Communications to the Editor

Chem. Pharm. Bull.
31(11)4181—4184(1983)

FORMATION OF N,1-BIS[5-(3-PHENYL)-[1,2,4]OXADIAZOLYL]DIMETHYLAMINES[1)]

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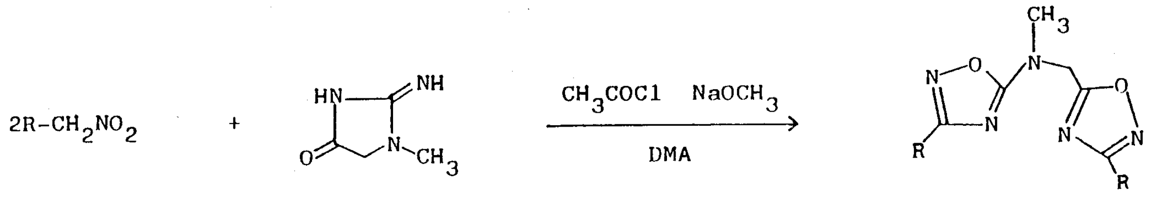
N,1-Bis[5-(3-substituted)-[1,2,4]oxadiazolyl]dimethylamines (3) were synthesized through the reaction of creatinine (2) with primary aliphatic nitro compounds (1) and acetyl chloride. The structural determination of 3 by single crystal X-ray analysis is reported.

KEYWORDS —— creatinine; primary aliphatic nitro compound; phenylnitromethane; N,1-bis[5-(3-phenyl)-[1,2,4]oxadiazolyl]dimethylamine; X-ray analysis

The authors are progressively interested in studying the extensive application of one-step synthesis of various heterocycles[2)] containing an N-O bond by use of nitrile oxides generated *in situ* through the O-acylation of primary aliphatic nitro compounds (1) with acetyl chloride in aprotic polar solvents. We describe here a new type of oxadiazolyldimethylamines (3).[3)] N,1-Bis[5-(3-phenyl)-[1,2,4]oxadiazolyl]dimethylamine (3a) was obtained by the reaction of phenylnitromethane (1a) with creatinine (2) in the above-mentioned reaction as shown in Chart 1. The compound 3a (R=phenyl) was obtained as follows: In a typical experiment, 226 mg (0.5 mmol) of 2 was added to a solution of phenylnitromethane (274 mg, 2.0 mmol) and acetyl chloride (0.14 ml, 2.0 mmol) in N,N-dimethylacetamide (DMA; 7 ml) with 1N sodium methoxide in methanol (1.8 ml) upon cooling to 0°C. The mixture was stirred at room temperature overnight. After neutralization with 10% aqueous sodium hydrogencarbonate followed by benzene extraction, further purification by column chromatography on silica gel (hexane-ethyl acetate, 3:1) was carried out. The main product 3a (105 mg), colorless needles in a yield of 63%, gave a single spot on TLC; 3a: mp 137-138°C (from methanol). IR νmax (KBr) cm^{-1}: 1645 (oxadiazole C=N). ^{1}H-NMR (δ in CDCl$_3$, 90 MHz): 3.38 (3H,s,NCH$_3$), 5.05 (2H,s,NCH$_2$), 7.3-7.6 (6H,m,2 X phenyl H-3,4,5), 7.9-8.2 (4H,m,2 X phenyl H-2,6). ^{13}C-NMR (δ in $CDCl_3$, 25.1 MHz): 36.8 (q,NCH_3), 47.0 (t,NCH_2), 126.5 (s,phenyl C-ipso), 127.6 and 127.8 (each d, phenyl C-meta), 128.9 and 129.2 (each d,phenyl C-ortho), 131.2 and 131.7 (each d, phenyl C-para), 169.0 and 169.2 (each s,N=C(N)-ph), 171.8 (s,N=C(O)-CH_2), 174.9 (s, N=C(O)-N). This procedure was applied to the analogs (1), i.e. p-tolylnitromethane$^{4)}$ (1b) and p-chlorophenylnitromethane$^{5)}$ (1c). The corresponding 3b and 3c were obtained respectively, 3b: mp 151-152°C (methanol), yield 62% and 3c: mp 187-189°C (benzene-petroleum ether), 60%. Both nitroethane (1d) and 1-nitropropane (1e) gave the corresponding 3d and 3e in poor yields; 3d: bp 76-83°C/4 Torr,$^{6)}$ and 3e: bp 92-93°C/4 Torr.



1 2 3

R= a:C_6H_5, b:p-$CH_3C_6H_4$, c:p-ClC_6H_4, d:CH_3, and e:C_2H_5

Chart 1

The structure of 3a was determined by single crystal X-ray analysis. A very thin platy crystal of approximate dimensions 0.1 X 0.6 X 0.03 mm was mounted on a Philips PW1100 diffractometer and the cell parameters and the intensity data were measured with graphite monochromated CuKα radiation. The crystal data: N,1-bis[5-(3-phenyl)-[1,2,4]oxadiazolyl]dimethylamine, $C_{18}H_{15}N_5O_2$, MW= 333.4. Triclinic space group P$\bar{1}$, Z=2, Dcal=1.363 gcm^{-3}. a=9.741(5), b=13.679(7), c=6.300(3) Å, α=91.03(5), β=100.42(5), γ=99.78(5)°, V=812.6 Å^3.

Of the total of 3338 reflections within the 2θ range of 6° through 150°, 2054 were measured as above the 2σ(I) level and were used for the structure determination. The structure was solved by the direct method using MULTAN$^{7)}$ and refined by the block-diagonal matrix least-squares method. The final R value was 0.053 including all the 15 hydrogen atoms.$^{8)}$ A perspective drawing of the molecular structure is illustrated in Fig. 1 showing the bond lengths and conformations. The molecule consists of two nearly identical halves of the 3-phenyl[1,2,4]oxadiazolyl moiety linked together by the dimethylamine group. The corresponding bond lengths and angles are very close to each other and the differences are almost within the limits of experimental errors. The largest differences are seen in the C(10)-N(12)-C(14)-C(15) group where the C(10)-N(12) bond [1.337(4) Å] has a partial double bond character due to extension of the double bond out of the oxadiazole ring. Thus the N(12) atom possesses a completely planer configuration with the C(10), C(13), and C(14) atoms and the tortional angle, N(11)-C(10)-N(12)-C(14), is almost cis [2.5(4)°]. The C(15)-C(14) bond, on the other hand, has the length 1.490(4) Å and far less double bond character. The torsional angle, N(16)-C(15)-C(14)-N(12) is 25.8(4)°. The benzene ring and the oxadiazole ring are almost coplaner with the torsion angles C(5)-C(6)-C(7)-N(11) = -0.8(4)° and C(25)-C(20)-C(17)-N(16) = 1.9(4)° and the C-C bonds connecting the two rings, C(6)-C(7) and C(20)-C(17), are 1.461(5) Å and 1.460(4) Å, respectively showing a partial double bond character.

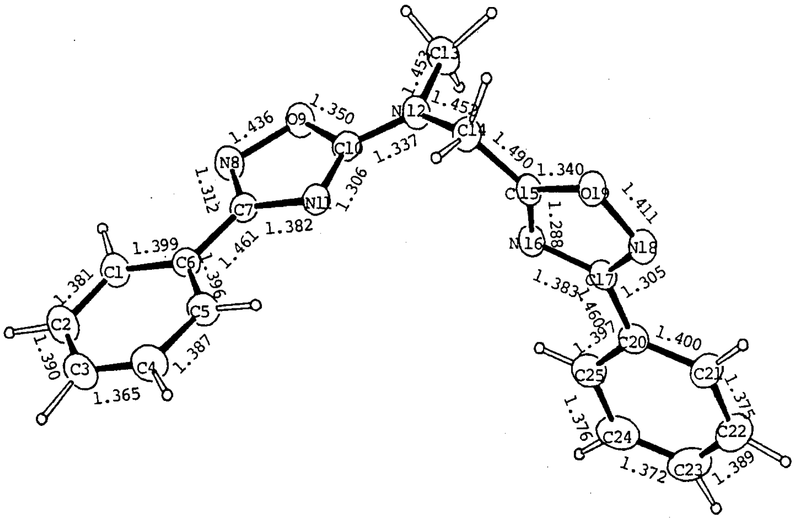


Fig. 1. Molecular Structure of the Compound 3a, Bond Lengths (Å), and Numbering of Atoms

Further detailed study are now in progress.

ACKNOWLEDGEMENT The authors are grateful to Director Dr. Hamao Umezawa, Institute of Microbial Chemistry, for his kind advice and support of the analyses.

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(Received August 20, 1983)