 ± 1 at % ^{18}O that was equidistributed between all three O atoms. This last conclusion was arrived at from the mass spectrum which bore witness to the fact that the tosyl cation contained 13 ± 1 at % ^{18}O (i.e. 2/3 of the initial amount), direct formation of this cation from the molecular ion (rather than from TosO$^+$) being confirmed first, by the presence of the metastable *m/e* 97 peak and secondly, by the absence of the TosO$^+$ peak (*m/e* 171) in the spectrum. These results shed light on the thermal decomposition mechanism of β-phenylazoxy toxylate (XVI). If phenyl tosylate would have resulted directly from homolytic rupture of XVI at the Ph—N and N—O bonds with subsequent recombination of the Ph· and TosO· radicals, or via the cyclic transition state XX, the resultant product would not have contained excess ^{18}O. With an intramolecular mechanism of the thermal decomposition through the cyclic transition states XXI and XXII, whereas if only the phenyl tosylate would contain the ^{18}O label, it would be entirely at the ester oxygen in the case of XXI and only at the SO$_2$ group in the case of XXII. Hence, azoxy tosylate (XVI) transforms to phenyl tosylate (XIX) not directly, but after preliminary isomerization to N-nitroso-O-tosylphenylhydroxylamine (XVII), in which the tosyl residue is bound already with the labelled O atom and which is practically the sole precursor of phenyl

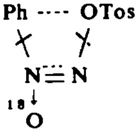
---

* Cupferron-^{18}O was prepared by analogy with the known synthesis of the unlabelled compound (Organic Syntheses, Coll. vol. I, p. 177, N.Y. 1946).

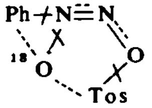
tosylate (XIX). As can be seen from the equal distribution of the ^{18}O label further transformation of the nitroso ester (XVII) to the phenyl tosylate (XIX) involves homolysis of the N—O bond and formation of the tosyloxy radical (XVIII), wherein all O atoms are chemically equivalent. Another product of this homolysis is the radical VII, stemming directly from compound XVII without oxygen migration. Subsequent decomposition of the radical VII to Ph· apparently proceeds by Stevens' mechanism (see Scheme 1), the reaction between the phenyl and tosyloxy (XVIII) radicals affording phenyl tosylate (XIX).*

SCHEME 2

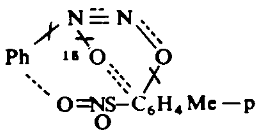




XX



XXI



XXII

It should be stressed that although the acyl migration we have discovered explains quite simply the formation of all the thermolytic products of β-phenylazoxy tosylate and makes superfluous the supposition of oxygen migration in the azoxy grouping, this in itself does not preclude the possibility of interconversion of the radicals V and VII via the oxadiaziridinyl radical VI.

It is noteworthy that the rearrangement of β-phenylazoxy tosylate (IV) to N-nitroso-O-tosyl-N-phenylhydroxylamine (VIII), in all probability occurs also under mass spectrometric conditions. Since the mass spectrum of the azoxy ester (IV) can be taken only at 100°,† one cannot fully exclude the possibility that the actual cause of the rearrangement under such conditions is the effect of temperature rather than of the electron impact.‡ There is no molecular ion peak in the mass spectrum of β-phenylazoxy tosylate IV (see Table 1), the ion of largest mass $(M\text{-}30)^+$ arising from elimination of NO. Assignment of the peaks was carried out by comparison of the mass spectra of the non-labelled IV, ^{15}N-labelled XIII and ^{18}O-labelled XVI compounds (Table 1). It is to be noted that in the two latter cases the eliminated NO group contained no excess heavy isotope. Most likely such fragmentation is the result

---

* Here the radical mechanism is assumed for the decomposition of compound XVII although it should be pointed out that reaction by an ion pair mechanism could not be completely excluded.

† At this temperature β-phenylazoxy tosylate does not suffer thermal decomposition, as can be seen from the unvariability of the mass spectrum with time (1 hr). However rapid decomposition occurs at 115°: the *m/e* 262, 137, 107 and certain other peaks decreases (to 1/20–1/30 the initial intensity in 1 hr), whereas at the same time there is a 15-fold increase in intensity of the *m/e* 248 $(PhOTos)^+$ peak.

‡ Such an assumption holds only for the case of very rapid thermal rearrangement in the cristalline state.

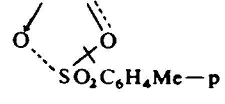
of preliminary isomerization of the azoxy ester (IV) to N-nitroso-O-tosylphenylhydroxylamine (VIII), but in principle the rearrangement IV → X may also serve for explanation of NO elimination. The second mass spectrometric fragmentation route of the azoxy ester (IV) involves elimination of the tosyl residue with the formation of the $(PhN_2O_2)^+$ cation (*m/e* 137). The available data do not permit solution of the question as to whether this cation directly forms from the molecular ion of the azoxy ester (IV) or the latter first isomerizes to the nitroso ester (VIII) or the intermediate form (X).

TABLE 1. *m/e* VALUES AND RELATIVE INTENSITIES (IN % OF I_{max}) OF THE PRINCIPAL PEAKS IN THE MASS SPECTRA OF PHENYLAZOXY TOSYLATE (IV), IV-^{15}N (XIII) AND IV—^{18}O (XVI) AT 100°

Compound \ *m/e*	264	263	262	248	172	157	156	155	139	138	137
IV	0.6	1.0	6.0	1.5	1.2	4.5	7.0	70	2.0	1.5	7.0
XIII	0.8	4.9	2.4	1.5	1.2	4.5	7.0	70	2.1	4.9	2.8
XVI	1.5	0.7	4.5	1.5	1.2	4.5	7.0	70	4.0	0.7	5.0

Compound \ *m/e*	123	122	121	109	108	107	106	105	92	91	77
IV	2.0	1.2	2.0	8.0	7.0	35	2.0	7.0	12	100	62
XIII	2.0	1.2	2.0	3.7	25	13	1.7	1.3	12	100	62
XVI	2.0	1.2	2.0	9.0	4.5	25	1.0	3.0	12	100	62

The results described in this paper show that systems of the type —N(→O)═X—OAcyl (A) are actually capable of transforming into systems of the type —N(OAcyl)—X═O (B), such transformation in light of the above said apparently being possible also for acetoxynitrones (X═C—; Acyl═Ac). In the latter case the most stable is system B, whereas in the case of the azoxy tosylate (X═N; Acyl═Tosyl) such a system is so unstable that it undergoes breakdown under the same conditions under which it forms from A. Possibly this too may be the case in the nitrosylation of N,O-dibenzoylhydroxylamine[10] in which the apparently formed N-nitroso ester (B: X═N; Acyl═PhCO) immediately decomposes to $(PhCO)_2O$ and N_2O. As for the mechanism of isomerization of β-phenylazoxy toxylate (IV) into the nitroso ester (VIII), this reaction apparently involves O,O′ migration of the acyl residue to the more negative oxygen atom (like that in the case of C-acetoxynitrones) and proceeds via the 5-membered cyclic transition state (XXIII).



XXIII

REFERENCES

[1] L. A. Neiman, S. V. Zhukova, L. B. Senyavina and M. M. Shemyakin, *Zh. Obshch. Khim.* **38**, 1480 (1968)
[2] E. J. Janzen and B. J. Blackburn, *J. Am. Chem. Soc.* **90**, 5909 (1968)
[3] E. H. White and D. W. Grisley, *Ibid.* **83**, 1191 (1961)

[4] T. E. Stevens, *J. Org. Chem.* **29**, 311 (1964)
[5] E. A. Dorko and T. E. Stevens, *Chem. Commun.* 871 (1966)
[6] T. E. Stevens, *J. Org. Chem.* **32**, 1641 (1967)
[7] R. B. Woodward and C. Wintner, *Tetrahedron Letters* 2689 (1969)
[8] S. S. Hecht and F. D. Greene, *J. Am. Chem. Soc.* **89**, 6762 (1967)
[9] L. A. Neiman, V. I. Maimind and M. M. Shemyakin, *Tetrahedron Letters* 3157 (1965)
[10] T. Koenig, T. Fithian, M. Tolela, S. Markwell and D. Rogers, *J. Org. Chem.* **34**, 952 (1969)