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Microwave-accelerated synthesis of psychoactive deuterated *N,N*-dialkylated-[$\alpha,\alpha,\beta,\beta$-$d_4$]-tryptamines

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A large number of *N,N*-dialkylated tryptamines are known to induce psychoactive effects in humans. This has resulted in their increased attention within clinical and forensic communities. Deuterated tryptamines are ideal for use as internal standards during MS bioanalysis or of use in biochemical NMR studies. The present study reports on a microwave-enhanced synthesis of 22 *N,N*-dialkylated-[$\alpha,\alpha,\beta,\beta$-d4]-tryptamines *via* the reduction with lithium aluminium deuteride of glyoxalylamide precursors obtained by the procedure of Speeter and Anthony. Syntheses were carried out using a single-mode system under elevated pressure conditions where anhydrous tetrahydrofuran was used as the solvent at 150°C. Good yields were obtained within 5 min.

Keywords: Hallucinogens; Microwaves; Deuteration; Clinical; Forensic

Introduction

Numerous tryptamines, such as serotonin (5-hydroxytryptamine, 5-HT), melatonin, and several related compounds play an important part in the neurochemistry of the human brain. Furthermore, *N*-monomethyltryptamine and *N,N*-dimethyltryptamine (DMT), have been identified in various human tissues.[1–3] A large number of *N,N*-dialkylated tryptamine derivatives, including DMT, are capable of inducing altered states of consciousness in humans and the term 'hallucinogen' is often used in an attempt to describe their powerful impact on perception, mood and cognition. Several *N,N*-dimethylated tryptamines are found in various plants and fungi which have been used since ancient times for recreational and religious purposes, and this has led to a long-standing interest in the chemistry and biological activity of these compounds. The most common naturally-occurring representatives include DMT, *O*-phosphoryl-4-hydroxy-*N,N*-dimethyltryptamine (psilocybin), 5-methoxy-*N,N*-dimethyltryptamine (5-MeO-DMT) and 5-hydroxy-*N,N*-dimethyltryptamine (bufotenin).[4,5] (Scheme 1A)

In recent years, DMT and psilocybin have been the focus of intense research within the pharmacology, neuroscience, and psychiatry communities and has included human clinical studies of these and related compounds.[6–11] Psychoactivity is greatly affected by substitution on the indole ring, the side-chain carbons and by alkylation of the side-chain nitrogen. Most of the psychoactive *N,N*-disubstituted derivatives may show oral activity, due to their refractoriness to metabolism by monoamine oxidases (MAOs). Homologation of the *N,N*-dialkyl substituents appears to diminish potency and only derivatives possessing *N,N*-dimethyl substituents exist naturally.[12–15]

Due to a renewed interest in the role of such compounds in understanding mechanisms of perception, there is a need for a fast and simple preparation of deuterated *N,N*-dialkylated tryptamine standards. This is based, in part, on the presence of several dimethylated derivatives in human biofluids and tissues and the question about their function is not fully resolved.[1,3,16–18] Rat brain levels of DMT and 5-MeO-DMT have been determined successfully following intraperitoneal (IP) injection and an isotope dilution method was successfully employed using deuterated DMT and 5-MeO-DMT as internal standards.[19] The use of $\alpha,\alpha,\beta,\beta$-$d_4$ derivatives provided indications for a differential pharmacological response when compared with nondeuterated tryptamines which merits further

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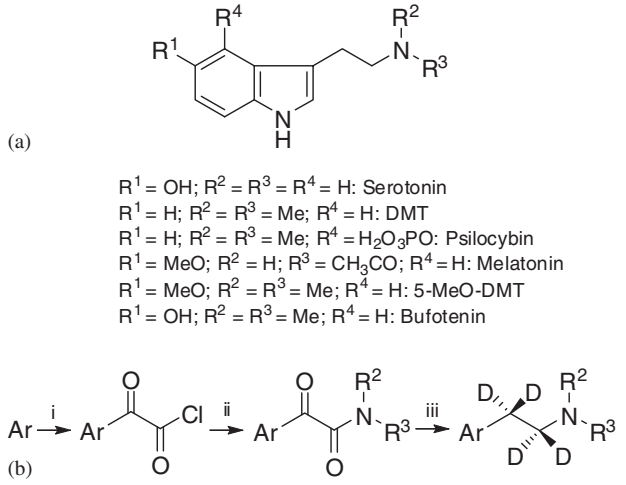


Scheme 1. (a) Commonly found naturally-occurring tryptamine derivatives. (b) Synthesis of deuterated *N,N*-disubstituted tryptamine derivatives *via* the synthetic route of Speeter & Anthony. i. oxalyl chloride; ii: amine; iii: $LiAlD_4$; $R^2 = R^3 =$ alkyl; Ar = 5-methoxyindole or indole. For structures of tryptamines **1–22**, see Table 1.

investigations. This has been attributed to the *in vivo* kinetic isotope effect where, for example, d_4-DMT was observed to exhibit prolonged behavioural effects in rats.[20] Correspondingly, deuteration also affected pharmacokinetic parameters which resulted in significantly increased rat brain levels following IP injections. This allowed for the identification of minor metabolic pathways without the use of pharmacological intervention such as MAO inhibition.[21,22] Further, the fact that a number of *N,N*-dialkylated tryptamines are often classified as controlled substances results in an increased demand for deuterated standards for forensic purposes.

A convenient method for the synthesis of *N,N*-dialkylated tryptamines is based on the route of Speeter and Anthony.[23] This involves acylation of an indole with oxalyl chloride followed by reaction with the appropriate amine to give an indol-3-yl-glyoxalylamide. This amide is then reduced with lithium aluminium hydride to the tryptamine product. Replacement of the metal hydride with lithium aluminium deuteride (LAD) conveniently affords the desired $\alpha,\alpha,\beta,\beta$-$d_4$ derivatives (Scheme 1B). Previous studies have focused on the preparation of *N,N*-dimethylated or mono-methylated derivatives only *via* the Speeter and Anthony procedure.[12,24–29]

Microwave-accelerated reactions are increasingly used in drug discovery and organic synthesis because they allow for a high-throughput approach in which syntheses can be carried out within minutes.[30–32] To the best of the authors' knowledge, this study appears to be the first application of a microwave-accelerated reduction of glyoxalylamides using LAD, to give a range of novel symmetrically and asymmetrically substituted $\alpha,\alpha,\beta,\beta$-$d_4$ derivatives.

Experimental

Materials

Silica gel for flash chromatography (particle size 40–63 μm), silica gel aluminium thin-layer chromatography (TLC) plates were obtained from VWR (UK). All other solvents, reagents, and lithium aluminium deuteride (98 atom %) were purchased from Aldrich (UK) and were of analytical grade.

Instrumentation

NMR spectra were recorded using a Bruker Avance 300 spectrometer at 300.1 MHz (^{1}H-NMR) or 75.5 MHz (^{13}C-NMR). Tryptamine spectra were taken in $CDCl_3$ and chemical shifts are reported relative to TMS at $\delta = 0$ ppm. NMR spectra were obtained by ^{1}H, proton decoupled ^{13}C, DEPT-135, HSQC and HMBC experiments. When d_6-DMSO was used, chemical shifts were determined relative to the residual solvent peak at $\delta = 2.51$ (^{1}H-NMR) and $\delta = 39.6$ ppm (^{13}C-NMR).

Microwave-accelerated syntheses were carried out using a monomode CEM Explorer (UK) microwave system. Operation settings were: microwave power 250 W, temperature 150°C, maximum pressure 280 psi, ramp time 5 min, hold time 5 min. Reactions were performed in glass microwave tubes, closed with *Intellivent* caps (CEM) and contents of the vessel were continuously stirred by a Teflon-coated magnetic stir bar (10 × 3 mm). Temperature, pressure and power profiles were monitored using the ChemDriver software version 3.6.0. Each reaction was carried out in duplicate.

A Micromass LCT orthogonal acceleration time-of-flight mass spectrometer (Micromass, UK) equipped with an electrospray ionisation source was operated in positive mode. Samples were introduced using a flow injection method *via* a Harvard Apparatus (Pump 11) (Massachusetts, USA) syringe pump at 20 μL/min. The instrument was tuned and calibrated in the mass range of 100–1000 Da using a sodium formate solution (0.005 M in 50:50 acetonitrile-water). Exact mass measurements of the tryptamine products were based on the protonated molecules $[M+H]^+$. Both *N,N*-diallylglyoxalylamides were detected as sodiated adducts $[M+Na]^+$. Leucine enkephalin (1 μg/mL) was used as lock mass standard after instrument calibration. Operation settings were: capillary voltage: 3000 V, sample cone voltage: 30 V, RF lens: 250 V, desolvation temperature: 150°C, source temperature: 100°C, acceleration: 200 V, cone gas flow: 22 L/h, desolvation gas flow: 602 L/h. Data acquisition was carried out using MassLynx version 4.0 SP2. Isotopic purities were determined after direct infusion and integration of mass peak areas.

General procedure for the microwave-accelerated synthesis of N,N-disubstituted [α,α,β,β-d$_4$]-tryptamine derivatives (1–22)

Tryptamines were synthesised in duplicate by the reduction of the appropriate indol-3-yl-*N,N*-dialkylated glyoxalylamides (available from previous work [33]) with lithium aluminium deuteride (LAD). The preparation of 5-MeO-d_4-DALT **11** and d_4-DALT **22** required the syntheses of the corresponding glyoxalylamides, which are reported here

The appropriate indole (5.44 mmol; 5-methoxyindole: 800 mg; indole: 637 mg) was dissolved in 150 mL anhydrous ether and stirred on ice for 30 min. Oxalyl chloride (2.07 g, 16.3 mmol) was added dropwise, stirred for 30 min on ice, and kept at −20°C for 4 h. The crystalline orange or yellow α-oxo acid chlorides were filtered and washed three times with cold anhydrous ether (50 mL) and dried *in vacuo* for 3 h at room temperature to give a yield of 1.19 g (5.00 mmol, 92%) for 5-methoxyindol-3-yl-glyoxalyl chloride and 1.02 g (4.90 mmol, 90%) for indol-3-yl-glyoxalyl chloride, respectively.

N,N-Diallylamine (760 mg, 7.81 mmol, 0.966 mL) was added dropwise to an ice-cold solution of 5-methoxyindol-3-yl-glyoxalyl

chloride (619 mg, 2.60 mmol) or indol-3-yl-glyoxalyl chloride (540 mg, 2.60 mmol) dissolved in 100 mL anhydrous tetrahydrofuran (THF). The mixture was stirred on ice for 4 h. The solvent was evaporated under reduced pressure to give a crude solid that was purified by flash chromatography (CH_2Cl_2-MeOH, 9:1). The solvent was evaporated under reduced pressure and recrystallised from methanol/ethyl acetate and dried overnight under vacuum.

5-Methoxyindol-3-yl-N,N-diallylglyoxalylamide

Yield: 64%. ^{1}H-NMR (d_6-DMSO): 12.18 (NH-1, br s), 8.03 (1H, s, H-2), 7.62 (1H, d, H-4, *J* 2.4 Hz), 7.44 (1H, d, H-7, *J* 8.5 Hz), 6.92 (1H, dd, H-6, *J* 8.9, 2.4 Hz), 5.89 (1H, ddt, $^3J_{trans}$ 16.7 Hz, $^3J_{cis}$ 10.7 Hz, ^3J 5.7 Hz, CH=CH_2), 5.74 (1H, ddt, $^3J_{trans}$ 17.2 Hz, $^3J_{cis}$ 10.3 Hz, ^3J 5.7 Hz, CH=CH_2), 5.27 (1H, ddt ~ dq, *J* 7.2, 1.5 Hz, CH=CH), 5.24-5.22 (1H, m, CH=CH), 5.16 (1H, ddt ~ dq, *J* 12.9, 1.5 Hz, CH=CH), 5.135 (1H, ddt ~ dq, *J* 5.7, 1.5, CH=CH), 4.03 (2H, d, N-CH_2, *J* 5.7 Hz), 3.86 (2H, d, N-CH_2, *J* 5.7 Hz), 3.81 (3 H, s, OCH_3). ^{13}C-NMR: 185.8 (CO-*β*), 167.3 (CO-*α*), 155.9 (C-5), 137.0 (C-2), 133.2 (CH=CH_2), 132.7 (CH=CH_2), 131.6 (C-7a), 125.8 (C-3a), 118.3 (CH=CH_2), 117.7 (CH=CH_2), 113.4 (C-7), 113.3 (C-6), 112.8 (C-3), 102.7 (C-4), 55.3 (OCH_3), 49.2 (N-CH_2), 45.6 (N-CH_2). HRESIMS theory $[M+Na]^+$: 321.1215; observed: 321.1230.

*Indol-3-yl-N,N-diallylglyoxalylamide (**22a**)*

Yield: 621 mg (2.87 mmol, 55%). ^{1}H-NMR (d_6-DMSO): 12.28 (NH-1, br s), 8.14-8.12 (1H, m, H-4), 8.1 (1H, s, H-2), 7.58-7.52 (1H, m, H-7), 7.29 (1H, td, H-6, *J* 7.2, 1.8 Hz), 7.26 (1H, td, H-5, *J* 7.2, 1.5 Hz), 5.89 (1H, ddt, $^3J_{trans}$ 16.7 Hz, $^3J_{cis}$ 10.7 Hz, ^3J 5.7 Hz, CH=CH_2), 5.74 (1H, ddt, $^3J_{trans}$ 17.2 Hz, $^3J_{cis}$ 10.3 Hz, ^3J 5.7 Hz, CH=CH_2), 5.27 (1H, ddt ~ dq, *J* 7.2, 1.5 Hz, CH=CH), 5.24-5.22 (1H, m, CH=CH), 5.16 (1H, ddt ~ dq, *J* 12.9, 1.5 Hz, CH=CH), 5.14 (1H, ddt ~ dq, *J* 5.7, 1.5 Hz, CH=CH), 4.03 (2H, d, N-CH_2, *J* 5.7 Hz), 3.86 (2H, d, N-CH_2, *J* 5.7 Hz). ^{13}C-NMR: 185.9 (CO-*β*), 167.3 (CO-*α*), 137.1 (C-2), 136.8 (C-7a), 133.1 (CH=CH_2), 132.7 (CH=CH_2), 124.9 (C-3a), 123.5 (C-6), 122.5 (C-5), 120.9 (C-4), 118.3 (CH=CH_2), 117.7 (CH=CH_2), 112.9 (C-7), 112.6 (C-3), 49.2 (N-CH_2), 45.6 (N-CH_2). HRESIMS theory $[M+Na]^+$: 291.1109; observed: 291.1092.

To a microwave tube were added a stirrer bar and the corresponding glyoxalylamide (0.5 mmol). Ice-cold anhydrous THF (3 mL) was added under a stream of nitrogen and LAD (126 mg, 3 mmol) was added under a stream of nitrogen with vigorous stirring on ice. The tube was sealed and the reaction mixture was heated in the microwave system under the conditions described above. At the end of the reaction the mixture was transferred to a conical flask and cooled on ice. The tubes were then rinsed with 3 × 8 mL THF and the washings were added to the flask. Excess deuteride was destroyed by the dropwise addition of 5 mL water, followed by 4 mL 20% NaOH and 5 mL water. The volume of THF was increased by adding another 20 mL. The precipitated inorganic salts were removed by filtration and washed with 30 mL THF. The filtrate was evaporated under reduced pressure and the resulting oily residue was dissolved in 60 mL chloroform, 1 mL 20% NaOH, and 10 mL water, and thoroughly shaken in a separating funnel. The organic layer was separated and two additional chloroform extractions (20 mL) from the remaining alkaline aqueous phases were carried out. The combined organic fractions were then pooled and washed with distilled water (2 × 40 mL) with saturated aqueous NaCl (40 mL). The organic phase was evaporated under reduced pressure and the resulting product was purified by flash chromatography ($CHCl_3$/MeOH/NH_4OH: 8/2/0.1). The free base products were dried overnight *in vacuo* over P_2O_5 to yield the desired, mostly solid, tryptamine derivatives.

*5-Methoxy-N,N-dimethyl-[α,α,β,β-d_4]-tryptamine (**1**)*

Yield: 82 mg (0.37 mmol, 74%). ^{1}H-NMR: 8.00 (NH-1, br s), 7.23 (1H, d, H-7, *J* 8.7 Hz,), 7.05 (1H, d, H-4, *J* 2.3 Hz), 6.99 (1H, d, H-2, *J* 2.3 Hz), 6.85 (1H, dd, H-6, *J* 8.7, 2.3 Hz), 3.86 (3H, s, OCH_3), 2.37 (6H, s, N-CH_3). ^{13}C-NMR: 153.8 (C-5), 131.6 (C-7a), 127.9 (C-3a), 122.5 (C-2), 113.7 (C-3), 111.9 (C-6 and C-7), 100.8 (C-4), 56.0 (OCH_3), 45.4 (N-CH_3). HRESIMS theory $[M+H]^+$: 223.1748; observed: 223.1740.

*5-Methoxy-N-methyl-N-ethyl-[α,α,β,β-d_4]-tryptamine (**2**)*

Yield: 95 mg (0.40 mmol, 80%). ^{1}H-NMR: 7.96 (NH-1, br s), 7.23 (1H, d, H-7, *J* 8.5 Hz,), 7.05 (1H, d, H-4, *J* 2.4 Hz), 7.00 (1H, d, H-2, *J* 2.3 Hz), 6.85 (1H, dd, H-6, *J* 8.7, 2.4 Hz), 3.86 (3H, s, OCH_3), 2.57 (2H, q, N-CH_2, *J* 7.2 Hz), 2.37 (3H, s, N-CH_3), 1.13 (3H, t, N-CH_2-CH_3, *J* 7.2 Hz). ^{13}C-NMR: 153.8 (C-5), 131.5 (C-7a), 127.9 (C-3a), 122.4 (C-2), 113.8 (C-3), 111.9 (C-6 and C-7), 100.8 (C-4), 56.0 (OCH_3), 51.3 (N-CH_2), 41.6 (N-CH_3), 12.3 (N-CH_2-CH_3). HRESIMS theory $[M+H]^+$: 237.1905; observed: 237.1917.

*5-Methoxy-N-methyl-N-n-propyl-[α,α,β,β-d_4]-tryptamine (**3**)*

Yield: 96 mg (0.38 mmol, 76%). ^{1}H-NMR: 7.94 (NH-1, br s), 7.23 (1H, d, H-7, *J* 8.5 Hz,), 7.05 (1H, d, H-4, *J* 2.4 Hz), 7.00 (1H, d, H-2, *J* 2.3 Hz), 6.85 (1H, dd, H-6, *J* 8.8, 2.1 Hz), 3.86 (3H, s, OCH_3), 2.45 (2H, m, N-CH_2-CH_2), 2.38 (3H, s, N-CH_3), 1.56 (2H, sext, N-CH_2-CH_2, *J* 7.5 Hz), 0.93 (3H, t, N-CH_2-CH_2-CH_3, *J* 7.5 Hz). ^{13}C-NMR: 153.8 (C-5), 131.6 (C-7a), 127.9 (C-3a), 122.5 (C-2), 113.9 (C-3), 111.9 (C-6 and C-7), 100.8 (C-4), 59.8 (N-CH_2-CH_2), 56.0 (OCH_3), 42.2 (N-CH_3), 20.4 (N-CH_2-CH_2), 12.1 (N-CH_2-CH_2-CH_3). HRESIMS theory $[M+H]^+$: 251.2061; observed: 251.2051.

*5-Methoxy-N-methyl-N-isopropyl-[α,α,β,β-d_4]-tryptamine (**4**)*

Yield: 96 mg (0.38 mmol, 76%). ^{1}H-NMR: 7.96 (NH-1, br s), 7.23 (1H, d, H-7, *J* 8.8 Hz,), 7.06 (1H, d, H-4, *J* 2.4 Hz), 7.00 (1H, d, H-2, *J* 2.1 Hz), 6.85 (1H, dd, H-6, *J* 8.7, 2.3 Hz), 3.86 (3H, s, OCH_3), 2.97 (1H, sept, N-CH, *J* 6.6 Hz), 2.37 (3H, s, N-CH_3), 1.07 (6H, d, N-CH-CH_3, *J* 6.6 Hz). ^{13}C-NMR: 153.9 (C-5), 131.5 (C-7a), 128.0 (C-3a), 122.3 (C-2), 114.2 (C-3), 112.1 (C-6), 111.8 (C-7), 100.9 (C-4), 56.0 (OCH_3), 53.6 (N-CH), 30.3 (N-CH_3), 18.0 (N-CH-CH_3). HRESIMS theory $[M+H]^+$: 251.2061; observed: 251.2075.

*5-Methoxy-N,N-diethyl-[α,α,β,β-d_4]-tryptamine (**5**)*

Yield: 97 mg (0.39 mmol, 78%). ^{1}H-NMR: 7.98 (NH-1, br s), 7.23 (1H, d, H-7, *J* 8.9 Hz,), 7.06 (1H, d, H-4, *J* 2.4 Hz), 6.99 (1H, d, H-2, *J* 2.3 Hz), 6.85 (1H, dd, H-6, *J* 8.9, 2.4 Hz), 3.86 (3H, s, OCH_3), 2.70 (4H, q, N-CH_2, *J* 7.2 Hz), 1.12 (6H, t, N-CH_2-CH_3, *J* 7.2 Hz). ^{13}C-NMR: 153.9 (C-5), 131.5 (C-7a), 127.9 (C-3a), 122.2 (C-2), 114.4 (C-3), 112.1 (C-6), 111.8 (C-7), 100.8 (C-4), 55.9 (OCH_3), 46.9 (N-CH_2), 11.8 (N-CH_2-CH_3). HRESIMS theory $[M+H]^+$: 251.2061; observed: 251.2074.

*5-Methoxy-N-ethyl,N-n-propyl-[α,α,β,β-d_4]-tryptamine (**6**)*

Yield: 95 mg (0.36 mmol, 72%). ^{1}H-NMR: 7.98 (NH-1, br s), 7.23 (1H, d, H-7, *J* 8.7 Hz,), 7.05 (1H, d, H-4, *J* 2.3 Hz), 6.99 (1H, d, H-2, *J* 2.1 Hz), 6.85 (1H, dd, H-6, *J* 8.7, 2.4 Hz), 3.86 (3H, s, OCH_3), 2.69

(2H, q, N-C$\underline{H}_2$-CH$_3$, *J* 7.2 Hz), 2.55 (2H, m, N-C$\underline{H}_2$-CH$_2$), 1.56 (2H, m, N-CH$_2$-C$\underline{H}_2$), 1.11 (3H, t, N-CH$_2$-C$\underline{H}_3$, *J* 7.2 Hz), 0.92 (3H, t, N-CH$_2$-CH$_2$-C$\underline{H}_3$, *J* 7.3 Hz). ^{13}C-NMR: 153.9 (C-5), 131.5 (C-7a), 128.0 (C-3a), 122.3 (C-2), 114.2 (C-3), 112.1 (C-6), 111.8 (C-7), 100.8 (C-4), 56.0 (OCH$_3$), 55.5 (N-C$\underline{H}_2$-CH$_2$), 47.5 (N-C$\underline{H}_2$-CH$_3$), 20.1 (N-CH$_2$-C$\underline{H}_2$-CH$_3$), 12.0 (N-CH$_2$-CH$_2$-C$\underline{H}_3$), 11.7 (N-CH$_2$-C$\underline{H}_3$). HR-ESIMS theory [M+H]$^+$: 265.2218; observed: 265.2230.

*5-Methoxy-N-ethyl-N-isopropyl-[α,α,β,β-d$_4$]-tryptamine (**7**)*

Yield: 94 mg (0.36 mmol, 72%). ^{1}H-NMR: 7.93 (NH-1, br s), 7.23 (1H, d, H-7, *J* 8.7 Hz,), 7.06 (1H, d, H-4, *J* 2.4 Hz), 7.00 (1H, d, H-2, *J* 2.3 Hz), 6.85 (1H, dd, H-6, *J* 8.7, 2.4 Hz), 3.86 (3H, s, OCH$_3$), 3.10 (1H, sept, N-CH, *J* 6.6), 2.62 (2H, q, N-CH$_2$, *J* 7.2 Hz), 1.14 (3H, t, N-CH$_2$-C$\underline{H}_3$, *J* 7.2 Hz), 1.06 (6H, d, N-CH-C$\underline{H}_3$, *J* 6.6 Hz). ^{13}C-NMR: 153.9 (C-5), 131.5 (C-7a), 128.0 (C-3a), 122.3 (C-2), 114.4 (C-3), 112.1 (C-6), 111.8 (C-7), 100.9 (C-4), 55.9 (OCH$_3$), 50.6 (N-CH), 44.2 (N-CH$_2$), 18.5 (N-CH-C$\underline{H}_3$), 14.0 (N-CH$_2$-C$\underline{H}_3$). HRESIMS theory [M+H]$^+$: 265.2218; observed: 265.2232.

*5-Methoxy-N,N-di-n-propyl-[α,α,β,β-d$_4$]-tryptamine (**8**)*

Yield: 103 mg (0.37 mmol, 74%). ^{1}H-NMR: 7.91 (NH-1, br s), 7.24 (1H, d, H-7, *J* 8.7 Hz,), 7.05 (1H, d, H-4, *J* 2.4 Hz), 6.99 (1H, d, H-2, *J* 2.4 Hz), 6.85 (1H, dd, H-6, *J* 8.7, 2.4 Hz), 3.86 (3H, s, OCH$_3$), 2.55 (4H, m, N-C$\underline{H}_2$), 1.56 (4H, m, N-CH$_2$-C$\underline{H}_2$), 0.91 (6H, t, N-CH$_2$-C$\underline{H}_3$, *J* 7.3 Hz). ^{13}C-NMR: 153.9 (C-5), 131.5 (C-7a), 128.0 (C-3a), 122.3 (C-2), 114.3 (C-3), 112.1 (C-6), 111.8 (C-7), 100.8 (C-4), 56.1 (N-CH$_2$), 56.0 (OCH$_3$), 20.1 (N-CH$_2$-C$\underline{H}_2$), 12.0 (N-CH$_2$-C$\underline{H}_3$). HRESIMS theory [M+H]$^+$: 279.2374; observed: 279.2360.

*5-Methoxy-N,N-diisopropyl-[α,α,β,β-d$_4$]-tryptamine (**9**)*

Yield: 108 mg (0.39 mmol, 78%). ^{1}H-NMR: 7.92 (NH-1, br s), 7.23 (1H, d, H-7, *J* 9.2 Hz,), 7.06 (1H, d, H-4, *J* 2.6 Hz), 6.98 (1H, d, H-2, *J* 2.3 Hz), 6.85 (1H, dd, H-6, *J* 8.9, 2.4 Hz), 3.86 (3H, s, OCH$_3$), 3.13 (2H, sept, N-CH, *J* 6.6 Hz), 1.09 (12H, d, N-CH-C$\underline{H}_3$, *J* 6.6 Hz). ^{13}C-NMR: 153.9 (C-5), 131.4 (C-7a), 128.1 (C-3a), 122.2 (C-2), 114.8 (C-3), 112.0 (C-6), 111.8 (C-7), 101.0 (C-4), 55.9 (OCH$_3$), 49.2 (N-CH), 20.7 (N-CH-C$\underline{H}_3$). HRESIMS theory [M+H]$^+$: 279.2374; observed: 279.2390.

*5-Methoxy-N,N-diisobutyl-[α,α,β,β-d$_4$]-tryptamine (**10**)*

Yield: 119 mg (0.39 mmol, 78%). ^{1}H-NMR: 7.79 (NH-1, br s), 7.23 (1H, d, H-7, *J* 8.7 Hz,), 7.03 (1H, d, H-4, *J* 2.4 Hz), 6.97 (1H, d, H-2, *J* 2.4 Hz), 6.84 (1H, dd, H-6, *J* 8.8, 2.4 Hz), 3.87 (3H, s, OCH$_3$), 2.20 (4H, d, N-CH$_2$, *J* 7.3 Hz), 1.73 (2H, non, N-CH$_2$-C$\underline{H}$, *J* 6.8 Hz), 0.90 (12H, d, N-CH$_2$-CH-C$\underline{H}_3$, *J* 6.6 Hz). ^{13}C-NMR: 153.8 (C-5), 131.4 (C-7a), 128.1 (C-3a), 122.2 (C-2), 114.7 (C-3), 112.0 (C-6), 111.8 (C-7), 101.0 (C-4), 63.9 (N-CH$_2$), 56.0 (OCH$_3$), 26.9 (N-CH$_2$-C$\underline{H}$), 20.1 (N-CH$_2$-CH-C$\underline{H}_3$). HRESIMS theory [M+H]$^+$: 307.2687; observed: 307.2673.

*5-Methoxy-N,N-diallyl-[α,α,β,β-d$_4$]-tryptamine (**11**)*

Yield: 95 mg (0.34 mmol, 68%). ^{1}H-NMR: 7.87 (NH-1, br s), 7.24 (1H, d, H-7, *J* 8.8 Hz,), 7.02 (1H, d, H-4, *J* 2.4 Hz), 6.97 (1H, d, H-2, *J* 2.4 Hz), 6.84 (1H, dd, H-6, *J* 8.7, 2.3 Hz), 5.93 (2H, ddt, $^3J_{trans}$ 17.1 Hz, $^3J_{cis}$ 10.2 Hz, ^3J 6.6 Hz, C$\underline{H}$=CH$_2$), 5.23 (2H, ddd, $^3J_{trans}$ 17.1 Hz, ^2J 3.3 Hz, ^4J 1.5 Hz, CH=C$\underline{H}_{cis}$), 5.16 (2H, ddt, $^3J_{cis}$ 10.2 Hz, ^2J 2.2 Hz, ^4J 1.1 Hz, CH=C$\underline{H}_{trans}$), 3.85 (3H, s, OCH$_3$), 3.23 (4H, dt, ^3J 6.6 Hz, ^4J 1.2 Hz, N-C$\underline{H}_2$). ^{13}C-NMR: 153.9 (C-5), 135.9 (N-CH$_2$-C$\underline{H}$), 131.4 (C-7a), 127.9 (C-3a), 122.3 (C-2), 117.4 (CH=C$\underline{H}_2$), 114.3 (C-3), 112.1 (C-6), 111.8 (C-7), 100.8 (C-4), 56.9 (N-CH$_2$), 55.9 (OCH$_3$). HRESIMS theory [M+H]$^+$: 275.2061; observed: 275.2050.

*N,N-Dimethyl-[α,α,β,β-d$_4$]-tryptamine (**12**)*

Yield: 77 mg (0.40 mmol, 80%). ^{1}H-NMR: 8.13 (NH-1, br s), 7.60 (1H, d, H-4, *J* 7.7 Hz,), 7.34 (1H, d, H-7, *J* 7.5 Hz), 7.18 (1H, td, H-6, *J* 7.5, 1.3 Hz), 7.10 (1H, td, H-5, *J* 7.3, 1.2 Hz), 7.00 (1H, d, H-2, *J* 2.4 Hz), 2.19 (6H, s, N-CH$_3$). ^{13}C-NMR: 136.5 (C-7a), 127.5 (C-3a), 121.8 (C-6 and C-2), 119.0 (C-5), 118.8 (C-4), 113.9 (C-3), 111.3 (C-7), 45.3 (N-CH$_3$). HRESIMS theory [M+H]$^+$: 193.1643; observed: 193.1655.

*N-Methyl-N-ethyl-[α,α,β,β-d$_4$]-tryptamine (**13**)*

Yield: 80 mg (0.39 mmol, 78%). ^{1}H-NMR: 8.08 (NH-1, br s), 7.61 (1H, d, H-4, *J* 7.7 Hz,), 7.34 (1H, dt, H-7, *J* 7.9, 1.1 Hz), 7.18 (1H, td, H-6, *J* 7.5, 1.1 Hz), 7.11 (1H, td, H-5, *J* 7.7, 1.1 Hz), 7.01 (1H, d, H-2, *J* 2.4 Hz), 2.57 (2H, q, N-CH$_2$, *J* 7.2 Hz), 2.38 (3H, s, N-CH$_3$), 1.13 (3H, t, N-CH$_2$-C$\underline{H}_3$, *J* 7.2 Hz). ^{13}C-NMR: 136.3 (C-7a), 127.6 (C-3a), 121.8 (C-6 and C-2), 119.1 (C-5), 118.8 (C-4), 114.4 (C-3), 111.3 (C-7), 51.3 (N-CH$_2$), 37.2 (N-CH$_3$), 12.3 (N-CH$_2$-C$\underline{H}_3$). HRESIMS theory [M+H]$^+$: 207.1799; observed: 207.1808.

*N-Methyl-N-n-propyl-[α,α,β,β-d$_4$]-tryptamine (**14**)*

Yield: 82 mg (0.37 mmol, 74%). ^{1}H-NMR: 8.06 (NH-1, br s), 7.60 (1H, d, H-4, *J* 7.7 Hz,), 7.34 (1H, d, H-7, *J* 7.7 Hz), 7.18 (1H, td, H-6, *J* 7.9, 1.3 Hz), 7.11 (1H, td, H-5, *J* 7.7, 1.3 Hz), 7.01 (1H, d, H-2, *J* 2.4 Hz), 2.45 (2H, m, N-CH$_2$), 2.38 (3H, s, N-CH$_3$), 1.56 (2H, m, N-CH$_2$-C$\underline{H}_2$), 0.92 (3H, t, N-CH$_2$-CH$_2$-C$\underline{H}_3$, *J* 7.3 Hz). ^{13}C-NMR: 136.3 (C-7a), 127.5 (C-3a), 122.0 (C-6), 121.5 (C-2), 119.2 (C-5), 118.8 (C-4), 114.3 (C-3), 111.1 (C-7), 59.7 (N-C$\underline{H}_2$-CH$_2$), 42.1 (N-CH$_3$), 20.3 (N-CH$_2$-C$\underline{H}_2$), 12.0 (N-CH$_2$-CH$_2$-C$\underline{H}_3$). HRESIMS theory [M+H]$^+$: 221.1956; observed: 221.1944.

*N-Methyl-N-isopropyl-[α,α,β,β-d$_4$]-tryptamine (**15**)*

Yield: 82 mg (0.37 mmol, 74%). ^{1}H-NMR: 8.04 (NH-1, br s), 7.61 (1H, d, H-4, *J* 7.7 Hz,), 7.35 (1H, d, H-7, *J* 8.1 Hz), 7.19 (1H, td, H-6, *J* 8.0, 1.1 Hz), 7.12 (1H, td, H-5, *J* 7.5, 1.1 Hz), 7.03 (1H, d, H-2, *J* 2.4 Hz), 2.98 (1H, sept, N-CH, *J* 6.6 Hz), 2.38 (3H, s, N-CH$_3$), 1.07 (6H, d, N-CH-C$\underline{H}_3$, *J* 6.6 Hz). ^{13}C-NMR: 136.3 (C-7a), 127.6 (C-3a), 121.8 (C-6), 121.6 (C-2), 119.1 (C-5), 118.8 (C-4), 114.4 (C-3), 111.3 (C-7), 53.5 (N-CH), 37.2 (N-CH$_3$), 18.1 (N-CH-C$\underline{H}_3$). HRESIMS theory [M+H]$^+$: 221.1956; observed: 221.1967.

*N,N-Diethyl-[α,α,β,β-d$_4$]-tryptamine (**16**)*

Yield: 85 mg (0.39 mmol, 78%). ^{1}H-NMR: 8.11 (NH-1, br s), 7.61 (1H, d, H-4, *J* 7.7 Hz,), 7.34 (1H, d, H-7, *J* 7.9 Hz), 7.18 (1H, td, H-6, *J* 7.0, 1.3 Hz), 7.11 (1H, td, H-5, *J* 7.0, 1.3 Hz), 7.00 (1H, d, H-2, *J* 2.3 Hz), 2.68 (4H, q, N-CH$_2$, *J* 7.2 Hz), 1.11 (6H, t, N-CH$_2$-C$\underline{H}_3$, *J* 7.2 Hz). ^{13}C-NMR: 136.3 (C-7a), 127.6 (C-3a), 121.9 (C-6), 121.4 (C-2), 119.2 (C-5), 118.8 (C-4), 114.5 (C-3), 111.1 (C-7), 46.9 (N-CH$_2$), 11.8 (N-CH$_2$-C$\underline{H}_3$). HRESIMS theory [M+H]$^+$: 221.1956; observed: 221.1966.

*N-Ethyl-N-n-propyl-[α,α,β,β-d$_4$]-tryptamine (**17**)*

Yield: 91 mg (0.39 mmol, 78%). ^{1}H-NMR: 8.04 (NH-1, br s), 7.60 (1H, d, H-4, *J* 7.7 Hz,), 7.35 (1H, d, H-7, *J* 8.1 Hz), 7.18 (1H, td, H-6, *J* 7.5, 1.3 Hz), 7.11 (1H, td, H-5, *J* 7.3, 1.1 Hz), 7.01 (1H, d, H-2, *J* 2.4

Hz), 2.69 (2H, q, N-CH$_2$-CH$_3$, *J* 7.2 Hz), 2.55 (2H, m, N-CH$_2$-CH$_2$), 1.56 (2H, m, N-CH$_2$-CH$_2$), 1.11 (3H, t, N-CH$_2$-CH$_3$, *J* 7.2 Hz), 0.92 (3H, t, N-CH$_2$-CH$_2$-CH$_3$, *J* 7.3 Hz). ^{13}C-NMR: 136.3 (C-7a), 127.6 (C-3a), 121.8 (C-6), 121.5 (C-2), 119.1 (C-5), 118.8 (C-4), 114.4 (C-3), 111.2 (C-7), 55.6 (N-CH$_2$-CH$_2$), 47.5 (N-CH$_2$-CH$_3$), 20.2 (N-CH$_2$-CH$_2$), 12.2 (N-CH$_2$-CH$_2$-CH$_3$), 12.1 (N-CH$_2$-CH$_3$). HRESIMS theory $[M+H]^+$: 235.2112; observed: 235.2125.

*N-Ethyl-N-isopropyl-[α,α,β,β-d$_4$]-tryptamine (**18**)*

Yield: 89 mg (0.38 mmol, 76%). ^{1}H-NMR: 8.01 (NH-1, br s), 7.61 (1H, d, H-4, *J* 7.9 Hz,), 7.35 (1H, dt, H-7, *J* 8.1, 1.1 Hz), 7.17 (1H, td, H-6, *J* 7.5, 1.1 Hz), 7.11 (1H, td, H-5, *J* 7.7, 1.2 Hz), 7.03 (1H, d, H-2, *J* 2.2 Hz), 3.10 (1H, sept, N-CH, *J* 6.6 Hz), 2.65 (2H, quart, N-CH$_2$, *J* 7.2 Hz), 1.14 (3H, t, N-CH$_2$-CH$_3$, *J* 7.2 Hz), 1.07 (6H, d, N-CH-CH$_3$, *J* 6.6 Hz). ^{13}C-NMR: 136.3 (C-7a), 127.6 (C-3a), 121.8 (C-6), 121.5 (C-2), 119.1 (C-5), 118.9 (C-4), 114.7 (C-3), 111.1 (C-7), 50.5 (N-CH), 44.2 (N-CH$_2$), 18.6 (N-CH-CH$_3$), 14.0 (N-CH$_2$-CH$_3$). HRESIMS theory $[M+H]^+$: 235.2112; observed: 235.2101.

*N,N-Di-n-propyl-[α,α,β,β-d$_4$]-tryptamine (**19**)*

Yield: 98 mg (0.39 mmol, 78%). ^{1}H-NMR: 8.05 (NH-1, br s), 7.60 (1H, d, H-4, *J* 7.9 Hz,), 7.34 (1H, d, H-7, *J* 8.0 Hz), 7.18 (1H, td, H-6, *J* 8.0, 1.3 Hz), 7.11 (1H, td, H-5, *J* 7.5, 1.1 Hz), 7.00 (1H, d, H-2, *J* 2.3 Hz), 2.53 (4H, m, N-CH$_2$), 1.54 (4H, m, N-CH$_2$-CH$_2$), 0.91 (6H, t, CH$_3$, *J* 7.3 Hz). ^{13}C-NMR: 136.3 (C-7a), 127.6 (C-3a), 121.9 (C-6), 121.4 (C-2), 119.2 (C-5), 118.8 (C-4), 114.6 (C-3), 111.1 (C-7), 56.2 (N-CH$_2$), 20.3 (N-CH$_2$-CH$_2$), 12.2 (CH$_3$). HRESIMS theory $[M+H]^+$: 249.2269; observed: 249.2280.

*N,N-Diisopropyl-[α,α,β,β-d$_4$]-tryptamine (**20**)*

Yield: 99 mg (0.40 mmol, 80%). ^{1}H-NMR: 7.97 (NH-1, br s), 7.61 (1H, d, H-4, *J* 8.1 Hz,), 7.35 (1H, d, H-7, *J* 8.1 Hz), 7.18 (1H, td, H-6, *J* 7.5, 1.1 Hz), 7.11 (1H, td, H-5, *J* 7.5, 1.1 Hz), 7.02 (1H, d, H-2, *J* 2.3 Hz), 3.13 (2H, sept, N-CH, *J* 6.6 Hz), 1.10 (12H, d, N-CH-CH$_3$, *J* 6.6 Hz). ^{13}C-NMR: 136.3 (C-7a), 127.8 (C-3a), 121.9 (C-6), 121.4 (C-2), 119.2 (C-5), 119.1 (C-4), 115.1 (C-3), 111.2 (C-7), 49.2 (N-CH), 20.9 (N-CH-CH$_3$). HRESIMS theory $[M+H]^+$: 249.2269; observed: 249.2283.

*N,N-Diisobutyl-[α,α,β,β-d$_4$]-tryptamine (**21**)*

Yield: 104 mg (0.38 mmol, 76%). ^{1}H-NMR: 7.90 (NH-1, br s), 7.59 (1H, d, H-4, *J* 7.7 Hz,), 7.34 (1H, d, H-7, *J* 7.9 Hz), 7.18 (1H, td, H-6, *J* 8.0, 1.1 Hz), 7.11 (1H, td, H-5, *J* 7.7, 1.1 Hz), 7.00 (1H, d, H-2, *J* 2.3 Hz), 2.20 (4H, d, N-CH$_2$, *J* 7.3 Hz), 1.73 (2H, non, N-CH$_2$-CH, *J* 6.8 Hz), 0.90 (12H, d, N-CH$_2$-CH-CH$_3$, *J* 6.6 Hz). ^{13}C-NMR: 136.2 (C-7a), 127.6 (C-3a), 121.8 (C-6), 121.4 (C-2), 119.0 (C-5), 118.8 (C-4), 114.9 (C-3), 111.0 (C-7), 63.8 (N-CH$_2$), 26.8 (N-CH$_2$-CH), 21.0 (N-CH$_2$-CH-CH$_3$). HRESIMS theory $[M+H]^+$: 277.2582; observed: 277.2592.

*N,N-Diallyl-[α,α,β,β-d$_4$]-tryptamine (**22**)*

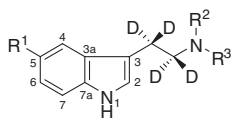
Yield: 85 mg (0.35 mmol, 70%). ^{1}H-NMR: 7.96 (NH-1, br s), 7.59 (1H, d, H-4, *J* 7.7 Hz,), 7.33 (1H, d, H-7, *J* 7.9 Hz), 7.18 (1H, td, H-6, *J* 8.1, 1.1 Hz), 7.10 (1H, td, H-5, *J* 8.1, 1.1 Hz), 6.99 (1H, d, H-2, *J* 2.3 Hz), 5.93 (2H, ddt, $^3J_{trans}$ 17.1 Hz, $^3J_{cis}$ 10.2 Hz, ^3J 6.6 Hz, CH=CH$_2$), 5.23 (2H, ddd, $^3J_{trans}$ 17.1 Hz, ^2J 3.3 Hz, ^4J 1.5 Hz, CH=CH$_{cis}$), 5.16 (2H, ddt, $^3J_{cis}$ 10.2 Hz, ^2J 2.2 Hz, ^4J 1.1 Hz, CH=CH$_{trans}$), 3.23 (4H, dt, ^3J 6.6 Hz, ^4J 1.2 Hz, N-CH$_2$). ^{13}C-NMR: 136.3 (C-7a), 135.8 (N-CH$_2$-CH), 127.6 (C-3a), 121.9 (C-6), 121.4 (C-2), 119.2 (C-5), 118.9 (C-4), 117.4 (CH=CH$_2$), 114.6 (C-3), 111.1 (C-7), 56.9 (N-CH$_2$). HRESIMS theory $[M+H]^+$: 245.1956; observed: 245.1969.

Results and discussion

The reduction of indol-3-yl-glyoxalylamides with lithium aluminium deuteride (LAD) provides a convenient method for the preparation of α,α,β,β-d$_4$ *N,N*-dialkylated tryptamines. This is typically carried out by heating at reflux in an anhydrous aprotic solvent (e.g. THF) for 2–16 hours.[12,24–29] There have also been examples where diethyl ether has been employed but the low boiling point of this solvent can result in significantly prolonged reaction times and incomplete reduction.[34] In cases where deuteration on the indole nucleus was desired, platinum-catalysed exchange reactions have been employed for the preparation of d$_5$-DMT and d$_5$-bufotenin. These included a 24 h reflux with deuterated acids. [17,19,35] Two examples have recently been reported for the synthesis of *N,N*-d$_{10}$-DET and *N,N*-d$_6$-DPT *via* tryptamine alkylation with d$_5$-iodoethane and 1,1,1-d$_3$-3-bromopropane, respectively. In both cases the reaction mixture was stirred for 5 days.[28]

In an attempt to apply a rapid method for the glyoxalylamide reduction a microwave-based procedure was developed. Previous work in this laboratory indicated that under the microwave-accelerated conditions used, reaction times above 20 min did not appear to increase yields. Correspondingly, this method was applied to the synthesis of α,α,β,β-d$_4$-DMT

Table 1. Structures of synthesised tryptamines 1–22, and commonly used abbreviations.



No.	R1	R2	R3	Name
1	MeO	Me	Me	5-MeO-d$_4$-DMT
2	MeO	Me	Et	5-MeO-d$_4$-MET
3	MeO	Me	Pr	5-MeO-d$_4$-MPT
4	MeO	Me	iPr	5-MeO-d$_4$-MIPT
5	MeO	Et	Et	5-MeO-d$_4$-DET
6	MeO	Et	Pr	5-MeO-d$_4$-EPT
7	MeO	Et	iPr	5-MeO-d$_4$-EIPT
8	MeO	Pr	Pr	5-MeO-d$_4$-DPT
9	MeO	iPr	iPr	5-MeO-d$_4$-DIPT
10	MeO	iBu	iBu	5-MeO-d$_4$-DIBT
11	MeO	allyl	allyl	5-MeO-d$_4$-DALT
12	H	Me	Me	d$_4$-DMT
13	H	Me	Et	d$_4$-MET
14	H	Me	Pr	d$_4$-MPT
15	H	Me	iPr	d$_4$-MIPT
16	H	Et	Et	d$_4$-DET
17	H	Et	Pr	d$_4$-EPT
18	H	Et	iPr	d$_4$-EIPT
19	H	Pr	Pr	d$_4$-DPT
20	H	iPr	iPr	d$_4$-DIPT
21	H	iBu	iBu	d$_4$-DIBT
22	H	allyl	allyl	d$_4$-DALT

Table 2. Isotopic purities of synthesised tryptamines 1–22.

No.	D0 (%)	D1 (%)	D2 (%)	D3 (%)	D4 (%)
1	0.35	0.60	2.89	2.34	93.83
2	0.25	0.76	0.45	1.72	96.82
3	0.39	0.26	0.52	1.92	96.92
4	0.03	0.03	1.35	1.77	97.52
5	0.21	0.54	0.43	1.82	97.01
6	1.25	0.59	0.87	1.77	95.52
7	0.86	0.49	0.60	1.63	96.43
8	0.46	0.26	0.49	1.94	96.85
9	2.13	0.77	1.23	1.55	94.30
10	0.31	0.30	0.77	1.79	96.83
11	0.54	0.20	0.34	0.56	98.35
12	0.21	2.74	0.92	1.57	94.56
13	0.15	1.40	0.50	1.65	96.35
14	1.95	0.82	0.41	1.68	95.15
15	0.93	0.44	2.77	1.09	94.78
16	0.99	0.77	0.92	1.66	95.68
17	0.18	0.34	0.21	0.25	97.23
18	0.36	0.23	0.29	1.78	97.33
19	1.75	0.53	0.60	1.59	95.53
20	0.75	0.31	0.24	1.55	97.15
21	0.41	0.44	1.39	1.64	96.11
22	1.22	1.04	0.92	1.51	95.31

(Table 1).[36] When this was compared with shortened reaction times of 5, 10, and 15 min, it was interesting to observe that comparable yields and product purities were obtained (HPLC analysis, data not shown). These findings led to the application of a 5 min reduction to the preparation of 22 *N*,*N*-dialkylated $\alpha,\alpha,\beta,\beta$-$d_4$-tryptamines (Table 1) with good yields.

Isotopic purities were determined by direct infusion LC-MS analysis and are summarised in Table 2. Ideally, when using deuterated internal standards, the D_0 contribution would be observed to be as close to zero as possible and for compounds 6, 9, 14, 19 and 22 however, the D_0 value was observed to be $>1\%$. The reasons for this are currently unknown.

Reactions were carried out using a single-mode microwave in combination with 10 mL pressurised vessels. This approach allows for the generation of a homogeneous field with high power densities and increased reproducibility.[37] The use of pressurised vessels and self-sealing septa enabled the reactions to be run at elevated temperatures above the boiling point of THF ($\sim$66°C). A reaction temperature of 150°C was ultimately chosen after evaluation of several temperatures ranging from 120 to 180°C and purity analysis by HPLC (data not shown). Microwave treatment causes rapid heating (within seconds), particularly if solvents are used which easily absorb microwaves. In comparison with solvents such as ethanol or ethylene glycol, THF is known to show relatively poor dielectric properties which can hamper the conversion of electromagnetic energy into heat.[30] Under the conditions used, the target temperature of 150°C was reached within 30 seconds. The use of pressurised vessels allowed for the reduction to be run at significantly elevated temperatures in order to accelerate reaction times. LAD is a powerful reducing agent that required careful handling. It was necessary to leave sufficient headspace when only 3 mL of THF was used in order to avoid vessel failure due to excessive pressure formation above 300 psi. Accordingly, the scale was restricted to 0.05 mmol starting material in order to minimise the amounts of LAD employed. Since the microwave system used in this study was equipped with a 24 vessel autosampler, scale-up considerations were not significantly hampered.

Conclusion

Application of a microwave-accelerated procedure to the reduction of glyoxalylamides with lithium aluminium deuteride was suitable for the preparation of deuterated psychoactive tryptamines. The advantage of a pressurised vessel microwave system was that the reaction only required 5 min, whereas traditional heating under reflux conditions take 2–16 h for the same reduction. This procedure gave good yields and a rapid approach for the production of deuterated tryptamines that can be used for future forensic, pharmacologic and pharmacokinetic studies.

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