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Arylation of Adamantanamines: IX.* Copper(I)-Catalyzed Arylation of Adamantane-Containing Amines

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Abstract—Copper(I)-catalyzed arylation of 14 adamantane-containing amines with iodobenzene, 1-fluoro-4-iodobenzene, 1-iodo-4-(trifluoromethyl)benzene, and 1-iodo-4-methoxybenzene has been studied under the conditions optimized previously. The yields of the N-arylation products have been shown to depend in a complicated manner on the amine structure, steric environment of the amino group, and substituent nature in iodobenzene.

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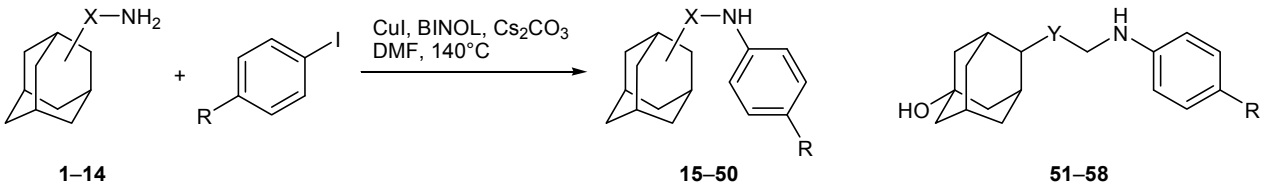
Over many years various adamantane derivatives occupy an important place among organic compounds interesting from the viewpoint of their biological activity [2, 3]. This is related to high lipophilicity of the adamantane fragment which facilitates penetration through cell membranes, lipophilic layer, and viral shells and thus enables adamantane-containing molecules to affect various biochemical processes. Amino, amide, hydroxy, and alkoxy groups capable of forming hydrogen bonds are introduced into active molecules to ensure their effective interaction with various proteins and receptors. Furthermore, the required conformational rigidity and appropriate geometry for effective binding can be achieved via introduction of various aromatic fragments. The spectrum of biological activity of such compounds is very broad. For example, dopamantine showed a high activity against *Plasmodium berghei* parasites that cause malaria [4]. Various 1-substituted adamantanes even at a nanomolar concentration are active against HSV-2 herpes viruses [5] and act as cholecystokinin A receptor agonists [6] and ligands for peroxisome proliferator-activated receptors (PPARs) [7] and ionotropic glutamate receptor (NMDA) [8]. Particular attention is given to fluorine-containing aryl-substituted adamantane derivatives. Biological activity of organofluorine compounds is well known; about 20% of organic pharmaceuticals and agrochemicals contain fluorine atoms. Among other compounds, fluoroaromatics attract interest [9]. Compounds containing adamantane and fluoroaryl fragments in a single molecule exhibit antitubercular [10] and anti-inflammatory activity [11] and inhibit topoisomerase II [12] and P2RX7 purinoceptor [13]. Adamantane derivatives possessing a trifluoromethylaryl substituent were also found to display various activities: they inhibit 11-β-hydroxysteroid dehydrogenase [14, 15] and melanin-concentrating hormone (MHC1) [16], as well as selectively bind to cannabinoid CB2 receptor [17]. Thus, the high biological potential of adamantane-containing arenes makes the synthesis of new compounds of this series an important problem.

While studying copper-catalyzed arylation and heteroarylation of amines and polyamines, we found that thorough selection of a catalytic system for each reactant pair is very important [18–20]. In particular, in

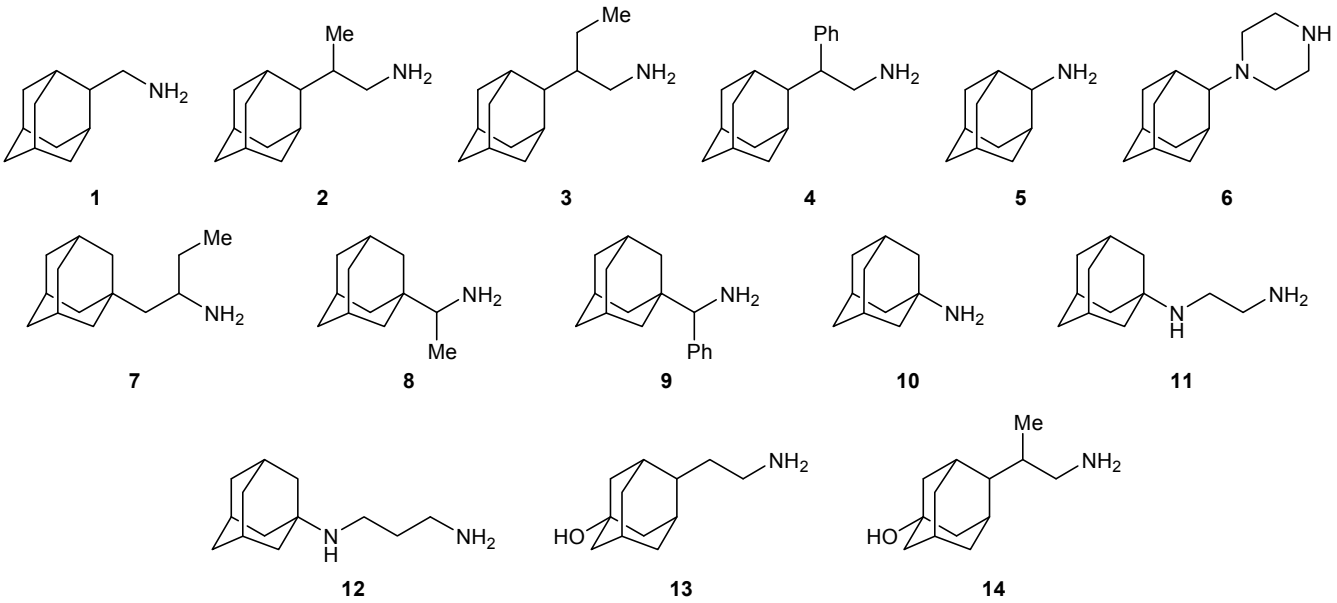
* For communication VIII, see [1].

Scheme 1.



1–14 **15–50** **51–58**

15–50, R = H, F, CF_3, OMe (see table); **51**, Y = CH_2, R = H; **52**, Y = CH_2, R = F; **53**, Y = CH_2, R = CF_3; **54**, Y = CH_2, R = OMe; **55**, Y = $CHCH_3$, R = H; **56**, Y = $CHCH_3$, R = F; **57**, Y = $CHCH_3$, R = CF_3; **58**, Y = $CHCH_3$, R = OMe.



the preceding communication [1] we have convincingly demonstrated that the catalytic system CuI–*rac*-BINOL [1,1′-bi(naphthalen-2-ol)] is the most efficient in the synthesis of *N*-aryl-substituted adamantane-containing amines. In this work we studied the arylation of 14 adamantane-containing amines with different spatial environments of the amino group. The arylating agents were iodobenzene, 1-fluoro-4-iodobenzene, 1-iodo-4-(trifluoromethyl)benzene, and 1-iodo-4-methoxybenzene (Scheme 1). The reactions were carried out in DMF at 140°C under argon using 1.25 equiv of aryl iodide and the catalytic system CuI–*rac*-BINOL–Cs_2CO_3 (10 mol % of CuI and 20 mol % of BINOL); the amine concentration was 0.5 M, and the reaction time was 24 h (unoptimized). The results are collected in the table.

The examined amines may be classed as follows: (1) 2-substituted adamantane derivatives **1**–**4** with gradually increasing steric hindrances at the amino group; (2) adamantane-2-amine (**5**) in which the amino group is directly linked to the adamantane core at the 2-position; (3) piperazine derivative **6** with a secondary amino group as a part of the ring; (4) 1-substituted adamantane derivatives **7**–**10** with different steric hindrances at the amino group; (5) diamines **11** and **12** containing sterically unhindered primary amino group and sterically hindered secondary amino group; (6) amino alcohols **13** and **14**.

On the whole, the arylation of amines **1**–**3** with iodobenzene, 1-fluoro-4-iodobenzene, and 1-iodo-4-(trifluoromethyl)benzene afforded good yields of the corresponding *N*-aryl derivatives in the range 50–65%. An exception was the reaction of amine **3** with iodobenzene, where the yield of **23** reached 82% (run no. 9). As might be expected, the yields of **18**, **22**, and **26** (run. nos. 4, 8, 12) in the reactions with 1-iodo-4-methoxybenzene were lower due to positive mesomeric effect of the methoxy group, which hampers substitution of iodine. Lower yields were also observed in the reactions of amine **4** with iodobenzene and 1-fluoro-4-iodobenzene (run nos. 13, 14); however, the yield of **30** in the arylation of **4** with 1-iodo-4-methoxybenzene (run no. 16) was comparable with the results obtained with amines **1**–**3**. Adamantane-2-amine (**5**) was more reactive, and the yield of its arylation product **31** was higher (78%, run no. 17).

Copper(I)-catalyzed arylation of adamantane-containing amines **1**–**14**

Run no.	Amine	XNH_2 or Y	Aryl iodide	Product	Yield, %
1	**1**	2-(CH_2NH_2)	PhI	**15**	58
2	**1**	2-(CH_2NH_2)	4-FC_6H_4I	**16**	47
3	**1**	2-(CH_2NH_2)	4-$CF_3C_6H_4I$	**17**	65
4	**1**	2-(CH_2NH_2)	4-$MeOC_6H_4I$	**18**	38
5	**2**	2-[CH(Me)CH_2NH_2]	PhI	**19**	59
6	**2**	2-[CH(Me)CH_2NH_2]	4-FC_6H_4I	**20**	51
7	**2**	2-[CH(Me)CH_2NH_2]	4-$CF_3C_6H_4I$	**21**	51
8	**2**	2-[CH(Me)CH_2NH_2]	4-$MeOC_6H_4I$	**22**	43
9	**3**	2-[CH(Et)CH_2NH_2]	PhI	**23**	82
10	**3**	2-[CH(Et)CH_2NH_2]	4-FC_6H_4I	**24**	52
11	**3**	2-[CH(Et)CH_2NH_2]	4-$CF_3C_6H_4I$	**25**	50
12	**3**	2-[CH(Et)CH_2NH_2]	4-$MeOC_6H_4I$	**26**	36
13	**4**	2-[CH(Ph)CH_2NH_2]	PhI	**27**	45
14	**4**	2-[CH(Ph)CH_2NH_2]	4-FC_6H_4I	**28**	35
15	**4**	2-[CH(Ph)CH_2NH_2]	4-$CF_3C_6H_4I$	**29**	58
16	**4**	2-[CH(Ph)CH_2NH_2]	4-$MeOC_6H_4I$	**30**	38
17	**5**	2-NH_2	PhI	**31**	78
18	**6**	2-[N(CH_2CH_2)$_2$NH]	PhI	**32**	32
19	**6**	2-[N(CH_2CH_2)$_2$NH]	4-FC_6H_4I	**33**	74
20	**6**	2-[N(CH_2CH_2)$_2$NH]	4-$CF_3C_6H_4I$	**34**	54
21	**6**	2-[N(CH_2CH_2)$_2$NH]	4-$MeOC_6H_4I$	**35**	67
22	**7**	1-[CH_2CH(Et)NH_2]	PhI	**36**	46
23	**7**	1-[CH_2CH(Et)NH_2]	4-FC_6H_4I	**37**	43
24	**7**	1-[CH_2CH(Et)NH_2]	4-$CF_3C_6H_4I$	**38**	39
25	**7**	1-[CH_2CH(Et)NH_2]	4-$MeOC_6H_4I$	**39**	39
26	**8**	1-[CH(Me)NH_2]	PhI	**40**	42
27	**8**	1-[CH(Me)NH_2]	PhI[a]	**40**	54
28	**9**	1-[CH(Ph)NH_2]	PhI	**41**	10
29	**9**	1-[CH(Ph)NH_2]	PhI[a]	**41**	15
30	**10**	1-NH_2	PhI	**42**	81
31	**10**	1-NH_2	4-FC_6H_4I	**43**	78
32	**10**	1-NH_2	4-$CF_3C_6H_4I$	**44**	86
33	**10**	1-NH_2	4-$MeOC_6H_4I$	**45**	20[b]
34	**11**	1-($NHCH_2CH_2NH_2$)	PhI	**46**	38
35	**12**	1-($NHCH_2CH_2CH_2NH_2$)	PhI	**47**	57
36	**12**	1-($NHCH_2CH_2CH_2NH_2$)	4-FC_6H_4I	**48**	63
37	**12**	1-($NHCH_2CH_2CH_2NH_2$)	4-$CF_3C_6H_4I$	**49**	75
38	**12**	1-($NHCH_2CH_2CH_2NH_2$)	4-$MeOC_6H_4I$	**50**	58

Contd.

Run no.	Amine	XNH_2 or Y	Aryl iodide	Product	Yield, %
39	**13**	CH_2	PhI	**51**	62
40	**13**	CH_2	4-FC_6H_4I	**52**	68
41	**13**	CH_2	4-$CF_3C_6H_4I$	**53**	75
42	**13**	CH_2	4-$MeOC_6H_4I$	**54**	52
43	**14**	CHMe	PhI	**55**	67
44	**14**	CHMe	4-FC_6H_4I	**56**	75
45	**14**	CHMe	4-$CF_3C_6H_4I$	**57**	65
46	**14**	CHMe	4-$MeOC_6H_4I$	**58**	51

[a] 3 equiv of iodobenzene.
[b] Conversion of 1-iodo-4-methoxybenzene 20%.

Secondary cyclic amine **6** showed different reactivity: its reaction with iodobenzene gave only 32% of arylation product **32** (run no. 18), whereas the yields in the reaction of **6** with substituted iodobenzenes were considerably higher (54–74%), and the arylation with 1-iodo-4-methoxybenzene was much more efficient than the reactions with amines **1**–**4** (compound **35** was formed in 67% yield; run no. 21).

Amine **7** containing a branched substituent in position *1* of the adamantane fragment displayed similar reactivity to amine **4** (run nos. 22–25); rimantadine (**8**) gave rise to arylation product **40** in a moderate yield which can be improved by using 3 equiv of iodobenzene (run nos. 26, 27). The amino group in **9** turned out to be most sterically shielded, and the yield of **41** was as low as 15% even in the reaction with excess iodobenzene (run no. 29). On the other hand, adamantan-1-amine (**10**) demonstrated unexpectedly high reactivity which ensured high yields of the arylation products with iodobenzene and its *p*-fluoro and *p*-(trifluoromethyl) derivatives (78–86%; run nos. 30–32); however, the conversion of **10** in the reaction with electron-rich 1-iodo-4-methoxybenzene was low (run no. 33).

As we showed previously, the presence of an ethylenediamine fragment in molecule **11** could negatively affect Cu(I)-catalyzed arylation of this compound [21]. In fact, its reaction with iodobenzene was characterized by a moderate yield (run no. 34). The arylation of trimethylenediamine derivative **12** was significantly more effective, and compounds **47**–**50** were obtained in 57–75% yields (run nos. 25–28); in this reaction, the activity of 1-iodo-4-methoxybenzene was comparable to that of iodobenzene.

The arylation of amino alcohols **13** and **14** selectively involved the amino group, and no concurrent *O*-arylation was observed to an appreciable extent. The yields of the arylation products with iodobenzene, 1-fluoro-4-iodobenzene, and 1-iodo-4-(trifluoromethyl)benzene ranged from 62 to 75% (run nos. 39–41 and 43–45); the reactions of **13** and **14** with 1-iodo-4-methoxybenzene also afforded fairly good yields (**54**, 52%; **58**, 51%; run nos. 42, 46).

Thus, the detailed study of the arylation of adamantane-containing amines differing by the structure and position of the substituent bearing the amino group showed that the yields in the reactions of some substrates with 1-iodo-4-methoxybenzene were noticeably lower than in the reactions with iodobenzene and its derivatives with electron-withdrawing substituents. However, the reactions with other substrates revealed no significant differences in the reactivities of these arylating agents. In most cases, the conversion of 1-iodo-4-methoxybenzene was incomplete, and the reactions were accompanied by side formation of its dimerization product, 4,4′-dimethoxybiphenyl. On the other hand, in a few cases a decrease in the yields of the arylation products was observed in going from iodobenzene to 1-fluoro-4-iodobenzene, which may be rationalized assuming a contribution of side reactions other than amination with the more reactive aryl iodide. Analogous relations were observed by us previously while studying Cu(I)-catalyzed arylation of di- and polyamines [22].

On the whole, systematic studies of Cu(I)-catalyzed arylation and heteroarylation of amines and polyamines are important for successful development of catalytic methodologies, as follows from the analysis

of the state of organic synthesis in Russia [23]; in addition, this is of primary significance for the improvement of chemical education quality [24].

EXPERIMENTAL

The ^{1}H and ^{13}C NMR spectra were recorded on a Bruker Avance-400 spectrometer at 400 and 100.6 MHz, respectively, using $CDCl_3$ as solvent and reference ($CHCl_3$, δ 7.25 ppm; $CDCl_3$, δ_C 77.00 ppm). The mass spectra (MALDI-TOF, positive ion detection) were obtained on a Bruker Daltonics Ultrafex instrument using 1,8,9-trihydroxyanthracene as matrix and poly(ethylene glycols) PEG-200 and PEG-300 as internal standards. Silica gel Merck (40/60) was used for preparative column chromatography. Commercially available iodobenzene, 1-fluoro-4-iodobenzene, 1-iodo-4-(trifluoromethyl)benzene, 1-iodo-4-methoxybenzene, cesium carbonate, copper(I) iodide, and *rac*-BINOL were used without additional purification. Adamantane-containing amines **1**–**4**, **13**, **14** [25], **5** [26], **6** [27], **7**–**9** [28], and **10**–**12** [29–31] were synthesized according to known procedures. Dimethylformamide was distilled over calcium hydride in an inert atmosphere.

Compounds 15–58 (*general procedure*). A two-necked flask was charged under argon with copper(I) iodide (0.05 mmol, 9.5 mg), *rac*-BINOL (0.1 mmol, 27 mg), and aryl iodide (0.625 mmol), and 1 mL of DMF, adamantane-containing amine (0.5 mmol), and cesium carbonate (250 mg, 0.75 mmol) were added. The mixture was heated with stirring for 24 h, cooled to room temperature, and diluted with methylene chloride (5 mL), the precipitate was filtered off and washed with methylene chloride (5 mL), and the organic phase was washed with water (5 mL), dried over 4-Å molecular sieves, and evaporated under reduced pressure (1 mm). The spectral characteristics of compounds **31** [32], **41** [28], and **42** [33] were consistent with those given in the literature.

***N*-(Adamantan-2-ylmethyl)aniline (15)** was synthesized from 83 mg of amine **1** and 128 mg of iodobenzene. Yield 70 mg (58%). ^{1}H NMR spectrum, δ, ppm: 1.59 d (2H, ^3J = 12.1 Hz), 1.73–1.79 m (8H), 3.22 br.d (2H, ^3J = 5.8 Hz), 3.61 br.s (1H), 6.62 d (2H, ^3J = 8.3 Hz), 6.68 t (1H, ^3J = 7.3 Hz), 7.18 t (2H, ^3J = 7.8 Hz). ^{13}C NMR spectrum, δ_C, ppm: 27.9, 28.3, 30.4 (2C), 31.8 (2C), 38.1, 38.9 (2C), 44.1, 46.4, 112.5 (2C), 116.8, 129.1 (2C), 148.6. Mass spectrum: *m*/*z* 242.210 $[M + H]^+$. $C_{17}H_{24}N$. Calculated: *M* + H 242.191.

***N*-(Adamantan-2-ylmethyl)-4-fluoroaniline (16)** was synthesized from 83 mg of amine **1** and 138 mg of 1-fluoro-4-iodobenzene. Yield 61 mg (47%). ^{1}H NMR spectrum, δ, ppm: 1.59 d (2H, ^3J = 11.9 Hz), 1.75 br.s (5H), 1.81–2.00 m (8H), 3.17 d (2H, ^3J = 6.8 Hz), 3.48 br.s (1H), 6.54 d.d (2H, $^3J_{HH}$ = 9.0, $^4J_{HF}$ = 4.4 Hz), 6.88 d.d (2H, $^3J_{HH}$ = 9.0, $^3J_{HF}$ = 8.7 Hz). ^{13}C NMR spectrum, δ_C, ppm: 27.9, 28.3, 30.4 (2C), 31.8 (2C), 38.1, 38.9 (2C), 44.2, 47.2, 113.3 d (2C, $^3J_{CF}$ = 6.7 Hz), 115.5 d (2C, $^2J_{CF}$ = 21.9 Hz), 145.1, 155.5 d ($^1J_{CF}$ = 234.4 Hz). Mass spectrum: *m*/*z* 260.193 $[M + H]^+$. $C_{17}H_{23}FN$. Calculated: *M* + H 260.181.

***N*-(Adamantan-2-ylmethyl)-4-(trifluoromethyl)-aniline (17)** was synthesized from 83 mg of amine **1** and 170 mg of 1-iodo-4-(trifluoromethyl)benzene. Yield 100 mg (65%). ^{1}H NMR spectrum, δ, ppm: 1.61 d (2H, ^3J = 11.6 Hz), 1.76 br.s (5H), 1.83–1.98 m (8H), 3.24 t (2H, ^3J = 6.2 Hz), 4.01 br.s (1H), 6.59 d (2H, ^3J = 8.6 Hz), 7.39 d (2H, ^3J = 8.6 Hz). ^{13}C NMR spectrum, δ_C, ppm: 27.8, 28.2, 30.3 (2C), 31.7 (2C), 38.1, 38.8 (2C), 44.0, 45.9, 111.5 (2C), 126.5 (2C), 151.0; two quaternary carbon signals were not identified. Mass spectrum: *m*/*z* 310.165 $[M + H]^+$. $C_{18}H_{23}F_3N$. Calculated: *M* + H 310.178.

***N*-(Adamantan-2-ylmethyl)-4-methoxyaniline (18)** was synthesized from 83 mg of amine **1** and 146 mg of 1-iodo-4-methoxybenzene. Yield 51 mg (38%). ^{1}H NMR spectrum, δ, ppm: 1.58 d (2H, ^3J = 11.7 Hz), 1.75 br.s (5H), 1.81–1.97 m (8H), 3.17 d (2H, ^3J = 7.1 Hz), 3.74 s (3H), 6.59 d (2H, ^3J = 8.8 Hz), 6.78 d (2H, ^3J = 8.8 Hz); NH signal was not identified. Mass spectrum: *m*/*z* 272.192 $[M + H]^+$. $C_{18}H_{26}NO$. Calculated: *M* + H 272.201.

***N*-[2-(Adamantan-2-yl)propyl]aniline (19)** was synthesized from 97 mg of amine **2** and 128 mg of iodobenzene. Yield 79 mg (59%). ^{1}H NMR spectrum, δ, ppm: 0.99 d (3H, ^3J = 6.6 Hz), 1.40 d (1H, ^3J = 10.6 Hz), 1.52–1.60 m (3H), 1.70–2.00 m (12H), 2.77–2.83 m (1H), 3.29 d (1H, ^2J = 12.0 Hz), 3.69 br.s (1H), 6.62 d (2H, ^3J = 8.3 Hz), 6.68 t (1H, ^3J = 7.3 Hz), 7.18 t (2H, ^3J = 7.6 Hz). ^{13}C NMR spectrum, δ_C, ppm: 16.0, 27.6, 27.9, 29.1, 29.2, 31.6, 31.9, 32.1, 38.1, 39.1, 39.2, 47.5, 47.9, 112.4 (2C), 116.7, 129.1 (2C), 148.6. Mass spectrum: *m*/*z* 270.230 $[M + H]^+$. $C_{19}H_{28}N$. Calculated: *M* + H 270.222.

***N*-[2-(Adamantan-2-yl)propyl]-4-fluoroaniline (20)** was synthesized from 97 mg of amine **2** and 138 mg of 1-fluoro-4-iodobenzene. Yield 73 mg (51%). ^{1}H NMR spectrum, δ, ppm: 0.97 d (3H, ^3J = 6.6 Hz), 1.39 d (1H, ^3J = 10.6 Hz), 1.51–1.58 m (3H),

1.70–1.99 m (12H), 2.72–2.79 m (1H), 3.23 d (1H, ^2J = 13.6 Hz), 3.55 br.s (1H), 6.54 d.d (2H, $^3J_{HH}$ = 8.8, $^4J_{HF}$ = 4.4 Hz), 6.88 d.d (2H, $^3J_{HH}$ = $^3J_{HF}$ = 8.8 Hz). ^{13}C NMR spectrum, δ_C, ppm: 16.0, 27.6, 27.9, 29.1, 29.3, 31.6, 32.0, 32.1, 38.1, 39.1, 39.2, 47.5, 48.6, 113.3 d (2C, $^3J_{CF}$ = 7.6 Hz), 115.5 d (2C, $^2J_{CF}$ = 22.8 Hz), 145.1, 155.5 d ($^1J_{CF}$ = 233.5 Hz). Mass spectrum: *m*/*z* 288.209 $[M + H]^+$. $C_{19}H_{27}FN$. Calculated: *M* + H 288.213.

***N*-[2-(Adamantan-2-yl)propyl]-4-(trifluoromethyl)aniline (21)** was synthesized from 97 mg of amine **2** and 170 mg of 1-iodo-4-(trifluoromethyl)benzene. Yield 86 mg (51%). ^{1}H NMR spectrum, δ, ppm: 0.97 d (3H, ^3J = 6.6 Hz), 1.39 d (1H, ^3J = 10.5 Hz), 1.55 d (2H, ^3J = 11.6 Hz), 1.60 d (1H, ^2J = 13.9 Hz), 1.73–2.09 m (12H), 2.82 d.d.d (1H, ^2J = 12.4, ^3J = 8.1, 5.9 Hz), 3.30 d.t (1H, ^2J = 12.4, ^3J = 3.4 Hz), 4.12 br.s (1H), 6.59 d (2H, ^3J = 8.5 Hz), 7.39 d (2H, ^3J = 8.5 Hz). ^{13}C NMR spectrum, δ_C, ppm: 15.9, 27.6, 27.8, 29.0, 29.3, 31.6, 31.9, 32.1, 38.0, 39.0, 39.2, 47.4 (2C), 111.4 (2C), 126.4 (2C), 151.1; two quaternary carbon signals were not identified. Mass spectrum: *m*/*z* 338.215 $[M + H]^+$. $C_{20}H_{27}F_3N$. Calculated: *M* + H 338.210.

***N*-[2-(Adamantan-2-yl)propyl]-4-methoxyaniline (22)** was synthesized from 97 mg of amine **2** and 146 mg of 4-methoxy-1-iodoanisole. Yield 64 mg (43%). ^{1}H NMR spectrum, δ, ppm: 0.79 d (3H, ^3J = 6.7 Hz), 1.39 d (1H, ^3J = 10.7 Hz), 1.50–1.57 m (3H), 1.72–2.02 m (12H), 2.75 d.d (1H, ^2J = 12.1, ^3J = 8.1 Hz), 3.24 d.d (1H, ^2J = 12.1, ^3J = 2.8 Hz), 3.74 s (3H), 6.58 d (2H, ^3J = 8.8 Hz), 6.78 d (2H, ^3J = 8.8 Hz); NH proton signal was not identified. Mass spectrum: *m*/*z* 300.227 $[M + H]^+$. $C_{20}H_{30}NO$. Calculated: *M* + H 300.233.

***N*-[2-(Adamantan-2-yl)butyl]aniline (23)** was synthesized from 104 mg of amine **3** and 128 mg of iodobenzene. Yield 116 mg (82%). ^{1}H NMR spectrum, δ, ppm: 0.91 t (3H, ^3J = 7.5 Hz), 1.40 d.quint (1H, ^2J = 14.6, ^3J = 7.3 Hz), 1.55–1.61 m (3H), 1.77 br.s (3H), 1.83–1.99 m (10H), 3.04 d.t (1H, ^2J = 11.9, ^3J = 5.8 Hz), 3.23 d.d.d (1H, ^2J = 11.9, ^3J = 4.8, 3.9 Hz), 3.59 br.s (1H), 6.64 d (2H, ^3J = 7.8 Hz), 6.70 t (1H, ^3J = 7.3 Hz), 7.20 d.d (2H, ^3J = 8.3, 7.5 Hz). ^{13}C NMR spectrum, δ_C, ppm: 9.8, 20.6, 27.7, 27.9, 28.8, 29.1, 31.8, 32.0, 37.0, 38.1, 39.3 (2C), 42.7, 44.5, 112.4 (2C), 116.7, 129.1 (2C), 148.7. Mass spectrum: *m*/*z* 284.245 $[M + H]^+$. $C_{20}H_{30}N$. Calculated: *M* + H 284.238.

***N*-[2-(Adamantan-2-yl)butyl]-4-fluoroaniline (24)** was synthesized from 104 mg of amine **3** and 138 mg of 1-fluoro-4-iodobenzene. Yield 78 mg (52%). ^{1}H NMR spectrum, δ, ppm: 0.86 t (3H, ^3J = 7.4 Hz), 1.37 d.quint (1H, ^2J = 14.8, ^3J 7.4 Hz), 1.50–1.56 m (3H), 1.73 br.s (3H), 1.75–1.92 m (10H), 2.92–2.98 m (1H), 3.10–3.17 m (1H), 3.47 br.s (1H), 6.53 d.d (2H, $^3J_{HH}$ = 8.5, $^4J_{HF}$ = 4.2 Hz), 6.86 d.d (2H, $^3J_{HH}$ = 8.5, $^3J_{HF}$ = 8.5 Hz). ^{13}C NMR spectrum, δ_C, ppm: 9.8, 20.5, 27.6, 27.9, 28.7, 29.1, 31.7, 32.0, 36.9, 38.2, 39.2 (2C), 43.4, 44.4, 113.1 d (2C, $^3J_{CF}$ = 6.7 Hz), 115.4 d (2C, $^2J_{CF}$ = 21.9 Hz), 145.1, 155.3 d ($^1J_{CF}$ = 234.4 Hz). Mass spectrum: *m*/*z* 302.223 $[M + H]^+$. $C_{20}H_{29}FN$. Calculated: *M* + H 302.228.

***N*-[2-(Adamantan-2-yl)butyl]-4-(trifluoromethyl)aniline (25)** was synthesized from 104 mg of amine **3** and 170 mg of 1-iodo-4-(trifluoromethyl)benzene. Yield 88 mg (50%). ^{1}H NMR spectrum, δ, ppm: 0.87 t (3H, ^3J = 7.1 Hz), 1.37 d.quint (1H, ^2J = 13.4, ^3J = 6.7 Hz), 1.51–1.60 m (3H), 1.73 br.s (3H), 1.76–1.96 m (10H), 2.98–3.06 m (1H), 3.17–3.26 m (1H), 3.98 br.s (1H), 6.59 d (2H, ^3J = 8.0 Hz), 7.38 d (2H, ^3J = 8.0 Hz). ^{13}C NMR spectrum, δ_C, ppm: 9.8, 20.5, 27.6, 27.9, 28.8, 29.2, 31.7, 32.0, 36.9, 38.1, 39.2 (2C), 42.3, 44.4, 111.5 (2C), 126.5 (2C), 151.1; two quaternary carbon signals were not identified. Mass spectrum: *m*/*z* 352.218 $[M + H]^+$. $C_{21}H_{29}F_3N$. Calculated *M* + H 352.225.

***N*-[2-(Adamantan-2-yl)butyl]-4-methoxyaniline (26)** was synthesized from 104 mg of amine **3** and 146 mg of 1-iodo-4-methoxybenzene. Yield 56 mg (36%). ^{1}H NMR spectrum, δ, ppm: 0.87 t (3H, ^3J = 7.3 Hz), 1.37 d.quint (1H, ^2J = 14.1, ^3J = 7.1 Hz), 1.51–1.57 m (3H), 1.73 br.s (3H), 1.78–1.95 m (10H), 2.93–2.98 m (1H), 3.16 d.d (1H, ^2J = 11.7, ^3J = 2.7 Hz), 3.74 s (3H), 6.58 d (2H, ^3J = 8.7 Hz), 6.78 d (2H, ^3J = 8.7 Hz); NH proton signal was not identified. ^{13}C NMR spectrum, δ_C, ppm: 9.7, 20.5, 27.6, 27.9, 28.7, 29.1, 31.7, 32.0 36.9, 38.1, 39.2 (2S), 43.6, 44.4, 55.7, 113.6 (2C), 114.8 (2C), 143.1, 151.6. Mass spectrum: *m*/*z* 314.254 $[M + H]^+$. $C_{21}H_{32}NO$. Calculated: *M* + H 314.248.

***N*-[2-(Adamantan-2-yl)-2-phenylethyl]aniline (27)** was synthesized from 128 mg of amine **4** and 128 mg of iodobenzene. Yield 72 mg (45%). ^{1}H NMR spectrum, δ, ppm: 1.33 br.s (1H), 1.40 d (1H, ^3J = 11.9 Hz), 1.60–2.12 m (12H), 2.20 br.s (1H), 3.08 d.d (1H, ^2J = 11.4, ^3J = 11.4 Hz), 3.26 d.d.d (1H, ^2J = 11.4, ^3J = 11.4, 3.3 Hz), 3.32–3.37 m (1H), 3.65–3.74 m (1H), 6.54 d (2H, ^3J = 7.7 Hz), 6.71 t (1H, ^3J = 7.3 Hz), 7.17 t (2H, ^3J = 7.9 Hz), 7.21–7.38 m (5H). Mass spectrum: *m*/*z* 332.231 $[M + H]^+$. $C_{24}H_{30}N$. Calculated: *M* + H 332.238.

***N*-[2-(Adamantan-2-yl)-2-phenylethyl]-4-fluoroaniline (28)** was synthesized from 128 mg of amine **4** and 138 mg of 1-fluoro-4-iodobenzene. Yield 61 mg (35%). ^{1}H NMR spectrum, δ, ppm: 1.33 br.s (1H), 1.41 d (1H, ^3J = 13.9 Hz), 1.60–2.16 m (12H), 2.20 br.s (1H), 3.03–3.10 m (1H), 3.26 d.d.d (1H, ^2J = 10.9, ^3J = 10.9, 3.8 Hz), 3.31–3.37 m (1H), 3.60–3.67 m (1H), 6.47 d.d (2H, $^3J_{HH}$ = 8.8, $^4J_{HF}$ = 4.4 Hz), 6.87 d.d (2H, $^3J_{HH}$ = 8.8, $^3J_{HF}$ = 8.8 Hz), 7.20–7.37 m (5H). Mass spectrum: *m*/*z* 350.225 $[M + H]^+$. $C_{24}H_{29}FN$. Calculated: *M* + H 350.228.

***N*-[2-(Adamantan-2-yl)-2-phenylethyl]-4-(trifluoromethyl)aniline (29)** was synthesized from 128 mg of amine **4** and 170 mg of 1-iodo-4-(trifluoromethyl)benzene. Yield 116 mg (58%). ^{1}H NMR spectrum, δ, ppm: 1.35 br.s (1H), 1.42 d (1H, ^3J = 11.6 Hz), 1.62–2.12 m (12H), 2.20 br.s (1H), 3.12 d.d (1H, ^2J = ^3J = 11.6 Hz), 3.22–3.30 m (1H), 3.68–3.76 m (2H), 6.51 d (2H, ^3J = 8.7 Hz), 7.22 d (2H, ^3J = 8.7 Hz), 7.28 t (1H, ^3J = 7.0 Hz), 7.32–7.36 m (2H), 7.39 d (2H, ^3J = 8.7 Hz). Mass spectrum: *m*/*z* 400.217 $[M + H]^+$. $C_{25}H_{29}F_3N$. Calculated: *M* + H 400.225.

***N*-[2-(Adamantan-2-yl)-2-phenylethyl]-4-methoxyaniline (30)** was synthesized from 128 mg of amine **4** and 146 mg of 1-iodo-4-methoxybenzene. Yield 68 mg (38%). ^{1}H NMR spectrum, δ, ppm: 1.30 br.s (1H), 1.37 d (1H, ^3J = 10.5 Hz), 1.60–2.12 m (12H), 2.18 br.s (1H), 3.03 d.d (1H, ^2J = ^3J = 11.1 Hz), 3.24 d.d.d (1H, ^2J = 10.9, ^3J = 10.9, 3.8 Hz), 3.60–3.67 m (1H), 3.73 s (3H), 6.49 d (2H, ^3J = 8.7 Hz), 6.76 d (2H, ^3J = 8.7 Hz), 7.19–7.34 m (5H); NH proton was not identified. Mass spectrum: *m*/*z* 362.252 $[M + H]^+$. $C_{25}H_{32}NO$. Calculated: *M* + H 362.248.

1-(Adamantan-2-yl)-4-phenylpiperazine (32) was synthesized from 110 mg of amine **6** and 128 mg of iodobenzene. Yield 47 mg (32%). ^{1}H NMR spectrum, δ, ppm: 1.42 d (2H, ^3J = 11.4 Hz), 1.64–1.72 m (4H), 1.78–1.90 m (4H), 2.06–2.14 m (4H), 2.38–2.48 m (1H), 2.58–2.63 m (4H), 3.18–3.22 m (4H), 6.83 t (1H, ^3J = 7.3 Hz), 6.93 d (2H, ^3J = 8.2 Hz), 7.08–7.12 m (2H). Mass spectrum: *m*/*z* 297.238 $[M + H]^+$. $C_{20}H_{29}N_2$. Calculated: *M* + H 297.233.

1-(Adamantan-2-yl)-4-(4-fluorophenyl)piperazine (33) was synthesized from 110 mg of amine **6** and 138 mg of 1-fluoro-4-iodobenzene. Yield 116 mg (74%). ^{1}H NMR spectrum, δ, ppm: 1.42 d (2H, ^3J = 11.9 Hz), 1.65–1.74 m (4H), 1.78–1.90 m (4H), 2.05–2.12 m (4H), 2.39–2.46 m (1H), 2.57–2.61 m (4H), 3.10–3.14 m (4H), 6.88 d (2H, $^3J_{HH}$ = 8.8, $^4J_{HF}$ = 4.6 Hz), 6.93–6.98 m (2H). ^{13}C NMR spectrum, δ_C, ppm: 27.2, 27.3, 28.9 (2C), 31.3 (2C), 37.2 (2C), 37.7, 49.5 (2C), 50.5 (2C), 67.5, 115.3 d (2C, $^2J_{CF}$ = 21.2 Hz), 117.3 d (2C, $^3J_{CF}$ = 6.8 Hz), 148.1, 156.9 d ($^1J_{CF}$ = 237.7 Hz). Mass spectrum: *m*/*z* 315.220 $[M + H]^+$. $C_{20}H_{28}FN_2$. Calculated: *M* + H 315.224.

1-(Adamantan-2-yl)-4-[4-(trifluoromethyl)-phenyl]piperazine (34) was synthesized from 110 mg of amine **6** and 170 mg of 1-iodo-4-(trifluoromethyl)-benzene. Yield 98 mg (54%). ^{1}H NMR spectrum, δ, ppm: 1.42 d (2H, ^3J = 11.6 Hz), 1.66–1.73 m (4H), 1.79–1.90 m (4H), 2.01–2.10 m (4H), 2.38–2.44 m (1H), 2.54–2.59 m (4H), 3.23–3.27 m (4H), 6.90 d (2H, ^3J = 8.5 Hz), 7.46 d (2H, ^3J = 8.5 Hz). ^{13}C NMR spectrum, δ_C, ppm: 27.2, 27.3, 28.9 (2C), 31.3 (2C), 37.1 (2C), 37.7, 48.2 (2C), 49.2 (2C), 67.3, 114.0 (2C), 126.2 (2C), 153.3; two quaternary carbon signals were not identified. Mass spectrum: *m*/*z* 365.227 $[M + H]^+$. $C_{21}H_{28}F_3N_2$. Calculated: *M* + H 365.220.

1-(Adamantan-2-yl)-4-(4-methoxyphenyl)piperazine (35) was synthesized from 110 mg of amine **6** and 146 mg of 1-iodo-4-methoxybenzene. Yield 109 mg (67%). ^{1}H NMR spectrum, δ, ppm: 1.41 d (2H, ^3J = 11.0 Hz), 1.64–1.73 m (4H), 1.77–1.89 m (4H), 1.99–2.12 m (4H), 2.36–2.42 m (1H), 2.56–2.60 m (4H), 3.06–3.10 m (4H), 3.74 s (3H), 6.82 d (2H, ^3J = 8.8 Hz), 6.89 d (2H, ^3J = 8.8 Hz). ^{13}C NMR spectrum, δ_C, ppm: 27.2, 27.3, 28.8 (2C), 31.2 (2C), 37.1 (2C), 37.7, 49.5 (2C), 50.8 (2C), 55.3, 67.4, 114.2 (2C), 117.6 (2C), 145.7, 153.4. Mass spectrum: *m*/*z* 327.239 $[M + H]^+$. $C_{21}H_{31}N_2O$. Calculated: *M* + H 327.244.

***N*-[1-(Adamantan-1-yl)butan-2-yl]aniline (36)** was synthesized from 104 mg of amine **7** and 128 mg of iodobenzene. Yield 65 mg (46%). ^{1}H NMR spectrum, δ, ppm: 0.90 t (3H, ^3J = 7.4 Hz), 1.03 d.d (1H, ^2J = 14.4, ^3J = 7.2 Hz), 1.17 d.d (1H, ^2J = 14.4, ^3J = 7.8 Hz), 1.20–1.35 m (2H), 1.52 br.s (6H), 1.61–1.72 m (6H), 1.93 br.s (3H), 3.38 br.s (1H), 6.54 d (2H, ^3J = 7.8 Hz), 6.64 t (1H, ^3J = 7.3 Hz), 7.16 t (2H, ^3J = 7.8 Hz); NH proton signal was not identified. ^{13}C NMR spectrum, δ_C, ppm: 9.8, 28.6 (3C), 28.9, 32.3, 37.0 (3C), 43.0 (3C), 49.3, 50.1, 112.6 (2C), 116.2, 129.2 (2C), 147.5. Mass spectrum: *m*/*z* 284.243 $[M + H]^+$. $C_{20}H_{30}N$. Calculated: *M* + H 284.238.

***N*-[1-(Adamantan-1-yl)butan-2-yl]-4-fluoroaniline (37)** was synthesized from 104 mg of amine **7** and 138 mg of 1-fluoro-4-fluorobenzene. Yield 65 mg (43%). ^{1}H NMR spectrum, δ, ppm: 0.88 t (3H, ^3J = 7.3 Hz), 1.15 d.d (1H, ^2J = 14.7, ^3J = 8.2 Hz), 1.22–1.32 m (2H), 1.41–1.55 m (7H), 1.58–1.70 m (6H), 1.92 br.s (3H), 3.24–3.31 m (1H), 6.45 d.d (2H, $^3J_{HH}$ =

8.7, $^4J_{HF}$ = 4.2 Hz), 6.86 d.d (2H, $^3J_{HH}$ = 8.7, $^3J_{HF}$ = 8.7 Hz); NH proton signal was not identified. ^{13}C NMR spectrum, δ_C, ppm: 9.7, 28.6 (3C), 28.8, 32.3, 36.9 (3C), 43.0 (3C), 50.0 (2C), 113.2 d (2C, $^3J_{CF}$ = 6.8 Hz), 115.5 d (2C, $^2J_{CF}$ = 21.9 Hz), 143.9, 155.0 d ($^1J_{CF}$ = 233.5 Hz). Mass spectrum: *m*/*z* 302.233 $[M + H]^+$. $C_{20}H_{29}FN$. Calculated: *M* + H 302.228.

***N*-[1-(Adamantan-1-yl)butan-2-yl]-4-(trifluoromethyl)aniline (38)** was synthesized from 104 mg of amine **7** and 170 mg of 1-iodo-4-(trifluoromethyl)benzene. Yield 68 mg (39%). ^{1}H NMR spectrum, δ, ppm: 0.89 t (3H, ^3J = 7.5 Hz), 1.04 d.d (1H, ^2J = 14.8, ^3J = 9.7 Hz), 1.16 d.d (1H, ^2J = 14.8, ^3J = 8.5 Hz), 1.19–1.37 m (2H), 1.52 br.s (6H), 1.60–1.68 m (6H), 1.92 br.s (3H), 3.42 br.s (1H), 3.71 br.s (1H), 6.52 d (2H, ^3J = 8.5 Hz), 7.37 d (2H, ^3J = 8.5 Hz). ^{13}C NMR spectrum, δ_C, ppm: 9.4, 28.2 (3C), 28.6, 32.0, 36.6 (3C), 42.6 (3C), 48.7, 49.6, 111.2 (2C), 126.2 (2C), 149.5; two quaternary carbon signals were not identified. Mass spectrum: *m*/*z* 352.229 $[M + H]^+$. $C_{21}H_{29}F_3N$. Calculated: *M* + H 352.225.

***N*-[1-(Adamantan-1-yl)butan-2-yl]-4-methoxyaniline (39)** was synthesized from 104 mg of amine **7** and 146 mg of 1-iodo-4-methoxybenzene. Yield 61 mg (39%). ^{1}H NMR spectrum, δ, ppm: 0.88 t (3H, ^3J = 7.2 Hz), 1.15 d.d (1H, ^2J = 14.5, ^3J = 7.8 Hz), 1.20–1.32 m (2H), 1.42–1.54 m (7H), 1.59–1.70 m (6H), 1.92 br.s (3H), 3.28 br.s (1H), 3.73 br.s (1H), 3.74 s (3H), 6.50 d (2H, ^3J = 8.8 Hz), 6.77 d (2H, ^3J = 8.8 Hz). ^{13}C NMR spectrum, δ_C, ppm: 9.8, 28.6 (3C), 28.9, 32.4, 37.0 (3C), 43.0 (3C), 50.0, 50.2, 55.7, 113.9 (2C), 114.9 (2C), 141.9, 151.3. Mass spectrum: *m*/*z* 314.241 $[M + H]^+$. $C_{21}H_{32}NO$. Calculated: *M* + H 314.248.

***N*-[1-(Adamantan-1-yl)ethyl]aniline (40)** was synthesized from 90 mg of amine **8** and 128 mg of iodobenzene. Yield 53 mg (42%). ^{1}H NMR spectrum, δ, ppm: 1.06 d (3H, ^3J = 6.6 Hz), 1.45–1.59 m (3H), 1.61–1.77 m (9H), 1.99 br.s (3H), 3.07 d.q (1H, ^3J = 9.9, 6.6 Hz), 3.42 d (1H, ^3J = 9.9 Hz), 6.59 d (2H, ^3J = 8.6 Hz), 6.62 t (1H, ^3J = 7.2 Hz), 7.14 t (2H, ^3J = 7.8 Hz). ^{13}C NMR spectrum, δ_C, ppm: 14.4, 28.4 (3C), 36.5, 37.1 (3C), 38.7 (3C), 57.4, 112.8 (2C), 116.3, 129.1 (2C), 148.6. Mass spectrum: *m*/*z* 256.219 $[M + H]^+$. $C_{18}H_{26}N$. Calculated: *M* + H 256.207.

***N*-(4-Fluorophenyl)adamantan-1-amine (43)** was synthesized from 76 mg of amine **10** and 138 mg of 1-fluoro-4-iodobenzene. Yield 96 mg (78%). ^{1}H NMR spectrum, δ, ppm: 1.56–1.71 m (6H), 1.76–1.79 m (6H), 2.09 br.s (3H), 6.75–6.80 m (2H), 6.85–6.90 m (2H); NH proton signal was not identified. ^{13}C NMR spectrum, δ_C, ppm: 29.6 (3C), 36.4 (3C), 43.6 (3C), 46.2, 115.1 d (2C, $^2J_{CF}$ = 21.9 Hz), 122.5 d (2C, $^3J_{CF}$ = 7.6 Hz), 141.5, 155.5 d ($^1J_{CF}$ = 231.8 Hz). Mass spectrum: *m*/*z* 246.152 $[M + H]^+$. $C_{16}H_{21}FN$. Calculated: *M* + H 246.166.

***N*-[4-(Trifluoromethyl)phenyl]adamantan-1-amine (44)** was synthesized from 76 mg of amine **10** and 170 mg of 1-iodo-4-(trifluoromethyl)benzene. Yield 127 mg (86%). ^{1}H NMR spectrum, δ, ppm: 1.66–1.74 m (6H), 1.94–1.96 m (6H), 2.14 br.s (3H), 6.79 br.s (2H), 7.36 d (2H, ^3J = 8.6 Hz). Mass spectrum: *m*/*z* 296.158 $[M + H]^+$. $C_{17}H_{21}F_3N$. Calculated: *M* + H 296.163.

***N*-(Adamantan-1-yl)-*N*′-phenylethane-1,2-diamine (46)** was synthesized from 97 mg of diamine **11** and 128 mg of iodobenzene. Yield 51 mg (38%). ^{1}H NMR spectrum, δ, ppm: 1.55–1.80 m (12H), 2.14 br.s (3H), 2.84 t (2H, ^3J = 5.7 Hz), 3.16 q (2H, ^3J = 5.2 Hz), 4.14 br.s (1H), 6.63 d (2H, ^3J = 8.2 Hz), 6.69 t (1H, ^3J = 6.9 Hz), 7.16 t (2H, ^3J = 7.6 Hz). Mass spectrum: *m*/*z* 271.106 $[M + H]^+$. $C_{18}H_{27}N_2$. Calculated: *M* + H 271.217.

***N*-(Adamantan-1-yl)-*N*′-phenylpropane-1,3-diamine (47)** was synthesized from 104 mg of diamine **12** and 128 mg of iodobenzene. Yield 81 mg (57%). ^{1}H NMR spectrum, δ, ppm: 1.58–1.71 m (12H), 1.76 quint (2H, ^3J = 6.3 Hz), 2.07 br.s (3H), 2.74 br.t (2H, ^3J = 4.9 Hz), 3.19 t (2H, ^3J = 6.1 Hz), 6.61 d (2H, ^3J = 8.0 Hz), 6.69 t (1H, ^3J = 7.2 Hz), 7.18 t (2H, ^3J = 7.5 Hz); NH proton signals were not identified. ^{13}C NMR spectrum, δ_C, ppm: 29.4 (3C), 30.0, 36.5 (3C), 38.8, 42.5 (3C), 43.1, 50.5, 112.5 (2C), 116.8, 129.0 (2C), 148.6. Mass spectrum: *m*/*z* 285.238 $[M + H]^+$. $C_{19}H_{29}N_2$. Calculated: *M* + H 285.233.

***N*-(Adamantan-1-yl)-*N*′-(4-fluorophenyl)-propane-1,3-diamine (48)** was synthesized from 104 mg of diamine **12** and 138 mg of 1-fluoro-4-iodobenzene. Yield 95 mg (63%). ^{1}H NMR spectrum, δ, ppm: 1.54–1.69 m (12H), 1.71 br.s (2H), 2.04 br.s (3H), 2.71 br.s (2H), 3.10 br.t (2H, ^3J = 5.2 Hz), 3.34 br.s (1H), 6.50 d.d (2H, $^3J_{HH}$ = 8.5, $^4J_{HF}$ = 3.9 Hz), 6.85 d.d (2H, $^3J_{HH}$ = 8.5, $^3J_{HF}$ = 8.5 Hz). ^{13}C NMR spectrum, δ_C, ppm: 29.4 (3C). 29.9, 36.6 (3C), 38.9, 42.5 (3C), 43.9, 50.5, 113.3 d (2C, $^3J_{CF}$ = 6.7 Hz), 115.3 d (2C, $^2J_{CF}$ = 21.9 Hz), 145.0, 155.5 d ($^1J_{CF}$ = 233.5 Hz). Mass spectrum: *m*/*z* 303.221 $[M + H]^+$. $C_{19}H_{28}FN_2$. Calculated: *M* + H 303.224.

***N*-(Adamantan-1-yl)-*N*′-[4-(trifluoromethyl)-phenyl]propane-1,3-diamine (49)** was synthesized from 104 mg of diamine **12** and 170 mg of 1-iodo-4-

(trifluoromethyl)benzene. Yield 132 mg (75%). ^{1}H NMR spectrum, δ, ppm: 1.58–1.72 m (12H), 1.75 br.s (2H), 2.07 br.s (3H), 2.76 br.s (2H), 3.19 br.s (2H), 6.56 d (2H, ^3J = 8.2 Hz), 7.38 d (2H, ^3J = 8.2 Hz); NH proton signals were not identified. ^{13}C NMR spectrum, δ_C, ppm: 29.4 (4C), 36.6 (3C), 39.0, 42.6 (3C), 43.1, 50.7, 111.4 (2C), 126.4 (2C), 151.1; two quaternary carbon signals were not identified. Mass spectrum: *m*/*z* 353.215 $[M + H]^+$. $C_{20}H_{28}F_3N_2$. Calculated: *M* + H 353.220.

***N*-(Adamantan-1-yl)-*N*′-(4-methoxyphenyl)-propane-1,3-diamine (50)** was synthesized from 104 mg of diamine **12** and 146 mg of 1-iodo-4-methoxybenzene. Yield 91 mg (58%). ^{1}H NMR spectrum, δ, ppm: 1.55–1.70 m (12H), 1.73 br.s (2H), 2.05 br.s (3H), 2.71 br.s (2H), 3.11 br.s (2H), 3.73 s (3H), 6.57 d (2H, ^3J = 8.6 Hz), 6.77 d (2H, ^3J = 8.6 Hz); NH proton signals were not identified. ^{13}C NMR spectrum, δ_C, ppm: 29.3 (3C), 29.4, 36.4 (3C), 38.7, 42.3 (3C), 43.9, 50.4, 55.5, 113.8 (2C), 114.6 (2C), 142.8, 151.6. Mass spectrum: *m*/*z* 315.248 $[M + H]^+$. $C_{20}H_{31}N_2O$. Calculated: *M* + H 315.244.

4-(2-Anilinoethyl)adamantan-1-ol (51) was synthesized from 98 mg of amino alcohol **13** and 128 mg of iodobenzene. Yield 84 mg (62%). ^{1}H NMR spectrum, δ, ppm: 1.36 d (2H, ^3J = 12.3 Hz), 1.65–1.80 m (12H), 1.91 br.s (2H), 2.06 br.s (1H), 3.08 br.s (2H), 3.64 br.s (1H), 6.58 d (2H, ^3J = 7.7 Hz), 6.66 t (1H, ^3J = 7.3 Hz), 7.15 t (2H, ^3J = 7.9 Hz). ^{13}C NMR spectrum, δ_C, ppm: 30.0 (2C), 30.1, 31.5, 33.7 (2C), 40.7, 42.3, 45.6, 46.1 (2C), 67.8, 112.5 (2C), 116.9, 129.0 (2C), 148.2. Mass spectrum: *m*/*z* 272.193 $[M + H]^+$. $C_{18}H_{26}NO$. Calculated: *M* + H 272.201.

4-[2-(4-Fluoroanilino)ethyl]adamantan-1-ol (52) was synthesized from 98 mg of amino alcohol **13** and 138 mg of 1-fluoro-4-iodobenzene. Yield 98 mg (68%). ^{1}H NMR spectrum, δ, ppm: 1.36 d (2H, ^3J = 12.5 Hz), 1.62–1.81 m (12H), 1.90 br.s (2H), 2.05 br.s (1H), 3.03 br.s (2H), 3.51 br.s (1H), 6.51 d.d (2H, $^3J_{HH}$ = 8.7, $^4J_{HF}$ = 4.4 Hz), 6.85 d.d (2H, $^3J_{HH}$ = 8.7, $^3J_{HF}$ = 8.7 Hz). ^{13}C NMR spectrum, δ_C, ppm: 30.0 (2C), 30.2, 31.6, 33.8 (2C), 40.8, 43.0, 45.6, 46.1 (2C), 67.8, 113.4 d (2C, $^3J_{CF}$ = 6.8 Hz), 115.5 d (2C, $^2J_{CF}$ = 21.9 Hz), 144.7, 155.5 d ($^1J_{CF}$ = 235.2 Hz). Mass spectrum: *m*/*z* 290.186 $[M + H]^+$. $C_{18}H_{25}FNO$. Calculated: *M* + H 290.192.

4-{2-[4-(Trifluoromethyl)anilino]ethyl}adamantan-1-ol (53) was synthesized from 98 mg of amino alcohol **13** and 170 mg of 1-iodo-4-(trifluoromethyl)-benzene. Yield 127 mg (75%). ^{1}H NMR spectrum, δ, ppm: 1.35 d (2H, ^3J = 12.8 Hz), 1.61–1.78 m (12H), 1.88 br.s (2H), 2.03 br.s (1H), 3.04–3.11 m (2H), 4.15 br.s (1H), 6.54 d (2H, ^3J = 8.2 Hz), 7.33 d (2H, ^3J = 8.2 Hz). ^{13}C NMR spectrum, δ_C, ppm: 29.9 (2C), 30.0, 31.1, 33.6 (2C), 40.5, 41.6, 45.5, 46.0 (2C), 67.5, 111.3 (2C), 126.2 (2C), 150.7; two quaternary carbon signals were not identified. Mass spectrum: *m*/*z* 340.192 $[M + H]^+$. $C_{19}H_{25}F_3NO$. Calculated: *M* + H 340.189.

4-[2-(4-Methoxyanilino)ethyl}adamantan-1-ol (54) was synthesized from 98 mg of amino alcohol **13** and 146 mg of 1-iodo-4-methoxybenzene. Yield 78 mg (52%). ^{1}H NMR spectrum, δ, ppm: 1.35 d (2H, ^3J = 12.4 Hz), 1.60–1.80 m (12H), 1.90 br.s (2H), 2.04 br.s (1H), 3.03 br.s (2H), 3.34 br.s (1H), 3.71 s (3H), 6.55 d (2H, ^3J = 8.5 Hz), 6.75 d (2H, ^3J = 8.5 Hz). ^{13}C NMR spectrum, δ_C, ppm: 30.0 (3C), 31.6, 33.7 (2C), 40.7, 43.3, 45.6, 46.1 (2C), 55.6, 67.7, 113.8 (2C), 114.7 (2C), 142.5, 151.7. Mass spectrum: *m*/*z* 302.218 $[M + H]^+$. $C_{19}H_{28}NO_2$. Calculated: *M* + H 302.212.

4-(1-Anilinopropan-2-yl)adamantan-1-ol (55) was synthesized from 105 mg of amino alcohol **14** and 128 mg of iodobenzene. Yield 95 mg (67%). ^{1}H NMR spectrum, δ, ppm: 0.99 d (3H, ^3J = 6.8 Hz), 1.25–1.53 m (3H), 1.62–1.99 m (10H), 2.10 s (1H), 2.14 s (1H), 2.21 s (1H), 2.77–2.84 m (1H), 3.29 br.d (1H, ^2J = 11.9 Hz), 3.70 br.s (1H), 6.61 d (2H, ^3J = 8.3 Hz), 6.68 t (1H, ^3J = 7.3 Hz), 7.17 t (2H, ^3J = 7.5 Hz). ^{13}C NMR spectrum, δ_C, ppm: 16.1, 30.0, 30.1, 30.6, 31.3, 31.4, 31.7, 45.5, 46.1, 46.2 (2C), 47.9, 67.7, 112.4 (2C), 116.8, 129.1 (2C), 148.4. Mass spectrum: *m*/*z* 286.213 $[M + H]^+$. $C_{19}H_{28}NO$. Calculated: *M* + H 286.217.

4-[1-(4-Fluoroanilino)propan-2-yl]adamantan-1-ol (56) was synthesized from 105 mg of amino alcohol **14** and 138 mg of 1-fluoro-4-iodobenzene. Yield 114 mg (75%). ^{1}H NMR spectrum, δ, ppm: 0.97 d (3H, ^3J = 6.7 Hz), 1.22–1.42 m (3H), 1.56–1.96 m (10H), 2.08 s (1H), 2.11 s (1H), 2.16 s (1H), 2.72–2.79 m (1H), 3.21 br.d (1H, ^2J = 11.4 Hz), 3.63 br.s (1H), 6.51 d.d (2H, $^3J_{HH}$ = 8.7, $^4J_{HF}$ = 4.3 Hz), 6.86 d.d (2H, $^3J_{HH}$ = 8.7, $^3J_{HF}$ = 8.7 Hz). ^{13}C NMR spectrum, δ_C, ppm: 16.1, 30.0, 30.1, 30.6, 31.4 (2C), 31.7, 45.5, 46.1, 46.2 (2C), 48.7, 67.9, 113.3 d (2C, $^3J_{CF}$ = 6.8 Hz), 115.5 d (2C, $^2J_{CF}$ = 21.9 Hz), 144.9, 155.4 d ($^1J_{CF}$ = 234.4 Hz). Mass spectrum: *m*/*z* 304.211 $[M + H]^+$. $C_{19}H_{27}FNO$. Calculated: *M* + H 304.208.

4-{1-[4-(Trifluoromethyl)anilino]propan-2-yl}-adamantan-1-ol (57) was synthesized from 105 mg from amino alcohol **14** and 170 mg of 1-iodo-4-(trifluoromethyl)benzene. Yield 115 mg (65%). ^{1}H NMR

spectrum, δ, ppm: 0.93 d (3H, ^3J = 6.6 Hz), 1.18–1.40 m (3H), 1.59–1.97 m (10H), 2.03 s (1H), 2.07 s (1H), 2.12 s (1H), 2.72–2.80 m (1H), 3.24 d.d (1H, ^2J = 12.4, ^3J = 3.0 Hz), 4.23 br.s (1H), 6.54 d (2H, ^3J = 8.6 Hz), 7.32 d (2H, ^3J = 8.6 Hz). ^{13}C NMR spectrum, δ_C, ppm: 16.0, 30.0, 30.1, 30.6, 31.3 (2C), 31.6, 45.4, 46.0, 46.2 (2C), 47.4, 67.4, 111.3 (2C), 126.3 (2C), 150.9; two quaternary carbon signals were not identified. Mass spectrum: *m/z* 354.208 $[M + H]^+$. $C_{20}H_{27}F_3NO$. Calculated: M + H 354.204.

4-[1-(4-Methoxyanilino)propan-2-yl]adamantan-1-ol (58) was synthesized from 105 mg of amino alcohol **14** and 146 mg of 1-iodo-4-methoxybenzene. Yield 80 mg (51%). ^{1}H NMR spectrum, δ, ppm: 0.96 d (3H, ^3J = 6.6 Hz), 1.20–1.41 m (3H), 1.55–1.96 m (10H), 2.05 s (1H), 2.10 s (1H), 2.16 s (1H), 2.70–2.80 m (1H), 3.21 br.d (1H, ^2J = 14.9 Hz), 3.74 s (3H), 6.54 d (2H, ^3J = 8.3 Hz), 6.75 d (2H, ^3J = 8.3 Hz); NH proton signal was not identified. ^{13}C NMR spectrum, δ, ppm: 16.1, 30.0, 30.1, 30.5, 31.2, 31.3, 31.4, 45.4, 46.1, 46.2 (2C), 48.9, 55.6, 67.6, 114.7 (2C), 116.2 (2C), 142.7, 151.6. Mass spectrum: *m/z* 316.237 $[M+H]^+$. $C_{20}H_{30}NO_2$. Calculated M + H 316.228.

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