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Synthesis of [^{11}C]/(^{13}C)amines *via* carbonylation followed by reductive amination

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Twelve ^{11}C-labelled amines were prepared *via* ^{11}C-carbonylation followed by reductive amination. The ^{11}C-carbonylation was performed in the presence of tetrakis(triphenylphosphine)palladium using aryl iodides or aryl triflates, [^{11}C]carbon monoxide and phenyl-/methylboronic acid. The [^{11}C]ketones formed in this step were then transformed directly into amines by reductive amination using different amines in the presence of $TiCl_4$ and $NaBH_3CN$. The ^{11}C-labelled amines were obtained with decay-corrected radiochemical yields in the range 2–78%. The radiochemical purity of the isolated products exceeded 98%. (^{13}C)Benzhydryl-phenyl-amine was synthesised and analysed by NMR spectroscopy for confirmation of the labelling position. Specific radioactivity was determined for the same compound. The reference compounds were prepared by reductive amination of ketones using conventional reaction conditions and three of the compounds were novel. The presented approach is a new method for the synthesis of [^{11}C]/(^{13}C)amines.

Introduction

The non-invasive imaging technique, positron emission tomography (PET) has become the tool of choice for many diagnostic medical applications. Moreover, it has recently been indicated that PET could be a potential tool in drug development.[1] The demand for new methods for the labelling of biologically interesting compounds with short-lived positron emitting radionuclides is increasing with the expanding use of PET in biomedical research. The most commonly used radionuclides for PET studies are ^{18}F, ^{11}C, ^{76}Br, ^{68}Ga and ^{15}O. Among these, ^{11}C is particularly interesting since most biologically important compounds are organic molecules and ^{11}C can be introduced into these molecules by substitution of a carbon atom. Moreover its half-life ($t_{½}$ = 20 min) allows both repeated PET studies in the same object within a relatively short time frame, and multi-step tracer syntheses. Another important consequence of the short half-life and the production methods of ^{11}C, is that high levels of specific radioactivity can be achieved.

The methods so far most commonly used for the synthesis of ^{11}C-labelled compounds are *S*-, *O*- and *N*-methylations using [^{11}C]methyl iodide or [^{11}C]methyl triflate.[2] Other methods like the Grignard reaction using [^{11}C]carbon dioxide[3] or C–C coupling reactions using [^{11}C]methyl iodide and organometallic reagents[4] are also used but less frequently. Carbonylation using [^{11}C]carbon monoxide has recently become an increasingly employed ^{11}C-labelling strategy and methods have been developed for the synthesis of a wide range of ^{11}C-labelled carbonyl compounds such as ketones,[5] amides,[6] imides,[7] hydrazides,[8] *etc*. Recently, the synthesis of ^{11}C-labelled ketones by the Suzuki coupling reaction was reported.[9] The successful synthesis of [^{11}C]ketones stimulated us to investigate the possibility of converting the [^{11}C]ketones to [^{11}C]amines since the amine group is a key functional group in many pharmaceutical agents. Reductive amination of carboxylic acids and [^{11}C]magnesium halide carboxylates was applied several years ago for the preparation of [^{11}C]amines[3b] and recently [^{11}C]acetone was used in a reductive amination with 1-phenylpiperazine.[10] In this work, we have explored the scope and limitations of transformations of various [^{11}C]ketones prepared by carbonylation using [^{11}C]carbon monoxide to different [^{11}C]amines.

Results and discussion

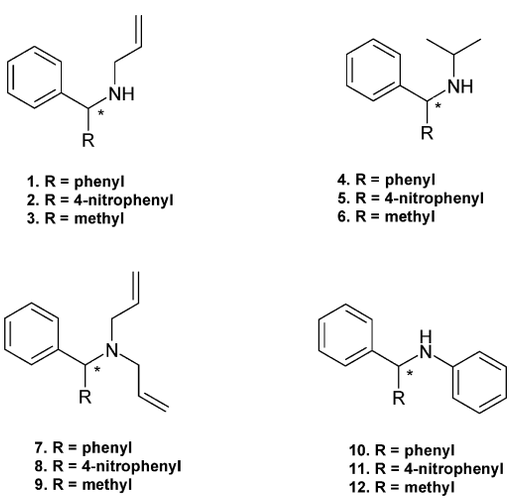
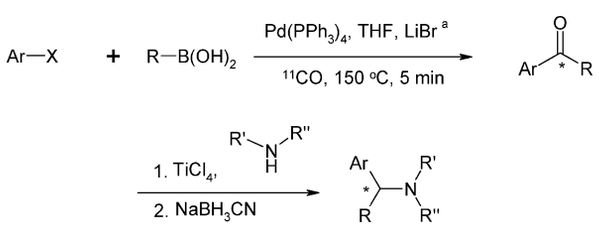


Fig. 1 Target molecules. * = ^{11}C.

The ^{11}C-labelled amines were synthesised by a route based on [^{11}C]carbonylation followed by reductive amination (Scheme 1). Carbonylation was performed in a micro autoclave of 200 μL volume using aryl iodide or triflate, tetrakis(triphenylphosphine)palladium(0), phenyl or methylboronic acids and a low concentration (typically *ca.* 10 to 100 μM) of [^{11}C]carbon monoxide. In this study a standardised procedure based on a 5 min carbonylation was used. However, this time may not be



Scheme 1 X = I, OTf, Ar = phenyl, 4-nitrophenyl; R = phenyl, methyl; R′ = allyl, isopropyl, methylene, phenyl; R″ = H, allyl. * = ^{11}C. a: used in the case where X = OTf.

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Table 1 Trapping efficiency and radiochemical yields for the ^{11}C-amines shown in Fig. 1

Entry	Amine	Ketone	Product	TE (%)[a]	RYC[b], %, (*n*)[c]	LC-MS [ESI+], *m*/*z* (M + 1)
1	**16**	**13**	**1**	94	66 (34)	224
2	**16**	**14**	**2**	57	35 (18)	269
3	**16**	**15**	**3**	90	44 (20)	162
4	**17**	**13**	**4**	93	53 (28)	226
5	**17**	**14**	**5**	55	37 (17)	271
6	**17**	**15**	**6**	92	45 (18)	164
7	**18**	**13**	**7**	95	5	—
8	**18**	**14**	**8**	54	2	—
9	**18**	**15**	**9**	92	39 (15)	202
10	**19**	**13**	**10**	96	78 (49)	260
11	**19**	**14**	**11**	57	36 (17)	305
12	**19**	**15**	**12**	95	49 (26)	198

[a] TE = Trapping Efficiency, decay-corrected, the fraction of radioactivity left in the crude product after purge with nitrogen. [b] RCY = radiochemical yield; decay-corrected and determined by analytical LC on the basis of radioactivity in the crude product before nitrogen purging and the purity of crude product. The value is the mean value of at least 3 experiments. [c] Values in parentheses are the isolated yields.

optimal for all cases. The [^{11}C]ketones obtained in this step were reductively aminated using $TiCl_4$, amines and $NaBH_3CN$. Three [^{11}C]ketones (Fig. 2) and four amines (Fig. 3) were selected in this investigation and all of the amines were reacted with all of the ketones. The [^{11}C]ketones were prepared by ^{11}C-carbonylation of aryl iodide or triflate and phenyl-/methyl-boronic acids. [^{11}C]4-Nitro-benzophenone was prepared from 4-nitro-phenyl triflate using the same reaction conditions described in our previous report,[9] but [^{11}C]benzophenone and [^{11}C]acetophenone were prepared from iodobenzene since iodobenzene gave higher radiochemical yields in these cases.

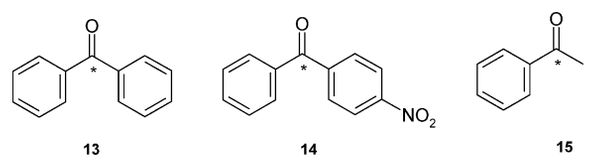


Fig. 2 Ketones used in the syntheses. * = ^{11}C.

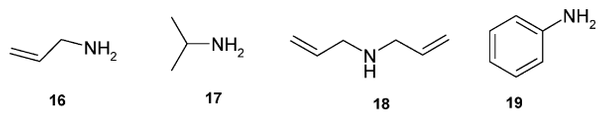


Fig. 3 Amines used in the syntheses.

The decay-corrected radiochemical yields (determined by analytical HPLC) of the [^{11}C]amines, calculated from [^{11}C]-carbon monoxide, were in the range of 2 to 78% (Table 1). The radiochemical yield was lowest (2%) (entry 8 in Table 1) when the secondary amine, diallylamine (**18**) was reacted with [^{11}C]4-nitro-benzophenone and a low radiochemical yield (5%) (entry 7 in Table 1) also was obtained when the same amine was reacted with [^{11}C]benzophenone. The reason for these low radiochemical yields may be steric hindrance, since the same amine gave a higher radiochemical yield (39%) (entry 9 in Table 1) when reacted with [^{11}C]acetophenone where steric hindrance is less. The steric factor is less important when a longer reaction time was used *e.g.* in the synthesis of reference compounds. The radiochemical yields for amines **2**, **5**, **8** and **11** (entries 2, 5, 8 and 11 respectively in Table 1) prepared from [^{11}C]4-nitro-benzophenone were lower as the formation of [^{11}C]4-nitro-benzophenone itself was low. In all cases the isolated radiochemical yields for [^{11}C]amines were lower (as low as 50%) than the analytical yields (Table 1) *i.e.* a substantial amount of product was lost during the isolation and purification. After the reductive amination, a precipitate was obtained and a lot of radioactivity was trapped in the precipitate and could not be removed. Further technological development is needed to improve the recovery of the radioactive product.

The radiochemical purity of the isolated product exceeded 98%. The identities of the labelled compounds were assessed using radio HPLC and LC-MS. Compounds **7** and **8** could not be analysed by LC-MS owing to the low concentrations. They were characterised by radio HPLC with co-injection of non-radioactive reference compounds and comparing the retention times for the UV and radioactivity peaks. Compound **10** was labelled in parallel with ^{11}C and ^{13}C, and the ^{13}C-labelled product was analysed by ^{13}C NMR for confirmation of the labelling position. The ^{13}C spectrum displayed only one peak at 63.19 ppm (Fig. 4) which corresponded to the –CH– carbon and matched with the same peak observed for the reference compound. The specific radioactivity was determined for compound **10** and the obtained value was 213 GBq μmol^{-1}, 50 min after a 10 μA bombardment. We expect that this procedure will increase the possibility of producing compounds with high specific radioactivity, although it was not the focus of this research.

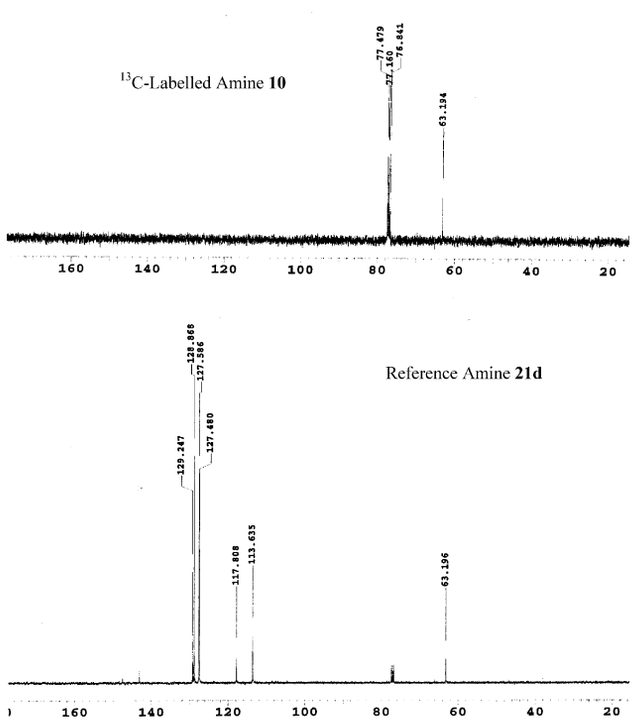


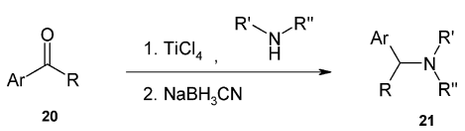
Fig. 4 ^{13}C NMR spectra of ^{13}C-labelled and reference benzhydryl-phenyl-amine.

Reductive aminations of aldehydes and ketones are frequently used methods for the synthesis of amines.[11] The reducing agents used for this purpose are hydride donors, usually sodium cyanoborohydride ($NaBH_3CN$).[12] Reductive aminations of hindered or biaryl ketones were performed using $NaBH_3CN$ together with titanium(IV) chloride[13] or

titanium(IV) isopropoxide.[14] Although these methods required several hours of reaction time (which is not appropriate in a synthesis with the short half-lived ^{11}C), we could successfully use $NaBH_3CN$ in combination with $TiCl_4$ and complete the reaction within 6 min using our reaction conditions. In a conventional synthesis, the reductive amination of ketones using $TiCl_4$ and $NaBH_3CN$ required 2 mol equivalent of amines. But in the labelling synthesis, a large excess of cold reagents is used in order to avoid side reactions and most importantly to obtain a reasonable reaction rate. If equimolar amounts (compared with the labelled ketones) were used, the reaction rate would be *ca.* 10^{-4} times lower. Therefore the optimal concentration of amines required was determined experimentally. The optimisation was performed for compound **10** and the optimal concentration of amine (97.5 mM) was then used for other compounds.

After carbonylation, the product was collected in a 5 mL vial and reductive amination was performed directly in that vial. The reagents were added in two steps. Amine and $TiCl_4$ were added first and the mixture was allowed to stand for 3 min at 60 °C, then the second reagent, $NaBH_3CN$, was added and the same temperature maintained for another 3 min. In most cases the reductive amination was completed after 6 min (checked by radio HPLC). When allylamine, isopropylamine or aniline were used the ^{11}C-ketones were consumed completely. But when diallylamine was reacted with ketones **13** and **14**, about 50% of the ^{11}C-ketones remained unreacted in the standardised experiment.

All reference compounds except *N*-allyl-α-methylbenzylamine were prepared with good to excellent yields by reductive amination of different ketones with different amines in the presence of $TiCl_4$ and $NaBH_3CN$ (Scheme 2) under the conventional reaction conditions.[12] Three of these compounds, **21e**, **21f** and **21g** were new. Both ^1H and ^{13}C NMR data for the known compounds **21a**,[15] **21c**,[15] **21d**[16] and **21k**[17] are available in the literature and our data were compared with these for the identification. NMR data for the other compounds and MS data for all of the prepared reference amines are presented in this report.



Scheme 2 Ar = R = Ph, R′ = allyl, R″ = H (**21a**), Ar = R = Ph, R′ = isopropyl, R″ = H (**21b**), Ar = R = Ph, R′ = R″ = allyl (**21c**), Ar = R = Ph, R′ = phenyl, R″ = H (**21d**), Ar = Ph, R = 4-nitro-phenyl, R′ = allyl, R″ = H (**21e**), Ar = Ph, R = 4-nitro-phenyl, R′ = isopropyl, R″ = H (**21f**), Ar = Ph, R = 4-nitro-phenyl, R′ = R″ = allyl (**21g**), Ar = Ph, R = 4-nitro-phenyl, R′ = phenyl, R″ = H (**21h**), Ar = Ph, R = methyl, R′ = isopropyl, R″ = H (**21i**), Ar = Ph, R = methyl, R′ = R″ = allyl (**21j**), Ar = Ph, R = methyl, R′ = phenyl, R″ = H (**21k**),

Experimental

General

The reference compound, *N*-allyl-α-methylbenzylamine and all of the reagents except tetrakis(triphenylphosphine)palladium and boronic acids, were obtained from Aldrich. Tetrakis-(triphenylphosphine)palladium and phenyl-and methylboronic acids were obtained from Lancaster. Freshly distilled THF (distilled from sodium/benzophenone under nitrogen) was used in the labelling reactions.

[^{11}C]Carbon dioxide was produced by the Scanditronix MC-17 cyclotron at Uppsala Imanet AB using the $^{14}N(p,\alpha)^{11}C$ reaction with 17 MeV protons in a gas target containing nitrogen (AGA, Nitrogen 6.0) and 0.1% oxygen (AGA. Oxygen 4.8). [^{11}C]Carbon monoxide was produced by reducing [^{11}C]carbon dioxide in a zinc furnace at 400 °C using a remote controlled work station.[18]

Liquid chromatographic analysis (LC) was performed with a Beckman 126 gradient pump and a Beckman 166 variable wavelength UV-detector in series with a β^+-flow detector. The following mobile phases were used: triethylamine (0.1% in H_2O), pH 9 (A1) and acetonitrile (B1), 0.01 M formic acid in H_2O (A2) and methanol (B2). The identity and radiochemical purity of the labelled products were assessed by analytical LC: solvent A1–B1 (70 : 30); linear gradient to 0 : 100 in 10 min, flow 1.5 mL min^{-1}, wavelength 254 nm. A Jones Chromatography Genesis C_{18}, 5 µm, 250 × 4.6 mm (i.d.) column was used for this analysis. For semi-preparative LC, a Beckman Ultrasphere ODS C_{18}, 5 µm, 250 × 10 mm (i.d.), column was used with a flow of 4 mL min^{-1}. The mobile phases used were A1–B1(70 : 30); linear gradient to 0 : 100 in 10 min.

Synthia, an automated synthesis system, was used for LC injection and fraction collection.[19] The Beckman System Gold chromatography software package was used for data collection and LC control. Radioactivity was measured in an ion chamber, Veenstra Instrumenten bv, VDC-202. For coarse estimations of radioactivity during production, a portable dose-rate meter was used, Långenäs eltekniska AB. The non-radioactive compounds were characterised by ^1H and ^{13}C NMR and GC-MS. NMR spectra were recorded on a Varian Unity-400 NMR instrument. [D_1]Chloroform was used as the internal standard. LC-MS was performed using a Micromass VG Quattro with electrospray ionisation (ESI+). A Beckman 126 pump, a CMA 240 autosampler and a Jones Chromatography Genesis C_{18} (5 µm, 250 × 4.6 mm id) column were used. Mobile phases were A2 and B2. GC-MS was performed with a Finnigan GCQ mass spectrometer coupled to a Finnigan Q-GC.

Synthesis of ^{11}C-amines (1–12)

The ^{11}C-Carbonylation was performed as described previously[9] using tetrakis(triphenylphosphine)palladium(0) (5.0 mg, 4.3 µmol), aryl iodide/triflate (30.8 µmol) and phenyl- or methylboronic acid (49.2 µmol). The crude product was transferred to a pre-evacuated, septum-fitted vial (5 mL) and the radioactivity was measured. The vial was purged with nitrogen to remove the unreacted [^{11}C]carbon monoxide and the radioactivity was measured again to determine the trapping efficiency. Titanium tetrachloride (500 µL of 1 M solution in CH_2Cl_2, 0.5 mmol) and an amine (87.8 µmol) were added and the mixture was heated for 3 min at 60 °C. Sodium cyanoborohydride (500 µL of 1 M solution in MeOH, 0.5 mmol) was added and the mixture was heated for an additional 3 min at the same temperature. The reaction was quenched with slow addition of aqueous sodium hydroxide (500 µL of 2 M aqueous solution) and filtered. The crude product was analysed with HPLC together with a small amount of the reference compound for identification of the product. The non-isolated radiochemical yield was determined by multiplying the purity of the crude product by the trapping efficiency. The volume of the filtrate was reduced to 1 mL by heating at 60 °C and purging with nitrogen. Methanol (1 mL) and water (0.5 mL) were added and the resulting mixture was injected onto the semi-preparative LC. The collected fractions were analysed by analytical HPLC to determine the radiochemical purity and also analysed by LC-MS using electrospray ionisation (ESI+) for final characterisation of the product.

Synthesis of ^{13}C-benzhydryl-phenyl-amine

Tetrakis(triphenylphosphine)palladium(0) (6.0 mg, 10.6 µmol) and iodobenzene (10 µL, 18.2 mg, 89.3µmol) were placed in a vial (1 mL), flushed with nitrogen and dissolved in THF (200 µL). Phenylboronic acid (10 mg, 82.0 µmol) was dissolved in THF (200 µL) and added to the previous solution. The resulting mixture was loaded into the injection loop. The reagent mixture and (^{13}C)carbon monoxide were transferred under pressure (35 MPa) into the micro-autoclave (200 µL). The

micro-autoclave was heated (150 °C) for 10 min. The crude product was transferred to a pre-evacuated, septum-fitted vial (5 mL). Titanium tetrachloride (1 mL of 1 M solution in CH_2Cl_2, 1.0 mmol) and aniline (20 μL, 20.4 mg, 219 μmol) were added and the mixture was heated for 5 min at 60 °C. Sodium cyanoborohydride (1 mL of 1 M solution in MeOH, 1.0 mmol) was added and the mixture heated for an additional 5 min at the same temperature. The reaction mixture was quenched by slow addition of aqueous sodium hydroxide (1 mL of 2 M aqueous solution) and filtered. The volume of the filtrate was reduced to 1 mL by heating at 60 °C and purging with nitrogen. Methanol (1 mL), water (1 mL) and a sufficient amount of the previously synthesised corresponding ^{11}C-labelled compound were added. The product was purified by semi-preparative LC using the same chromatographic method as described for ^{11}C-labelled compound. The radioactive fraction was collected and evaporated under reduced pressure to yield the title compound. The residue was dissolved in $CDCl_3$ and analysed by NMR spectroscopy.

δ_C (100 MHz, $CDCl_3$): 63.19.

Preparation of reference compounds

General method. The procedure is exemplified by the preparation of allyl-benzhydryl-amine (**21a**). Benzophenone (1.0 g, 5.5 mmol) was dissolved in dry CH_2Cl_2 (30 mL) and $TiCl_4$ (6.0 mL of 1.0 M solution in CH_2Cl_2, 6.0 mmol) was added. The mixture was cooled to 0 °C and allylamine (0.9 mL. 0.68 g, 11.9 mmol) was added. The resulting mixture was stirred for 3 h at ambient temperature under argon. The reaction was quenched with a methanolic solution of $NaBH_3CN$ (10 mL of 6.5 M solution, 6.5 mmol) and stirred for an additional 1 h at the same temperature. The mixture was made basic (pH ~10) with 5 M aqueous solution of NaOH and filtered. The filtrate was partitioned between ethyl acetate (100 mL) and water (100 mL). The organic layer was separated, washed with water (2 × 100 mL) and brine (100 mL), dried over $MgSO_4$ and concentrated under reduced pressure. The crude product was dissolved in ether, acidified (pH ~2) with conc. HCl and extracted with water. The water extract was made basic (pH ~11) with aqueous ammonia (28%) and extracted with ether. The ether extract was dried over $MgSO_4$ and the solvent was removed under reduced pressure to give the title compound as a yellowish oil.

Compounds **21d**, **21h** and **21k** were purified by column chromatography using pentane/ether (90 : 10) as the eluent.

Allyl-benzhydryl-amine (21a). Yield 95%, yellow oil, (lit[20] bp 105–110 °C). GC-MS (EI): *m/z* = 223 ($M^{\bullet+}$, 4%), 180 (26%), 167 (51%), 146 (100%), 104 (28%), 91 (37%).

Benzhydryl-isopropyl-amine (21b). Yield 90%, colourless oil (lit[21] bp 181.5–182.0 °C). δ_H (400 MHz, $CDCl_3$): 7.5 (m, 4H), 7.3–7.4 (m, 4H), 7.3 (m, 1H), 5.1 (s, 1H), 2.8 (m, 1H), 1.5 (bs, 1H), 1.2 (m, 6H). δ_C (100 MHz, $CDCl_3$): 144.6, 128.4, 127.4, 126.8, 64.3, 46.1, 23.28. GC-MS (EI): *m/z* = 225 ($M^{\bullet+}$, 3%), 210 (21%), 167 (100%), 148 (23%), 106 (10%).

Diallyl-benzhydryl-amine (21c). Yield 62%, yellow oil. GC-MS (EI): *m/z* = 263 ($M^{\bullet+}$, 24%), 220 (36%), 186 (51%), 167 (100%), 152 (19%), 96 (13%).

Benzhydryl-phenyl-amine (21d). Yield 95%, colourless oil (lit[22] bp 160–180 °C). GC-MS (EI): *m/z* = 259 ($M^{\bullet+}$, 9%), 180 (4%), 167 (100%), 104 (3%), 77 (14%).

Allyl-[(4-nitro-phenyl)-phenyl-methyl]amine (21e). Yield 85%, yellow oil. δ_H (400 MHz, $CDCl_3$): 8.1 (d, 2H), 7.6 (d, 2H), 7.3 (m, 4H), 7.2 (m, 1H), 5.9 (m, 1H), 5.1–5.2 (m, 2H), 4.9 (s, 1H), 3.2 (d, 2H), 1.7 (bs, 1H). δ_C (100 MHz, $CDCl_3$): 151.6, 147.1, 142.7, 136.3, 128.9, 128.1, 127.7, 127.3, 123.8, 116.3, 66.0, 50.4. GC-MS (EI): *m/z* = 268 ($M^{\bullet+}$, 18%), 267 (85%), 251 (32%), 227 (22%), 191 (69%), 180 (68%), 165 (100%), 146 (60%), 91 (19%), 77 (16%).

Isopropyl-[(4-nitro-phenyl)-phenyl-methyl]-amine (21f). Yield 69%, yellow crystal, mp 78–79 °C. δ_H (400 MHz, $CDCl_3$): 8.1 (d, 2H), 7.6 (d, 2H), 7.3 (m, 4H), 7.2 (m, 1H), 5.0 (s, 1H), 2.7–2.8 (m, 1H), 1.4 (bs, 1H), 1.1 (m, 6H). δ_C (100 MHz, $CDCl_3$): 152.3, 146.9, 143.3, 128.8, 128.1, 127.5, 127.3, 123.7, 64.1, 46.5, 23.3, 23.1. GC-MS (EI): *m/z* = 270 ($M^{\bullet+}$, 5%), 255 (78%), 212 (100%), 193 (7%), 166 (43%), 153 (8%), 106 (5%).

Diallyl-[(4-nitro-phenyl)phenyl-methyl]-amine (21g). Yield 70%, yellow oil. δ_H (400 MHz, $CDCl_3$): 8.1 (d, 2H), 7.6 (d, 2H), 7.3 (m, 4H), 7.2 (m, 1H), 5.9 (m, 2H), 5.1–5.2 (m, 4H), 5.0 (s, 1H), 3.1–3.2 (m, 4H). δ_C (100 MHz, $CDCl_3$): 150.5, 146.8, 140.1, 134.9, 128.9, 128.7, 128.6, 127.6, 123.6, 117.8, 69.1, 52.5. GC-MS (EI): *m/z* = 308 ($M^{\bullet+}$, 15%), 267 (10%), 231 (39%), 212 (100%), 186 (39%), 166 (95%), 154 (19%), 96 (27%), 91 (10%).

[(4-Nitro-phenyl)-phenyl-methyl]-phenyl-amine (21h). Yield 75%, yellow crystal, mp 122 °C (lit.[23] mp 120–121 °C). δ_H (400 MHz, $CDCl_3$): 8.1 (d, 2H), 7.6 (d, 2H), 7.3–7.6 (m, 5H), 7.1–7.2 (m, 2H), 6.7 (m, 1H), 6.5 (m, 2H), 5.5 (s, 1H), 4.2 (bs, 1H). δ_C (100 MHz, $CDCl_3$): 150.3, 147.3, 146.7, 141.8, 129.3, 129.2, 128.3, 128.1, 127.7, 124.1, 118.5, 113.6, 62.9. GC-MS (EI): *m/z* = 304 ($M^{\bullet+}$, 42%), 212 (100%), 166 (44%), 77 (40%).

Isopropyl-(1-phenyl-ethyl)-amine (21i). Yield 83%, yellow oil (lit.[24] bp 176–177). δ_H (400 MHz, $CDCl_3$): 7.3 (m, 4H), 7.2 (m, 1H), 3.9 (q, 1H), 2.6 (m, 1H), 1.3 (d, 3H), 1.2 (bs, 1H), 1.0 (m, 6H). δ_C (100 MHz, $CDCl_3$): 146.2, 128.4, 126.7, 126.4, 55.1, 45.5, 24.9, 24.1, 22.3. GC-MS (EI): *m/z* = 163 ($M^{\bullet+}$, 25%), 148 (100%), 106 (44%), 77 (12%).

Diallyl-(1-phenyl-ethyl)-amine (21j). Yield 86%, brown oil (lit.[25] bp 103–104). δ_H (400 MHz, $CDCl_3$): 7.3 (m, 4H), 7.2 (m. 1H), 5.8 (m, 2H), 5.1–5.2 (m, 4H), 3.9 (q, 1H), 3.1 (m, 4H), 1.4 (d, 3H). δ_C (100 MHz, $CDCl_3$): 144.2, 136.7, 128.1, 127.7, 126.7, 116.7, 58.4, 52.7, 17.2. GC-MS (EI): *m/z* = 201 ($M^{\bullet+}$, 5%), 186 (100%), 105 (26%), 11 (10%).

Phenyl-(1-phenyl-ethyl)-amine (21k). Yield 91%, colourless oil (lit.[26] bp 132–134). GC-MS (EI): *m/z* = 197 ($M^{\bullet+}$, 10%), 182 (39%), 165 (37%), 106 (100%), 77 (22%).

Acknowledgements

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