PREPARATION AND ISOMERIZATION OF 3- AND 4-PHENYLFUROXANS

L. I. Khmel'nitskii, T. I. Godovikova,
N. A. Ruleva, B. N. Khasapov,
and S. S. Novikov*

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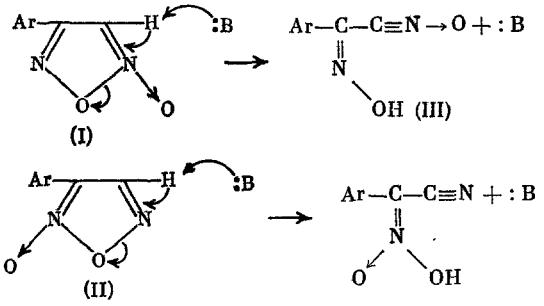
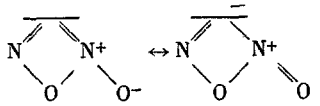
Monoarylfuroxans undergo isomerization with opening of the heterocyclic ring on treatment with bases, which remove a proton from the heterocycle:



4-Phenylfuroxan (I, Ar = Ph) reacts much more readily with bases than does 3-phenylfuroxan (II, Ar = Ph). Thus, (I) isomerizes readily at room temperature in sodium carbonate solution [1], whereas (II) isomerizes slowly (over several days) in NaOH solution, but rapidly on heating in ethanolic EtONa [2].†

It might be supposed that the reason for the increased ease of removal of a proton from (I) is a reduction in the electron density at C^3 of the furoxan ring, resulting from the electron-acceptor properties of the nitrogen atom of the N-oxide group. However, in the ^{13}C NMR spectra of dimethylfuroxan, benzofuroxan [4], benzotrifuroxan [5], and dibenzofuroxan [6], the chemical shift (CS) of the C atom bonded to the N-oxide group is shifted to higher field by 40 ppm with respect to the second C atom of the furoxan ring. This is taken to indicate increased electron density at the first C atom as compared with the second, as a result of a large contribution by the resonance structure with negatively charged carbon [4].



Such a large shift in the signal is hardly likely to be due solely to the magnetic anisotropy of the N-oxide group, since it is generally accepted that the maximum shift arising from this effect is no greater than 15 ppm. Thus, the relative reactivities of the isomeric monophenylfuroxans do not correspond to the electron densities at the C atoms of the furoxan ring, such as has been established for disubstituted furoxans. This led us to check directly (and also by ^{13}C NMR) the relative electron densities of the C atoms of the heterocycle in the isomeric phenylfuroxans themselves.

The information in the literature on these compounds is contradictory. In [7], three isomers of phenylglyoxime (PGO) were isolated for the first time, and their configurations established as amphi (hydroxyls rotated away from the phenyl group), anti, and syn. Reactions of each of these with N_2O_4 afforded (I) [8]. Only two modifications of PGO were known previously, namely the α and β forms, which reacted with N_2O_4 to give different products: (I) from the α form [9, 10], and phenylnitrofuroxan from the β form [9]. Further, oxidation of

*Deceased.

†In [2], isomer (I) is incorrectly assigned the structure (III), and isomer (II) is assigned a phenyldioxadiazine structure [3].

N. D. Zelinskii Institute of Organic Chemistry, Academy of Sciences of the USSR, Moscow.
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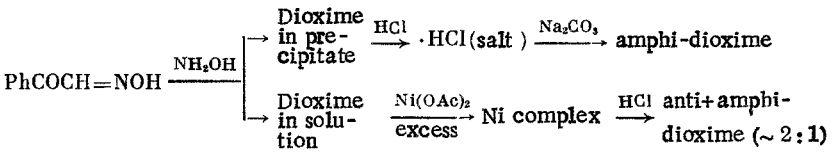
the β form with HNO_3 gave (II) [11-13]. Thus, the information on the effects of oxidizing agents on PGO is not entirely self-consistent.

It was first of all necessary to establish the nature of the α and β forms used in [9, 10]. To judge from the properties of the Ni^{2+} complexes [9, 14], they correspond to the amphi and anti isomers described in [7]. The α form, like the amphi isomer, gave a yellowish-green complex with Ni diacetate (of composition 1 mole dioxime: 1 atom Ni), which was insoluble in water but soluble in dilute AcOH; the β form, like the anti isomer, gave a red complex (2 moles of dioxime: 1 atom Ni) which was insoluble in water and AcOH. The melting points were unreliable as properties of the modifications of PGO, since at 160° the α form undergoes substantial conversion into the β form [14]. Different samples of the α form melted between 168 and 176° [14], whereas in [7] an mp of 178-180° is given for the amphi isomer. The mp of the β form was given as 180° in [9], whereas two modifications of the anti isomer with mp's of 166-168° and 177-180° were reported in [7]. In our experiments, the amphi isomer had mp 179-180°, and the anti isomer 165-170°. According to other literature sources, the mp is variable [7]. Furthermore, according to [7], it is possible by choosing certain isomer mixtures to obtain mp's which have been reported elsewhere for the pure isomers.

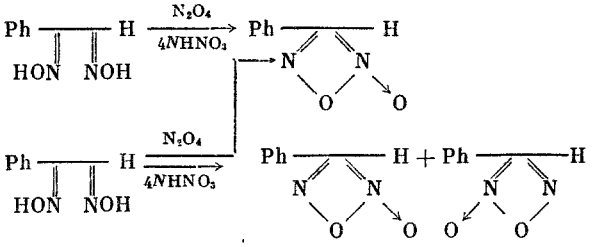
We have employed the CS in the PMR spectra, given in [7], to characterize the isomers, namely amphi 8.4 (CH) and 11.7 ppm (OH), anti 7.8 (CH), 11.4 and 11.6 ppm (OH), syn 7.4 (CH) and 11.4 ppm (OH) (in DMSO). Using these criteria, we have shown that the α form, obtained via the hydrochloride [14], is the pure amphi isomer, and the β form, isolated from the mother liquors with an excess of Ni acetate [14], is the anti isomer, contaminated by significant amounts of the amphi isomer.



Reaction of the α and β forms with N_2O_4 afforded (I) in 69 and 25% yields, respectively. The reaction product was isolated by steam distillation (Ponzio, [9]). The product from the reaction with the β form contained, even before recrystallization, 59% of carbon instead of the 46.6% required for phenylnitrofuroxan. The IR spectrum did not contain absorption bands due to the nitro group, and therefore the formation of phenylnitrofuroxan from the β form of PGO could not be confirmed.

When the calculated amount of Ni acetate was added to the β form, the anti isomer was obtained almost free from the amphi isomer. Treatement of this with 4 N HNO_3 afforded (II) contaminated by ~30% of (I), whereas treatment of the amphi isomer with this reagent gave (I) containing only traces of (II). If the β form of PGO, with an anti:amphi composition of 45:55, is reacted with HNO_3, the ratio of (II) to (I) in the product is ~40-60.

Thus, the amphi form of PGO affords (I) on treatment with either reagent, whereas the anti form on treatment with N_2O_4 gives (I), and on treatment with HNO_3, predominantly (II).



In order to obtain (II) in the pure state, it is best to thermally isomerize (I). Different products have been reported for the thermal isomerization of (I) on boiling in p- and o-xylene, namely (II) [10], and 3-phenyl-5-hydroxy-1,2,4-oxadiazole (mp 202°) [15, 16], respectively. We have shown that the sole isomerization product in either solvent is (II).

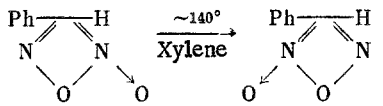
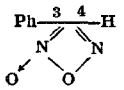
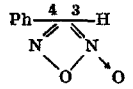
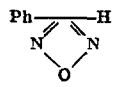
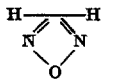


TABLE 1. ^1H and ^{13}C NMR Spectral Data for Isomeric Phenylfuroxans and Related Compounds. δ, ppm from TMS (internal standard)

Compound		δH in heterocycle	δC				
			in heterocycle		in benzene ring		
			CPh	CH	C^1	$C^{2,3}$	C^4
	(I)	8,50	115,1	145,5	123,6	130,6 126,8	132,1
	(II)	7,22	158,9	103,9	127,8	131,2 128,3	133,4
	(IV)	8,52	156,7	141,7	127,0	131,1 129,2	132,8
		8,30	–	141,9	–	–	–

$\delta(CPh)_{II} - \delta(CPh)_I = 43.8$ ppm; $\delta(CPh)_{II} - \delta(CPh)_{IV} = 2.2$ ppm;
$\delta(CH)_I - \delta(CH)_{II} = 41.6$ ppm; $\delta(CH)_I - \delta(CH)_{IV} = 3.8$ ppm.

In order to identify isomers (I) and (II) with confidence, we have examined their ^1H and ^{13}C NMR spectra (see Table 1), in comparison with those of furazan and phenylfurazan as model compounds. The CS of the heterocyclic proton provided a satisfactory measure of the content of each phenylfuroxan isomer in the mixture. Conclusive assignment of the signal at δ 7.22 ppm in the PMR spectrum of (I) to C^3–H was obtained by selective ^{13}C–^1H decoupling.

Comparison of the CS of the C atoms in the heterocycle shows that in both the phenylfuroxan isomers, as in the disubstituted furoxans, the C^3 atom undergoes a large upfield shift as compared with atom C^4. On comparing one isomer with the other in respect of the same fragments (CPh or CH) bonded to the N-oxide group, the shift is of approximately the same magnitude (~40 ppm) as for the same fragments in symmetrically disubstituted furoxan. The direction of the shift shows that the electron density at the C atom of the CH group in (I) is greater than that in (II), and hence the proton should be more difficult to remove from (I) than from (II). Since the relative reactivities of the isomers towards bases are precisely the opposite of what would be expected from the relative electron densities at the C atom of the CH fragment, it must be concluded that the electron density in the ground state is not the decisive factor in the detachment of a proton from monophenylfuroxans by bases.

By comparing the CS of the C atom of the CPh or CH fragment of the "furazan" moiety of the molecule with that of the corresponding moiety of phenylfurazan and furazan, it will be seen that the effect of the N-oxide group on the C atom which is not bonded to it is far smaller (a CS of 2-4 ppm) than that of the atom to which is is bonded, and is opposite in sense, resulting in a reduction in electron density.

EXPERIMENTAL

^1H and ^{13}C NMR spectra were recorded on Perkin–Elmer 12 and JEOL JNM PS-100 instruments (60 MHz for ^1H, and 25.15 MHz for ^{13}C), as 10-15% solutions in CH_2Cl_2. Isonitrosoacetophenone was obtained as in [9].

Preparation and Isolation of the α and β Forms of Phenylglyoxime (PGO). To a solution of 10 g (67.5 mmole) of isonitrosoacetophenone in 20 ml of ethanol, heated to 75-80°C, was added a solution of 5.3 g (76.4 mmole) of hydroxylamine hydrochloride and 11.8 g (86.7 mmole) of AcONa in 15 ml of water. The solution was yellow in color. After keeping for 12 h at 75-80°, the mixture was cooled to ~20°, and the crystals of PGO filtered off (yield 8 g; 73%). The α form of PGO was obtained from the solid, and the β form from the filtrate.

a) The solid was dissolved in 50 ml of absolute ethanol, and dry HCl was passed into the solution with ice-cooling for 0.5 h. The colorless precipitate of α-PGO hydrochloride was filtered off, decomposed with dilute aqueous sodium carbonate, and the resulting material was

extracted with ether. Removal of the ether from the extract left 4.5 g of the α form, mp 178-182° (the pure amphi form, from its PMR spectrum). PMR spectrum (δ, ppm, DMSO): 7.42 m (Ph), 8.63 s (CH), 11.7 s (2 OH). Data from [7] (δ, ppm, DMSO): 7.4 m (Ph), 8.4 s (CH), 11.7 s (2 OH). IR spectrum (ν, cm^{-1}, KBr): 3250 br, 1475 med, 1295 med, 1115 med, 1085 weak, 1010 med, 960 s, 935 med, 815 weak, 790 s, 710 med.

b) The filtrate was evaporated, the residue was dissolved in 100 ml of 50% aqueous ethanol, and 40 g of $Ni(OAc)_2 \cdot 4H_2O$ as a 20% aqueous solution, heated to 60-70° and containing a few drops of glacial acetic acid, was added. The red nickel complex which separated was filtered off, washed with alcohol and ether, decomposed with dilute HCl, and the solution was extracted with ether. Removal of the ether afforded 0.5 g (4.5%) of β-PGO, mp 160°, containing 67% of the anti isomer (from the ratio of the CH peaks for the amphi and anti isomers at 8.60 and 8.00 ppm, respectively).

To isolate the anti isomer, 14.3 g (87.3 mmole) of β-PGO was dissolved in 200 ml of 50% ethanol, and 25.4 g (102.1 mmole) of $Ni(OAc)_2 \cdot 4H_2O$ was added in aqueous solution. The red Ni complex which separated was filtered off, decomposed with dilute HCl, and extracted with ether to give 6.4 g of anti-PGO, mp 165-170° (from $CHCl_3$).

PMR spectrum (δ, ppm, DMSO): 7.23 m (Ph), 7.90 s (CH), 11.4 and 11.6 (2 OH). Data from [7] (δ, ppm, DMSO): 7.4 m (Ph), 7.8 s (CH), 11.4 and 11.6 (2 OH). IR spectrum (ν, cm^{-1}, KBr): 3300 broad, 1425 med, 1300 weak, 1270 weak, 1115 weak, 1085 weak, 1015 weak, 970 s, 810 med, 755 weak, 725 weak, 700 weak.

Reaction of N_2O_4 with amphi-Phenylglyoxime. To a solution of 2.5 g (15.3 mmole) of amphi-PGO in 25 ml of anhydrous ether was added at 0-5° 1.5 g (16.3 mmole) of N_2O_4. The brown reaction mixture gradually turned green, and colorless crystals of (I) began to separate. After keeping for 1 h, the crystals were filtered off. Evaporation of the filtrate to a small volume afforded a further small amount of product. In all there was obtained 1.7 g (69%) of (I), mp 106-107°, raised by recrystallization from alcohol to 108-109°. PMR spectrum (δ, ppm, CH_2Cl_2): 7.20 s (CH), 7.44 m (Ph). Data from [7] (δ, ppm, $CDCl_3$, from TMS): 7.4-7.9 (Ph), 7.26 s (CH).

Reaction of N_2O_4 with β-Phenylglyoxime (anti:amphi = 2:1). To a solution of 1 g (6.1 mmole) of the oxime in 20 ml of anhydrous ether was added at 20-25° 1 g (10.9 mmole) of N_2O_4. The brown solution gradually turned green and became lighter in color. After 1 h, the reaction mixture was washed with water, the ether removed by distillation, and the pale yellow solid residue was subjected to steam distillation. Yield 0.24 g (24%) of (I), mp 95-98° (from alcohol). A mixed sample with material from the preceding experiment had mp 100-104°. Found C 58.97; H 3.71% (before steam distillation): C 59.2; H 3.94% (after steam distillation). $C_8H_6N_2O_2$. Calculated: C 59.26; H 3.73%. PMR spectrum (δ, ppm, CH_2Cl_2): 7.25 s (CH), 7.50 m (Ph).

Isomerization of 4-Phenylfuroxan (I) and 3-Phenylfuroxan (II). A solution of 1 g (6.1 mmole) of (I) in 10 g of p-xylene was boiled for 1 h (138.5°). After removal of the solvent, the residue was steam distilled to give 0.25 g (25%) of (II), mp 104-106°; after recrystallization from alcohol, mp 107-108°.

Isomerization in o-xylene by the same method afforded 8.3% of (II).

PMR spectrum (δ, ppm, CH_2Cl_2): 7.48 m and 7.79 m (Ph), 8.50 s (CH). IR spectrum (ν, cm^{-1}, KBr): 3140 weak, 1610 s, 1505 s, 1460 med, 1410 med, 1345 weak, 1300 weak, 1270 weak, 1220 weak, 1090 s, 995 weak, 920 s, 890 weak, 815 s.

Reaction of Nitric Acid with amphi-Phenylglyoxime. To 10 ml of 4 N HNO_3 at 20-25° was added in portions 1 g (6.1 mmole) of amphi-PGO. Oxides of nitrogen were evolved, and the temperature rose slightly. After 24 h, the reaction mixture was poured into water (~50 ml) and steam distilled to give 0.35 g (35%) of (I), slightly comtaminated with (II) (from the PMR spectrum), mp 95-100°.

Reaction of Nitric Acid with anti-Phenylglyoxime. To 20 ml of 4 N HNO_3 at ~20° was added in portions 2 g (12.2 mmole) of anti-PGO. The reaction mixture became dark in color, oxides of nitrogen being evolved at the same time. After 24 h it was poured into water, and steam distilled to give 0.6 g (30%) of a mixture of (II) and (I), mp 105-106°, in a ratio of ~7:3 (from the PMR spectrum).

Reaction of Nitric Acid with β-Phenylglyoxime (anti:amphi = 2:1). To 10 ml of 4 N HNO_3 was added in portions 1 g (6.1 mmole) of β-PGO. Oxides of nitrogen were evolved, and after 24 h the mixture was poured into water and steam distilled to give 0.3 g (30%) of a mixture of (II) and (I), mp 68-70°, in a ratio of ~4:6 (from the PMR spectrum).

CONCLUSIONS

1. amphi-Phenylglyoxime is converted into 4-phenylfuroxan by N_2O_4 or 4 N HNO_3; anti-phenylglyoxime gives 4-phenylfuroxan with N_2O_4, but predominantly 3-phenylfuroxan with 4 N HNO_3.

2. 4-Phenylfuroxan isomerizes on boiling in o- or p-xylene to 3-phenylfuroxan.

3. The distribution of electron density in the ground state is not the decisive factor governing the removal of a proton from phenylfuroxans by bases.

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GENERATION AND PROPERTIES OF EPISULFONIUM INTERMEDIATES.

7.* GENERATION OF EPISULFONIUM IONS FROM 1,3-BUTADIENE AND ISOPRENE

Yu. B. Kal'yan, M. Z. Krimer, and V. A. Smit

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Addition of covalent sulfenyl halides to 1,3-dienes is known to give the 1,2-adducts only, which subsequently isomerize with greater or lesser ease to the 1,4-isomers (on treatment with acids and/or heating) [2-4]. The aim of the present investigation was to develop a method for converting butadiene and isoprene [(I), R^1 = H or Me] into the corresponding episulfonium ions (ESI), and to obtain data on the reactivity of the latter, particularly in respect of their rearrangement to 2,5-dihydrothiophenium salts.

It has been found that the most convenient route to ESI from (I) is by the direct reaction of the diene with the cationoid reagent $ArS^{\oplus}Y^{\ominus}$ (Y = BF_4^- or SbF_6^-), which may be previously prepared in solution, or generated directly at the moment of reaction (methods A and

*For part 6, see [1].

N. D. Zelinskii Institute of Organic Chemistry, Academy of Sciences of the USSR, Moscow. Institute of Chemistry, Academy of Sciences of the Moldavian SSR, Kishinev.

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