NPC Natural Product Communications

2015
Vol. 10
No. 4
581 - 584

Concise Synthesis of *N,N*-Dimethyltryptamine and 5-Methoxy-*N,N*-dimethyltryptamine Starting with Bufotenine from Brazilian *Anadenanthera* ssp.

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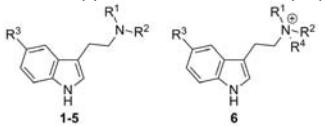
Received: September 9th, 2014; Accepted: February 17th, 2015

Bufotenine (**1**, 5-hydroxy-*N,N*-dimethyltryptamine) was isolated from seeds of *Anadenanthera* spp., a tree widespread in the Brazilian cerrado, using an efficient acid-base shakeout protocol. The conversion of bufotenine into *N,N*-dimethyltryptamine (**4**) and 5-methoxy-*N,N*-dimethyltryptamine (**5**) was accomplished through an innovative and short approach featuring the use of novel bufotenine-aminoborane complex (**7**). Furthermore, an easy methodology for conversion of bufotenine into 5-hydroxy-*N,N,N*-trimethyltryptamine (**6**) was well-established. This is the first study that highlights bufotenine as a resource for the production of *N,N*-dimethyltryptamines for either pharmacological and toxicological investigations or for synthetic purposes.

Keywords: *Anandenanthera*, Bufotenine, Bufotenine-aminoborane complex, Bufotenidine, *N,N*-Dimethytryptamine, 5-Methoxy-*N,N*-dimethyltryptamine.

The narcotic snuff (*cohoba*) of *Piptadenia* ssp. has been used in syncretic religious ceremonies in Central and South America since ancient times [1], even though bufotenine (**1**, HDMT) was first isolated in 1954 from seeds of *P. peregrina* Benth (*Anadenanthera peregrina* L. Speg.) by Stromberg [2]. HDMT together with some related indoleamines and corresponding *N*-oxides were isolated from *P. peregrina* and related species [3]. Fellows and Bell [4] studying indole metabolism in *P. peregrina* showed an unusual direct enzymatic hydroxylation of tryptamine (**2**) to serotonin (**3**), suggesting the latter as the biosynthetic precursor of HDMT instead of DMT (**4**) (Table 1). The occurrence and quantitative detection of **1** in other vegetal sources, such as hardinggrass (*Phalaris* spp.) [5], *takini*, a shamanic potion from latex of *Brosimum acutifolium* [6], and *Citrus* species [7] were also reported. Furthermore, HDMT has been found in three arboreal amphibian species of the *Osteocephalus* (*O. taurinus*, *O. oophagus*, and *O. langsdorffii*), as well as in the marine invertebrate *Paramuricea clavata* [8].

Table 1: Structure of bufotenine (**1**) and related indolamines (**2**-**6**).



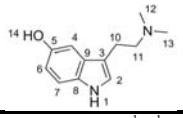
Compds	R^1	R^2	R^3	R^4	Name(s)
1	Me	Me	OH	-	5-Hydroxy-*N,N*-dimethyltryptamine, bufotenine, HDMT
2	H	H	H	-	Tryptamine
3	H	H	OH	-	Serotonin, 5-HT
4	Me	Me	H		*N,N*-Dimethyltryptamine, DMT
5	Me	Me	OMe	-	5-Methoxy-*N,N*-dimethyltryptamine, MDMT
6	Me	Me	OH	Me	5-Hydroxy-*N,N,N*-trimethyltryptamine, bufotenidine, cinobufotenine

Since the discovery of HDMT and its relatives in the skin of Bufo toads (*e.g. B. alvarius*, *B. marinus*, *B. vulgaris*, *B. garganizans*), writings have been controversial over the psychedelic effects of toads and bufotenine [9]. Likewise, **1** has become the center of scientific debate since its detection in human urine, and extensive literature surrounding *N,N*-dimethyltryptamines in humans fluids has been reviewed [10]. It is noteworthy that patients with mental illnesses such as autistic spectrum disorder (ASD) and schizophrenia have exhibited significant urinary levels of HDMT, suggesting that this alkaloid plays a role in ASD and schizophrenia and may be correlated with hyperactivity scores in autism [11]. Interest in the metabolism and pharmacokinetics, plus understanding the mechanism of action, of tryptamine derivatives has been growing in recent years, mostly for antipsychotic drugs that act directly on the serotonin 2A receptor (5-HT_{2A}). Studies for mapping the binding site pocket of the 5-HT_{2A} receptor revealed its high affinity for serotonergic ligands HDMT and LSD [12]. Investigations using recombinant cytochrome P_{450} isoenzymes showed that MDMT acts as a nonselective 5-HT agonist and causes many physiological and behavioral changes. Besides, it is *O*-demethylated by polymorphic CYP2D6 to generate HDMT, a metabolite more potent than DMT [13]. Latterly, it was demonstrated that coadministration of the monoamine oxidase A (MAO-A) inhibitor, harmaline, increases systemic exposure to MDMT and HDMT. These data provided a fused model including the inhibition of MAO-A- and CYP2D6-catalyzed MDMT metabolism by harmaline to describe blood harmaline, DMT, and HDMT PK profiles [14]. The synergistic action of these alkaloids is considered to be the basis of the psychotropic action of ayahuasca [15], a beverage that has been officially incorporated in rituals of religious groups in Brazil to facilitate self-knowledge and introspection, deserving the attention of researchers [16]. Up-to-date, the hallucinogen DMT was identified as a potent endogenous agonist for the sigma-1 receptor [17] and more recently it was shown to inhibit the indolethylamine-*N*-methyltransferase (INMT) responsible for the transfer of one or more methyl groups to small molecules such as endogenous indole-containing compounds, through a mixed competitive and noncompetitive mechanism [18].

This work describes a different protocol for the isolation of bufotenine (**1**) from seeds of *Anadenanthera* spp., a widespread tree of the Brazilian cerrado, and focuses on the synthesis of DMT (**4**) and MDMT (**5**) starting with **1**.

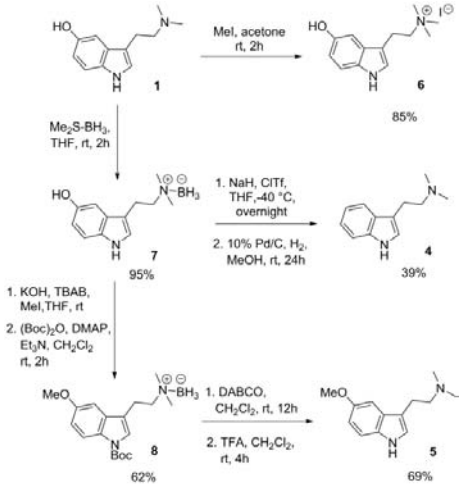
Preliminary extractions of bufotenine from seeds of *Anadenanthera* were carried out in full accordance with the literature [2], which yielded the alkaloid in about 1%. The requirement to collect **1** in sufficient quantity for pharmacological studies, as well as to access synthetic routes designed for *N*,*N*-dimethyltryptamines, encouraged us to improve the extraction methodology. As pointed out in the experimental section, using a modified version of the classic acid-base shakeout method and avoiding chlorinated organic solvents, bufotenine was selectively extracted in 2.4% from *A. colubrina* and 4% from *A. peregrina* (greater than the above described). The HR-ESIMS of **1** showed a quasi-molecular ion peak at m/z 205.1335 [M + H]$^+$ corresponding to the formula $C_{12}H_{17}N_2O$. ^{1}H-, ^{13}C- and two-dimensional (COSY, HMQC and HMBC) NMR experiments were also used to accomplish bufotenine identification. The ^{1}H and ^{13}C NMR assignments are given in Table 2, in accordance with the numbered structure.

Table 2: ^{1}H and ^{13}C NMR spectral data for isolated bufotenine (**1**).[a]



Position	δ_H	δ_C	APT	^{1}H-^{1}H COSY	HMBC
1	-	-	-	-	-
2	6.64 (s)	122.6	CH	-	H-10
3	-	111.4	C	-	H-2, H-4, H-10, H-11
4	6.87 (d, 2.4)	102.2	CH	-	H-6
5	-	159.7	C	-	H-6, H-7
6	6.86 (dd, 8.5; 2.4)	111.1	CH	H-7	H-4, H-7
7	6.89 (dd, 8.5; 0.64)	111.4	CH	H-6	H-6
8	-	131.6	C	-	H-4, H-6
9	-	127.9	C	-	H-2, H-7
10	2.54 - 2.51 (m)	22.9	CH_2	H-11	H-11
11	2.30 - 2.26 (m)	59.8	CH_2	H-10	H-10, H-12/H-13
12, 13	1.93 (s)	43.9	CH_3	-	H-11, H-12/C-13
14	9.63 (s)	-	-	-	-

[a] ^{1}H NMR (300 MHz) and ^{13}C NMR (75 MHz) were performed in methanol-d_4.



Scheme 1: Synthetic path for DMT (**4**), MDMT (**5**), bufotenidine (**6**) from HDMT **(1)**.

Scheme 1 outlines our approach to the synthesis of the title compounds. After several attempts, **1** was first over *N*-methylated in mild conditions (without basic catalysis) furnishing 5-hydroxy-*N*,*N*,*N*-trimethyltryptamine (**6**) in 85%, after crystallization from acetone. However our efforts to convert this ammonium salt into DMT (**4**) failed in the final step, which was selective mono *N*-demethylation. To overcome this limitation, **1** was converted into an aminoborane complex (**7**) with borane-dimethyl sulfide**.** Then, DMT (**4**) was prepared in 39% overall yield from **7** by transforming the 5-OH group into an *O*-Tf moiety, which was removed by catalytic hydrogenation. The aminoborane complex (**7**) was treated with iodomethane under PTC (KOH powder, TBAB in dried THF), followed by protection of the indole amine group with Boc to afford **8**. The latter was subsequently treated with DABCO and TFA for removal of both protecting groups, furnishing MDMT (**5**) in 69% overall yield (Scheme 1). All intermediates and targets covered in the synthetic path were characterized by HR-ESIMS, IR-FT and ^{1}H and ^{13}C plus two-dimensional (COSY, HMQC, HMBC) NMR experiments. Table 3 shows the ^{13}C NMR assignments for **4** to **8**.

The HR-ESIMS of **6** showed an ion peak at m/z 219.1493 [M + H]$^+$, corresponding to the formula $C_{13}H_{20}N_2O$. The structure of **6** could be determined based on characteristic signals at δ_H 3.16 (9H, s) and δ_C 52.6 (3C) relative to the methyl group by comparison with those of **1** at δ_H2.27 (6H, s) and δ_C 45.2 (2C).The aminoborane complex (**7**) was established from the ion peak at m/z 241.1495 corresponding to the [M + Na]$^+$ ion. Its IR spectrum exhibited bands at 2388, 2313 and 2279 cm^{-1} (borane group). The ^{1}H and ^{13}C NMR spectra of compound **7** were rather similar to those of **1**, except for chemical shifts related to methylene and methyl groups. The structure of the novel derivative was further confirmed by X-ray crystallographic methods (Figure 1).

Table 3: ^{13}C NMR data for **4**, **5**, **7** (75 MHz, methanol-d_4), **6** (75 MHz, DMSO-d_6) and **8** (75 MHz, $CDCl_3$).

Position	**4**	**5**	**6**	**7**	**8**
1-NH	-	-	-	-	-
2-CH	123.7	122.6	124.3	121.6	123.2
3-C	112.0	99.7	107.8	108.8	118.5
4-CH	118.7	99.8	102.7	100.7	101.8
5-CO or 5-CH	118.9	153.5	150.8	148.5	149.7
6-CH	121.7	111.5	112.3	110.2	112.6
7-CH	109.5	111.1	112.1	109.9	115.9
8-C	136.7	132.0	131.2	130.4	130.1
9-C	127.1	127.4	127.8	126.5	131.4
10-CH_2	20.9	22.6	19.2	18.7	23.4
11-CH_2	57.6	59.7	52.6	63.4	59.1
12, 13-NCH_3	43.0	43.8	65.7	49.3	43.4
14-OCH_3	-	55.0	-	-	55.7
15-COO (Boc group)	-	-	-	-	155.7

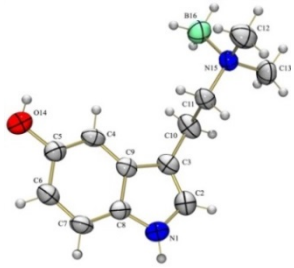


Figure 1: An ORTEP-3 representation (50% probability displacement ellipsoids) of the asymmetric unit of the aminoborane complex (**7**).

N,*N*-Dimethyltryptamine (**4**), $C_{12}H_{17}N_2$, showed a [M + H]$^+$ ion in its HR-ESIMS at m/z 189.1482. The ^{1}H NMR, aromatic region was observed at δ_H 7.03-7.16 (2H, m); 7.19 (1H, s); 7.39 (1H, d, *J* = 8.1 Hz); 7.59 (1H, d, *J* = 7.69 Hz) corresponding to 5-H, 6-H, 2-H, 7-H, and 6-H, respectively. In comparing with the precursor **7**, the signal for C-5 moves from δ_C 148.5 to 118.7. The ^{1}H and ^{13}C NMR spectra of the intermediate **8** showed additional signals correlated with 5-methoxyl (δ_H 3.86, 3H, s; δ_C 55.7), *tert*-butyl (δ_H, 1.65, 9H, s; δ_C, 83.1, 28.1) and carboxyl (δ_C 155.7) groups in comparison with **7**. Its IR spectrum exhibited absorption at 2365, 2314 and 2267 cm^{-1} (borane group) and at 1754 cm^{-1} (Boc group). The HR-ESIMS of MDMT (**5**), in the positive mode, revealed a peak at m/z 219.1493 [M + H]$^+$, indicating $C_{13}H_{18}N_2O$ as the molecular formula. The ^{1}H and ^{13}C NMR spectra of **5** showed a methoxyl group (δ_H 3.82, 3H, s; δ_C, 55.0) but lacked a Boc group. The IR spectra of **4** and **5** did not exhibit absorptions related to the borane group.

Herein bufotenine was efficiently isolated from seeds of *Anadenanthera* and employed for a partial synthesis of DMT (**4**)

and MDMT (**5**). Furthermore, bufotenine was effortlessly converted into an aminoborane complex (**7**) and trimethyl ammonium salt (**6**). As far as we know, this is the first time that such protocols are reported, including the description of the aminoborane complex (**7**). The synthesized dimethyltryptamines will serve as analytical standards for future pharmacological studies.

Experimental

General: Chemicals and absorbents were purchased from commercial sources. Commercial aluminum sheets (silica gel 60, F_{254}/0.2 mm) were used for analytical TLC and compounds were visualized with UV light, sulfuric acid/vanillin, or Dragendorff's reagent. CC was carried out on silica gel 60. NMR spectra were recorded at 25°C on a Varian Mercury Plus spectrometer (7.05 T) operating at 300 MHz for ^{1}H and 75.46 MHz for ^{13}C. Chemical shifts (δ) were reported in parts per million (ppm) relative to tetramethylsilane (TMS) for ^{1}H NMR and deuterated solvent (methanol-d_4 and DMSO-d_6) for ^{13}C NMR. Coupling constants were reported as *J* (Hz). IR (KBr) spectra were measured on a Varian FT 640-IR. HR-ESIMS were obtained on a Micro TOF Bruker Daltonics Inc.

Plant material: Seeds of *Anadenanthera* were collected during August-September of 2009 and 2011 around the University of Brasilia, in cerrado *sensu strito* vegetation at an altitude of 1030 m. Voucher specimens were authenticated by Fagg CW and deposited in the Herbarium (UB), UnB, CEP 70919970, Brasilia DF, Brazil, under codes Fagg CW 1739, *Anadenanthera peregrina* (L.) Speg. var. *peregrina*, and Fagg CW 1737, *Anadenanthera colubrina* (Vell.) Brenan var. *cebil* (Griseb.) Altschul.

Extraction and isolation of bufotenine (1): Air-dried seeds of *Anadenanthera* species (50 g) were powdered in a domestic blender and defatted with *n*-hexane (80 mL x 3) under magnetic stirring for 2 h at 25°C. After filtering, the residual solid was extracted with MeOH (80 mL x 4) with magnetic stirring for 2 h at 25°C. The filtered methanolic extract was concentrated in vacuum to 80 mL and diluted with H_2O (100 mL). The resulting mixture was stirred for 2 h with aqueous 2 M HCl (40 mL), neutralized with solid Na_2CO_3 (7.0 g), and extracted with AcOEt (20 mL x 10). The combined extract was dried over Na_2SO_4 and evaporated in vacuum to afford a brown amorphous solid, which was recrystallized from AcOEt to yield **1** [yellowish pale solid, 2.0 g (1.2%) for *A. colubrina* and 2.0 g (4%) for *A. peregrine*].
R_f: 0.45 (MeOH-AcOEt-NH_4OH 1:1:0.1).
MP: 150-155ºC (lit. [2] 146-147°C).
IR (KBr): 3409, 2945, 1623, 1468, 1245, 1056, 827, 796, 504 cm^{-1}.
^{1}H and ^{13}C NMR (methanol-d_4): Table 2.
HR-ESIMS: *m/z* 205.1335 (calc. 205.1341 for $C_{12}H_{17}N_2O$, $[M + H]^+$).

5-Hydroxy-N,N,N-trimethyltryptamine (6): A mixture of **1** (0.204 g, 1.0 mmol) and iodomethane (0.283 g, 2.0 mmol) in acetone (3.0 mL) was stirred at 25°C for 3 h, under N_2. Then the solvent was evaporated in vacuum and the residual solid was recrystallized from acetone to give **6** (amorphous yellowish solid, 0.186 g, 85%).
MP: 210-214ºC (lit. [19] 211-215°C).
IR (KBr): 3347, 3413, 1617, 1456, 1201, 1096, 616 cm^{-1}.
^{1}H NMR (300 MHz, DMSO-d_6): 3.05-3.10 (2H, m), 2.18 (9H, s), 3.54-3.57 (2H, m), 6.63 (1H, dd, *J* = 8.4; 2.31 Hz), 6.88 (1H, d, *J* = 2.14 Hz), 7.14 (d, *J* = 3.21 Hz), 7.16 (1H, s), 8.64 (1H, s), 10.64 (1H, sl).
^{13}C NMR (75 MHz, DMSO-d_6): Table 3.
HR-ESIMS: *m/z* 219.1493 (calc. 219.1497 for $C_{13}H_{20}N_2O$, $[M + H]^+$).

Bufotenine-aminoborane complex (7): To a solution of **1** (1.02 g, 5.0 mmol) in THF, dried prior to use, was added 10 M Me_2S-BH_3 in THF (0.75 mL, 7.5 mmol). The mixture was stirred at 0°C for 2 h, under N_2. After concentration, the residue was dissolved in CH_2Cl_2 (40 mL). The organic layer was washed with 10% aqueous NH_4OH (100 mL x 3), dried over Na_2SO_4, and evaporated in vacuum. CC (*n*-hexane:AcOEt 2:1) of the residue afforded **7** (white crystals, 1.03 g, 95%).
R_f: 0.3 (*n*-hexane-AcOEt 2:1)
MP: 123-125°C.
IR (KBr): 3395, 3028, 2894, 1697, 1576, 1485, 1220, 927, 698 cm^{-1}
^{1}H NMR (300 MHz, methanol-d_4): 2.58 (6H, s), 2.91-2.96 (2H, m), 3.05-3.09 (2H, m), 6.68 (1H, dd, *J* = 8.7; 2.7 Hz), 6.95 (1H, d, *J* = 2.7 Hz), 6.17 (1H, dd, *J* = 8.7; 2.7 Hz).
^{13}C NMR (75 MHz, methanol-d_4): Table 3.
HR-ESIMS: *m/z* 241.1495 (calc. 241.1488 for $C_{12}H_{19}BN_2ONa$, $[M + Na]^+$).

Crystal data for complex (7): Crystallographic measurements were collected on a Bruker CCD SMART APEX II single crystal diffractometer with Mo Kα radiation (0.71073 Å) at 296K, processed with SAINT and corrected for absorption using SADABS [20]. Experimental data can be found on file deposited at the Cambridge Crystallographic Data Centre with CCDC number 1022431. The structures were solved by Direct Methods using SHELXS-97 and subsequent Fourier-difference map analyses yielded the positions of the non-hydrogen atoms; the refinement was performed using SHELXL-97 [21]. Molecular graphics, ORTEP-3, software were used to prepare material for publication, WinGX-Routine. $C_{12}H_{19}N_2OB$; *M* = 218.10; monoclinic, space group *P21*; a = 5.849(3) Å, *b* = 7.671(4) Å, *c* = 13.763(6) Å; $\alpha = \gamma =$ 90º, β = 92.160(3)º; *V* = 617.17(5) Å^3; Z = 2; D_c = 1.174 g.cm^{-1}; *F*(000) = 236; colorless block, size 0.49 x 0.28 x 0.15 mm; 2423 independent measured reflections, refinement based on F^2 to give R_1 [$F^2 > 4\sigma(F^2)$] = 0.048; w_2 = 0.106 for 5791 observed reflections, and 151 parameters.

N,N-Dimethyltryptamine (4): A mixture of NaH (0.06 g, 2.4 mmol, 60% in mineral oil) and **7** (0.436 g, 2.0 mmol) in THF was stirred at -40°C for 20 min, under N_2. ClT_f (0.6 mL, 8.0 mmol) was added dropwise and stirring was continued for an additional 12 h. The mixture was diluted with CH_2Cl_2 (50 mL), the organic phase washed with 10% aqueous NH_4OH (10 mL x 3) and brine (10 mL), dried over Na_2SO_4 and concentrated in vacuum. The residue was diluted in MeOH and Pd-C (10% Pd, 0.235 g, 0.22 mmol) was added; the reaction flask was degassed and fitted with a balloon filled with H_2. Stirring was maintained at 25°C for 24 h. Afterwards, the mixture was filtered through Celite® with MeOH, the filtrate concentrated in vacuum, and CC (AcOEt-Et_3N 1:1.0 x 10^{-3}) of the residue afforded **4** (yellow solid, 0.147 g, 39%).
R_f: 0.40 (MeOH-AcOEt-NH_4OH, 1:1:0.1).
MP: 37-40°C (lit. [22] 38-40°C).
IR (KBr): 3416, 2928, 1639, 1550, 1460, 1262, 1044, 740 cm^{-1}.
^{1}H NMR (300 MHz, methanol-d_4): 2.81 (6H, s), 3.10-3.15 (2H, m), 3.28-3.32 (2H, m), 7.03-7.16 (2H, m), 7.19 (1H, s), 7.39 (1H, d, *J* = 8.1 Hz), 7.59 (1H, d, *J* = 7.69 Hz), 10.37 (1H, sl).
^{13}C NMR (75 MHz, methanol-d_4): Table 3.
HR-ESIMS: *m/z* 189.1482 (calc. 189.1392 for $C_{12}H_{17}N_2$, $[M + H]^+$).

5-Methoxy-N-Boc bufotenine-aminoborane complex (8): A mixture of KOH powder (0.05 g, 0.75 mmol), TBAB (0.05 g, 0.13 mmol), and **7** (0.109 g, 0.50 mmol) in dried THF was stirred at 25°C for 20 min, under N_2. Then, iodomethane (0.05 mL, 0.75 mmol) was added and stirring was continued for 12 h. Then, the solvent was evaporated in vacuum, the residue dissolved in CH_2Cl_2

(10 mL), washed with H_2O (3 mL x 3), the organic layer dried over Na_2SO_4 and concentrated. The residue was treated with catalytic DMAP, $(Boc)_2O$ (0.109 g, 0.50 mmol), and Et_3N (0.2 mL, 1.5 mmol) in CH_2Cl_2. After 2 h of stirring at 25°C, H_2O (3 mL) was added, the organic layer removed, the aqueous phase extracted with CH_2Cl_2 (7 mL x 3) and the combined extracts dried over Na_2SO_4 and concentrated. CC (*n*-hexane: AcOEt 2:1) of the residue afforded **8** (white solid, 102 mg, 62%).
R_f: 0.45 (*n*-hexane-AcOEt 2:1)
MP: 134-136ºC.
IR (KBr): 3406, 2945, 2387, 2278, 1584, 1489,1214, 1169, 801cm^{1}.
^{1}H NMR (300 MHz, $CDCl_3$): 1.65 (9H, s), 2.34 (6H, s), 2.60-2.66 (2H, m), 2.81-286 (2H, m), 3.86 (3H, s), 6.92 (1H, dd, *J* = 8.84, 2.46 Hz), 6.95 (1H, d, *J* = 2.46 Hz), 7.38 (1H, s), 7.90 1H, sl).
^{13}C NMR (75 MHz, methanol-d_4): Table 3.

5-Methoxy-N,N-dimethyltryptamine (5): A mixture of **8** (90 mg, 0.3 mmol) and DABCO (0.07 g, 0.6 mmol) in CH_2Cl_2 (4.0 mL) was stirred at 25°C for 2 h, under N_2. The mixture was diluted with CH_2Cl_2 (10 mL), washed with H_2O and brine, dried over Na_2SO_4, and evaporated in vacuum. The residue was stirred with TFA in CH_2Cl_2 (0.5:1 mL) at 25°C. The solvent was removed in vacuum at 25°C and the residue was submitted to CC (AcOEt-Et_3N 1:1.0x10^{-3}) to give **5** (yellow oil, 41 mg, 69%).
R_f: 0.43 (MeOH-AcOEt-NH_4OH 1:1:0.1).
IR (KBr): 3297, 1582, 1457, 1360, 904, 848, 796 cm^{-1}.
^{1}H NMR (300 MHz, methanol-d_4): 2.39 (6H, s), 2.68-2.74 (2H, m), 2.90-2.95 (2H, m,), 3.82 (3H, s), 6.75 (1H, dd, *J* = 8.84, 2.46 Hz), 7.01 (1H, d, *J* = 2.46 Hz), 7.03 (1H, s), 7.22 (1H, d, *J* = 8.82 Hz).
^{13}C NMR (75 MHz, methanol-d_4): Table 3.
HR-ESIMS: *m/z* 219.1493 (calc. 219.1497 for $C_{13}H_{18}N_2O$, $[M + H]^+$).

Acknowledgments - Financial support from CNPq/FINEP, CAPES, and FAP-DF. CAPES provided scholarship for M.L.A.

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