THE REACTION OF β-AMINOALCOHOLS WITH 1,2-BENZENEDICARBOXALDEHYDE --A CORRECTION

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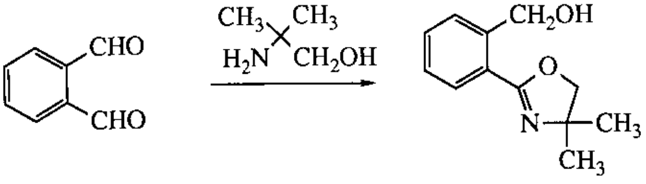
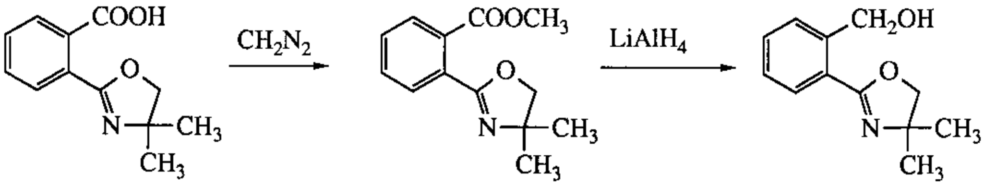
Abstract - The structure of the compound obtained from the reaction of 2-amino-2-methyl-1-propanol with 1,2-benzenedicarboxaldehyde is revised.

Shipchandler[1] reported the reaction of 2-amino-2-methyl-1-propanol with 1,2-benzenedicarboxaldehyde gave a product, mp 78-79°C. He assigned the product the ortho-substituted phenyloxazoline structure (I). We have repeated this reaction and obtained a product identical to that reported by Shipchandler (our melting point 76-77°C). However, attempted hydrolysis of this compound with mild acid failed.



I

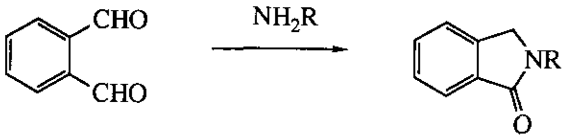
We have synthesized the proposed 2-(4,4-dimethyl-2-oxazolin-2-yl)benzenemethanol (I) by another route. The reaction of 2-(4,4-dimethyl-2-oxazolin-2-yl)benzoic acid (II)[2] with diazomethane gave the ester (III). This ester was reduced with lithium aluminum hydride to give the desired 2-(4,4-dimethyl-2-oxazolin-2-yl)benzenemethanol (I') in 88% yield.



IV III I'

The product I' obtained by lithium aluminum hydride reduction was different from I obtained by Shipchandler. The proton chemical shifts for the lithium aluminum hydride product I' were at 1.40 (methyl), 4.12 (oxazolinyl methylene), and 4.60 ppm (benzylic methylene) while the shifts for Shipchandler's product I were at 1.43, 3.88, and 4.50 ppm.

The reaction of 1,2-benzenedicarboxaldehyde with anilone (or other amines) leads to the substituted 1,3-dihydro-1-oxo-2H-isoindole (IVa).[3] We examined structures I and I' by ^{13}C nmr to determine if I or I' could be the isoindole IVb. We obtained the ^{13}C spectra of I and I' as well as of isoindole IVc (R=H) and 2-phenyl-4,4-dimethyl-2-oxazoline (V).[4] The results are shown in the Table. The chemical shifts match very well for oxazolines V and I'. The chemical shifts for isoindole IVc and Shipchandler's I also match very well. The isoindole carbonyl groups are shifted to lower frequency than the oxazoline imine carbons and the amidomethylene is shifted to higher frequency than the oxymethylene of the oxazolidine. Therefore, we believe that the product isolated by Shipchandler from 1,2-benzenedicarboxaldehyde and 2-amino-2-methyl-1-propanol should be formulated as 1,3-dihydro-1-oxo-2H-isoindole (IVb).[5]

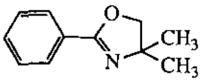
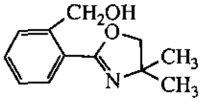


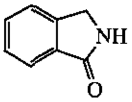
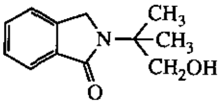
IV a,b   a, R = C_6H_5

b, R = $C(CH_3)_2CH_2OH$

Table

^{13}C Chemical Shifts

		C=N	CH_2O	quat-C	CH_3	CH_2OH
V		161.85	78.93	67.43	28.32	----
I'		162.23	78.74	67.95	28.44	64.55

		C=O	CH_2N	quat-C	CH_3	CH_2OH
IVc		172.4	46.01	-----	-----	-----
IVb (I)		169.71	49.20	59.45	23.80	70.02

EXPERIMENTS

Melting and boiling points are uncorrected. The following instruments were used: Thomas-Hoover melting point apparatus (uncorrected), Perkin-Elmer Infracord (ir), Varian T-60 and Varian XL 300 spectrometers (nmr). Microanalyses were performed by the Microanalytical Laboratories of American Cyanamid Company, Medical Research Division.

Methyl 2-(4,4-Dimethyl-2-oxazolin-2-yl)benzoate (III)

To a suspension of 2.9 g (13.7 mmol) of 2-(4,4-dimethyl-2-oxazolin-2-yl)benzoic acid (II), mp 176.5-179°C (lit.[2] mp 175.5-176.3°C), in 65 ml of anhydrous ether, cooled to 0°C, was added an ethereal solution of diazomethane until the yellow color persisted. After stirring for 1 h, the excess diazomethane was decomposed with acetic acid and the solvent removed in vacuo to give the ester III in quantitative yield; ir (neat): 1750, 1650, m 1250, 1120, 1100, 1050, 965, 770, and 735 cm^{-1}; nmr ($CDCl_3$): 1.38 (s, 6H, CH_3), 3.86 (s, 3H, OCH_3), 4.08 (s, 2H, CH_2), and 7.50 (m, 4H, aromatic). Anal. Calcd. for $C_{13}H_{15}NO_3$ C, 66.94; H, 6.48; N, 6.00. Found: C, 66.59; H, 6.72; N, 5.83.

2-(4,4-Dimethyl-2-oxazolin-2-yl)benzenemethanol (I)

To a suspension of 0.40 g (5.26 mmol) of lithium aluminum hydride, 50% in oil, in 10 ml of anhydrous ether was added 2.20 g (9.44 mmol) of ester III in 10 ml of anhydrous ether at a rate to boil the ether. Then the reaction was heated at reflux for an additional 30 min. After cooling, the reaction mixture was treated with 0.4 ml of 2N sodium hydroxide and then 0.6 ml of water. After stirring for 1 h, the ethereal solution was filtered through solid magnesium sulfate and the filtrate concentrated in vacuo. The residue was distilled bulb to bulb to give 1.7 g (88%) of benzyl alcohol I, bp 115°C (bath temp)/0.5 mm Hg; ir (neat): 3300m, 1640, 1030, 1020, 1015, 960, 780, and 750 cm^{-1}; nmr ($CDCl_3$): 1.40 (s, 6H, $(CH_3)_2$), 4.12 (s, 2H, CH_2), 4.60 (d, 2H, J = 8Hz, CH_2OH), 6.60 (t, 1H, J = 8Hz, OH), 7.39 (m, 3H, aromatic), and 7.8 (m, 1H, aromatic). Anal. Calcd. for $C_{12}H_{15}NO_2$:C, 70.22; H, 7.37; N, 6.82. Found: C, 70.38: H, 7.72; N, 6.55.

REFERENCES AND NOTES

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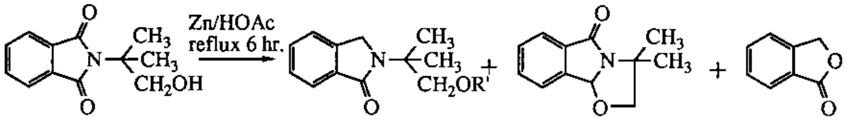
2. S. Chaloupka, P. Viltorelli, H. Heimgartner, H. Schmid, H. Link, K. Bernauer, and W. E. Oberhansli, Helv. Chim. Acta, 61, 2116 (1978).
3. G. Grabe and R. Pictet, Ann., 247, 302 (1888); J. Thiele and J. Schneider, ibid., 369, 287 (1909); T. DoMinh, A. L. Johnson, J. E. Jones, and P. P. Senise, Jr., J. Org. Chem., 42, 4217 (1977).
4. R. N. Boyd and R. H. Hansen, J. Amer. Chem. Soc., 75, 5896 (1953).
5. We attempted to prepare the suggested structure IVb directly by a zinc-acetic acid reduction of the phthalimide VI and isolated the products shown. The yields were determined by vpc and the retention time of IVb was the same as the material isolated by Shipchandler. However, the yield of isoindole IVb was considered too low to constitute a structure proof.



VI

IVb R' = H (4.1%)

R' = $COCH_3$ (16.4%)

(53.4%)

(19.8%)

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