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N-Lithio-N,N′,N″,N″-tetramethyldiethylenetriamine and N′-Lithio-N,N,N″,N″-tetramethyldiethylenetriamine; Oxidative Coupling of Aminomethyllithium Derivatives

Hendrikus Luitjes [a], Marius Schakel [a] & Gerhard W. Klumpp [a]
[a] Scheikundig Laboratorium, Vrije Universiteit, De Boelelaan 1083, 1081 HV, Amsterdam, The Netherlands

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N-LITHIO-*N,N',N'',N''*-TETRAMETHYLDIETHYLENETRIAMINE AND *N'*-LITHIO-*N,N,N'',N''*-TETRAMETHYLDIETHYLENETRIAMINE; OXIDATIVE COUPLING OF AMINOMETHYLLITHIUM DERIVATIVES

Hendrikus Luitjes, Marius Schakel, Gerhard W. Klumpp*

Scheikundig Laboratorium Vrije Universiteit,
De Boelelaan 1083, 1081 HV Amsterdam,The Netherlands

ABSTRACT: *N*-lithio-*N,N',N",N"*-tetramethyldiethylenetriamine (**I**-Li) is formed from 2,5,8,11-tetramethyl-2,5,8,11-tetraazadodecane (**III**) or from 2,5,8,11,14,17-hexamethyl-2,5,8,11,14,17-hexaazaoctadecane (**IV**) with *n*-BuLi or *sec*-BuLi, respectively, its isomer *N'*-lithio-*N,N,N",N"*,-tetramethyldiethylene-triamine (**II**-Li) from tris(2-dimethylaminoethyl)amine (**V**) with *n*-BuLi. **IV** results from treatment of *N*-lithiomethyl-*N,N',N",N"*-tetramethyldiethylenetriamine (PMDTA-Li) with 1,2-dibromoethane.

Linear and cyclic (tertiary) polyamines are of great interest in chemistry and biochemistry as selective complexation agents for many cations.[1] By complexation of lithium, they activate organolithiums to function as potent polymerization catalysts[2] and metalation agents.[3] Studies of the properties imbued by complexation are advantageously carried out with compounds containing the C-Li and tertiary polyamine moieties within the same molecule.[4] Molecules containing a suitably placed polyamine group can react with organolithium reagents in modes otherwise not observed.[5]

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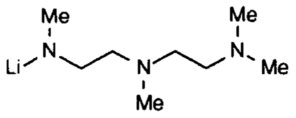
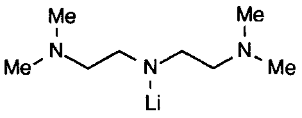
* To whom correspondence should be addressed

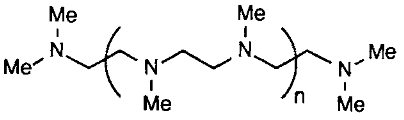
Tertiary polyamines or compounds containing tertiary polyamine groups may be prepared *via* the corresponding secondary polyamines, following well-described[6] routes for the assemblage of small building blocks and a final polyalkylation step. Problems with selectivity can arise in such an approach. We now report the easy preparation of the lithium amides **I**-Li and **II**-Li indicated in the title. By reaction with a suitable electrophile they permit the introduction of the moieties **I** or **II**, respectively, into a target molecule. Also reported is the preparation of the tertiary polyamine **IV** from two identical synthons.



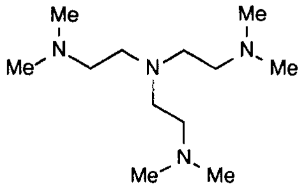
I-Li



II-Li



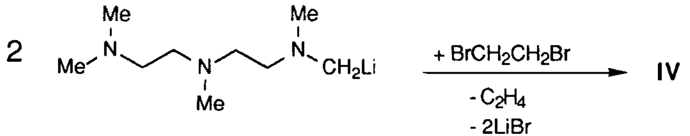
III : n = 1
IV : n = 2



V

I-Li and **II**-Li are formed when the polyamines **III** or **IV** and **V**, respectively, are treated with an alkyllithium (eq. 1-3). Of the co-products, dimethylvinylamine (eq. 1, 3), which, under the conditions of reaction, will be lithiated[5] was evidenced in the reaction mixtures by ^{13}C nmr signals at 142 and 76

III + *n*-BuLi → BuH + $Me_2NCH=CH_2$ + **I**-Li (1)
IV + 2 *sec*-BuLi → 2 BuH + HC≡CH + 2 **I**-Li (2)
V + *n*-BuLi → BuH + $Me_2NCH=CH_2$ +**II**-Li (3)



PMDTA-Li

(4)

ppm,[7] acetylene (eq. 2) was not proven but its formation is reasonable. **IV** was obtained by oxidative coupling of *N*-lithiomethyl-*N,N',N",N"*-tetramethyldiethylenetriamine (PMDTA-Li)[8] with 1,2-dibromoethane. (eq. 4).

Experimental

N,N,N',N",N"-pentamethyldiethylenetriamine (PMDTA), tris(2-amino-ethyl)amine and triethylenetetramine are commercially available and were used without purification. The butyllithiums used are also commercially available (1.6 M *n*-BuLi in hexane and 1.3 M *sec*-BuLi in cyclopentane). The N-methylations of triethylenetetramine and tris(2-aminoethyl)amine were performed by a literature procedure[9] and yielded the compounds **III** and **V**, respectively. *n*-Pentane was distilled from $LiAlH_4$ and the reactions were carried out in an argon atmosphere in dry glass equipment. ^1H- and ^{13}C-NMR spectra were recorded in $CDCl_3$ at 200 and 50 MHz. respectively.

General Procedure for N-dealkylation

To solutions of amines **III**-**V** (10 mmol) in pentane (40 ml) at -78 °C butyllithium was added dropwise (see Table). After addition the reaction mixture was stirred onehour at 0 °C followed by one hour at room temperature. Quenching with aqueous NaOH (5M, 20 ml), extraction with dichloromethane (3x 50 ml), drying over $MgSO_4$, and short path destillation (75 mm, bath: 95°C) gave **I**-H and **II**-H as colourless oils (85-90 %).

N,N,N',N"-tetramethyldiethylenetriamine (I-H)

^1H NMR (δ, ppm): 2.62 (2H, t, J 5.5 Hz, CH_2), 2.5-2.3 (6H, m, CH_2), 2.38 (3H, s, CH_3), 2.18 (3H, s, CH_3), 2.17 (6H, s, CH_3); ^{13}C NMR (δ, ppm): 57.19 (1CH_2), 56.82 (1CH_2), 55.81 (1CH_2), 49.17 (1CH_2), 45.53 (2CH_3), 42.72 (1CH_3), 36.06 (1CH_3).

Bis(2-dimethylaminoethyl)amine (II-H)

^1H NMR (δ, ppm): 2.65 (4H, t, J 6.3 Hz, CH_2), 1.98 (4H, t, J 6.3 Hz, CH_2), 2.16 (12H, s,CH_3); ^{13}C NMR (δ, ppm): 58.99 (2CH_2), 47.35 (2CH_2), 45.35 (4CH_3).

Table 1. Preparation of **I**-Li and **II**-Li.

Amine	RLi(equiv.	Product	Yield(%)[a]
III	*n*-BuLi (2.0)	**I**-Li	88
IV	*sec*-BuLi (2.0)	**I**-Li	85
V	*n*-BuLi (1.0)	**II**-Li	91

[a] Isolated yields of **I**-H and **II**-H after quench with water. Conversions were 100% by GC.

2,5,8,11,14,17-hexamethyl-2,5,8,11,14,17-hexaazaoctadecane (IV) To a stirred solution of PMDTA (30.5 mmol) in pentane (160 ml) at -78 °C wasadded dropwise a solution of *sec*-BuLi (30.5 mmol). After addition the reaction mixture was allowed to stir at room temperature for one hour. The reaction mixture was cooled to -78 °C and a solution of 1,2-dibromoethane (15 mmol) in pentane (20 ml) was added dropwise. After fifteen minutes, the cooling bath was removed, the reaction mixture was stirred for one hour at room temperature and was then quenched with an aqueous solution of NaOH (5M, 30 ml). After extraction with dichloromethane (3x 50 ml), the combined organic layers were dried over $MgSO_4$, filtered and concentrated in vacuo. Short path destillation ($2.3 \cdot 10^{-3}$ mm, bath: 75°C) gave **IV** as a colourless oil (3.8 g, 73 %). ^1H NMR (δ, ppm): 2.5-2.3 (8H, m, CH_2), 2.43 (12H, s, CH_2), 2.18 (12H, s, CH_3), 2.16 (12H, s, CH_3). ^{13}C NMR (δ, ppm): 57.23 (CH_2), 55.96 (CH_2), 55.80 ($2CH_2$), 45.71 ($6CH_3$), 42.88 ($4CH_3$).

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