N-(2-Hydroxyethyl)-4-(*p*-nitrobenzylidene)-1,4-dihydropyridine (DHP) from the Reaction of 4-(*p*-Nitrobenzyl)pyridine (NBP) with Ethylene Oxide

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The title reaction was carried out and characterization of the alkylation product (DHP, II) lead to the conclusion that it had a 1,4-dihydropyridine structure, rather than a pyridinium ion structure. The ^{13}C- and ^{1}H-nmr spectra, and the colors were especially important in establishing the structure.

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The use of 4-(*p*-nitrobenzyl)pyridine (I,NBP) as a chemical monitor for ethylene oxide (2) and for other alkylation reagents (3) has been reported. Carbowax solutions of NBP (I), a light yellow compound, spread on white filter paper comprise indicator paper that can be used to monitor the presence of ethylene oxide (4). Ethylene oxide is detected by the conversion of the white indicator papers, upon treatment with gaseous ethylene oxide, to a red-purple (or violet) color. Herein, we describe the preparative scale synthesis of this red-purple compound, its characterization and the determination of its structure.

Addition of ethylene oxide to NBP (I) in methanol solution or treatment of thin layers of Carbowax and alcohol solution with ethylene oxide, give rise to a red-purple compound. We now show (see below) the structure of the red-purple compound (in solution, solid crystalline forms are often dark green) to be *N*-(2-hydroxyethyl)-4-(*p*-nitrobenzylidene)-1,4-dihydropyridene (DHP, II). Samples of solid DHP (II) can be recrystallized (mp 147°); this compound is most interestingly nearly immobile on silica gel thin-layer chromatography (tlc); development with a variety of solvents did not move the red-purple spot sufficiently to allow its characterization. This compound (II) is, however, quite mobile on reverse-phase tlc (R_f= 0.66-0.67). We found that the R_f value of the red-purple compound produced in the preparative scale operations to be identical to the R_f value of samples isolated by extraction from indicator papers.

Molecular weight determined and quantitative elemental analyses (see experimental) of the red-purple compound agreed with structure II. The presence of the aromatic ring, the nitro group and the hydroxyl group are supported by the infrared spectrum. The color and the nuclear magnetic resonance (nmr) spectra are crucial in determining the postion of the π-bonds in this compound. This approach has been used before (3), and in like manner,our ^{1}H nmr data (Table I) and color observations support the dihydropyridine structure (II), rather than a pyridinum structure (III). Structures such as the latter have been reported to be colorless (3). Treatment of dihydropyridine II with acid converts II to a colorless compound, presumably pyridinium compond IV. Treatment of

STRUCTURES

NBP (I)

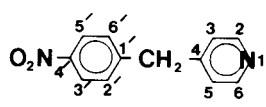
DHP (II)

(III)

(IV)

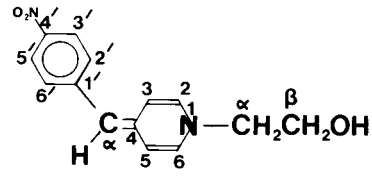
Table I

NMR Spectra of NBP (I) and of DHP (II)



NBP(I)

^{13}C NMR (a)



(II)

DHP

DBP (b)			DHP (b)			
assignment	δ	int (c)	assignment	δ	int (c)	o.r.d. mult (d)
C_2, C_6	149.83	m	C_2, C_6	116.5	w	d
*C_3, C_5	123.71	m	C_3, C_5	108.0	w	d
C_4	148.62	w	C_4	138.64	m	s
C_α	39.71	s	C_α	100.38	m	d
C_1'	146.28	w	C_4'	148.36	m	s
C_2', C_6'	130.16	m	*C_2', C_6'	123.28	s	d
*C_3', C_5'	124.20	m	*C_3', C_5'	124.30	s	d
C_4'	147.65	w	C_1'	141.73	m	s
			C_α'	57.11	m	t
			C_β'	60.33	m	t

^{1}H NMR (b)

NBP (e)				DHP (f)			
Assignment	δ	integ	mult (g)	assignment	δ	integ	mult
H_2,H_6	8.59	2H	m	H_2,H_6	7.00	2H	d (J = 9 Hz) (h)
H_3,H_5	7.15	2H	d (J = 6 Hz)	H_3,H_5	6.0-6.6	2H	m
H_α	4.12	2H	s	H_α	5.3	1.0H	s
H_2', H_6'	7.38	2H	d (J = 9 Hz)	H_2', H_6'	7.20	2H	d (J = 9 Hz)
H_3', H_5'	8.22	2H	d (J = 9 Hz)	H_3', H_5'	7.80	2H	d (J = 9 Hz)
				H_α', H_β'	3.4-3.8 (i)	4H	bs (m?)

(a) Determined on a Varian-CFT-20 instrument (20 MHz). (b) DMSO-d_6 solvent; deterium lock on solvent, δ = 0.00 for TMS carbons (^{13}C nmr) or protons (^{1}H nmr). (c) Intensity of proton-decoupled singlet: s = strong, m = medium, w = weak, b = broad. (d) Multiplicity of off-resonance decoupled multiplets; s = singlet, d = doublet, t = triplet, m = undefined multiplet. (e) Determined on Perkin Elmer R-20 instrument, 60 MHz. (f) Determined on Jeol-JMN-PS-100 (PFT) instrument; 100 MHz. (g) Multiplicity of ^{1}H signals: m = undefined multiplet, s = singlet, d = doublet, t = triplet, bs = broadened singlet. (h) Multiplicity visible only after heavy water treatment of DMSO-d_6 solution. (i) Signal overlapped by water signal. Position of OH proton of II not clearly established; weak signals in δ 5.8-6.6 area not identified.

the colorless compound with base regenerates the purple color. Our ^{1}H and ^{13}C nmr data are presented in Table I; the ^{13}C data for II are important in establishing the attached 2-hydroxyethyl group since the ^{13}C triplets at δ57.11 and 60.33 in the off-resonance decoupled spectrum as well as the 4H δ 3.4-3.8(^{1}H nmr) signal pinpoint the hydroxyethyl methylene groups of II.

EXPERIMENTAL

Elemental analyses were performed by Baron Consulting Co., Orange, Ct. Nmr spectra were taken on Perkin Elmer R-20 (^{1}H), Varian CFT-20 (^{13}C) and Jeol-JMN-PS-100 instruments. Ir spectra were taken on a Perkin Elmer 621 spectrometer and uv spectra on a Cary 219 spectrometer.

NBP (I) was obtained from Aldrich Chemicals and from Eastman. The purity of commerical NBP was variable, giving melting point of 66-72° (lit. (5), 74°) and the lower melting material showed two spots on silica gel tlc (ethyl acetate solvent, R_f of I = 0.60). Recrystallization of impure I from ethyl acetate/cyclohexane sovent pair gave pure NBP (mp 70-71°, one spot on tlc).

Preparation of *N*-(2-hydroxyethyl)-4-(*p*-nitrobenzylidene)-1,4-dihydropyridine (II,DHP).

A reflux apparatus was charged with 3.0 g (0.0014 moles) of 4-(*p*-nitrobenzyl)pyridine [I, NBP] dissolved in 15.0 ml of absolute methanol. To this was added 6.0 ml of liquid ethylene oxide and this solution was heated at *ca.* 37° for two hours. The reaction mixture was cooled under tap water until green precipitate had formed. This precipitate was collected by filtration, washed with ethyl acetate, and dried under dry nitrogen gas. This resulted in a 43% yield (1.57 g, 0.006 moles of crude DHP (II) as a green solid. This material showed a small amount of NBP on silica gel tlc; in view of the quantitative nmr results on such samples, it must be a minor amount. Samples such as these were used for nmr, ir and uv analyses. Tlc analysis on reverse-phase chromatographic sheets (RP-2, Darmstadt-Merck) gave the following results: 50%/50% = methanol/triethylamine, R_f = 0.03; 52.4%/41.9%/5.2%/0.5% = 50 ml/40 ml/5 ml/0.5 ml = acetonitrile/ethanol/water/formic acid, R_f = 0.66-0.67.

Tlc analysis on normal silica gel, using 50 ml/50 ml/10 ml = triethylamine/methanol/concentrated ammonium hydroxide, moved the DHP only slightly (R_f less than 0.1).

The precipitate recovered from a run such as described above was dried under dry nitrogen resulting in green needles, mp. 147° (melting gave an intractable amorphous globule).

Samples, prepared as described above, were dried over phosphorous pentoxide (overnight, room temperature).

Anal. Calcd. for $C_{14}H_{14}N_2O_3$: C, 65.13; H, 5.47; N, 10.85. Found: C, 64.89; H, 5.44; N, 11.09.

The uv-vis spectra showed that the green crystals dissolved in acetone gave λ max at 555 nm ($\epsilon = 2.11 \times 10^3$). Although the DHP is usually green in the solid state, solutions of DHP have a red-purple color and DHP shows as a red-purple spot on the tlc; ir spectrum of DHP (potassium bromide): 3430, b,s (OH stretch); 3050, m (aromatic and olefinic C-H stretch); 2840, w, 2820, w (aliphatic C-H stretch); 1645, s (ring C=C stretch), 1583, s (C=C stretch); 1529, s (asym. NO_2 stretch); 1420 m; 1408 m; 1380 w; 1335 m; (sym NO_2 stretch); 1280 s; 1190 m; 1163 s; 1142 m; 1108 m; 1077 m; 950 w; 935 w; 872 w; 846 m; 804 m; 736 w; 687 w; 589 s; 550 s; 525 m; 503 m.

REFERENCES AND NOTES

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