

## The 2:2 Adducts from Glutaraldehyde and 1-Substituted Ethylenediamines

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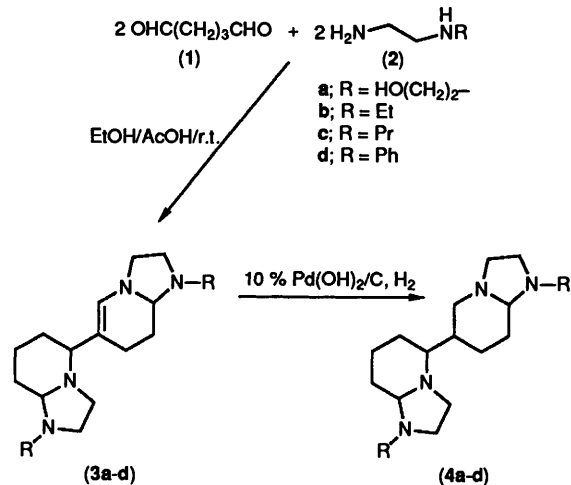
The reaction of glutaraldehyde (1) with *N*-substituted ethylenediamines (2) afforded the 2:2 adducts, 6-octahydroimidazo[1,2-*a*]pyridin-5-ylhexahydroimidazo[1,2-*a*]pyridine (3).

Glutaraldehyde is a useful annulating reagent for constructing heterocycles. So far, several reactions have been reported for the preparations of piperidine derivatives from primary amines and tetracarboxylhydridoferrate,<sup>1</sup> pyrido-oxazine-6-carbonitriles from glutaraldehyde dicyanohydrin and 3-aminopropanol,<sup>2</sup> oxazolizopiperidine-6-carbonitriles from ethanolamine and cyanide ion,<sup>3</sup> and pyridopyridine-6-carbonitriles from 1-methylpropane-1,3-diamine and cyanide ion.<sup>4</sup>

The products in these reactions, in all cases, were the 1:1 adducts of glutaraldehyde and the amines.

In connection with our work on saturated fused heterocycles using *N*-hydroxyethylenediamine (2a),<sup>5</sup> we have examined the reaction with glutaraldehyde (1). The reaction was achieved by the addition of (2a) to (1) in EtOH containing a drop of AcOH to afford the unexpected 2:2 adduct (3a). This reaction was extended to *N*-substituted ethylenediamines (2b-d) to afford the corresponding 2:2 adducts (3b-d). The results are shown in the Table.

Structural assignment for the products were made on the basis of spectral data and elemental analyses. The mass spectra indicated that the parent ions were equivalent to the sum of two molecules each of (1) and (2) minus four molecules of water. The IR spectra showed the characteristic strong absorptions for the C=C double bond of the enamine entity (1660–1650 cm<sup>-1</sup>) whilst in the <sup>1</sup>H NMR spectra, the enamine methine  $\alpha$ -proton signal appeared at  $\delta$  6.0–6.4. The <sup>13</sup>C NMR spectrum of (3b) showed 18 carbons, from 12 of which it was possible to calculate the ratio of each carbon for the two isomers. The DEPT method exhibited two methyl group carbons ( $\delta$  13.7 and 13.8), 11 methylene carbons ( $\delta$  19.5–51.2), and 3 methine carbons ( $\delta$  66.8, 77.8, and 83.8) and enamine  $\alpha$ - and  $\beta$ -carbons ( $\delta$  129.0 and 112.1). These results strongly supported the assigned structure of (3). Further, the catalytic hydrogenation of (3b) over 10% Pd(OH)<sub>2</sub>/C afforded the corresponding dihydrogenated compound (4), the structure of which was confirmed by the absence



Scheme 1.

of peaks for the enamine  $\alpha$ - and  $\beta$ -carbons in the <sup>13</sup>C NMR spectrum.

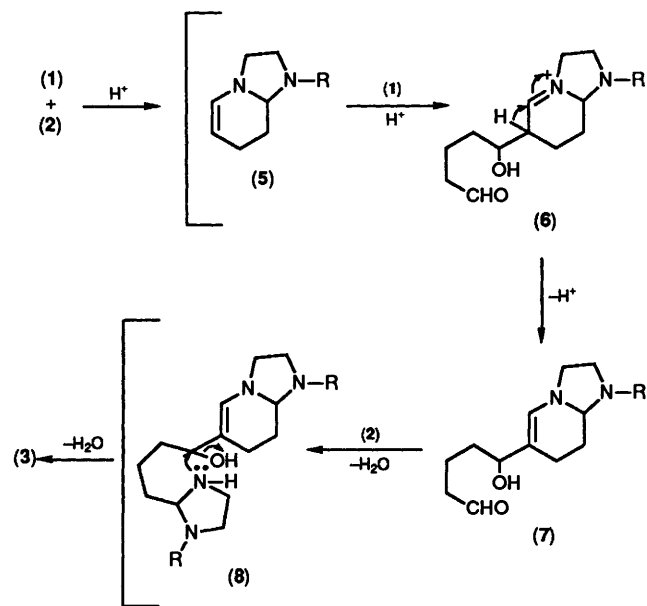
The reaction was assumed to proceed as follows: formation of unstable enamine intermediate (5) which then electrophilically attacks the aldehyde (1) to give, via (6), (7). Reaction of the latter with (2) affords (8), which undergoes dehydration to (3).

### Experimental

1-Ethyl-6-(1-ethyloctahydroimidazo[1,2-*a*]pyridin-5-yl)-1,2,3,7,8,8a-hexahydroimidazo[1,2-*a*]pyridine (3b).—A solution of (1) (50% w/v in water; 2.0 ml, 10 mmol) in EtOH (20 ml) was gradually added to a solution of (2) (10 mmol) in EtOH (20 ml)

Table 1. Compounds (3a-d).

(3)	M.p. (b.p./mmHg) (°C)	Yield (%)	$m/z$ ( $M^+$ )	$\nu_{\max}$ (KBr)/ $\text{cm}^{-1}$
a	122	60	336	3 500 (OH), 1 650 (C=C)
b	156–157/0.5	52	304	1 660 (C=C)
c	128–130/0.2	42	332	1 660 (C=C)
d	94–95	56	400	1 660 (C=C)



Scheme 2.

containing a drop of AcOH, over 1 h at room temperature under an atmosphere of argon. The reaction mixture was stirred for 12 h and then evaporated to dryness under reduced pressure. The residue was dissolved in water (100 ml), and the aqueous solution was extracted with  $\text{CH}_2\text{Cl}_2$  ( $3 \times 20$  ml). Evaporation of the extract and distillation under reduced pressure of the

residue gave the product (1.6 g, 52%), b.p. 156–157 °C/0.5 mmHg (Found: C, 71.23; H, 10.75; N, 18.32%.  $\text{C}_{18}\text{H}_{32}\text{N}_4$  requires C, 71.00; H, 10.59; N, 18.40%);  $\nu_{\max}$ (film) 1 660 (C=C), 1 280, 1 215, 1 108  $\text{cm}^{-1}$ ;  $m/z$  304 ( $M^+$ , 100%), 275 (37%), 246 (21%), and 178 (65%);  $\delta_{\text{H}}$ ( $\text{CDCl}_3$ ) 1.09 (3 H, t,  $J$  7.3 Hz, Me), 1.15 (3 H, t,  $J$  7.3 Hz, Me), 1.18–1.63 (2 H, m,  $\text{CH}_2$ ), 1.81 (2 H, m,  $\text{CH}_2$ ), 1.89–2.43 (12 H, m,  $\text{CH}_2 \times 6$ ), 2.76–2.89 (3 H, m,  $\text{CH}_2$  and CH), 3.01–3.14 (2 H, m,  $\text{CH}_2$ ), 3.17–3.24 (2 H, m,  $\text{CH}_2$ ), 3.28 (1 H, q,  $J$  6.6 Hz, CH), 3.48 (1 H, m, CH), and 5.97 (1 H, s, CH=);  $\delta_{\text{C}}$ ( $\text{CDCl}_3$ ) 13.67, 13.75 (Me), 19.51 and 20.33, 22.89 and 23.03, 27.00 and 27.17, 29.19 and 29.30, 30.95 and 31.65, (C– $\text{CH}_2$ –C), 46.58 and 46.62, 47.88, 48.66, 48.85, 49.48, and 51.20 and 51.30 ( $\text{CH}_2\text{N}$ ), 66.79 and 67.32 (CHN), 77.40 and 77.75, 83.83, and

84.17 (NCHN), 112.11 and 112.46 (–C–), 128.95 and 129.17 (CN=).

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