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5-Methylenehexahydropyrrolo[1,2-*a*]imidazoles and 6-methyleneoctahydropyrrolo[1,2-*a*]pyrimidines in the reactions of 1-(alk-1-ynyl)-1-chlorocyclopropanes with lithium derivatives of 1,2- and 1,3-diaminoalkanes

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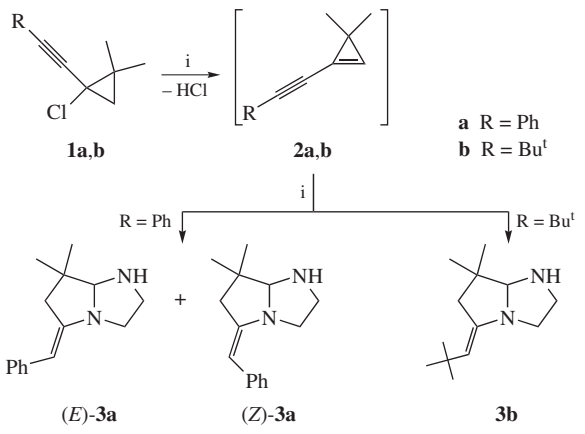
Unusual reactions of 1-(alk-1-ynyl)-1-chlorocyclopropanes with lithium derivatives of 1,2-diaminoethane, 1,3-diaminopropane and 1-methylamino-3-aminopropane in THF at 20 °C give previously unknown 5-methylenehexahydropyrrolo[1,2-*a*]imidazoles and 6-methyleneoctahydropyrrolo[1,2-*a*]pyrimidines with up to 60% yields.

Previously, we found that the treatment of 1-(alk-1-ynyl)-1-chlorocyclopropanes[1,2] with lithium *N*,*N*-dialkylamides yields alkynyl(dialkylamino)cyclopropanes,[3] whereas in similar reactions with lithium monoalkylamides, depending on the nature of substituent at the triple bond in starting alkynylchlorocyclopropanes **1**, conjugated iminocyclopropenes or substituted propa-1,2-dienes[4] were obtained. According to the published data,[3,4] these reactions proceed *via* intermediate formation of conjugated alkynylcyclopropenes **2**, which are characterized by the combination of two highly reactive fragments, a triple bond and an unsaturated three-membered ring. Therefore, it could be expected that by the interaction of alkynylchlorocyclopropanes **1** with lithium derivatives of 1,2- and 1,3-diaminoalkanes the latter due to the presence of two amino groups would consequently add to both unsaturated fragments of intermediate alkynylcyclopropenes **2** with formation of nitrogen-containing heterocyclic systems.

We found that the interaction of 1-chloro-2,2-dimethyl-1-phenylethynylcyclopropane **1a** and 1-chloro-2,2-dimethyl-1-(3,3-dimethylbut-1-ynyl)chlorocyclopropane **1b** with a four-fold excess of lithium (2-aminoethyl)amide in THF at 20 °C after aqueous workup gives previously unknown 5-methylenehexahydropyrrolo[1,2-*a*]imidazoles **3a**,**b**† in 60 and 35% yields, respectively. Compound **3a** is formed as a mixture of *E*- and *Z*-isomers in a ratio of 4:1, whereas **3b** with its bulky *tert*-butyl substituent, is obtained exclusively as the *E*-isomer (Scheme 1).



Scheme 1 *Reagents and conditions*: i, $LiNH(CH_2)_2NH_2$, THF, 20 °C, followed by treatment with H_2O.

Under the same conditions, the reaction of cyclopropane **1a** with lithium (3-aminopropyl)amide gives 8,8-dimethyl-6-(*E*)-phenylmethylideneoctahydropyrrolo[1,2-*a*]pyrimidine **4**‡ in 50% yield. The lithium derivative of 1-methylamino-3-aminopropane reacts with alkynylchlorocyclopropane **1a** unselectively.

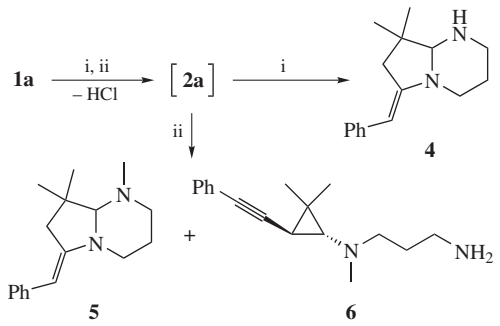
† Structures of all new compounds have been proved by ^1H and ^{13}C NMR spectroscopy. Spectra were recorded for solutions in $CDCl_3$ on Bruker AC-200p and Bruker AM-300 spectrometers (200 and 300 MHz for ^1H, 50 and 75 MHz for ^{13}C), using tetramethylsilane as an internal standard. Identification of *E*- and *Z*-isomers of compounds **3**–**5** was based on 2D-NOESY experiments.

General procedure for reactions of 1-(alk-1-ynyl)-1-chlorocyclopropanes **1a**,**b** *with lithium derivatives of diaminoalkanes.* A 1.6 M solution of BuLi in hexane (5 ml, 8 mmol) was added to the solution of corresponding diaminoalkane (10 mmol) in 15 ml of anhydrous THF, at 0 °C. Alkynylchlorocyclopropane **1a**,**b** (2 mmol) was added to the resulting mixture followed by stirring at room temperature for 2 h. After that reaction mixture was quenched with water and extracted with diethyl ether; the organic layer was washed three times with water and dried over anhydrous Na_2SO_4. After removal of the solvent, products **3a**,**b**, **4** or a mixture of compounds **5** and **6** were isolated by passage through a silica gel layer in hexane–diethyl ether as an eluent.

*7,7-Dimethyl-5-phenylmeth-(*E*)-ylenehexahydropyrrolo[1,2-*a*]imidazole* (*E*)-**3a**: ^1H NMR ($CDCl_3$) δ: 0.92 (s, 3H, Me), 1.20 (s, 3H, Me), 1.35 (br. s, 1H, NH), 2.76 (dd, 1H, C*H*HC=, *J* 15 Hz, *J* 1.3 Hz), 2.81 (dd, 1H, CH*H*C=, *J* 15 Hz, *J* 1.9 Hz), 3.1–3.22 (m, 4H, NCH_2CH_2N), 4.29 (s, 1H, CH), 5.36 (dd, 1H, PhC*H*=, *J* 1.9 Hz, *J* 1.3 Hz), 7.02 (br. t, 1H, *p*-H, *J* 7 Hz), 7.14 (br. d, 2H, *o*-H, *J* 7 Hz), 7.25 (br. t, 2H, *m*-H, *J* 7 Hz). ^{13}C NMR ($CDCl_3$) δ: 21.5 (Me), 26.4 (Me), 39.5 (*C*Me_2), 46.3, 47.9, 48.7 (3CH_2), 87.8 (NCHN), 96.7 (Ph*C*H=), 122.9, 126.4, 128.0 (Ph), 139.5 (C-1, Ph), 149.8 (PhCH=*C*).

*7,7-Dimethyl-5-phenylmeth-(*Z*)-ylenehexahydropyrrolo[1,2-*a*]imidazole* (*Z*)-**3a**: ^1H NMR ($CDCl_3$) δ: 0.99 (s, 3H, Me), 1.17 (s, 3H, Me), 1.35 (br. s, 1H, NH), 2.46 (dd, 1H, C*H*HC=, *J* 15.1 Hz, *J* 1.5 Hz), 2.52 (dd, 1H, CH*H*C=, *J* 15.1 Hz, *J* 1.4 Hz), 3.1–3.3 (m, 4H, NCH_2CH_2N), 4.29 (s, 1H, CH), 5.25 (dd, 1H, PhC*H*=, *J* 1.5 Hz, *J* 1.4 Hz), 7.0–7.35 (m, 5H, Ph). ^{13}C NMR ($CDCl_3$) δ: 21.3 (Me), 26.2 (Me), 38.4 (*C*Me_2), 46.6, 47.6, 52.2 (3CH_2), 90.3 (NCHN), 96.7 (Ph*C*H=), 123.2, 127.3, 127.6 (Ph), 138.5 (C-1, Ph), 149.7 (PhCH=*C*).

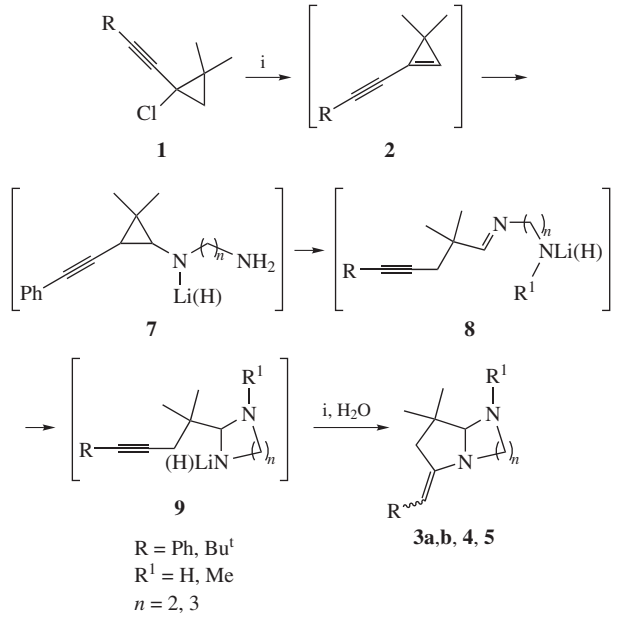
*7,7-Dimethyl-5-[2,2-dimethylprop-(*E*)-ylene]hexahydropyrrolo[1,2-*a*]-imidazole* **3b**: ^1H NMR ($CDCl_3$) δ: 0.91 (s, 9H, Bu^t), 1.05 (s, 6H, Me), 1.11 (s, 6H, Me), 1.82 (s, 2H, CH_2C=), 2.75–3.10 (m, 4H, NCH_2CH_2N), 3.89 (s, 1H, CH), 4.31 (s, 1H, Bu^{t}C*H*=). ^{13}C NMR ($CDCl_3$) δ: 19.7 (Me), 29.6 (Me), 29.9 (3Me), 32.2 (*C*Me_3), 41.5, 45.9, 48.1 (3CH_2), 42.1 (*C*Me_2), 90.2 (NCHN), 112.9 (Bu^t*C*H=), 127.1 (Bu^{t}CH=*C*). Found (%): C, 74.04; H, 11.52; N, 14.31. Calc. for $C_{12}H_{22}N_2$ (%): C, 74.17; H, 11.41; N, 14.42.



Scheme 2 *Reagents and conditions*: i, [$H_2N(CH_2)_3NHMe$ + BuLi], THF, 20 °C, followed by treatment with H_2O; ii, [$H_2N(CH_2)_3NHMe$ + BuLi], THF, 20 °C, followed by treatment with H_2O.

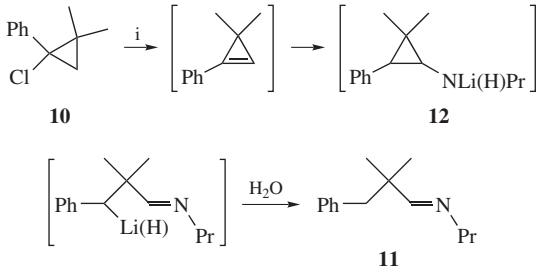
Due to the concurrence of primary and secondary amino groups, the formation of a mixture of corresponding *N*-methyl substituted pyrimidine **5**‡ (*E*-isomer) and aminocyclopropane **6**‡ in a 1.5:1 ratio is observed (Scheme 2).

Most likely, the reaction proceeds as depicted in Scheme 3. At first, starting cyclopropanes **1**, as was previously shown,[3,4] under the action lithium amides, undergo elimination of HCl with the formation of conjugated cyclopropenes **2**. Further, addition of an amide ion to the double bond of the cyclopropene ring takes place giving intermediate **7**, which isomerizes with opening of the three-membered ring into acyclic imine **8**. Under the reaction conditions the latter, due to the presence of an amino group, undergoes a cascade cyclization with consecutive participation of the C=N[5] and C≡C bonds *via* intermediate formation of monocyclic structure **9** (Scheme 3).



Scheme 3 *Reagents and conditions*: i, $LiNH(CH_2)_nNHR^1$, THF, 20 °C.

The possibility of previously unknown isomerization of secondary cyclopropylamines into acyclic imines of type **8**, which is a key step of the proposed mechanism, was demonstrated for the reaction of 1-chloro-2,2-dimethyl-1-phenylcyclopropane **10** with an excess of lithium propylamide. In this case, imine **11**,‡ arising obviously *via* the intermediate formation of aminocyclopropane **12**, was obtained in 52% yield (Scheme 4).



Scheme 4 *Reagents and conditions*: i, PrNHLi, $PrNH_2$, THF, 60 °C.

Thus, an original approach to previously unknown 5-methylenepyrrolo[1,2-*a*]imidazoles and 6-methyleneoctahydropyrrolo[1,2-*a*]pyrimidines, based on the reaction of 1-(alk-1-ynyl)-1-chlorocyclopropanes with lithium derivatives of 1,2- and 1,3-diaminoalkanes, has been developed.

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‡ *8,8-Dimethyl-6-phenylmeth-*(E)*-yleneoctahydropyrrolo[1,2-*a*]pyrimidine* **4**: ^{1}H NMR ($CDCl_3$) δ: 1.02 (s, 3H, Me), 1.19 (s, 3H, Me), 1.40 (br. s, 1H, NH), 1.60–1.72 (m, 1H, $NCH_2CH_2CH_2NH$), 2.55 (dd, 1H, C*H*HC=, *J* 16.3 Hz, *J* 2.0 Hz), 2.65–2.90 (m, 2H, $NCH_2CH_2CH_2NH$), 2.73 (dd, 1H, CH*H*C=, *J* 16.3 Hz, *J* 1.6 Hz), 3.21–3.35 [m, 1H, $NCH_2(CH_2)_2NH$], 3.50 (s, 1H, CH), 3.65–3.78 [m, 1H, $NCH_2(CH_2)_2NH$], 5.21 (dd, 1H, PhC*H*=, *J* 2.0 Hz, *J* 1.6 Hz), 6.99 (br. t, 1H, *p*-H, *J* 7 Hz). 7.19 (br. d, 2H, *o*-H, *J* 7 Hz), 7.25 (br. t, 2H, *m*-H, *J* 7 Hz). ^{13}C NMR ($CDCl_3$) δ: 21.8 (Me), 25.2 ($CH_2CH_2CH_2$), 25.8 (Me), 36.7 (CMe_2), 43.9, 44.0, 45.0 ($3CH_2$), 82.4 (NCHN), 93.7 (PhCH=), 122.8, 126.1, 128.1 (Ph), 139.7 (C-1, Ph), 146.6 (PhCH=*C*). Found (%): C, 78.56; H, 8.52; N, 12.94. Calc. for $C_{14}H_{18}N_2$ (%): C, 78,46; H, 8.47; N, 13.07.

1,1,8-Trimethyl-6-phenylmeth-(E)*-yleneoctahydropyrrolo[1,2-*a*]pyrimidine* **5**: ^{1}H NMR ($CDCl_3$) δ: 1.11 (s, 3H, Me), 1.27 (s, 3H, Me), 1.60–1.72 (m, 2H, $NCH_2CH_2CH_2NMe$), 2.29 (s, 3H, NMe), 2.53 (dd, 1H, C*H*HC=, *J* 16.3 Hz, *J* 2.1 Hz), 2.50–2.62 [m, 2H, $N(CH_2)_2CH_2NMe$], 2.72 (dd, 1H, CH_2C=, *J* 16.3 Hz, *J* 1.6 Hz), 2.75 (s, 1H, CH), 2.87–2.99 [m, 1H, NC*H*H$(CH_2)_2$NMe], 3.52–3.64 [m, 1H, NCH*H*$(CH_2)_2$NMe], 5.19 (dd, 1H, PhCH=, *J* 2.1 Hz, *J* 1.6 Hz), 6.98 (br. t, 1H, *p*-H, *J* 7 Hz), 7.19 (br. d, 2H, *o*-H, *J* 7 Hz), 7.24 (br. t, 2H, *m*-H, *J* 7 Hz). ^{13}C NMR ($CDCl_3$) δ: 22.4 (Me), 24.0 ($CH_2CH_2CH_2$), 27.9 (Me), 38.2 (CMe_2), 42.2 (NMe), 42.8, 45.9, 56.2 ($3CH_2$), 89.8, 93.0 (NCHN, PhCH=), 122.7, 126.2, 128.1 (Ph), 139.9 (C-1, Ph), 146.5 (PhCH=*C*).

*(*E*)-1-[3-Aminopropyl(methyl)amino]-2,2-dimethyl-3-phenylethynylcyclopropane* **6**: ^{1}H NMR ($CDCl_3$) δ: 1.09 (d, 1H, C≡CCH, *cyclo*-C_3H_2, *J* 3.8 Hz), 1.21 (s, 3H, Me), 1.22 (s, 3H, Me), 1.35 (br. s, 2H, NH_2), 1.6–1.72 (m, 1H, $NCH_2CH_2CH_2NH_2$), 1.67 (d, 1H, NCH, *cyclo*-C_3H_2, *J* 3.8 Hz), 1.75–2.15 (m, 4H, $NCH_2CH_2CH_2N$), 2.25 (s, 3H, NMe), 7.1–7.4 (m, 5H, Ph). ^{13}C NMR ($CDCl_3$) δ: 19.3, 21.5, 22.0 (2Me, C≡C*C*H), 26.8 (CMe_2), 31.1 ($NCH_2CH_2CH_2N$), 40.6 [$N(CH_2)_2CH_2NH_2$], 41.8 (NMe), 55.6 ($MeNCH_2$), 59.9 (CHN), 78.8, 90.1 (C≡C), 124.2 (C-1, Ph), 127.2, 128.1, 131.4 (Ph).

2,2-Dimethyl-3-phenylpropenylidenepropylamine **11**: ^{1}H NMR ($CDCl_3$) δ: 0.84 (t, 3H, *Me*CH_2, *J* 7.4 Hz), 1.03 (s, 6H, 2Me), 1.50–1.71 (m, 2H, MeCH_2), 2.70 (s, 2H, PhCH_2), 3.32 (br. t, 2H, NCH_2, *J* 6.9 Hz), 7.05–7.30 (m, 5H, Ph), 7.54 (br. s, 1H, C*H*=NPr). ^{13}C NMR ($CDCl_3$) δ: 11.6 (*Me*CH_2), 23.9 (Me*C*H_2), 24.7 (2Me), 39.9 (CMe_2), 46.4 (*C*H_2Ph), 63.2 (NCH_2), 126.0, 127.4, 130.5 (Ph), 138.1 (C-1, Ph), 171.2 (*C*H=NPr). Found (%): C, 82.52; H, 10.33; N, 7.05. Calc. for $C_{14}H_{21}N$ (%): C, 82.70; H, 10.41; N, 6.89.