3'-Deoxy-3'-fluoroadenosine (3a). Compound **33** (0.3 g, 0.3 mmol) was treated with a mixture of CF_3CO_2H–$CHCl_3$ as described for **1b**. The crystalline **3a** (76.0 mg, 94%) had mp 210–211 °C (lit.[13] mp 205 °C; lit.[14] mp 211–212 °C). ^1H NMR of this sample was identical with that reported earlier.[14]

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Characterization of an Unexpected Product from a Monoamine Oxidase B Generated 2,3-Dihydropyridinium Species

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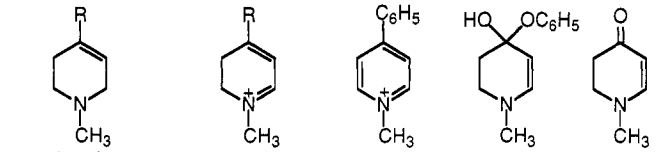
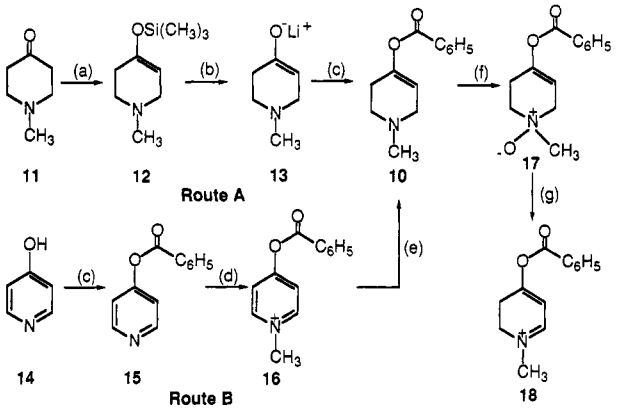
This report summarizes the unexpected properties of the 2,3-dihydropyridinium species generated by the monoamine oxidase B catalyzed oxidation of 4-(benzoyloxy)-1-methyl-1,2,3,6-tetrahydropyridine, an analog of the neurotoxic 4-phenyltetrahydropyridine derivative. Unlike the corresponding 4-aryloxy and 4-carbamoyloxy derivatives which undergo rapid hydrolytic cleavage via a 1,4-addition of water, the benzoyloxy metabolite undergoes a 1,2-addition reaction to yield a carbinolamine that subsequently rearranges to a β-keto aldehyde that was characterized as the corresponding pyrazole. From these results it appears that, under physiological conditions, 2,3-dihydropyridinium species in general may exist in equilibrium with the corresponding carbinolamines and ring-opened amino aldehydes, species which may be of importance in understanding the chemical and biological properties of these heterocyclic systems.

The neurotoxic cyclic allylamine 1-methyl-4-phenyl-1,2,3,6-tetrahydropyridine (**1**) is an excellent substrate for brain monoamine oxidase B (MAO-B) which catalyzes its bioactivation to the dihydropyridinium species **2**,[1,2] an unstable intermediate that spontaneously oxidizes to the putative ultimate toxin **3**.[3] In contrast to this behavior, the corresponding phenoxy derivative **4** generates the dihydropyridinium metabolite **5** which rapidly hydrolyzes, presumably via the hemiketal **6**, to yield the amino enone **7** and phenol. Analogous behavior has been observed with carbamoyloxy analogs (**8**, R' = CH_3 and C_6H_5) which are converted via **9** to **7** and dimethylamine or *N*-methylaniline.[4] The possibility of developing tetrahydropyridine derivatives bearing biologically active moieties that are released in the central nervous system following enzymatic bioactivation has prompted the chemical and metabolic studies on 4-(benzoyloxy)-1-methyl-1,2,3,6-tetrahydropyridine (**10**) reported in this paper.



Our initial synthetic approach to **10** (Scheme I, route A) involved treatment of the (trimethylsilyl)oxy derivative **12**, obtained from 1-methyl-4-piperidone (**11**) and trimethylsilyl chloride, with methyllithium in THF/HMPA to generate the corresponding lithium enolate **13**.[5] Reaction of **13** with benzoic anhydride afforded a moderate yield of the desired product **10**. An improved synthesis of the target compound (Scheme I, route B) proceeded through O-benzoylation of 4-hydroxypyridine (**14**) followed by treatment of the resulting 4-(benzoyloxy)pyridine (**15**) with iodomethane to yield the corresponding *N*-methylpyridinium species **16**. Reduction of **16** with sodium borohydride[6] gave the desired tetrahydropyridine **10** in 61% overall yield.

Scheme I. Synthetic Pathways to (Benzoyloxy)tetrahydropyridine 10[a]



[a] (a) $ClSi(CH_3)_3$, $(CH_3CH_2)_3N$; (b) CH_3Li, THF/HMPA; (c) $(C_6H_5O)_2O$; (d) CH_3I; (e) $NaBH_4$; (f) *m*-CPBA; (g) $(CF_3CO)_2O$.

Incubation of **10** with purified MAO-B isolated from beef liver led to the rapid formation of a compound with λ_{max} 283 nm to which we initially assigned the expected dihydropyridinium structure **18**. The formation of this product was completely inhibited by pretreatment of the enzyme preparation with 10^{-6} M deprenyl, a potent inactivator of MAO-B.[7] Furthermore, treatment of the

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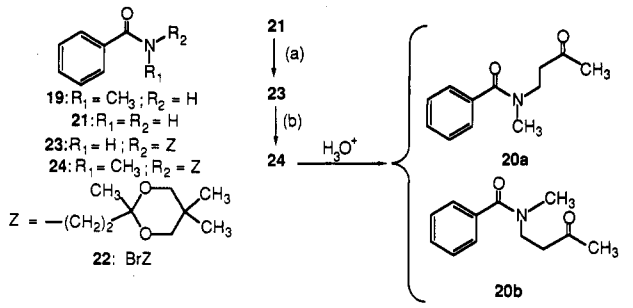
Scheme II. Synthesis of the Methyl Ketone 20[a]



[a] (a) 50% NaOH, $(Bu)_4^+HSO_4^-$, 22; (b) KOH, CH_3I, DMSO.

post-incubation mixture with sodium borohydride (to reduce the azomethine system)[8] or sodium cyanide (to add across the azomethine system)[9] led to the loss of the choromophore at 283 nm, behavior which is consistent with a dihydropyridinium moiety. On the other hand, this compound did not convert to the amino enone 7 (λ_{max} 324 nm) as expected. The possibility that 18 had undergone in situ autoxidation or disproportionation to yield the pyridinium product 16 as observed with some dihydropyridinium species[10] could be ruled out since 16 absorbs maximally at 243 nm.

These results argued that the 283-nm absorbing product was not the expected dihydropyridinium metabolite 18 and suggested an unexpected conversion of one of the radical intermediates thought to be involved in the MAO-B catalytic pathway[11] or of the dihydropyridinium species itself. An authentic sample 18 as its stable perchlorate salt was prepared by oxidation of the tetrahydropyridine 10 with *m*-chloroperoxybenzoic acid (*m*-CPBA) followed by treatment of the resulting *N*-oxide 17 with trifluoroacetic anhydride (Scheme I).[12] Compound 18 in acetonitrile displayed a stable chromophore which absorbed maximally at 300 nm. A solution of 18 in sodium phosphate buffer (pH 7.4) also absorbed maximally at 300 nm but within a few minutes the λ_{max} shifted to 283 nm, the same chromophore observed in the MAO-B incubation mixture of the tetrahydropyridine substrate 10. Based on these results, we suspected that 10 had undergone the expected MAO-B catalyzed oxidation to yield the dihydropyridinium metabolite 18 but that under the incubation conditions 18 was transformed to a product of unknown structure.

The GC-EI total ion current mass chromatogram of a dichloromethane extract obtained from a pH 7.4 buffered phosphate solution containing the 283-nm absorbing species displayed two major components, A and B. The mass spectrum of A ($M^{\bullet+}$ at *m/z* 135 and base peak at *m/z* 105) was identical to that of synthetic *N*-methylbenzamide (19, Scheme II). The mass spectrum of B exhibited a molecular ion at *m/z* 205 (10) and fragment ions at *m/z* 204 ($M^{\bullet+}$ – H, 10), 162 (204 fragment – CH_2CO, 15), 105 ($C_6H_5CO^+$, 100), and 77 ($C_6H_5^+$, 50), consistent with the methyl ketone derivative 20. An authentic sample of 20 was prepared by condensation of the sodium salt of benzamide (21)[13] with the methyl vinyl ketone synthon 22 followed by N-methylation[14] of the intermediate 23 and hydrolysis of the resulting N-methylated product 24 (Scheme II). The ambient temperature ^1H NMR spectrum of this product displayed all of the signals expected for 20 as pairs in a ratio of 3:1. Upon warming to 54 °C these pairs collapsed to broad peaks, suggesting the presence of a pair of rotamers, 20a and 20b. The GC-EI mass spectrum of synthetic 20 was identical to the corresponding spectrum of B observed in the anaylsis of the incubation mixture isolate.

The carbon composition (C_{12}) of 20 differs from that of the dihydropyridinium species 18 (C_{13}) by a one-carbon unit, suggesting that compound 20 was a thermal breakdown product of the corresponding β-keto acid 25 or β-keto aldehyde 26 (see Scheme III). Preparative thin layer chromatography of the above dichloromethane extract used for mass spectral analysis provided a partially purified sample of the 283-nm absorbing product which upon FAB mass spectral analysis exhibited a protonated molecular ion at *m/z* 234 and fragment ions at *m/z* 190 (MH^+ – CH_3CHO), 162 (190 fragment – CO), 147 (162 fragment – $^\bullet CH_3$), 136 [$(C_6H_5CONHCH_3)H^+$], and 105 ($C_6H_5CO^+$), consistent with the β-keto aldehyde 26. As observed with the enzyme-generated product, treatment of 26 with sodium borohydride (reduction of the carbonyl groups) and potassium cyanide (cyanohydrin formation) led to loss of the 283-nm chromophore due to the β-keto aldehyde moiety.[15] The observed thermal instability of 26 may be analogous to the metal-catalyzed thermal decarbonylation reactions of β-keto aldehydes.[16,17]

Treatment of the crude preparation of 26 with hydrazine gave a product displaying a GC-EI mass spectrum and parent ion exact mass consistent with the pyrazole 31 or its tautomer. As observed with the methyl ketone 20, the ^1H NMR signals appeared as pairs, this time in a rato of 3:2. All of the signals could be assigned satisfactorily on the basis of the pair of rotamers 31a and 31b (see Experimental Section).[15] Once again, upon heating each of the paired signals coalesced to a broad peak as would be expected of such rotamers. C-Formylation of the methyl ketone 20 also gave a crude sample of the β-keto aldehyde 26 which again was characterized as the pyrazole derivative 31. Finally compound 31 could be obtained by treating an MAO-B incubation mixture of the tetrahydropyridine 10 with hydrazine.

Collectively the above results establish that the fate of the dihydropyridinium metabolite derived from the MAO-B catalyzed oxidation of the (benzoyloxy)tetrahydropyridine 10 is different from that of related 4-substituted tetrahydropyridines (e.g., 4 and 8) that we have studied. Rather than the usual 1,4-attack of water resulting in amino enone formation, the (benzoyloxy)dihydropyridinium metabolite 18 undergoes 1,2-hydration to form the carbinolamine 28 (Scheme III). Carbon–nitrogen bond cleavage of 28 generates the amino aldehyde 29 which then rearranges via intermediate 30 to yield the β-keto aldehyde 26. The higher susceptibility of the ester moiety to the intramolecular aminolysis reaction compared to the carbamoyloxy moiety might explain the different fates of the dihydropyridinium metabolites derived from the corresponding tetrahydropyridine substrates. The results of this study argue that, under physiological con-

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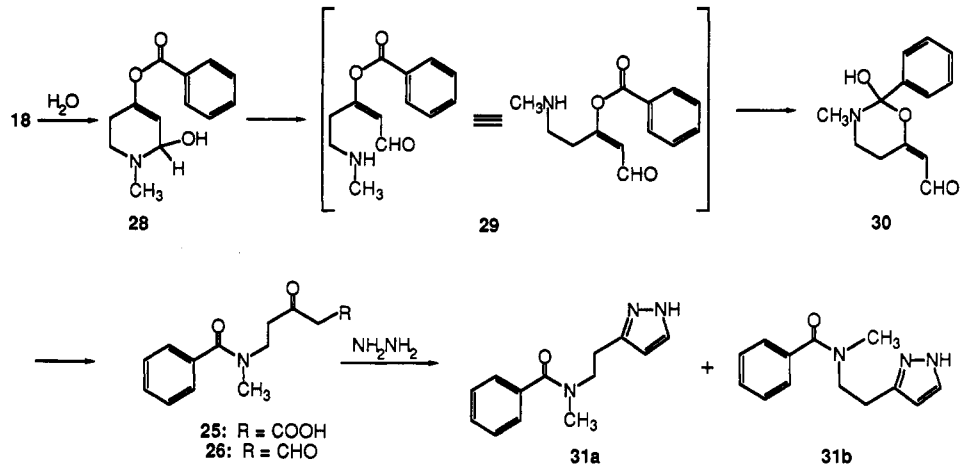
Scheme III. Proposed Mechanism for the Formation of the β-Keto Aldehyde 26 from the Dihydropyridinium Metabolite 18



ditions, 2,3-dihydropyridinium species in general exist in equilibrium with the corresponding carbinolamines and ring-opened amino aldehydes, an observation which may be valuable when attempting to interpret the chemical and biological behavior of these heterocyclic systems.

Experimental Section

Reactions requiring anhydrous conditions were carried out under a nitrogen atmosphere. ^{1}H NMR spectra were taken on a Bruker WP270SY 270-MHz spectrometer; chemical shifts are recorded in parts per million (ppm) relative to TMS as internal standard. FAB (using *p*-nitrobenzyl alcohol as matrix) and direct insertion probe high resolution EI mass spectra were obtained on a VG 7070 HF instrument and capillary column (HP-1) GC-EI mass spectra on a temperature programmed (50 °C for 1 min, 25 °C/min to 275 °C) HP 5890 gas chromatograph linked to an HP 5970B quadrupole mass spectrometer. UV spectra were taken on a Beckman DU-50 spectrophotometer. Elemental analyses were performed by Atlantic Microlab, Inc., Norcross, GA. Melting points were determined on a Thomas-Hoover melting point apparatus and are uncorrected.

1-Methyl-4-(benzoyloxy)-1,2,3,6-tetrahydropyridine (10). Method A. A mixture of 1-methyl-4-((trimethylsilyl)oxy)-1,2,3,6-tetrahydropyridine (12, 1 mL, 6 mmol), which was prepared according to the procedure of Wanner,[18] and methyllithium (4.5 mL of a 1.4 M ether solution, 6 mmol) in dry THF (15 mL) was stirred at room temperature for 6 h to form a clear yellow solution of the enolate. The mixture was treated with hexamethylphosphoramide (HMPA, distilled from CaH_2, 5 mL) followed by a solution of benzoic anhydride (1.4 g, 6 mmol) in THF (15 mL). After the reaction mixture was stirred for 1 h, it was poured into 50 mL of water, and the resulting mixture was extracted with hexane (30 mL × 2). The combined organic layers were washed with 5% sodium bicarbonate solution (50 mL) and dried (magnesium sulfate), and the solvent was removed in vacuo to afford a light oil. The product was purified further by chromatography (silica gel, ethyl acetate:methanol, 9:1) to yield **10** (550 mg, 42%) as a light yellow crystalline solid: mp 47–49 °C; UV λ_{max} (water) 233 nm (ε 12550); ^{1}H NMR ($CDCl_3$) δ 2.40 (m, 2 H, C 3), 2.42 (s, 3 H, N CH_3), 2.72 (t, 2H, C 2), 3.12 (d, 2 H, C 6), 5.52 (t, 1 H, C 5), 8.05–8.15 and 7.42–7.65 (m, 5 H, ArH); GC/MS (t_R 6.21 min) *m/z* (rel intensity) 217 ($M^{\bullet+}$, 10), 112 (40), 105 (100), 96 (35), 77 (45), 70 (30). Anal. Calcd for $C_{13}H_{15}NO_2$: C, 71.87; H, 6.96; N, 6.45. Found: C, 71.74; H, 6.98; N, 6.45.

Method B. A solution of 4-(benzoyloxy)pyridine (**15**, 2.0 g, 10 mmol)[19] and iodomethane (3.2 mL, 50 mmol) was stirred at room temperature in anhydrous acetone (30 mL) for 3 h. The precipitate obtained was filtered and recrystallized from acetone to give the iodide salt of the **4-(benzoyloxy)-1-methylpyridinium species 16** (2.56 g, 74%) as a light yellow crystalline solid: mp 203–205 °C dec; UV λ_{max} (water) 246 nm (ε 20180); ^{1}H NMR (CD_3OD) δ 4.48 (s, 3 H, N CH_3), 8.05–8.15 and 7.42–7.65 (m, 5 H, ArH), 8.16 (d, 2 H, C 3 and C 5), 9.02 (d, 2 H, C 2 and C 6); GC-EIMS [of the thermally generated **15** (t_R 5.94 min)] *m/z* rel intensity) 199 ($M^{\bullet+}$, 5), 105 (100), 77 (45), 51 (20). Anal. Calcd for $C_{13}H_{12}NO_2I$: C, 45.77; H, 3.55; N, 4.11. Found: C, 45.73; H, 3.57; N, 4.12. Sodium borohydride (224 mg, 5.88 mmol) was added to a solution of methiodide **16** (1 g, 2.94 mmol) in methanol (30 mL) at 0 °C. The reaction mixture was stirred for 5 min and then was concentrated in vacuo. The residue in 20 mL of water was extracted with ethyl acetate (2 × 30 mL). The organic layer was dried and evaporated in vacuo to give **10** (530 mg, 83%). The spectroscopic data of this product were identical with those reported above. The free base was converted to its oxalate salt in THF and was recrystallized from acetonitrile:ether: mp 196–197 °C.

Incubation of 4-(Benzoyloxy)-1-methyl-1,2,3,6-tetrahydropyridine (10) with MAO-B. MAO-B was isolated from bovine liver mitochondria by the procedure of Salach.[20] A pH 7.4, 0.1 M sodium phosphate buffered solution of the tetrahydropyridine **10** (0.5 mM, 0.5 mL total final volume) and MAO-B (0.05 unit, equivalent to 175 pmol, in 50 μL of buffer) was scanned at 37 °C from 360 to 220 nm at 5-min intervals for 90 min. The data were obtained as difference spectra with the $t = 0$ scan of the total mixture taken as background. A chromophore with λ_{max} 283 nm appeared and increased smoothly in intensity over the first 30 min and then remained stable (maximum absorbance of 0.7 OD unit) over the remaining 60 min.

1-Methyl-4-(benzoyloxy)-1,2,3,6-tetrahydropyridine *N*-Oxide (17). *m*-CPBA (1.34 g, 7.7 mmol) was added to a solution of 4-(benzoyloxy)-1,2,3,6-tetrahydropyridine (**10**, 1.0 g, 4.6 mmol) in dichloromethane (50 mL) at 0 °C. The reaction mixture was stirred for 1 h and evaporated in vacuo, and the residue was triturated with anhydrous ether (30 mL). The solid obtained was filtered and washed with ether to afford the *m*-chlorobenzoic acid salt of the *N*-oxide **17** (1.0 g, 55%). This salt (0.03 g) was passed through a short alumina column with dichloromethane and dichloromethane–methanol (9:1) to obtain the free base as a hydrate: mp 88–90 °C; ^{1}H NMR ($CDCl_3$) δ 2.8 (m, 2 H, C 3), 3.4 (s, 3 H, NCH_3), 3.65 (t, 2 H, C 2), 4.1 (d, 2 H, C 6), 5.55 (t, 1 H, C 5), 7.55 (t, 2 H, ArH), 7.65 (t, 1 H, ArH), 8.18 (d, 2 H, ArH). Anal. Calcd for $C_{13}H_{15}NO_3 \cdot 1.2H_2O$: C, 61.22; H, 6.82; N, 5.49. Found: C, 61.22; H, 6.88; N, 5.78.

1-Methyl-4-(benzoyloxy)-2,3-dihydropyridinium Perchlorate (18). A solution of trifluoroacetic anhydride (1 mL, 1.4 g, 6.6 mmol) in dichloromethane (10 mL) was added in a dropwise manner to a solution of the *m*-chlorobenzoic acid salt of the *N*-oxide **17** (0.500 g, 1.28 mmol) in dichloromethane (50 mL). The reaction mixture was stirred at 0 °C for 1 h and concentrated in vacuo to give a yellow oil which was treated with ethanolic perchloric acid (prepared by mixing one part of 95% ethanol and one part of 70% perchloric acid). Recrystallization of the resulting solid from acetonitrile and ether afforded the desired dihydro-

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pyridinium perchlorate **18** (0.370 g, 91%): mp 153–154 °C; ^{1}H NMR (CD_3CN) δ 3.1 (t, 2 H, C 3), 3.6 (s, 3 H, N CH_3), 4.0 (t, 2 H, C 2), 6.7 (d, 1 H, C 5), 7.55 (t, 2 H, ArH), 7.65 (t, 1 H, ArH), 8.18 (d, 2 H, ArH), 8.3 (d, 1 H, C 6). Anal. Calcd for $C_{13}H_{14}NO_6Cl$: C, 49.45; H, 4.46; N, 4.43. Found: C, 49.26; H, 4.47; N, 4.40.

Formation of the β-Keto Aldehyde 26 from the Dihydropyridinium Species 18. After being allowed to stand for a few minutes at room temperature, a solution of the dihydropyridinium perchlorate **18** (0.100 g, 0.3 mmol) in pH 7.4 buffered 0.1 M sodium phosphate solution (100 mL) was extracted with dichloromethane (2 × 100 mL) and the combined extracts were dried (sodium sulfate) and evaporated in vacuo. The residue thus obtained (50 mg) was loaded onto a preparative TLC plate (silica gel) which was developed three times with a mixture of ethyl acetate:hexane (4:1). The UV-active portion of the plate (R_f 0.2) was removed and extracted with acetone and the combined filtrate and washings were concentrated under a stream of nitrogen. The GC-EI mass spectrum of the residue showed two major components with retention times and mass spectra corresponding to those of *N*-methylbenzamide (t_R 4.9 min) and the methyl ketone **20** (t_R 6.6 min, see below). The FAB mass spectrum of this isolate was consistent with the β-keto aldehyde structure **26**: *m/z* (rel intensity) 234 (MH^+, 25), 190 (10), 162 (20), 147 (35), 136 (35), 105 (100).

4-(*N*-Benzoyl-*N*-methylamino)butan-2-one (20). A solution of 2-(2-bromoethyl)-2,5,5-trimethyldioxane (**22**, 2.9 g, 12 mmol) in benzene (10 mL) was added dropwise to an efficiently stirred mixture of benzamide (1.2 g, 10 mmol) in 50% aqueous sodium hydroxide (25 mL) and benzene (25 mL) containing tetrabutylammonium hydrogen sulfate (0.14 g, 0.4 mmol). After 2 h, the mixture was cooled to room temperature and ethyl acetate (25 mL) and water (25 mL) were added. The organic layer was washed with water (2 × 40 mL) and dried (sodium sulfate), and the solvent was removed in vacuo to yield the crude benzamide derivative **23** as an oil (1.5 g, 78%). A solution of crude **23** (0.39 g, 1.4 mmol) in DMSO (10 mL) was added to a suspension of potassium hydroxide (0.5 g, 8.9 mmol) in DMSO (5 mL), and the resulting mixture was stirred at room temperature for 15 min. Iodomethane (1.0 mL, 16 mmol) in DMSO (5 mL) was added and the reaction was allowed to proceed with stirring for 3 h. After additional water (30 mL) was added, the solution was extracted with ethyl acetate (30 mL) and the organic layer was washed with water (3 × 30 mL) and brine (30 mL), dried (sodium sulfate), and evaporated in vacuo. The oily residue containing the methylated product **24** in 5 mL of methanol and 5 mL of 10% hydrochloric acid was allowed to stir at room temperature for 1 h. Extraction of the mixture with ethyl acetate (15 mL) followed by purification of the extract by preparative TLC (ethyl acetate:hexane, 9:1) afforded 0.13 g (47%) of the methyl ketone **20** as a highly viscous oil: ^{1}H NMR (CD_3OD) 2.00 [s, 0.75 H, $COCH_3$ (minor rotamer)], 2.08 [s, 2.25 H, $COCH_3$ (major rotamer)], 2.70 [t, 0.5 H, CH_2CO (minor rotamer)], 2.81 [t, 1.5 H, CH_2CO (major rotamer)], 2.90 [s, 2.25 H, NCH_3 (major rotamer)], 2.96 [s, 0.75 H, NCH_3 (minor rotamer)] 3.47 [t, 0.5 H, NCH_2 (minor rotamer)], 3.68 [t, 1.5 H, NCH_2 (major)], 7.35 (m, 5 H, C_6H_5). Upon warming to 50 °C, the paired signals each coalesced into a broad peak. The resolved signals reappeared upon cooling; GC-EIMS-see text; UV (CH_3OH) end absorption. Anal. Calcd for $C_{12}H_{15}NO_2 \cdot 0.2H_2O$: C, 69.50; H, 7.31; N, 6.76. Found: C, 69.49; H, 7.30; N, 6.71.

3-[2-(*N*-Methyl-*N*-benzoylamino)ethyl]pyrazole (31). (a) From Dihydropyridinium Metabolite 18. Hydrazine sulfate (0.200 g, 1.5 mmol) was added to a solution of **18** (0.050 g, 0.15 mmol) in 0.1 M trisodium phosphate (25 mL), and the reaction, which was monitored by UV (disappearance of the 283-nm chromophore), was stirred at room temperature for 1.5 h. The solution then was extracted with ethyl acetate and the organic layer was dried (sodium sulfate) and evaporated in vacuo. The residue was purified by preparative TLC (ethyl acetate) to afford (0.025 g, 69%) of the desired pyrazole **31**: ^{1}H NMR[16] ($CDCl_3$) δ 2.9 [bs, 2.5 H, NCH_3 (major rotamer) and CH_2 (minor rotamer)], 3.1 [m, 2.5 H, CH_2 (minor rotamer) and NCH_3 (major rotamer)] 3.5 [t, 0.8 H, CH_2 (minor rotamer)] 3.8 [t, 1.2 H, CH_2 (major rotamer)] 5.9 [br s, 0.4 H, C 4 (minor rotamer)], 6.1 [br s, 0.6 H, C 4 (major rotamer)], 7.2 [br s, 0.4 H, C 3 (minor rotamer)] 7.28–7.42 (m, 5 H, ArH) 7.51 (br s, 0.6 H, C 3 major rotamer), 9.8 (br s, 1 H, NH); irradiation of the signal at 2.9 ppm caused the triplet at 3.5 ppm to collapse to a singlet while irradiation of the signal at 3.1 ppm caused the triplet centered at 3.8 ppm to collapse to a singlet. GC-EIMS (t_R 8.07 min) *m/z* (rel intensity) 229 (4), 228 (8), 148 (20), 105 (100), 77 (40). Direct insertion probe high resolution EI exact mass of parent ion. Calcd for $C_{13}H_{15}N_3O$: 229.1215123. Found: 229.120621.

(b) From Methyl Ketone 20. A solution of the methyl ketone **20** (20 mg, 0.1 mmol) and ethyl formate (74 mg, 1.0 mmol) in 5 mL of dry benzene was added to a stirred suspension of finely divided sodium (25 mg, 1.1 mmol) in 5 mL of benzene. After 24 h of stirring at room temperature, the reaction mixture was treated carefully with a few drops of water followed by addition of hydrazine sulfate (126 mg, 1 mmol). After an additional hour at room temperature, the reaction mixture was worked up with ethyl acetate to provide the pyrazole **31**, identical in all respects to that obtained from the dihydropyridinium species **18**.

Isolation and Identification of Pyrazole 31 from the MAO-B Incubation Mixture. The tetrahydropyridine **10** was incubated with MAO-B as described above. The metabolic reaction was stopped by addition of sodium triphosphate (0.001 g) and the resulting mixture (pH 11) was treated with hydrazine sulfate (0.003 g). The mixture was allowed to stand for 15 min and then was extracted with dichloromethane (2 mL). The organic layer was separated, dried (sodium sulfate), and evaporated under a stream of nitrogen to yield a residue which gave a GC-EI mass spectrum identical to that of the synthetic standard.

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