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Brief Articles

Synthesis, Structural Reassignment, and Biological Activity of Type B MAO Inhibitors Based on the 5*H*-Indeno[1,2-*c*]pyridazin-5-one Core

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The synthesis and enzyme inhibitor properties of reversible type B monoamine oxidase inhibitors are described. These compounds belong to the 5*H*-indeno[1,2-*c*]pyridazine family and possess a hydrophobic benzyloxy or 4,4,4-trifluorobutoxy side chain which, in contrast to a previous assignment, has been unambiguously located at C(8) of the heterocyclic moiety. Investigation of the regioisomeric structures establishes that substitution of the 5*H*-indeno[1,2-*c*]pyridazin-5-one core at C(7) vs C(8) dramatically influences the MAO-inhibiting properties of these compounds.

Introduction

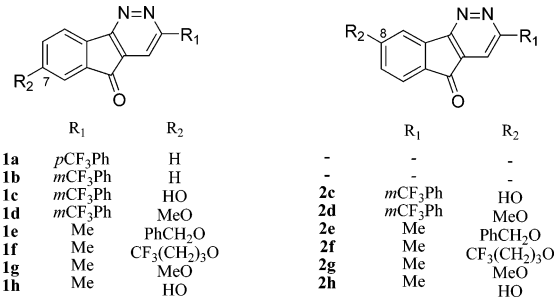
Numerous studies have established the potential utility of reversible and selective monoamine oxidase B (MAO-B) inhibitors, in particular in the treatment of neurodegenerative disorders, including Parkinson's disease (PD)[1] and Alzheimer's disease (AD)[2] as well as for tobacco detoxification.[3] The 5*H*-indeno[1,2-*c*]pyridazin-5-one-based structures **1a**−**d** have been reported by Kneubühler et al.[4,5] to be potent reversible and selective MAO-B inhibitors (Figure 1).[6]

The most active compound **1a** displayed an IC_{50} value for the inhibition of MAO-B of 90 nM whereas two related compounds bearing an hydroxy (**1c**) (IC_{50} = 5.10 μM) or a methoxy (**1d**) (IC_{50} of 1.91 μM) group on the fused aromatic ring showed considerably weaker MAO-B inhibitory properties than the corresponding unsubstituted analogue **1b** (IC_{50} = 0.28 μM).[5]

We recently reported, on the basis of an MAO-B pharmacophoric model, that compounds **1e** and **1f** (Figure 1) bearing, respectively, a benzyloxy and a 4,4,4-trifluorobutyloxy hydrophobic side chain in the 7-position of the 5*H*-indeno-[1,2-*c*]-pyridazin-5-one system would possess improved activity compared to **1a**.[7,8]

Results and Discussion

We planned to synthesize **1e** and **1f** by a demethylation−alkylation sequence starting from the common intermediate **1g**



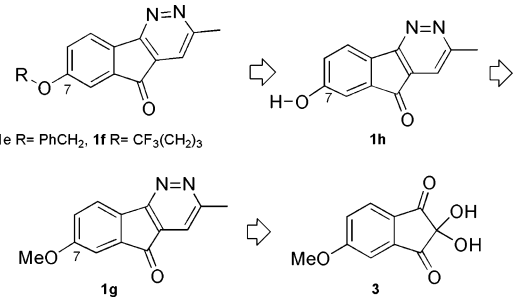
	R_1	R_2
1a	*p*CF_3Ph	H
1b	*m*CF_3Ph	H
1c	*m*CF_3Ph	HO
1d	*m*CF_3Ph	MeO
1e	Me	$PhCH_2O$
1f	Me	$CF_3(CH_2)_3O$
1g	Me	MeO
1h	Me	HO

	R_1	R_2
-	-	-
-	-	-
2c	*m*CF_3Ph	HO
2d	*m*CF_3Ph	MeO
2e	Me	$PhCH_2O$
2f	Me	$CF_3(CH_2)_3O$
2g	Me	MeO
2h	Me	HO

Figure 1. 5*H*-Indeno[1,2-*c*]pyridazin-5-ones derivatives discussed in this paper.

bearing a methoxy group at C-7. We expected to be able to prepare **1g** regioselectively from the commercially available methoxyninhydrin **3**, by analogy to the method already used by Kneubühler et al.[5] for related compounds **1c** and **1d**. This strategy moreover offers an opportunity to access a large variety of 7-alkoxy analogues (Scheme 1).

Scheme 1



Compound **3** was subjected to an acid-catalyzed aldol reaction (acetone in AcOH, 120 °C, 2 h), and the resulting adduct **4** was treated with an excess of hydrazine (aq hydrazine, AcOH, 20 °C, 3 h). Under these conditions,[5] the expected product

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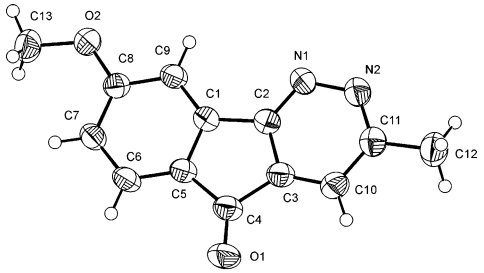
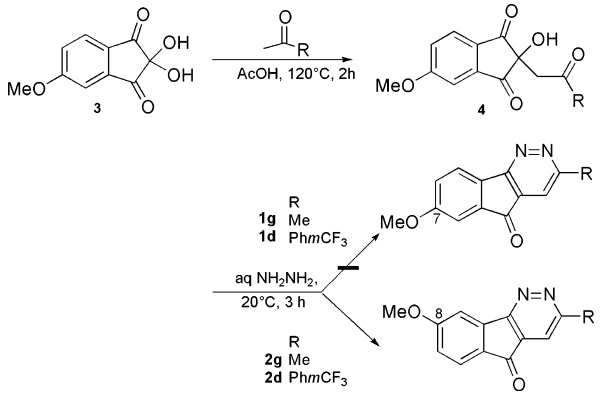


(2g)

Figure 2. The molecular structure of compounds **2g**. Displacement ellipsoids are drawn at the 50% probability level.

Scheme 2



should be 7-methoxy-3-methyl-5*H*-indeno[1,2-*c*]pyridazin-5-one **1g**. Unexpectedly, the yellow solid that separated from the reaction mixture proved to be 8-methoxy-3-methyl-5*H*-indeno-[1,2-*c*]pyridazin-5-one (**2g**, 71% yield; Scheme 2: R = Me), an isomer of the expected compound, as confirmed from the X-ray diffraction of a single crystal (obtained by slow evaporation from a concentrated solution of acetonitrile).

An ORTEP view of the conformation of **2g** is depicted in Figure 2. The final atomic coordinates and equivalent isotropic thermal parameters of the non-hydrogen atoms of **2g** are given as Supporting Information.

It has to be noted that control of the temperature is of prime importance for the regioselective formation of 8-methoxy-3-methyl-5*H*-indeno[1,2-*c*]pyridazin-5-one **2g**. Indeed, when the hydrazine hydrate is added to **4** at −10 °C, an intractable mixture of both regioisomers **2g** and **1g** is formed (**2g**/**1g**: 70/30) as shown by analyses of the ^{1}H NMR spectra.

These results led us to suspect that the original structural assignment for **1d** may have been incorrect.[5] To assess this, we repeated the reaction between **3** and methyl *m*-trifluoromethylphenyl ketone under the reported experimental conditions (Scheme 2: R = Ph*m*CF$_3$).[5] A mixture of two compounds was isolated and separated after repeated chromatographic purifications (SiO_2, CH_2Cl_2). The major isomer (47% yield, yellow, mp 214 °C) exhibits a ^{1}H NMR spectrum identical to that published[5] but its structure, confirmed by X-ray crystallography,[9] proved to be the C(8)-substituted compound **2d** instead of **1d** as originally described. The minor isomer (3.5% yield, orange, mp 204 °C), which has never been isolated previously, displays a ^{1}H NMR spectrum significantly different from that of **2d**. The structure of this product was confirmed by crystallography to be the regioisomer **1d**.[9]

The approach to our further studies required the synthesis of **2e** and **2f** instead of our original targets **1e** and **1f**. Our initial synthetic approach to **2e** and **2f** proceeded via the phenolic

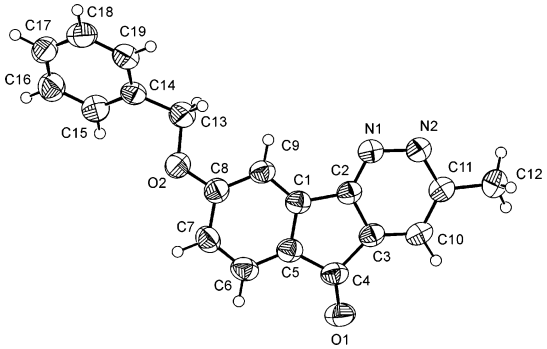
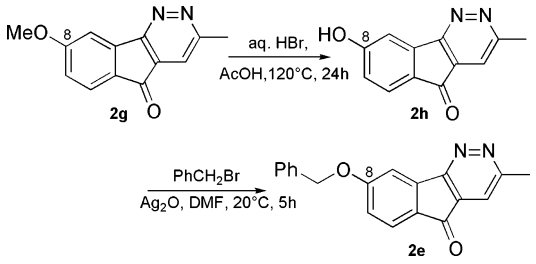


Figure 3. The molecular structure of compound **2e**. Displacement ellipsoids are drawn at the 50% probability level.

Scheme 3



intermediate **2h** (Figure 1) that, in turn, was to be generated by cleavage of the methyl ether present in **2g** (Scheme 3). Reaction of the latter with hydrobromic acid (aq HBr, AcOH, 120 °C, 24 h) produced **2h** as an intractable mixture of compounds. Alternative reagents such as thiolates[12,13] or selenolates[14,15] also led to disappointing results apparently due to the intrinsic instability of the resulting phenolate. Moreover, attempted methylation of **2h** in the crude reaction mixture with methyl iodide in the presence of potassium carbonate neither produced **2g** nor led to the recovery of **2h** after workup.

Benzylation of **2h**, present in the crude reaction mixture was, however, successfully achieved upon reaction with benzyl bromide in the presence of silver oxide and provided **2e** in modest yield (BnBr, Ag_2O, DMF, 20 °C, 5 h, 40% yield, Scheme 3).

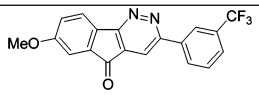
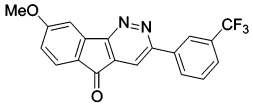
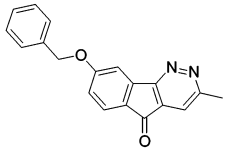
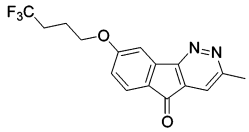
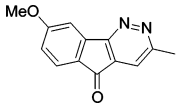
The X-ray diffraction analysis of compound **2e** confirmed its structure. Crystals were obtained by slow evaporation of a concentrated acetonitrile solution. The molecular structure of **2e**, with its atomic numbering scheme, is depicted in Figure 3. The final atomic coordinates and equivalent isotropic thermal parameters of the non-hydrogen atoms of **2e** are given as Supporting Information.

Since the approach depicted in Scheme 3 suffered from a poor yield in the final synthetic step and did not allow the synthesis of **2f**, we developed a slightly modified synthetic strategy that allowed us to produce the latter compound efficiently. This strategy is depicted in Scheme 4.

This novel approach uses commercially available and inexpensive 6-methoxy **6g$_1$** or 7-methoxy-1-indanone **6g$_2$** as starting material. These indanones have been transformed to the desired ninhydrins **3f** that possess the required alkoxy group on the fused aromatic ring and which, in turn, was regioselectively transformed to **2f** (Figure 1).

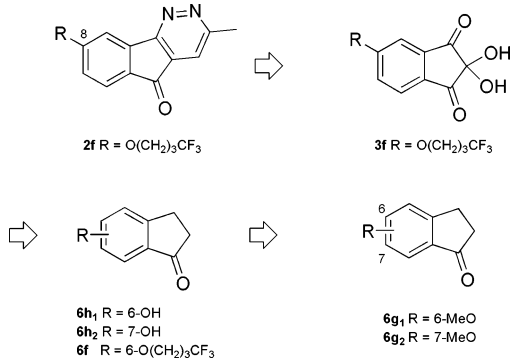
Demethylation of 6- or 7-methoxy-1-indanones (**6g$_1$** and **6g$_2$**) was our first goal since the analogous transformation was the weak step in our previous synthetic route (Scheme 3). As anticipated from our previous results, acid treatment of 6-methoxy-1-indanone **6g$_1$** (aq HBr, 120 °C, 0.6 h, 16%; 1.5 h, 40%; 4 h, 19%, Scheme 3) led to 6-hydroxy-1-indanone **6h$_1$** in a very

Table 1. MAO Inhibiting Properties for Compounds **1d**, **2d**, **2e**, **2f**, and **2g**

Compd	Structure	Mp (°C)	IC_{50} (nM)[i]	
			MAO-B	MAO-A
1d		204	38.0	> 1000
2d		214	0.10	> 1000
2e[ii]		168	170	> 1000
2f		116	14.0[iii]	> 1000[iii]
2g[ii]		175	> 1000	> 1000

[i] Standard errors less than 2%. [ii] Rat brain mitochondria. [iii] Taken from ref 8.

Scheme 4



modest yield. Use of lithium chloride[16] in DMF did not result in any improvements (130 °C, 26 h, 46% yield). Sodium ethylthiolate or sodium methylselenolate, which proved equally efficient, however, led to $\mathbf{6h}_1$ in good yield (DMF, 130 °C, 2 h, 70% yield, each). The same reaction carried out with the isomeric 7-methoxy-1-indanone $\mathbf{6g}_2$ proved to be much less efficient.

The next steps proceeded without major problems. O-alkylation of $\mathbf{6h}_1$ with 1-tosyl-4,4,4-trifluoro-butane gave an 86% yield of 4,4,4-trifluoromethylbutoxy-1-indanone **6f** (K_2CO_3, acetonitrile, 80 °C, 4 h, Scheme 4) which, in turn, underwent smooth oxidation with selenium dioxide[15,17] to afford 5-trifluorobutoxyninhydrin **3f** in 74% yield (3 equiv, dioxane, reflux, 6 h). Finally, treatment of **3f** sequentially with acetone and hydrazine [(i) acetone, AcOH, 120 °C, 2 h; (ii) aq hydrazine, AcOH, 20 °C, 24 h], as described above, gave **2f** (mp 116 °C, 40% yield), the structure of which has been unambiguously established by crystallography.[9]

MAO Inhibition. The findings described above are important, especially with respect to validation of previously reported structure−activity relationships.[5,7,8] In view of this, we have determined the MAO-A and MAO-B inhibitory properties of the newly isolated and characterized compound **1d**, and **2d** (Table 1). Intact mitochondria prepared from human placenta and baboon liver served as sources for MAO-A and MAO-B, respectively. Human placental mitochondria express MAO-A almost exclusively[10] while baboon liver mitochondria express almost exclusively MAO-B.[11] IC_{50} values for the inhibition of MAO-B by **1d** and **2d** were estimated to be 38.0 nM and 0.1 nM, respectively. Moreover, neither compound inhibited MAO-A at the maximum attained solubility (5 μM), confirming their very good selectivity profile. The current data document dramatic differences in MAO-B inhibitory potency of these indeno[1,2-*c*]pyradzin-5-one regioisomers and provide a compelling tool to refine the MAO-B pharmacophoric model previously reported by us.[8]

The MAO inhibitory potencies of compounds **2e** and **2g** have also been investigated (Table 1). Compound **2e**, which possesses a benzyloxy as side chain in the 8-position, exhibits a modest MAO-B inhibitory potency (IC_{50} = 170 nM). This compound does not inhibit MAO-A. Compound **2g**, which possesses a methoxy group in the 8-position, is without MAO-A and MAO-B inhibition properties. When compared with **2f** (Table 1), these data show that the replacement of the 4,4,4-trifluorobutoxy side chain of **2f** with a methoxy **2g** or a benzyloxy **2e** strongly decreases the MAO-B inhibiting properties of the compounds.

Conclusion

In conclusion, in this paper we show that a procedure described for the synthesis of 7-substituted 5*H*-indeno[1,2-*c*]-pyridazin-5-ones **1d** from methoxyninhydrin **3** affords, instead, its 8-substituted regioisomer **2d**. We have nevertheless isolated, from the reaction mixture, small amounts of 7-methoxy-5*H*-indeno[1,2-*c*]pyridazin-5-one **1d**.

The MAO inhibitory potencies of these compounds proved to be highly dependent on the position of the alkoxy-substituent. The 8-substituted derivative **2d** proved much more active than

its 7-regioisomer **1d**. These findings are of value when attempting to document the structure−activity relationships in these series and to rationalize the design of new potent and selective reversible MAO-B inhibitors.

Finally, as the demethylation−alkylation sequence was the weaker point in the synthesis of **2** from **3**, we have designed a novel synthetic strategy which efficiently allowed the synthesis of the trifluorobutyloxy analogue **2f**, which is expected to be widely applicable for the synthesis of the most biologically active 8-alkoxy-5*H*-indeno[1,2-*c*]pyridazin-5-ones.

Experimental Section

^{1}H and ^{13}C NMR spectra were obtained from a JEOL JNM EX 400 spectrometer (400 MHz for ^{1}H or 100.4 MHz for ^{13}C). The spectra were measured in $CDCl_3$ with TMS as internal standard (δ: 0.00 ppm). IR data reported in cm^{-1} were obtained using a BIO-RAD FTS 165 spectrophotometer. Those data are given as Supporting Information. Elemental analysis (C,H,N) were performed on a ThermoFinnigan flash EA112 analyzer and were within ±0.4% of the theoretical values. Analytical thin-layer chromatography (TLC) were performed on prefabricated, glass-backed plates SiO_2, $60PF_{254}$, 250 μm (Merck 5719). Compounds were visualized by UV illumination and by heating to 150 °C after spraying with phosphomolybdic acid/ethanol. All the reactions were performed in two necked round-bottomed flasks equipped with a septum stopper and an argon-filled balloon. Glassware were warmed prior to use and degassed at 0.1 mmHg. All transfers of reagents were performed via syringes.

3-Methyl-8-methoxy-5*H*-indeno[1,2-*c*]pyridazin-5-one 2g. A solution of methoxyninhydrin (500 mg, 2.4 mmol) and acetone (278 mg, 4.8 mmol, 2 equiv) in glacial acetic acid (6 mL) was heated to reflux at 120 °C over a period of 2 h. The mixture was evaporated in order to eliminate the excess of acetone. Upon cooling to room temperature, the orange mixture was diluted in glacial acetic acid (2 mL) and stirred with hydrazine hydrate 98% (209 mg, 4.2 mmol) for 2 h at room temperature under an inert atmosphere. The yellow solid which precipitates was collected after filtration, washed with pentane, and dried under vacuum (385 mg; 71% yield). TLC: R_f (100% AcOEt) 0.4. mp 175 °C. Calcd for $C_{13}H_{10}N_2O_2$: C, H, N.

3-(3-Trifluoromethyl)phenyl-8-methoxy-5*H*-indeno[1,2-*c*]pyridazin-5-one 2d and 3-(3-Trifluoromethyl)phenyl-7-methoxy-5*H*-indeno[1,2-*c*]pyridazin-5-one 1d. A solution of ninhydrin (0.178 g, 1 mmol) and (*m*-trifluoromethyl)phenyl methyl ketone (0.118 g, 1 mmol) in glacial acetic acid (5 mL) was heated at 110 °C for 2 h and then allowed to cool to room temperature. Addition of hydrazine hydrate (98%, 0.075 g, 1.5 mmol.) proceeded slightly exothermically and, after 4 h at 20 °C, yielded a precipitate which was collected after filtration, washed quickly with pentane (2 × 5 mL), and then dried under vacuum to afford 0.220 g of a solid.. The latter was purified by silica gel column chromatography and eluted with dichloromethane to produce small amounts of regioisomeric **2d** (R_f: 0.7) and **1d** (R_f: 0.66). The intermediate fraction containing a mixture of the two regioisomers was purified by three consecutive column chromatography runs on silica gel and finally led to the isolation of a yellow solid **2d** (0.172 g, 47%, mp 214 °C) and an orange solid **1d** (0.013 g, 3.5%, mp 204 °C). Calcd for $C_{19}H_{11}F_3N_2O_2$: C, H, N. Calcd for $C_{19}H_{11}F_3N_2O_2$: C, H, N.

3-Methyl-8-ol-5*H*-indeno[1,2-*c*]pyridazin-5-one 2h. A solution of 3-methyl-8-methoxy-5*H*-indeno[1,2-*c*]pyridazin-5-one (385 mg; 1.7 mmol) in 10 mL of aqueous HBr (47%)/glacial acetic acid (50:50) was refluxed at 120 °C for 24 h under an inert atmosphere. The mixture was then diluted in 80 mL of water and concentrated under vacuum. The residue was again diluted in 50 mL of water and concentrated under vacuum. The dark brown solid formed was dried under vacuum (0.5 mmHg) and used without any further purification in the next step of the synthesis.

3-Methyl-8-benzyloxy-5*H*-indeno[1,2-*c*]pyridazin-5-one 2e. Silver oxide (2.32 g, 10 mmol) was added at room temperature to a solution of 3-methyl-8-ol-5*H*-indeno[1,2-*c*]pyridazin-5-one **2h** (2.4 mmol; 500 mg) and benzyl bromide (1.59 g; 10 mmol) in 10 mL of anhydrous DMF. The mixture was stirred at room temperature under an inert atmosphere for 5 h. The crude suspension was then filtered and washed with ethyl acetate. The filtrate was evaporated to dryness under vacuum (0.5 mmHg) and the residue purified twice on a silica gel column (100% EtOAc) to yield a yellow solid (26 mg, 40% yield). TLC: R_f 0,7 (AcOEt); mp: 168 °C. Calcd for $C_{19}H_{14}N_2O_2$: C, H, N.

6-Hydroxy-1-indanone 6h$_1$. A solution of dimethyl diselenide (347 mg, 1.84 mmol) in anhydrous DMF (3 mL) was added dropwise to a suspension of NaH (110 mg, 3.69 mmol) in anhydrous DMF (1 mL). After stirring for 45 min at room temperature under an argon atmosphere, a solution of 6-methoxy-1-indenone (500 mg, 3.08 mmol) in anhydrous DMF (10 mL) was added and the resulting mixture stirred vigorously for 2 h at 130 °C. After cooling, the solution was poured into 10% hydrochloric acid (20 mL), extracted with chloroform (3 × 50 mL), dried over magnesium sulfate, filtered, and evaporated. The residue was purified by column chromatography over silica gel and eluted with CH_2Cl_2/AcOEt (3:1) to give **6h$_1$** (317 mg, 70%). TLC: R_f 0,2 (Pentane/AcOEt 7:3); mp 146 °C.

4,4,4-Trifluoromethylbutoxy-1-indanone 6f. 1-Tosyl-4,4,4-trifluorobutane (3.56 g, 12.6 mmol) was added to in a solution of **6h** (1.7 g, 11.4 mmol) in acetonitrile (15 mL) in which potassium carbonate (3.46 g, 25.08 mmol) is suspended. The resulting mixture was stirred for 4 h at 90 °C under an argon atmosphere and then cooled to room temperature. After evaporation of the solvents, the residue was poured into ethyl acetate, washed with water, dried over magnesium sulfate, filtered, and evaporated to dryness. The residue was purified by column chromatography over silica gel and eluted with pentane/AcOEt (7:3) to give **6f** (2.53 g, 86%). TLC: R_f 0,4. (pentane/AcOEt 7:3); mp 96 °C.

5-Trifluorobutoxyninhydrin 3f. 6f (1.8 g, 6.97 mmol) was added to a suspension of selenium dioxide (3.87 g, 34.8 mmol) in dioxane (10 mL). The suspension was then stirred for 4 h to reflux under an argon atmosphere and filtered, and the solvents were evaporated. The residue was poured into dichloromethane (30 mL) into which the unreacted SeO_2 precipitated. The SeO_2 was filtered off and the filtrate evaporated to dryness. The residue was purified by column chromatography over silica gel eluted with CH_2Cl_2/AcOEt (3:1) to give **3f** (1.56 g, 74%). TLC: R_f (CH_2Cl_2/AcOEt 7:3) 0.3.

3-Methyl-8-[4,4,4-trifluorobutoxy]-5*H*-indeno[1,2-*c*]pyridazin-5-one 2f. Acetone (572 mg, 9.8 mmol) was added to a solution of **3f** (1 g, 3.2 mmol) in glacial acetic acid (5 mL) which was then stirred under reflux for 2.5 h. After cooling, the solution was concentrated and hydrazine monohydrate (494 mg, 9.8 mmol) added. After stirring vigorously at room temperature for 24 h, the precipitate was filtered and washed with pentane (3x) to give **2f** (420 mg, 40%). TLC: R_f 0,5 (CH_2Cl_2/AcOEt 3:1); mp 116 °C. Calcd for $C_{16}H_{13}F_3N_2O_2$: C, H, N.

MAO Inhibition. Intact mitochondria prepared from human placenta and baboon liver served as sources for MAO-A and MAO-B, respectively. Mitochondria were prepared as described by Salach and Weyler[18] and stored in aliquots containing the equivalent of 5−12 mg protein at −70 °C in Eppendorf tubes. Before use, the original mitochondrial isolate was suspended in 200 μL of sodium phosphate buffer (100 mM, pH 7.4 containing 50% glycerol, w/v), and the protein concentration was determined by the method of Bradford.[19] The inhibition of MAO by the test compounds was evaluated by incubating the nonselective substrate 1-methyl-4-(1-methylpyrrol-2-yl)-1,2,3,6-tetrahydropyridine[20] (MMTP; 70 μM) with the mitochondrial homogenate (0.15 mg of protein/mL) and various concentrations of the test compounds. The K_m values of MMTP for MAO-A and MAO-B are 52.0 and 60.9 μM, respectively, in human placental and baboon liver tissue. The test compounds were dissolved in DMSO and added to the buffered incubation mixture such that the final DMSO concentration was 4%. The final volume of the incubation mixtures was 500 μL (in sodium phosphate buffer, pH 7.4), and the samples were incubated at 37 °C for 25 min. All samples were protected from light by

covering the incubation tubes (1.5 mL microcentrifuge tubes) with aluminum foil. The reactions were terminated by the addition of 20 μL perchloric acid (70% v/v) and centrifuged (16000*g* for 5 min), and the concentrations of the enzyme-generated dihydropyridinium metabolite $MMDP^+$ in the supernatant fractions were estimated spectrophotometrically at 420 nm ($\epsilon = 25000\ M^{-1}\ cm^{-1}$). These data were used to determine the velocity (v) of the MAO-catalyzed oxidation of MMTP. IC_{50} values were calculated from a sigmoidal dose−response nonlinear regression equation using GraphPad Prism version 3.02 (GraphPad software).

X-ray Diffraction. CCDC 282947 and CCDC 2828948 contain the supplementary crystallographic data for this paper. These data can be obtained free of charge via www.ccdc.cam.ac.uk/data_request/cif, or by e-mailing data_request@ccdc.cam.ac.uk, or by contacting The Cambridge Crystallographic Data Centre, 12, Union Road, Cambridge CB2 1EZ, UK; fax: +44 1223 336033.

Single crystals of compounds **2e** and **2g** were obtained by slow evaporation of concentrated solutions of acetonitrile. In both case, a suitable crystal was mounted on a quartz fiber on the goniometer head of a CAD4 Nonius diffractometer. After determination of the cell parameter using 25 well-centered reflections, complete diffraction data sets were collected. The structure was solved using direct methods and refined by full matrix least squares on F^2 using the program Shelxl97.[21] All non-hydrogen atoms were treated anisotropically while a riding model was applied for the hydrogens. Analytical and psi-scan corrections for absorption were introduced for **2e** and **2g**, respectively. Compound **2g**: monoclinic, *P*21/*c*, $a = 3.899(1)$ Å, $b = 26.078(1)$ Å, $c = 10.481(1)$ Å, $\alpha = 90.00°$, $\beta = 95.097\ (7)°$, $\gamma = 90.00°$, $V = 1061.5(3)$ Å^3, $Z = 4$ (four molecules in the asymmetric unit), $\mu = 0.802\ mm^{-1}$, $D_x = 1.416\ g\ cm^{-3}$, λ (Cu Kα) = 1.54178 Å, $F(000) = 472$, $T = 293$ K, 1319 unique reflections ($R_{int} = 0.0458$), $R_1 = 0.0467$ for 1319 $F_o > 2\sigma(F_o)$, $R_1 = 0.0920$ for all data (2083) and $wR_2 = 0.1100$, GOF = S = 1.039. Compound **2e**: Orthorhombic, P 21 21 21, $a = 4.061(1)$ Å, $b = 9.890(1)$ Å, $c = 36.633(4)$ Å, $\alpha = 90.00°$, $\beta = 90.00°$, $\gamma = 90.00°$, $V = 1471.3(4)$ Å^3, $Z = 4$ (four molecules in the asymmetric unit), $\mu = 0.726\ mm^{-1}$, $D_x = 1.365\ g\ cm^{-3}$, λ (Cu Kα) = 1.54178 Å, $F(000) = 632$, $T = 293$ K, 1744 unique reflections ($R_{int} = 0.0184$), $R_1 = 0.0528$ for 1744 $F_o > 2\sigma(F_o)$, $R_1 = 0.0931$ for all data (1744) and $wR_2 = 0.1209$, GOF = $S = 1.076$.

Supporting Information Available: Microanalytical data for all targeted compounds not included in the Experimental Section. Crystallographic parameters for the structure of compounds **2e** and **2g**. This material is available free of charge via the Internet at http://www.pubs.acs.org

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