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SYNTHESIS OF γ-PYRONEIMINE N-OXIDE A NOVEL NITRONE WITH ELECTRON RELEASING SUBSTITUENT

J. Asgarian Damavandy, M.A. Bigdeli and G. Mohammadi Ziarani

Department of Chemistry, Faculty of Science, Teacher Training University, Mofatteh Ave., Tehran, Islamic Republic of Iran

Abstract

N-Oxidation of 1,4-dihydro-2,6-dimethyl-1-phenyliminopyridine (7) with several peracids was attempted. The main compound obtained was 1-phenyl-2,6-dimethyl-4-pyridone (8), instead of the expected N-oxide (2). The reaction of phenylhydroxylamine with dimethylmethoxypyroxonium perchlorate, however, successfully gave the N-oxide (3), which belongs to a class of nitrones in which the diazomethine N-oxide group is conjugated with an electron releasing center.

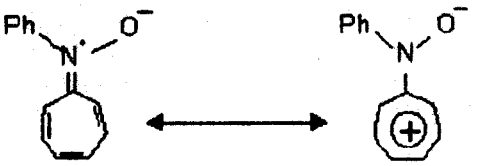
Introduction

Nitrones have been the subject of considerable research of both a fundamental and applied nature [1]. Syntheses and studies of conjugated nitrones, however, have remained largely unexploited.

We have previously studied both synthetic and reactivity aspects of nitrones which are conjugated with electron withdrawing quinone moieties [2,3]. We found that when the nitrone is conjugated with benzoquinone, for example, its 1,3-dipolar cycloaddition reactivity becomes minimal [2], whereas conjugation with naphtho- or anthraquinone has little effect on nitrone functionality and hence they are active in cycloaddition reaction [3].

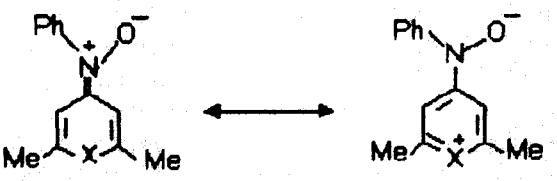
To gain a better understanding of the electronic effect, we undertake the syntheses of nitrones in which the electron donating groups are conjugated with nitrone moiety. The only reported example of such nitrone is compound (1) which showed typical nitrone reactivity, but with reverse regioselectivity [4]. The particularity of the nitrone was envisaged to be the conjugation of diazomethine N-oxide moiety with an electron donating center toward aromatization.

Keywords: N-Phenylpyroneimine N-oxide; γ-Pyroneimine N-oxide



(1)

In the present work, we have reported the synthesis of γ-pyroneimine N-oxide (3) in which the nitrone group enjoys the electron donation of the pyrone ring. We have also herein reported an approach, although not successful, toward the synthesis of analogous nitrone phenyliminopyridine N-oxide (2).

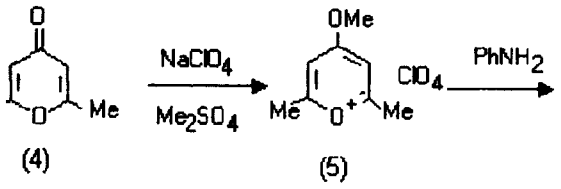


(a) (b)

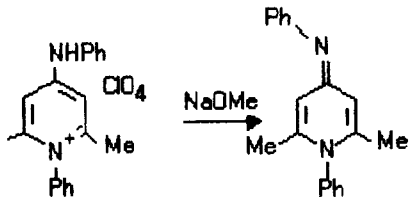
(2) x = N
(3) x = O

Results and Discussion

[-Oxidation of imines by peracids is one possible ral route for the preparation of nitrones [6]. Thus, limethyl-γ-pyrone (4) was chosen as starting ma- l for synthesis of the title nitrones (2 and 3). The ıture methods were followed for the preparation ıe corresponding pyridinum perchlorate salt (6). ;, reaction of (4) with dimethylsulphate followed ıe addition of sodium perchlorate gave dimethyl ıoxypyroxonium perchlorate (5) [7]. Addition of ne to (5) in methanol, and heating the reaction ure under reflux for one hour led to pyridinium (6) [8]. Deprotonation of the latter salt with so- ı methoxide gave the corresponding loneimine (7), which was separated as a yellow ipitate.



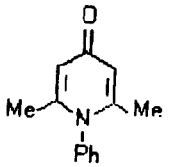
(4) (5)



(6) (7)

The infrared spectrum of (7) showed a band at) cm^{-1} which was assigned to C= N stretching vi- ion. The ^1H NMR spectrum comprised of multip- centered at δ 7.5 for 10 protons and δ 6.4 for two ons, which were assigned to phenyl and pyridone protons respectively. The resonance of two me- groups at the 2 and 6 positions of pyridone ring ar non-equivalent. They resonate at δ 1.9 and 4. It appears that one of the methyl groups which rrelative to the N-phenylimine group is strongly cted by the anisotropy of the phenyl group. Our npt to substitute only the methoxy group of the (5) with aniline under milder conditions always to the formation of (6). It appears that in the reac- of pyroxonium salt (5) with primary amine, both 4 2 positions of the pyroxonium ring are liable to- ds amine nitrogen, and nucleophilic substitution at ı positions is inevitable.

The N-oxidation of imine (7) was attempted using several peracids. They included perbenzoic, 3-chloroperbenzoic and peracetic acid. Addition of different peracids to the chloroform solution of imine (7) gave either an unidentifiable oily residue, not solidifying under different conditions, or N-phenyl-2,6-dimethyl-4-pyridone (8).



(8)

Since the direct N-oxidation failed to give the desired nitrone (2), preparation of the analogous nitrone (3) by a different method was achieved. Thus, addition of excess phenylhydroxylamine to salt (5) in ethanol gave an oily residue. The main product was identified as N-oxide (3). Probably phenylhydroxylamine acts as both nucleophile and deprotonating base. The elucidation of the nitrone structure was made from NMR, IR and mass spectrum. Infrared spectrum showed a C= N stretching band at 1681 cm^{-1}. A strong evidence for domination of structure (3b) came from the analysis of ^1H NMR spectrum. The two methyl groups of γ-pyrone ring resonate at the same chemical shift, i.e. δ 1.2, pointing to the fact that C-N bond rotation is fast enough and hence the two methyl groups experience an average magnetic effect of the nitrone moiety. Mass spectrum showed m/z at 199, attributable to deoxygenated nitrone molecular ion, which is typical for all nitrone fragmentation.

Experimental Section

Melting points were taken in open glass capillaries and are uncorrected. IR spectra were recorded in nujol on a Beckman Acculab 3 and Shimadzu Corporation Spectrophotometer. ^1H NMR spectra were obtained with Perkin Elmer 248 (60 MHz) and Bruker AC 80 (80 MHz) spectrometers. The shifts are given in scale with Me_4Si as internal standard. Mass spectra were run by Varian MAT 311 Mass Spectrometer.

Reaction of Pyroxonium Salt (5) with Aniline

A mixture of 2,6-dimethyl-4-methoxypyroxonium perchlorate (5) [7] (0.3 g, 1.2 mmol), aniline (0.279 g, 3 mmol) and methanol (2 ml) was heated under reflux for one hour followed by stirring at room temperature for three days. The solvent was removed under reduced pressure and the resulting solid was recrystal-

lized from methanol to give pyridinium salt (6) m.p. 222-224°C (0.21 g, 45% yield) (lit. [8] m.p. 222°C) as white crystals; IR ν_{max}(KBr) 3150, 1640, 1580, 1320 cm^{-1}; ^1H NMR δ ($(CD_3)_2SO$) 9.72-8 (m, 10H), 7.1 (s, 2H), 2.2 (s, 6H).

1,4-Dihydro-2,6-dimethyl-1-phenyl-4-phenyliminopyridine (7)

To the pyridinium salt (6) (0.31 g, 0.8 mmol) was added dropwise a concentrated solution of sodium methoxide until all salts were dissolved. The resulting yellow-coloured solution was evaporated in reduced pressure and the solid thus obtained was treated with CCl_4 (10 ml) and stirred for several hours at room temperature. The mixture was filtered off and the filtrate was concentrated under reduced pressure to afford iminopyridine (7), m.p. 144-148°C as yellow crystals, IRν_{max} (nujol) 1640, 1580, 1560, 1540, 1440, 1350, 750, 680 cm^{-1}; ^1H NMR δ ($CDCl_3$) 7.0-8.0 (m, 10H), 6.0-6.8 (m, 2H), 1.9 (s, 3H), 1.4 (s, 3H); mass spectrum m/z 274 (M^+, $C_{19}H_{18}N_2$).

Reaction of Imine (7) with Peracids

To iminopyridine (7) (0.1 g, 0.36 mmol) in benzene (2 ml) was added a solution of perbenzoic acid (0.1 g, 0.7 mmol) in benzene dropwise. The mixture was stirred at room temperature for 24 hours. The solution was extracted with sodium hydroxide solution (0.5 g, 0.012 mol) in water (40 ml), washed with water (10 ml) and dried over potassium sulphate. The solvent was evaporated under reduced pressure and the residue crystallized in ethanol to give 2,6-dimethyl-N-phenyl-4-pyridone (8), m.p. 197-197.5°C, (lit. [9] m.p. 196.5).

Several attempts using peracetic acid and 3-chloroperbenzoic acid gave similar results.

2,6-Dimethyl-4-phenylimino-4-pyrone N-oxide (3)

A mixture of pyroxonium salt (5) (0.81 g, 3.3 mmol) and phenyl hydroxylamine (0.71 g, 6.5 mmol) in ethanol (3 ml) was stirred at room temperature for one week. The resulting red-coloured solution was evaporated under reduced pressure and the residue was treated with chloroform (10 ml). The solution was dried over $MgSO_4$. It was chromatographed (dry-flash, petroleum ether 40-60°) to give N-oxide (3) as a low melting solid, m.p. 30-35°C (0.31 g, 43%); IR ν_{max}(KBr) 1481, 1436, 1317, 764, 682 cm^{-1}; ^1H NMR δ($CDCl_3$) 7.2-8.0 (m, 5H), 7.1 (s, 2H), 1.2 (s, 6H); mass spectrum m/z 199 (M^+-16, $C_{13}H_{13}NO_2$).

References

1. Tuarriello, J.J. *1-3, Dipolar cycloaddition chemistry*, (ed. A. Padwa), 12, 83-186. John Wiley and Sons, New York, (1984).
2. Damavandy, J.A. and Ahmadian, M. *J. Sci. I.R. Iran*, **1**, (3), 182, (1990).
3. Damavandy, J.A. and Jones, R.A.Y. *J. Chem. Soc. Perkin* 1, **3**, 712, (1981).
4. Houk, K.N., Domelsmith, L.N. and Muknerjee, D. *J. Amer. Chem. Soc.*, **100**, 1954, (1978).
5. Damavandy, J.A. and Mehrdad, M. *J.Sci. I.R. Iran.*, **1**, (2) 96, (1990).
6. Katritzky, A.R. and Lagowsky, J. *Chemistry of the heterocyclic N-oxide*, p. 22. Academic Press, (1971).
7. Anker, R.N. and Hook, A.H. *J. Chem. Soc.*, 117, (1946).
8. King, L.C. and Ozog, F.Z. *J. Org. Chem.*, **20**, 448, (1955).
9. Chauvelier, J. *Bull. Soc. Chim. France*, 734, (1954).