***N*-(2-Phenethyl)-3,5-diphenylpyrrole-2-carboxamide (7).** A mixture of 6.30 g (0.022 mol) of ethyl 2,4-diphenylpyrrole-5-carboxylate and 8.47 g (0.070 mol) of β-phenethylamine was heated at 240–250° for 8 hr. The dark brown liquid was cooled to room temperature and then induced to deposit crystals by addition of small amounts of ether and Skelly B solvent. The solid was washed with ether and crystallized from 95% ethanol to give 2.80 g (35%) of **7**: mp 177–179°; ir ($CHCl_3$) 3435 (NH), 1627 (amide C=O) cm^{-1}; nmr ($CDCl_3$) δ 2.68 (t, 2 H, J = 6.7 Hz), 3.52 (q, 2 H, J = 6.7 Hz), 5.85 (t, broad, 1 H), 6.49 (d, 1 H, J = 3 Hz), 6.9–7.8 (m, 15 H), 10.55 (s, broad, 1 H).

Anal. Calcd for $C_{25}H_{22}N_2O$: C, 81.93; H, 6.05; N, 7.65. Found: C, 82.14; H, 6.04; N, 7.60.

2-(3,4-Dihydro-1-isoquinolyl)-3,5-diphenylpyrrole (8). A mixture of 1.0 g (2.7 mmol) of **7** and 10 g of phosphorus pentoxide in 15 ml of anhydrous *p*-xylene was heated under reflux for 6 hr. The hot *p*-xylene layer was decanted from a black, insoluble residue. The residue was added to 600 ml of ice-cold water with stirring, and a brown solid which formed was collected by filtration, washed with water, and suspended in concentrated sodium hydroxide solution. The suspension was diluted with water and then neutralized with 6 *N* sulfuric acid. The mixture was extracted with benzene, and the benzene extract was washed with water and dried over anhydrous magnesium sulfate. The solvent was evaporated, and the residue was chromatographed on alumina by the dry column technique.[15] Elution with benzene produced a yellow band near the top of the column, and this was cut out and extracted with benzene. Evaporation of the benzene gave a brown solid, which was crystallized from 95% ethanol–Skelly B solvent. A crystalline product of mp 209–211° was recrystallized from acetone to give 0.20 g (21%) of **8**: mp 214–216°; ir ($CHCl_3$) 3440 (NH), 1601 (C=N) cm^{-1}; nmr ($CDCl_3$) δ 2.70 (t, 2 H, J = 7 Hz), 3.60 (t, 2 H, J = 7 Hz), 6.76 (s, 1 H), 6.8–7.8 (m, 14 H), 10.26 (s, broad, 1 H).

Anal. Calcd for $C_{25}H_{20}N_2$: C, 86.17; H, 5.79. Found: C, 86.14; H, 5.85.

2-(1-Isoquinolyl)-3,5-diphenylpyrrole (6). A mixture of 0.15 g (0.43 mmol) of **8** and 0.08 g of 10% palladium-on-carbon catalyst was suspended in 6 ml of decalin and refluxed in a nitrogen atmosphere, with stirring, for 5 hr. The mixture was filtered, and the filtrate was evaporated to dryness by application of a jet of air. The residue was triturated in petroleum ether, then crystallized from benzene–Skelly B solvent. The product, mp 221–223°, was chromatographed on alumina by the dry column technique.[14] Two yellow bands were developed by elution with benzene. The eluent of the first yellow band gave 0.06 g (40%) of **6** on evaporation, mp 226–228° (after recrystallization from 95% ethanol), also in admixture with the sample prepared by decarbethoxylation of **5**. The ir and nmr spectra of the two samples were identical.

Condensation of 1 (R = C_6H_5) with Ethyl *p*-Nitrocinnamate. The reaction of 2.32 g (6.66 mmol) of **1** (R = C_6H_5) with 1.45 g (6.55 mmol) of ethyl *p*-nitrocinnamate in 20 ml of dimethylformamide was carried out in the same manner as described previously for the corresponding ethyl cinnamate reaction. There was obtained 1.88 g (62%) of yellow crystals of ethyl 2-(1-isoquinolyl)-3-(*p*-nitrophenyl)-5-phenylpyrrole-4-carboxylate: mp 224–225°; ir ($CHCl_3$) 3440 (NH), 1700 (ester C=O), 1345 (NO_2), 1510 (NO_2) cm^{-1}; nmr ($CDCl_3$) δ 1.00 (t, 3 H, J = 7 Hz), 4.10 (q, 2 H, J = 7 Hz), 7.0–8.1 (m, 15 H), 13.80 (s, 1 H).

Anal. Calcd for $C_{28}H_{21}N_3O_4$: C, 72.56; H, 4.57; N, 9.07. Found: C, 72.72; H, 4.45; N, 8.89.

Condensation of 1 (R = C_6H_5) with Ethyl Acrylate. A mixture of 1.5 g (4.31 mmol) of **1** (R = C_6H_5), 3 ml of ethyl acrylate, and 30 ml of methylene chloride was heated under reflux as 95% ethanol was added slowly until the solution became clear, 70 ml being required. The solution was refluxed for another hr, and the solvents were removed by evaporation in a rotary evaporator. The reddish residue was extracted with 300 ml of benzene and chromatographed on neutral alumina to give a yellow, gummy material. This was induced to crystallize from a mixture of ethyl acetate and Skelly B solvent. There was obtained 0.99 g (67%) of ethyl 2-(1-isoquinolyl)-5-phenylpyrrole-3-carboxylate, mp 149–150°, also in admixture with a sample of the known[10] compound. The ir and nmr spectra of the two samples, taken in chloroform and deuteriochloroform, respectively, were identical.

Acknowledgment. This work was supported in part by a grant from the National Science Foundation.

Registry No.—**1** (R = C_6H_5), 33969-32-3; **5**, 53778-22-6; **6**, 53778-23-7; **7**, 53778-24-8; **8**, 53778-25-9; ethyl cinnamate, 103-36-6; ethyl 2,4-diphenylpyrrole-5-carboxylate, 53778-26-0; ethyl bromide, 74-96-4; 2,4-diphenylpyrrole, 3274-56-4; β-phenethylamine, 64-04-0; ethyl *p*-nitrocinnamate, 953-26-4; ethyl 2-(1-isoquinolyl)-3-(*p*-nitrophenyl)-5-phenylpyrrole-4-carboxylate, 53778-27-1; ethyl acrylate, 140-88-5.

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Synthesis of 2-Methylpiperidine-*2-d*. Choice of Reductive Methods from Azomethine Precursors[1]

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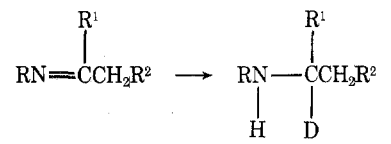
The synthesis of *2-d* 2-alkylamines by reductive methods from azomethine precursors (eq 1) is attended with some

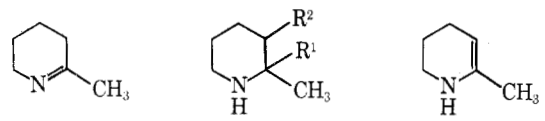


(1)

difficulties. We wish to report a simple method avoiding these problems.

Thus, catalytic deuteration (PtO_2) of 2-methyl-Δ^1-piperideine[2] in methyl acetate gave a product showing two signals of equal intensity for the methyl group in its NMR spectrum: a doublet (J = 6 Hz) at 1.05 ppm and a singlet at 1.05 ppm. From the ratio of methyl protons:methylene protons at C-3, 4, and 5 (m, 1.15–2.05 ppm):methylene protons at C-2 and 6 (m, 2.4–3.4 ppm), the composition of the mixture was 20% each of **2a** and **2b** and 30% each of **2c** and **2d**; mass spectral data confirmed *m/e* 99, 100, and 101.

This result may be explained by the possibility of rearrangement of the azomethine **1** to the tautomeric enamine **3**,[3] allowing hydrogen from position 3 to enter the pool. Olefins are known to isomerize on catalytic hydrogenation,[4] leading to a mixture of reduction products.[5] Alternatively, the known[4] reversibility of the hydrogenation step could result in the introduction of hydrogen (as DH) into the

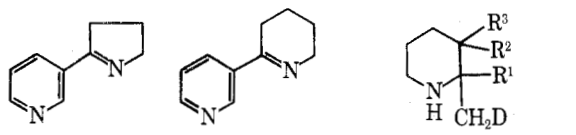


1 2a, $R^1 = R^2 = H$ 3

b, $R^1 = D$, $R^2 = H$

c, $R^1 = R^2 = D$

d, $R^1 = H$, $R^2 = D$



4 5 6a, $R^1 = R^2 = D$, $R^3 = H$

b, $R^1 = R^2 = R^3 = D$

deuterium pool, giving molecules containing more than two deuterium atoms. However, no exchange was observed (NMR) on submitting **2a** to the same catalytic deuteration conditions used above, so that the first explanation appears the more likely.

A similar effect may account for the results reported[6] on catalytic deuteration of myosmine **4** which yielded nornicotine-2-d_1 containing 65% d_1 and 35% d_0 species, and of anabasene **5** which afforded 70% d_1 and 30% d_0 species.

Sodium borohydride (usually in methanol or ethanol solution) has been shown[7,8] to be an effective reagent for the reduction of isolated Schiff bases, although this reduction is relatively slow[9,10] compared with that of aldehydes and ketones.[11] Two examples[12] of borodeuteride reduction of cyclic iminium salts are recorded in the yohimbine series, using deuteriomethanol as solvent.[13]

When **1** was reduced with sodium borodeuteride in D_2O and CH_3OD, the product showed a singlet for the methyl group (1.05 ppm) indicating the absence of hydrogen at C-2. The ratio of methyl:C-3, 4, and 5 methylene:C-6 methylene protons was, however, 2:4.6:2, and this together with mass spectral data (*m/e* 102 and 103) indicated a 1:1 mixture of **6a** and **6b.** Allylic deuterium exchange of **1** with the solvent thus appears to be a faster process than reduction.

In agreement with this conclusion, reduction of **1** with borodeuteride under identical conditions but using *aqueous methanol* gave pure **2b** in excellent yield, fully deuterated at C-2 only, as shown by the appearance of a singlet for the methyl group in its nmr spectrum.

Kinetic studies on the hydrolysis of hydroborate and of d_4-hydroborate,[14a] and of hydrogen exchange between hydroborate and water,[14b] suggested that the rate of exchange is only 6% of that for hydrolysis, and it has been shown[15] that there is very little isotopic exchange of sodium borohydride in aqueous solution at pH 9 and none[16] at pH 12. The preparation reported above confirms that borodeuteride reduction of Schiff bases, albeit slower than that of carbonyl, is fast enough to permit quantitative conversion of, e.g., **1** → **2b** to take place in protic solvents such as aqueous methanol without hydrogen exchange, double bond migration, or other side reactions.[17]

Experimental Section

2-Methylpiperidine-2-*d*. **1** (1g) was stirred with 0.42 g (1 mol) of $NaBD_4$ in 2 ml of CH_3OH and 3 ml of H_2O at 20° for 16 hr. Removal of CH_3OH, extraction with ether, and distillation of the dried (Na_2SO_4) extract gave 0.8 g (80%) of **2b:** bp 117°; mol wt, 100 (calcd for $C_6H_{12}DN$: 100), NMR ($CDCl_3$) δ 1.06 (s, 3 H), 1.15–2.05 (m, 6 H), 2.4–3.4 (m, 2 H). The product showed a single peak on GLC (10% Apiezon-L, 2% KOH on 80/100 Supelcon AW, column temp 70°) identical in retention time (2.88 min) with that of **2a** but different from that of **1** (4.3 min).

Registry No.—**1,** 1462-92-6; **2b,** 5382-40-2; $NaBD_4$, 15681-89-7.

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