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Addition of Organometallic Reagents to Nitriles Promoted by Titanium(IV) Isopropoxide as a Procedure of Synthesis of Primary *tert*-Alkylamines

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Abstract—Grignard reagents are able to add twice to nitriles in the presence of titanium(IV) isopropoxide providing primary *tert*-alkylamines in a fair yield. The conditions and structural features of reagents required for successful reaction were established. A possibility to apply two different organometallic reagents was demonstarated, in particular, the use of organolithium compounds in the second stage.

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The preparation of primary *tert*-alkylamines is a difficalt problem. One of the most general and widely used method of their synthesis is Ritter reaction providing the amines in two stages proceeding from nitriles and tertiary alcohols or alkenes capable of generating stable carbocations in acid medium [1]. An essential disadvantage of this procedure alongside the relatively low overall yield is the stringent deacylation condition in the last stage. A similar synthetic route to the primary *tert*-alkylamines, the reduction of *tert*-alkylazides obtained as a rule from the corresponding halides [2] or alcohols [3], is also inconvenient.

Although the addition oof organometallic reagents to ketimines is not regarded as a general procedure for the synthesis of *tert*-alkylamines [4], infrequently from the specifically substituted ketimines primary amines were obtained after deblocking [5]. However as a rule the addition of organolithium and organomagnesium reagents to N-metallated ketimines does not occur excluding the direct preparation of primary *tert*-alkylamines from nitriles and excess of the corresponding organometallic reagent. As exception may be cited, on the one hand, some nitriles with acceptor groups in the α-position [6], and on the other hand, allylmagnesium bromide [7] where the second stage apparently proceeded in a concerted mode. The only known organometallic reagents capable twice add to various nitriles are compounds formally described as $RCeCl_2$ obtained in situ from the corresponding organolithium reagents and $CeCl_3$ [8]. This method is however very expensive.

Tertiary cyclopropylamines are obtained by Kulinkovich–de Meijere reaction from tertiary amides and Grignard reagents in the presence of $(i\text{-PrO})_4Ti$ [9]. The attempts to prepare analogously primarily cyclopropylamines from nitriles and Grignard reagents were unsuccessful until it was found, that addition of $BF_3{\cdot}Et_2O$ to the end of the process forced the formation of the desired product [10]. However the practical application of this procedure revealed that at least with ethylmagnesium bromide disregarding the nitrile structure formed as side products the corresponding α,α-diethyl-alkyl-amines (3–5 mol%). It is presumable that their formation originates from the ability of $(i\text{-PrO})_4Ti$ not only to generate titanacyclopropane intermediates but also to operate as a Lewis acid increasing the electrophilicity of the carbon atom of the imine group. It was therefore of interest to differentiate both these types of reactivity directing it to the route leading to primary *tert*-alkylamines.

Inasmuch as cyclopropanation is possible only with Grignard reagents with β-hydrogen in the molecule, the most promising for preparation primary *tert*-alkylamines seem the Grignard reagents lacking this structural feature. We selected as test system propionitrile (**Ia**) –

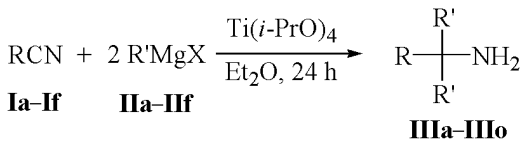
† Deceased.

Table 1. Primary *tert*-alkylamines RR'_2NH_2 obtained from nitriles RCN and Grignard reagents R'MgX

RCN	R	R'MgX	R'	X	Amine	Yield, %
Ia	Et	**IIa**	Ph	Br	**IIIa**	77
Ib	Me	**IIa**	Ph	Br	**IIIb**	57
Ic	$MeOCH_2CH_2$	**IIa**	P	Br	**IIIc**	40
Id	*i*-Pr	**IIa**	Ph	Br	**IIId**	55
Ie	Ph	**IIa**	Ph	Br	**IIIe**	55
Ia	Et	**IIb**	*p*-MeC_6H_4	Br	**IIIe**	65
Ie	Ph	**IIc**	*m*-$CF_3C_6H_4$	Br	**IIIg**	25
Ib	Me	**IId**	Bn	Cl	**IIIh**	40
Ia	Et	**IId**	Bn	Cl	**IIIi**	72
If	Pr	**IId**	Bn	Cl	**IIIj**	67
Id	*i*-Pr	**IId**	Bn	Cl	**IIIk**	28
Ic	$MeOCH_2CH_2$	**IId**	Bn	Cl	**IIIl**	35
Ie	Ph	**IId**	Bn	Cl	**IIIm**	64
Ie	Ph	**IIe**	Me	Cl	**IIIn**	44
Id	*i*-Pr	**IIe**	Me	Cl	**IIIo**	27
Ie	Ph	**IIf**	Et	Br	**IIIp**	60

phenylmagnesium bromide (**IIa**) – $(i\text{-PrO})_4Ti$. In procedure [10] to the solution of nitrile in ether first $(i\text{-PrO})_4Ti$ was added, then two equiv of Grignard reagent. This sequence of addition seemed questionable for the solution of the target problem; the primary generation of imine magnesium derivative looked more reasonable, and only afterwards should be performed activation of the intermediate obtained by $(i\text{-PrO})_4Ti$. One of the main problems was the molar ratio of the nitrile, Grignard reagent, and $(i\text{-PrO})_4Ti$. It turned out that at the use of 0.1 equiv of $(i\text{-PrO})_4Ti$ and 2 equiv of the Grignard reagent in ether the expected 1,1-diphenylpropylamine (**IIIa**) did not form at all, and at equimolar amount of $(i\text{-PrO})_4Ti$ it was obtained in a low yield (11%). The yield was successfully raised to 60% only by increasing the quantity of the Grignard reagent to three equivalents. Variation of reaction conditions showed that the best yield was obtained at room temperature: at low temperature (0°C) and at boiling the yield diminished (48 and 60% respectively). The addition of the second equiv of Grignard reagent to the magnesium imine derivative did not reuire much time: In 10 min the yield was 57%, in 1 h, 77%, after 24 h, the same 77%. The attempt to use THF as solvent resulted in decreased yield (25%) and more difficult purification of the product. Thus we demonstrated fundamental possibility to obtain in the reaction under study the target *tert*-alkylamines and to a certain degree optimized the preparation procedure.

To outline the limits of the reaction applicability we investigated nitriles and Grignard reagents of various structure (Table 1). Aliphatic and aromatic nitriles lacking labile hydrogen atoms gave with phenylmagnesium bromide (**IIa**) and substituted analogs **IIb** and **IIc** the corresponding primary *tert*-alkylamines **IIIa–IIIg** in 25–77% yields. Unexpectedly and quite in contrast to the data [7] with benzylmagnesium chloride (**IId**) the yields of primary *tert*-alkylamines **IIIh–IIIm** are quite plausible and reach in some events 60–70%. Methylmagnesium chloride (**IIe**) provided in reaction with benzonitrile (**Ie**) and isobutyronitrile (**Id**) the corresponding amines **IIIn–IIIo** in moderate yields.

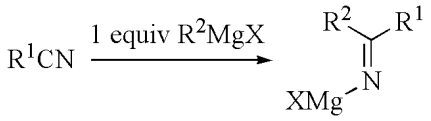


In all above reactions the Grignard reagents employed were incapable of cyclopropanation. An obvious interest consisted in revealing whether the primary *tert*-alkylamines could be obtained from a Grignard reagent containing a β-hydrogen under the conditions where the cyclopropanation was suppressed simply by changing the order of the reagents addition to the nitrile and by increasing the overall amount of the Grignard reagent. It proved that if in reaction of benzonitrile (**Ie**) with EtMgBr (**IIf**), the classical Grignard reagent for cyclopropanation, first would be added to the nitrile 3 equiv of reagent (**IIf**), and then 1 equiv of $(i\text{-PrO})_4Ti$ the main reaction product instead of 1-phenylcyclopropylamine became α,α-diethylbenzylamine (**IIIp**) (yield 60%).

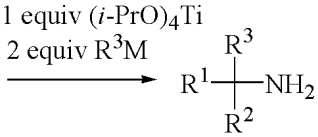
In reaction of benzyl cyanide with phenylmagnesium bromide (**IIa**) no amines were isolated from the reaction mixture. It is apparently due to the high CH-acidity of the benzyl cyanide resulting in side processes already at the stage of reaction with Grignard reagent. Vinylmagnesium chloride and ethynylmagnesium chloride although incapable to enter into the cyclopropanation neither give primary *tert*-alkylamines.

Another interesting problem was an extension of the application range of the reaction by successive addition to the nitrile two different Grignard reagents in order to obtain amines with three different substituents. This idea was fulfilled proceeding from propionitrile (**If**), methylmagnesium chloride (**IIe**), and phenylmagnesium bromide (**IIa**) (Table 2). One of the reasons of low yield of 1-methyl-1-phenylpropylamine (**IIIq**) was the formation of a side product, 1,1-diphenylpropylamine (**IIIa**).

Even wider prospects provides the use in the second stage of this cross-coupling of organolithium reagents characterized by a wide range of possible structures. In this way we succeeded in preparation of the corresponding *tert*-alkylamines **IIIr–IIIt** (Table 2).



Ia, If, Ig



IIIr–IIIt

The problem of the reaction mechanism is yet unsolved. If the action of $(i\text{-PrO})_4Ti$ is limited just to the increasing the electrophilicity of the carbon atom in the imine group then $(i\text{-PrO})_4Ti$ would be possible to be replaced by another Lewis acid. Yet at the attempt to use in this position $(i\text{-PrO})_3Al$, $BF_3{\cdot}Et_2O$, and $SnCl_4$ no primary *tert*-alkylamines were formed showing that $(i\text{-PrO})_4Ti$ was a unique coreagent in this reaction.

EXPERIMENTAL

^1H and ^{13}C NMR spectra were registered on spectrometers Bruker DPX-300 at operating frequencies 300.130 and 75.54 MHz, Varian Mercury-300 at operating frequencies 300.141 and 75.478 MHz, and Varian Unity-300 at operating frequencies 300.544 and 75.579 MHz. Chemical shifts were measured from the residual solvent signal [7.26 ($CHCl_3$), 77.0 ($CDCl_3$), 2.49 (DMSO-d_5), 39.7 ppm (DMSO-d_6)]. The mixture DMSO-d_6–CCl_4 was always 1:2 v/v. The coupling constants in the proton spectra were measured in the first order approximation. The multiplicity of signals in the ^{13}C NMR spectra was estimated using standard pulse sequences DEPT-135 and APT. To give the spectral information in a uniform format the following interpretation of DEPT-135 and APT spectra was done: For every signal in the ^{13}C NMR spectrum the type of carbon atom was indicated (C, CH, CH_2, CH_3). Mass spectra were measured on Finnigan MAT-95 instrument, electrospray ionization with registering positively charged species, and on Finnigan MAT Incos-50, electron impact ionization, ionizing electrons energy 70eV. Elemental analyses were carried out on an automatic CHN-analyzer HP-185 and in the laboratory of microanalysis, Institut für Organische und Biomolekulare Chemie, Georg-August-Universität Göttingen.

Table 2. Cross-coupling of nitriles R^1CN with various organometallic reagents

R^1CN	R^1	R^2MgX	R^2	X	R^3M	R^3	M	Amine	Yield, %
Ia	Et	**IIe**	Me	Cl	**IIa**	Ph	MgBr	**IIIq**	30
If	Pr	**IIa**	Ph	Br	**IIg**	2-furyl	Li	**IIIr**	25
If	Pr	**IIa**	Ph	Br	**IIh**	2-$PyCH_2$	Li	**IIIs**	55
Id	*i*-Pr	**IIa**	Ph	Br	**IIi**	2-thienyl	Li	**IIIt**	30

Primary *tert*-alkylamines IIIa–IIId, IIIh, IIIj–IIIp. General procedure. To a solution of 10 mmol of nitrile in 30–50 ml of ether was added within 15 min at room temperature while vigorously stirring 30 mmol of Grignard reagent (1–2 M solution in ether), and the mixture was stirred for 30 min more. Then 2.84 g (10 mmol) of $(i\text{-PrO})_4Ti$ was added (the solution usually became dark-brown). The reaction mixture was left overnight and then treated with 40 ml of 10% solution of NaOH. The suspension was filtered off from the precipitate of inorganic compounds, the precipitate was washed with dichloromethane. The organic layer was separated, the water layer was extracted with dichloromethane. The combined organic solutions were evaporated to dryness in a vacuum at 40°C, the residue was treated with a small quantity of ether and extracted with 5% solution of HCl. The combined acid solutions were washed with a small quantity of ether, alkalinized, and thrice extracted with ether. The combined organic solution was dried over sodium sulfate and evaporated to dryness in a vacuum. Amines obtained (save amines **IIIa** and **IIId**) were slowly crystallizing oily substances. They were converted into the corresponding hydrochlorides by acidifying their solution in dichloromethane with saturated HCl solution in ether or with several drops of concn. hydrochloric acid. The solution was evaporated to dryness, the hydrochlorides were additionally purified if necessary by passing through a bed of silica gel and/or by recrystallization from a mixture ethanol–ether.

Primary *tert*-alkylamines IIIe–IIIg. General procedure. The synthesis of these compounds is carried out by procedure identical to above described, but these amines are not extracted from the ether solution with 5% HCl solution. Their hydrochlorides crystallized within a night from the preliminary acidified ether-dichloromethane solution (amines **IIIe** and **IIIg**). Another

means of obtaining pure hydrochlorides consists in filtering of acidified reaction mixure through a silica gel bed, eluent $CHCl_3$–MeOH (amine **IIIf**).

1,1-Diphenylpropylamine (IIIa). Yield 77%, mp 70–72°C. ^{1}H NMR spectrum ($CDCl_3$), δ, ppm: 0.85 t (3H, *J* 7.8 Hz), 1.79 br.s (2H), 2.29 q (2H, *J* 7.8 Hz), 7.24–7.29 m (2H), 7.33–7.39 m (4H), 7.43–7.46 m (4H). ^{13}C NMR spectrum ($CDCl_3$), δ, ppm: 9.0 (CH_3), 35.5 (CH_2), 61.7 (C), 126.7 (CH), 127.1 (CH), 128.5 (CH), 149.1 (C). Mass spectrum (electron impact), *m/z* (I_{rel}, %): 182 $[M - C_2H_5]^+$ (100), 152 (2), 134 $[M - C_6H_5]^+$ (19), 115 (9), 104 $[M - C_6H_5 - C_2H_6]^+$ (43), 91 (22), 77 (34), 65 (3), 51 (18), 39 (5). Found, %: C 85.34; H 7.88; N 6.79. $C_{15}H_{17}N$. Calculated, %: C 85.26; H 8.11; N 6.63.

1,1-Diphenylethylamine hydrochloride (IIIb). Yield 57%, mp 228–229°C (229–231°C [11]).

3-Methoxy-1,1-diphenylpropylamine hydrochloride (IIIc). Yield 40%, mp 100–101°C. ^{1}H NMR spectrum (DMSO-d_6), δ, ppm: 2.74 t (2H, *J* 9.0 Hz), 3.15 s (3H), 3.30 t (2H, *J* 9.0 Hz), 7.33–7.42 m (10H), 8.30 br.s (3H). ^{13}C NMR spectrum (DMSO-d_6), δ, ppm: 37.7 (C), 58.2 (CH_3), 63.2 (CH_2), 67.8 (CH_2), 126.8 (CH), 128.1 (CH), 128.5 (CH), 141.0 (C). Mass spectrum (electrospray), *m/z* (I_{rel}, %): 242 $[M - Cl]^+$ (100).

2-Methyl-1,1-diphenylpropylamine (IIId). Yield 55%, mp 63–65°C. ^{1}H NMR spectrum ($CDCl_3$), δ, ppm: 0.92 d (6H, *J* 6.3 Hz), 1.76 br.s (2H), 2.98 septet (1H, *J* 6.6 Hz), 7.18–7.23 m (2H), 7.30–7.35 m (4H), 7.54–7.57 m (4H). ^{13}C NMR spectrum ($CDCl_3$), δ, ppm: 18.1 (CH_3), 35.1 (CH), 64.1 (C), 126.4 (CH), 127.0 (CH), 128.5 (CH), 148.4 (C). Mass spectrum (electron impact), *m/z* (I_{rel}, %): 224 $[M - H]^+$ (1), 182 $[M - C_3H_7]^+$ (100), 148 $[M - C_6H_5]^+$ (5), 115 (9), 104 $[M - C_6H_5 - C_3H_8]^+$ (43), 90 (8), 77 (35), 43 (12). Found, %: C 85.10; H 8.52; N 6.39. $C_{16}H_{19}N$. Calculated, %: C 85.29; H 8.50; N 6.22.

1,1,1-Triphenylmethylamine (IIIe). Yield 55%, mp 101–102°C (100–102 °C [12]).

1,1-Bis(4-methylphenyl)propylamine hydrochloride (IIIf). To isolate the target compound the acidified reaction mixture was passed through a silica gel bed (eluent $CHCl_3$–MeOH, 16:1). Yield 65%, mp 195–196°C. ^{1}H NMR spectrum ($CDCl_3$), δ, ppm: 0.83 t (3H, *J* 7.3 Hz), 2.36 s (6H), 2.49 q (2H, *J* 7.3 Hz), 7.10 d (4H, *J* 8.0 Hz), 7.26 d (4H, *J* 8.0 Hz), 9.52 br.s (3H). ^{13}C NMR spectrum ($CDCl_3$), δ, ppm: 8.9 (CH_3), 21.5 (CH_3), 32.5 (CH_2), 66.1 (C), 127.6 (CH), 129.5 (CH), 137.7 (C), 138.3 (C). Mass spectrum (electrospray), *m/z* (I_{rel}, %): 223 $[M - Cl - NH_3]^+$ (100). Found, %: C 74.17; H 8.07; N 5.06. $C_{17}H_{21}N$·HCl. Calculated, %: C 74.03; H 8.04; N 5.08.

α,α-Bis[3-(trifluoromethyl)phenyl]benzylamine hydrochloride (IIIg). Yield 25%, mp 165–168°C. ^{1}H NMR spectrum (DMSO-d_6–CCl_4), δ, ppm: 7.24–7.45 m (13H), 10.48 br.s (3H). ^{13}C (DMSO-d_6–CCl_4), δ, ppm: 68.5 (C), 124.5 q (C, *J* 273 Hz), 125.8 (CH), 126 (CH), 129.1 (CH), 129.3 (CH), 129.5 (CH), 130.7 q (C, *J* 31.9 Hz), 130.1 (CH), 133.2 (CH), 143.1 (C), 141.2 (C). Mass spectrum (electron impact), *m/z* (I_{rel}, %): 395 $[M - HCl - H]^+$ (1), 318 $[M - HCl - C_6H_5]^+$ (20), 250 $[M - HCl - C_7H_4F_3]^+$ (55), 182 (100), 172 (20), 145 (12), 104 (30), 77 (22), 51 (5). Found, %: C 58.59; H 3.69; N 3.47. $C_{21}H_{15}NF_6$·HCl. Calculated, %: C 58.41; H 3.73; N 3.24.

1,1-Dibenzylethylamine hydrochloride (IIIh). Yield 40%, mp 215–216°C. ^{1}H NMR spectrum (DMSO-d_6), δ, ppm: 1.44 s (3H), 2.90 d (2H, *J* 13.4 Hz), 3.10 d (2H, *J* 13.4 Hz), 7.25–7.36 m (10H), 8.26 br.s (3H). ^{13}C NMR spectrum (DMSO-d_6), δ, ppm: 22.1 (CH_3), 43.6 (CH_2), 56.1 (C), 126.8 (CH), 128.2 (CH), 130.8 (CH), 134.9 (C). Mass spectrum (electrospray), *m/z* (I_{rel}, %): 487 $[2M - Cl]^+$ (28), 226 $[M - Cl]^+$ (100). Found, %: C 73.17; H 7.54; N 5.22. $C_{16}H_{19}N$·HCl. Calculated, %: C 73.41; H 7.70; N 5.35.

1,1-Dibenzylpropylamine hydrochloride (IIIi). On acidifying the combined organic fractions hydrochloride precipitated, insoluble both in water and organic solvents. The precipitate was filtered off and was not further purified. Yield 72%, mp >250°C. ^{1}H NMR spectrum (DMSO-d_6–CCl_4), δ, ppm: 1.06 t (3H, *J* 7.3 Hz), 1.49 q (2H, *J* 7.3 Hz), 2.84 d (2H, *J* 13.8 Hz), 3.18 d (2H, *J* 13.8 Hz), 7.24–7.34 m (10H), 8.32 br.s (3H). ^{13}C NMR spectrum (DMSO-d_6), δ, ppm: 7.6 (CH_3), 26.8 (CH_2), 41.2 (CH_2), 58.7 (C), 126.9 (CH), 128.4 (CH), 130.9 (CH), 134.9 (C). Mass spectrum (electrospray), *m/z* (I_{rel}, %): 1067 $[4M - Cl]^+$ (46), 515 $[2M - Cl]^+$ (18), 479 $[2M - HCl - Cl]^+$ (10), 240 $[M - Cl]^+$ (100). Found, %: C 74.23; H 8.14; N 5.19. $C_{17}H_{21}N$·HCl. Calculated, %: C 74.03; H 8.04; N 5.08.

1,1-Dibenzylbutylamine hydrochloride (IIIj). Yield 67%, mp 196–198°C. ^{1}H NMR spectrum (DMSO-d_6), δ, ppm: 0.85 t (3H, *J* 6.9 Hz), 1.36–1.41 m (2H), 1.46–1.55 m (2H), 2.90 d (2H, *J* 13.7 Hz), 3.07 d (2H, *J* 13.7 Hz), 7.25–7.36 m (10H), 8.26 br.s (3H). ^{13}C NMR spectrum (DMSO-d_6), δ, ppm: 13.9 (CH_3), 15.8 (CH_2), 36.4 (CH_2), 41.6 (CH_2), 58.5 (C), 126.8 (CH), 128.2 (CH), 130.8 (CH), 134.9 (C). Mass spectrum (electrospray), *m/z* (I_{rel}, %): 1121 $[4M - Cl]^+$ (64), 543 $[2M -$

Cl]$^+$ (20), 254 [M – Cl]$^+$ (100). Found, %: C 74.25; H 8.02; N 4.59. $C_{18}H_{23}N$·HCl. Calculated, %: C 74.59; H 8.35; N 4.83.

1,1-Dibenzyl-2-methylpropylamine hydrochloride (IIIk). Yield 28%, mp 193–194°C. ^{1}H NMR spectrum (DMSO-d_6), δ, ppm: 1.05 d (6H, J 6.7 Hz), 1.78 septet (1H, J 6.7 Hz), 2.76 d (2H, J 14.2 Hz), 3.09 d (2H, J 14.3 Hz), 7.24–7.34 m (6H), 7.45–7.47 m (4H), 8.16 br.s (3H). ^{13}C NMR spectrum (DMSO-d_6), δ, ppm: 17.1 (CH_3), 31.5 (CH), 38.4 (CH_2), 61.4 (C), 126.7 (CH), 128.1 (CH), 131.0 (CH), 134.7 (C). Mass spectrum (electrospray), m/z (I_{rel}, %): 1121 [4M – Cl]$^+$ (100), 254 [M – Cl]$^+$ (60). Found, %: C 74.23; H 8.27; N 5.10. $C_{18}H_{23}N$·HCl. Calculated, %: C 74.59; H 8.35; N 4.83.

1,1-Dibenzyl-3-methoxypropylamine hydrochloride (IIIl). Yield 35%, mp 192–195°C. ^{1}H NMR spectrum (DMSO-d_6), δ, ppm: 1.71 t (2H, J 6.9 Hz), 2.92 d (2H, J 13.8 Hz), 3.06 d (2H, J 13.8 Hz), 3.21 s (3H), 3.59 t (2H, J 6.9 Hz), 7.25–7.38 m (10H), 8.26 br.s (3H). ^{13}C NMR spectrum (DMSO-d_6), δ, ppm: 33.6 (CH_2), 41.6 (CH_2), 57.4 (C), 57.8 (CH_3), 66.7 (CH_2), 126.6 (CH), 128.0 (CH), 130.7 (CH), 134.4 (C). Mass spectrum (electrospray), m/z (I_{rel}, %): 1189 [4M – Cl + 4H]$^+$ (51), 1188 [4M – Cl + 3H]$^+$ (53), 1187 [4M – Cl + 2H]$^+$ (100), 1185 [4M – Cl]$^+$ (93), 270 [M – Cl]$^+$ (57). Found, %: C 70.43; H 7.68; N 4.31. $C_{18}H_{23}NO$·HCl. Calculated, %: C 70.69; H 7.91; N 4.58.

1-Benzyl-1,2-diphenylethylamine hydrochloride (IIIm). Yield 64%, mp 105–107°C. ^{1}H NMR spectrum (DMSO-d_6), δ, ppm: 3.39 d (2H, J 13.6 Hz), 3.51 d (2H, J 13.9 Hz), 7.05–7.08 m (4H), 7.15–7.18 m (6H), 7.30–7.40 m (5H), 8.81 br.s (3H). ^{13}C NMR spectrum (DMSO-d_6), δ, ppm: 44.6 (CH_2), 62.9 (C), 126.4 (CH), 126.9 (CH), 127.6 (CH), 127.8 (CH), 127.9 (CH), 131.0 (CH), 134.3 (C), 138.4 (C). Mass spectrum (electrospray), m/z (I_{rel}, %): 288 [M – Cl]$^+$ (100). Found, %: C 78.15; H 6.63; N 4.51. $C_{21}H_{21}N$·HCl. Calculated, %: C 77.88; H 6.85; N 4.32.

α,α-Dimethylbenzylamine hydrochloride (IIIn). Yield 44%, mp 238–239°C (240–241°C [13]).

1,1,2-Trimethylpropylamine hydrochloride (IIIo). Yield 27%, mp >250°C (292°C [14]) ^{1}H NMR spectrum (DMSO-d_6), δ, ppm: 0.88 d (6H, J 6 Hz), 1.17 s (6H), 1.86 septet (1H, J 6 Hz), 8.14 br.s (3H). ^{13}C NMR spectrum (DMSO-d_6), δ, ppm: 16.9 (CH_3), 22.2 (CH_3), 35.0 (CH), 56.2 (C).

α,α-Diethylbenzylamine hydrochloride (IIIp). Yield 60%, mp 225–230°C (253°C [15]). ^{1}H NMR spectrum (DMSO-d_6), δ, ppm: 0.75 t (6H, J 9 Hz), 1.92–2.88 m (4H), 7.29–7.52 m (5H), 8.75 br.s (3H). ^{13}C NMR spectrum (DMSO-d_6), δ, ppm: 7.8 (CH_3), 31.4 (CH_2), 62.5 (C), 125.9 (CH), 127.4 (CH), 128.44 (CH), 139.4 (C).

1-Methyl-1-phenylpropylamine hydrochloride (IIIq). To a solution of 2.2 g (40 mmol) of propionitrile (**Ia**) in diethyl ether was added at room temperature while vigorous stirring 40 mmol of 3 M solution of MeMgCl (**IIe**) in THF, after 30 min was added in succession 11.64 g (41 mmol) of (i-PrO)$_4$Ti, and 80 mmol of 1.46 M solution of PhMgBr (**IIa**) in Et_2O. The reaction mixture was stirred for 24 h and worked up by the general procedure. The obtained hydrochloride was purified by column chromatography on silica gel (eluent $CHCl_3$–MeOH, 4:1). Yield 30%, mp 239–240°C (242–243°C [15]).

1-Phenyl-1-(2-furyl)butylamine hydrochloride (IIIr). To a solution of 1.7 g (25 mmol) of furan in 10 ml of THF was added at –10°C while stirring 25 mmol of 2.9 M solution of BuLi in hexane, and the stirring was continued at room temperature for 4 h. To a solution of 0.69 g (10 mmol) of butyronitrile (**If**) in 100 ml of diethyl ether was added at stirring 10 mmol of 1.1 M solution of PhMgBr (**IIa**) in Et_2O. After 30 min 2.84 g (10 mmol) of (i-PrO)$_4$Ti was added and afterwards a solution of 2-furyllithium (**IIg**). The reaction mixture was stirred at room temperature for 24 h more and then subjected to common workup. The obtained hydrochloride was purified by column chromatography on silica gel (eluent $CHCl_3$–MeOH 30:1). Yield 25%, mp 158–160°C. ^{1}H NMR spectrum (DMSO-d_6–CCl_4), δ, ppm: 0.93 t (3H, J 7.2 Hz), 1.15–1.45 m (2H), 2.25–2.42 m (2H), 6.46 m (1H), 6.57–6.58 m (1H), 7.29–7.37 m (5H), 7.55 m (1H), 9.47 br.s (3H). ^{13}C NMR spectrum (DMSO-d_6–CCl_4), δ, ppm: 14.7 (CH_3), 17.7 (CH_2), 41.1 (CH_2), 61.6 (C), 109.9 (CH), 111.2 (CH), 127.2 (CH), 128.6 (CH), 128.9 (CH), 130.5 (C), 143.4 (CH), 153.7 (C). Mass spectrum (electrospray), m/z (I_{rel}, %): 970 [4M – Cl]$^+$ (16), 199 [M – Cl – NH_3]$^+$ (100). Found, %: C 66.69; H 7.31; N 5.26. $C_{14}H_{17}NO$·HCl. Calculated, %: C 66.79; H 7.21; N 5.56.

1-(2-Picolyl)-1-phenylbutylamine hydrochloride (IIIs). To a solution of 2.33 g (25 mmol) 2-picoline in 10 ml of THF was added at –20°C 25 mmol of 2.9 M solution of BuLi in hexane, and the stirring was continued at room temperature for 1 h. To a solution of 0.69 g (10 mmol) of butyronitrile (**If**) in 100 ml of diethyl ether was added at stirring 10 mmol of 1.1 M solution of PhMgBr (**IIa**) in Et_2O. After 30 min 2.84 g (10 mmol) of

(i-PrO)$_4$Ti was added and afterwards a solution of 2-picolyllithium (**IIh**). The reaction mixture was stirred at room temperature for 24 h more and then subjected to common workup. The obtained hydrochloride was purified by column chromatography on silica gel (eluent $CHCl_3$–MeOH, 100:1). Yield 55%. ^{1}H NMR spectrum (DMSO-d_6), δ, ppm: 0.79 t (3H, J 7.3 Hz), 0.91–1.12 m (1H), 1.19–1.38 m (1H), 1.81–1.95 m (1H), 2.27–2.40 m (1H), 3.81 d (1H, J 14.1 Hz), 3.83 d (1H, J 14.2 Hz), 7.32–7.50 m (3H), 7.59 d (2H, J 9 Hz), 7.75–7.91 m (2H), 8.36 m (1H), 8.80 d (1H, J 6 Hz), 9.34 br.s (3H). ^{13}C NMR spectrum (DMSO-d_6), δ, ppm: 13.7 (CH_3), 16.1 (CH_2), 39.1 (CH_2), 42.9 (CH_2), 61.9 (C), 125.3 (CH), 125.6 (CH), 127.9 (CH), 128.6 (CH), 128.8 (CH), 138.9 (C), 142.7 (CH), 144.4 (CH), 150.5 (C). Mass spectrum (electrospray), m/z (I_{rel}, %): 241 [M – Cl]$^+$ (100).

2-Methyl-1-(2-thienyl)-1-phenylpropylamine (IIIt). To a solution of 4.08 g (25 mmol) of 2-bromo thiophene was added at –50°C while stirring 25 mmol of 2.5 M solution of BuLi in hexane, and the stirring at –60°C continued for 10 min. To a solution of 0.69 g (10 mmol) of isobutyronitrile (**Id**) in 100 ml diethyl ether was added at stirring 10 mmol of 1.1 M solution of PhMgBr (**IIa**) in Et_2O. After 30 min 2.84 g (10 mmol) of (i-PrO)$_4$Ti was added and afterwards a solution of 2-thienyllithium (**IIi**). The reaction mixture was stirred at room temperature for 24 h more and then subjected to common workup. The obtained hydrochloride was purified by column chromatography on silica gel (eluent $CHCl_3$–MeOH, 100:1). Yield 30%. ^{1}H NMR spectrum ($CDCl_3$), δ, ppm: 1.00 d (3H, J 5.9 Hz), 1.09 d (3H, J 5.8 Hz), 3.97 m (1H), 7.89–7.97 m (1H), 7.21–7.35 m (5H), 7.37–7.40 m (1H), 7.52–7.61 m (1H), 9.44 br.s (3H). ^{13}C NMR spectrum ($CDCl_3$), δ, ppm: 18.2 (CH_3), 18.4 (CH_3), 36.7 (CH), 67.9 (C), 125.8 (CH), 126.7 (CH), 127.3 (CH), 128.1 (CH), 128.2 (CH), 128.3 (CH), 138.7 (C), 143.6 (C). Mass spectrum (electrospray), m/z (I_{rel}, %): 215 [M – Cl – NH_3]$^+$ (100).

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