Tetrahedron Letters,Vol.30,No.19,pp 2477-2480,1989
Printed in Great Britain

0040-4039/89 $3.00 + .00
Pergamon Press plc

REACTIONS OF α-AMINOESTER IMINES WITH NITROSOBENZENE

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ABSTRACT: Arylidene imines of α-aminoesters react with nitrosobenzene at room temperature yielding a diarylnitrone and a Z-diimine.Adecuate mechanistic scheme is postulated to account for the products formed.

Imines of α-aminoester 1 exist in solution in tautomeric equilibrium with the corresponding azomethin-ylid[1] 2, as shown in Scheme I.

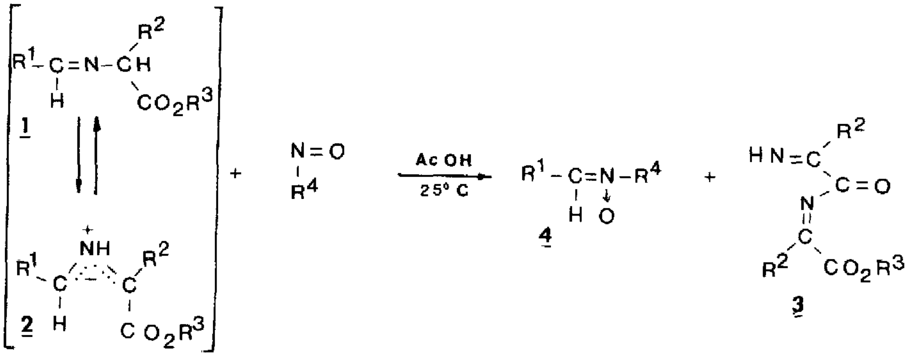
The formation of the 1,3-dipole is catalized by Lewis and Brönsted acids[2], bases[3] and metallic salts[4]. Both the dipole and the aza-allyl anion have been captured in a number of different ways, forming in each case the corresponding cycloadduct in good yields[2b,5-7].

The nitroso group is a good dipolarophile towards azomethine ylids that come from the prototropic migration in *Δ^2-oxazolin-5-ones, yielding Δ^4-* 1,2,4-oxadiazolin-3-carboxylic acids regiospecifically[8]. Also, methylene-N-phenylimines, which cannot form 1,3-dipoles, react with nitrosobenzene to yield 1,2,4-oxadiazetidines via 2 + 2 cycloaddition reaction[9].

This paper reports reactions of imines: 1a: N-benzylydene-α-phenylglycine ethyl ester; 1b: N-p-methoxybenzylydene-α-phenylglycine ethyl ester and 1c: N-methoxybenzylydene-α-p-methylphenylglycine methyl ester with nitroso and p-methylnitrosobenzene in acetic acid at room temperature. In each case, compound 3 and a nitrone 4 were obtained.

In a first reaction, imine 1a (2 mM) in 3 ml of acetic acid was reacted with nitrosobenzene (2 mM) at 25°C., until a colour change occurred (10 min.). The reaction was then stopped by adding water and then aqueous NaOH until pH 5. The resulting solution was extracted with ether. The ethereal extract was dried with $MgSO_4$ and evaporated to dryness. The ethereal residue was crystallysed from petroleum ether 40-60 and then from carbon tetrachloride. The product, C-phenyl-N-phenylnitrone 4a was obtained in 41% yield, mp=111°C.(lit.[10]=112°C.); the spectroscopic properties correspond to those of the product of the reaction between N-phenylhydroxylamine and benzaldehyde[10]. In addition to the nitrone, this reaction yields a product isolated as white crystals from petroleum ether, with the following characteristics: mp=164-5°C. and a R_f in di-n-butylether of

0.19; its elemental analysis was C:70.24; H:5.23; N:9.17 which fits well the required analysis for $C_{18}H_{16}N_2O_3$ (C:70.11; H:5.23; N:9.09). ^{1}H-NMR ($CDCl_3$)ppm: 9.05(s, broad, 1H); 8.65-8.38(m, 2H); 7.97-7.23(m, 8H); 4.33(q, J=7 Hz, 2H); 1.30(t, J=7 Hz, 3H). The signal at 9.05 ppm exchange with D_2O. IR (KBr) cm^{-1}: 3175, 3075, 1773, 1751, 1608. UV-VIS (CH_2Cl_2) λ_{max}=267 nm ε_{max}=18 204 $dm^3 mole^{-1} cm^{-1}$. When this compound was heated for two hours in a solution of ethanolic NaOH and then acidified with HCl, benzoic acid was produced together with abundant gas evolution. This compound fits structure 3a [α-imino-N-(1-ethoxycarbonylbenzylidene)-phenylacetamide]. The structural assignment was confirmed by ^{1}H-NMR with increasing amounts of Eu(fod)$_3$. The chemical shifts corresponding to the signal of the product are displaced as the $[Eu^{+3}]$ increases. There are linear relationships between the displacement of a chemical shift and the $[Eu^{+3}]$ added, where the slopes of these lines differ as follow: there is a large slope for a signal that integrates for 1H (NH); then, the displacement of a signal for two aromatic protons, as well as another aromatic signal (2H) both show moderate slopes. The methylene protons in the ethoxyl group show identical slopes than one of the aromatic signals; while there are small slopes for two aromatic signals with three protons each and three methyl protons. This observations correspond well with a complex where Eu^{+3} coordinates with 3a at the two imine nitrogens.



Reaction Nº	Imine	R1	R2	R3	R4:nitroso derivative
1	1a	Ph	Ph	Et	Ph
2	1b	p-MeO-Ph	Ph	Et	Ph
3	1b	p-MeO-Ph	Ph	Et	p-Me-Ph
4	1c	p-MeO-Ph	p-Me-Ph	Me	Ph

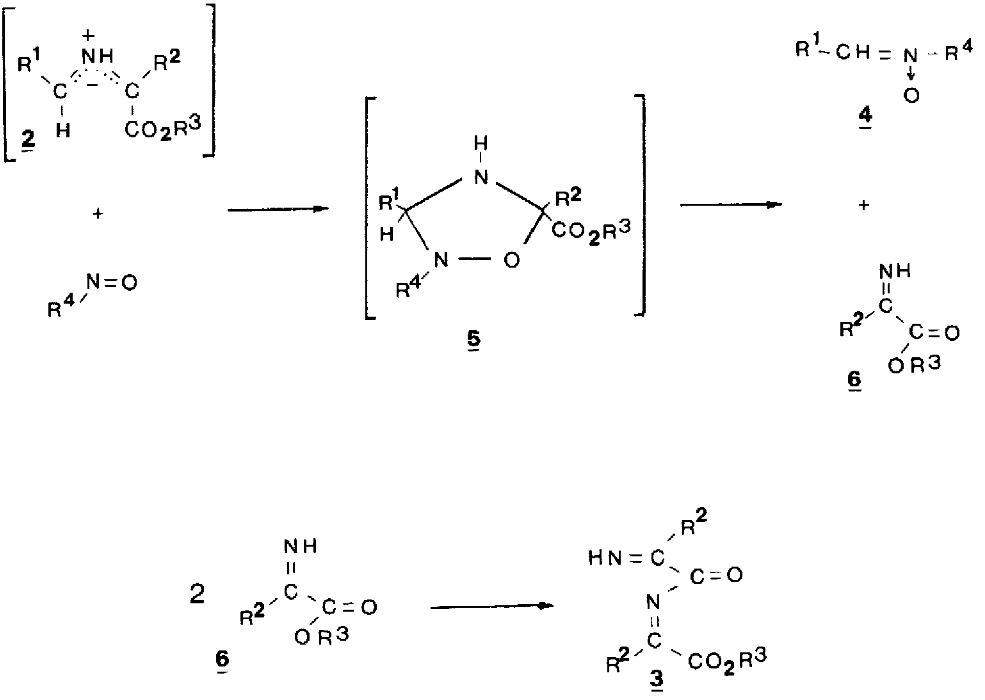
SCHEME I: Summary of reactions

In a second reaction, one equivalent of imine <u>1b</u>[11] was reacted with two equivalents of nitrosobenzene. After 10 minutes the reaction yielded 43% of C-p-methoxyphenyl-N-phenylnitrone <u>4b</u>, this reaction also produced 11% of <u>3a</u>.

In a third reaction, the imine <u>1b</u> was reacted with p-methylnitrosobenzene[13] where <u>4c</u> (C-p-methoxyphenyl-N-p-methylphenylnitrone)[12] was produced, this reaction also produced <u>3a</u>.

In a fourth reaction between imine <u>1c</u> and nitrosobenzene the products were nitrone <u>4b</u> and the compound <u>3b</u>. The latter product has the following characteristics: white crystals from petroleum ether 40-60; mp=176-8°C.; elemental analysis: C:71.11; H:5.76; N:8.73 ($C_{19}H_{18}N_2O_3$ requires C:70.79; H:5.63; N:8.69). ^{1}H-NMR (CCl_4) ppm: 10.1(s, broad, 1H) exchange with D_2O; 8.47(d, J_d=8 Hz, 2H); 7.53(d, J_d=8 Hz, 2H); 7.40-6.97(m, 4H); 3.73(s, 3H); 2.43(s, 3H); 2.33(s, 3H). IR (KBr) cm^{-1} : 3226(NH); 1754(C=0); 1613(C=N).

Our results show that the C-substituent in the nitrone comes from the C-substituent of the imine while the N-substituent comes from nitrosobenzene. Also, it can be seen that <u>3a</u> and <u>3b</u> must have a Z-geometry around the trisubstituted imine bond, because with an E-geometry an internal nucleophilic substitution would take place, which would yield a di-iminoquinone as a product.



<u>SCHEME II</u>: Mechanism postulated that yields the observed products

Scheme II shows that the reaction may consist in a concerted cycloaddition of tautomer 2 and the nitrosoderivative to yield an oxadiazolidine 5 followed by reverse 1,3-dipolar cycloaddition in a different sense to give imine 6 and nitrone 4 directly[14]. Further the imine 6 yields the product 3 via an nucleophilic substitution reaction.

ACKNOWLEDGEMENT: Financial support for this research from the Departamento Técnico de Investigación, U. de Chile (Project Q-2312-8824) is gratefully acknowledge.

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11. Imines 1a, 1b and 1c were obtained according to the method of Clark et al. (J. C. Clark, G. H. Phillips, M. R. Steer, J. Chem. Soc. Perkin I, 475 (1976)).
12. Nitrones: 4b mp=118°C. ^{1}H-NMR (CCl$_4$) ppm: 8.36(d, J$_d$=9 Hz, 2H); 7.90-7.63(m, with a singlet at 7.82, 3H); 7.53-7.23(m, 3H); 6.88(d, J$_d$=9 Hz, 2H); 3.87(s, 3H). IR (KBr) cm^{-1}: 1613 (C=N), 1470, 1408, 1266(N→O), 1067, 1029, 892, 778, 758 and 693 (J. Hammer and M. Macaluso, Chem. Rev. 64, 473-495 (1964).
    4c: mp=130°C. ^{1}H-NMR (CCl$_4$) ppm: 8.4(d, J$_d$=8 Hz, 2H); 7.78(d, J$_d$=8 Hz, 2H); 7.3(d, J$_d$=8 Hz, 2H); 3.9(s, 3H); 2.45(s, 3H). IR (KBr) cm^{-1}: 1605(C=N); 1256(N→O).
13. p-Methylnitrosobenzene was prepared according to the method of Ingold[9], which oxidises p-toluidin with $K_2S_2O_8$ and H_2SO_4 at 0-5°C.
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(Received in USA 31 January 1989)