Chemistry of Heterocyclic Compounds, Vol. 38, No. 4, 2002

CONDENSATION OF 2-PYRIDYL-METHYLLITHIUM NUCLEOPHILES AND PYRIDINE ELECTROPHILES AS A CONVENIENT SYNTHETIC ROUTE TO POLYDENTATE CHELATING N-DONOR LIGANDS*

N. Vedernikov[1], R. Miftakhov[1], S. V. Borisoglebski[1], K. G. Caulton[2], B. N. Solomonov[1]

Condensation of 2-pyridylmethyllithium or (6-methyl-2-pyridyl)methyllithium nucleophiles and pyridine, 2-picoline, or 4-tert-butylpyridine as electrophiles leads to new polydentate N-donor ligands, methyl-, tert-butyl-substituted tripyridinedimethanes, or to tripyridinedimethane itself, in good or high yields. Depending on the reagent ratio, solvent used, and reaction conditions, the corresponding intermediate dipyridinemethanes can be minor by-product or major products of the condensation. In contrast to 2-pyridylmethyllithium, lithiated 2-isopropylpyridine does not react with pyridine electrophiles. Vice versa, nucleophilic substitution at the C(2)-pyridine carbon of 2,2-bis(2-pyridyl)propane with 2-pyridylmethyllithium takes place to produce products of condensation of 2-isopropylpyridine and dipyridylmethyllithium. DFT calculations of the Gibbs free energies of reactions combined with pK_a values of the CH-acids involved help to explain the reactivity observed.

Keywords: 4-*tert*-butylpyridine, dipyridinemethanes, 2,6-lutidine, (6-methyl-2-pyridyl)methyllithium, 2-picoline, pyridine, 2-pyridylmethyllithium, tripyridinedimethanes, C–C bond cleavage, DFT calculations, condensation, Gibbs free energy of reaction, nucleophilic substitution.

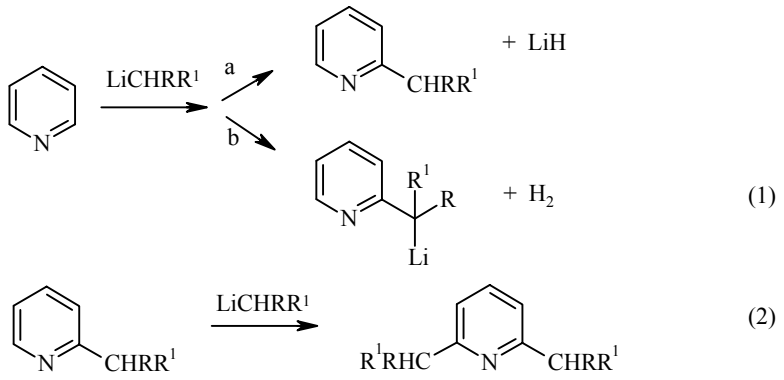
Ligands can play an extremely important role in determining the "face" of a transition metal atom in its complexes. So, chelating tridentate N-donor ligands and, first of all, facially chelating ones, turned out to be very effective in stabilizing alkylhydrido complexes of d^6 platinum metals [1-4]. Azaheterocycles are especially useful in this respect, in particular, owing to their resistance to oxidation and low basicity. Polypyridines [5] and derivatives of tris(2-pyridyl)methane [6] are the best known polydentate chelating ligands derived purely from pyridine, which have only limited coordination abilities and form correspondingly *mer*- (tri- and higher polypyridines) or *fac*(tris(2-pyridyl)methane ligands) chelates. Poly(2,6-pyridine)polymethanes (Scheme 1), which belong to other group of polypyridine ligands, are conformationally more flexible and therefore can be expected to be more variable in their coordination behavior. Unfortunately, till now they were much less accessible and rarely used ligands [7-13]. Here we report a convenient synthetic route to (substituted) tripyridinedimethanes and dipyridinemethanes, which can lead to extending the chemistry of this interesting

* Dedicated to M. G. Voronkov.

[1] Kazan State University, Kazan 420008, Russia; e-mail: ave@ksu.ru. [2] Department of Chemistry, Indiana University, Bloomington, IN 47405, USA; e-mail: caulton@indiana.edu. Translated from Khimiya Geterotsiklicheskikh Soedinenii, No. 4, pp. 471-481, April, 2002. Original article submitted July 6, 2001.

 0009-3122/02/3804-0406$27.00

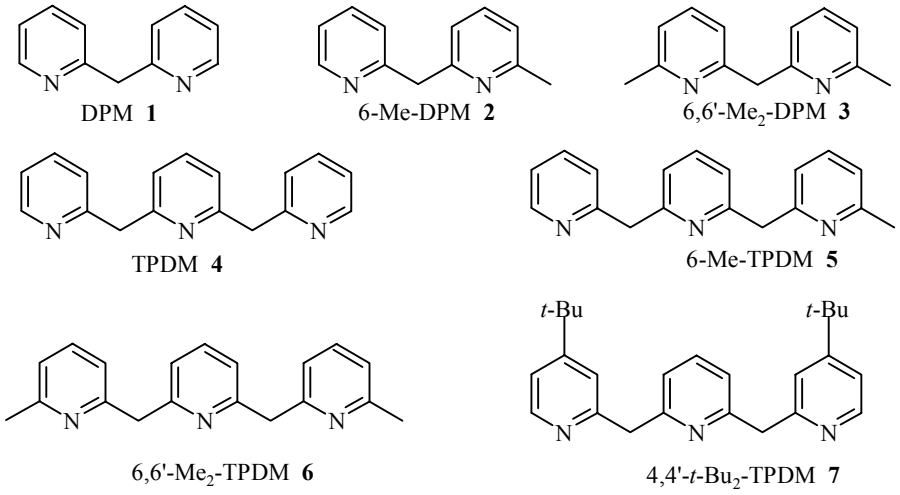
class of azaheteropolycycles. The synthetic method suggested in this work is based on a version of the Chichibabin reaction, which implies hydride nucleophilic substitution at the most electrophilic carbon atoms in position 2 or 6 of the pyridine ring with organyllithiums as nucleophiles and leads to 2-alkyl- or aryl- or 2,6-dialkyl- or diaryl-substituted pyridines [13]:



It is reasonable to expect that in the case of 2-pyridylmethyllithium (LiPic) or its analogs chosen as nucleophilic reagents ($LiCHRR^1$), this condensation could lead to dipyridinemethanes (Eq. (1), LiPic instead of $LiCHRR^1$) and further to tripyridinedimethanes (Eq. (2)). Indeed, some examples of such condensation of LiPic as a nucleophile and pyridine as electrophile leading to dipyridinemethane with 37% yield (DPM, Scheme 1) [14] or with 2-picoline leading to 6-methyl-2-pyridylpyridine (Me-DPM, Scheme 1) and 2-(6-methyl-2-pyridylmethyl)-6-(2-pyridylmethyl)pyridine (Me-TPDM, Scheme 1) [15] are known. No systematic study devoted to synthesis of ligands of the mentioned class has been reported yet.

Scheme 1

Representatives of dipyridylmethanes (dipyridinemethanes) and di(pyridylmethyl)pyridines (tripyridinedimethanes) synthesized

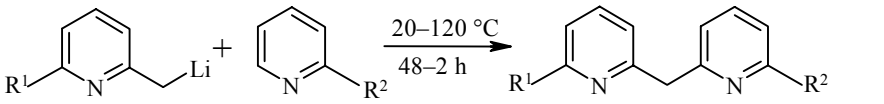


In this work condensation of pyridine and its easily available derivatives, 2-picoline, 4-*tert*-butylpyridine, and 2,6-lutidine, leading to seven poly-(2,6)-pyridinemethanes (Scheme 1) and three corresponding intermediate dipyridinemethanes has been studied. To simplify their notation we will use the

further abbreviations DPM for dipyridinemethane with substituent symbols indicated just before this abbreviation and the notation TPDM for tripyridinedimethane also with foregoing indication of symbols of substituents at two terminal pyridine rings.

RESULTS AND DISCUSSION

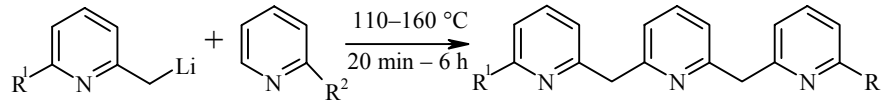
Dipyridylmethanes are formed according to Eq. (3):



(3)

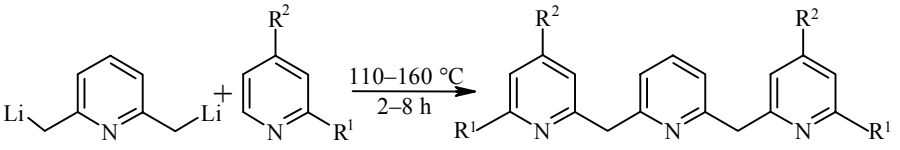
1 $R^1 = R^2 = H$; **2** $R^1 = H$, $R^2 = Me$; **3** $R^1 = R^2 = Me$

We have found that TPDM and compounds derived from it by substitution of hydrogen atoms in positions 6 or 4 of the two terminal pyridine rings with alkyl radical can be obtained in good or high yields according to Eqs. (4) and (5):



(4)

4 $R = R^1 = H$; **5** $R^1 = H$, $R = R^2 = Me$



(5)

6 $R^1 = Me$, $R^2 = H$; **7** $R^1 = H$, $R^2 = t$-Bu

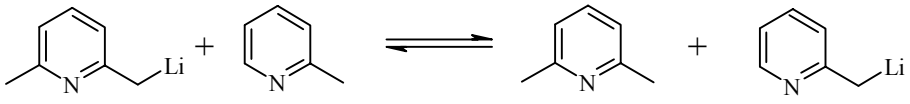
Reactions (4) and (5) proceed under significantly more severe conditions than those for reaction (3). Both lithium hydride precipitation and dihydrogen evolution occur in the course of these condensations. According to Eqs. (4), (5), the central pyridine ring of TPDM can originate from the electrophile, which undergoes one (picoline) or two consecutive (pyridine) attacks of the organolithium compound (Eq. (4)) or from the nucleophile (2,6-dilithiolutidine, Eq. (5)), which also serves twice in this role.

Lithiated picoline, LiPic (pK_a(PicH) 34), has been obtained by treatment of the corresponding CH-acid with butyllithium in either diethyl ether or glyme solution. The preparation of dilithiated lutidine turned out to be less convenient than the preparation of the monolithiated compound due to the incompleteness of butyllithium protodemetallation. We have shown that dilithiated lutidine can be efficiently replaced by two moles of LiLut. In all cases the ether solvent has been removed and the residual organolithium compound dried in high vacuum. Nevertheless, ether coordinated to lithium atoms remained in this solid and was liberated only in the course of its treatment with the electrophile–toluene mixture. The residual ether was then removed when the resulting reaction mixture was heated. Depending on the solvent used for the lithiation, a variable amount of the picoline to be metallated was transformed into the 6-butyl derivative in the course of a side reaction according to Eq. (1), being higher in ether solution and negligible in glyme. Lutidine metallation was an almost clean reaction. Ether bonded to organolithium nucleophile affected its reactivity, which was significantly higher in the case of diethylether solvates. As a result, glyme-solvated organolithiums turned out to be excellent in the synthesis of DPM, minimizing the formation of TPDM.

Table 1 includes results on the synthesis of DPM, Me-DPM, and Me_2-DPM under various conditions. The mildest conditions, room temperature, have been used in the case of DPM. In order to increase the rate of DPM formation, a 3-fold excess of pyridine was used (entry 1). The same reaction can be run with higher yield at increased temperature (entry 2). For a 1:1 reagent ratio and the same reaction conditions as in the entry (2), the yield of DPM is lower (entry 3). The most effective use of pyridine can be achieved if 2 moles of LiPic prepared in glyme are used per one mole of pyridine (entry 4) with the main by-product being 2,2'-bipyridine. The yield of DPM is significantly higher as compared with that reported earlier [14].

Following the same procedure (the use of LiPic prepared in glyme and either a 3-fold excess of PicH or a 2-fold excess of the nucleophile), satisfactory yields of Me-DPM on either LiPic or PicH correspondingly were obtained (entries 5, 6).

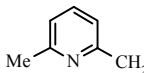
The main by-product observed in the case of the synthesis of Me_2-DPM was Me-DPM. Its formation can be explained by the proton transfer from the more acidic picoline to the anion of the less acidic lutidine:



leading to LiPic with its subsequent condensation with free picoline.

TABLE 1. Results of Condensation of Pyridine Electrophiles with 2-Pyridylmethyllithium Nucleophiles (Eq. (3), (4))

Entry	Compound	Reagents*	Reagents ratio*[2]	*t*, °C	Reaction time, h	NMR yield/ isolated yield, %
1	**1**	LiPic / Py	1* / 3	20	12	25 / 16
2	**1**	LiPic / Py	1* / 3	110	4	41 / 30
3	**1**	LiPic / Py	1* / 1	110	4	33 / 25
4	**1**	LiPic / Py	2 / 1*[3]	120	2	65 / 45
5	**2**	LiPic / PicH	1* / 3*[3]	20	48	41 / 30
6	**2**	LiPic / PicH	2 / 1*[3]	125	2	50 / 40
7	**3**	LiLut / LutH / PicH	1* / 1 / 1	160	3	32 / 20
8	**3**	LiLut / LutH / PicH	1* / 2 / 1	160	6	44 / 35
9	**3**	LiLut / LutH / PicH	1* / 4.5 / 1	160	6	55 / 45
10	**3**	LiLut / LutH / PicH	1* / 2 / 1 *[4]	120	8	56 / 45
11	**4**	LiLut / Py	2 / 1*	110	—*[5]	63 / 50
12	**5**	LiPic / PicH	2 / 1*	170	8	60 / 50
13	**6**	LiLut / LutH / PicH	2 / 0 / 1*	160	8	80 / 65
14	**6**	LiLut / LutH / PicH	2 / 0 / 1*	145	12	77 / 65
15	**7**	LiPic / *t*-BuPy	2 / 1*	115	5	65 / 50

* Organolithium compounds were obtained by lithiation of the appropriate methylpyridine with butyllithium in diethyl ether solution; Pic =  ; Lut =  , *t*-BuPy = 4-*tert*-butylpyridine.

*[2] Asterisk indicates compound on which yield is calculated.

*[3] An organolithium compound was obtained in 1,2-dimethoxyethane solution.

*[4] No toluene as co-solvent was used.

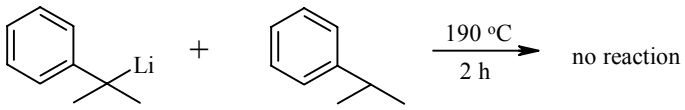
*[5] Includes 20 min heating at 110°C for ether distillation for reactions conducted at tempe-ratures higher than 20°C.

To shift the position of this equilibrium to the left, free lutidine was introduced into the reaction mixtures. Increase of the LutH/LiLut ratio from 1 to 2-4.5 allowed us to obtain Me_2-DPM of higher purity and in satisfactory yield (entries 7-9). Milder reaction conditions can be reached if no toluene as co-solvent is used (entry 10).

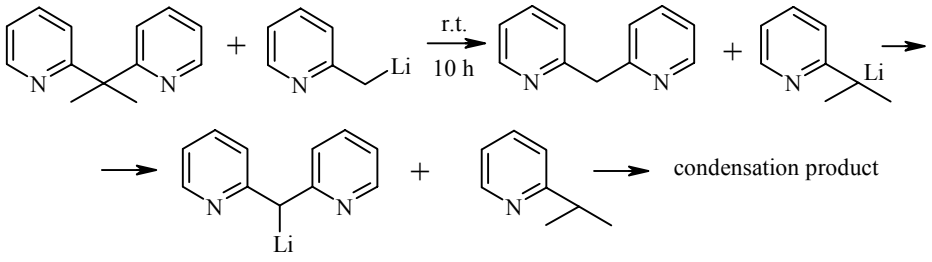
Thus, we can conclude that the simplest dipyridinemethanes can be obtained in satisfactory yields under mild conditions with a properly chosen reagent ratio.

The greater part of the TPDM ligands listed in Table 1 can be obtained *via* either Eqs. (4) or (5). Results optimized for one of the schemes possible for each of the TPDM compounds in Scheme 1 are given in Table 1. All of the tripyridinedimethanes were synthesized using organolithium compounds prepared in diethyl ether. When glyme was used instead of diethyl ether only small amounts of TPDM's were obtained with the major products being the corresponding DPM's. Tripyridinedimethane itself can be synthesized in good yield under milder conditions (entry 11) than those for Me-TPDM, in accordance with the higher electrophilicity of pyridine as compared with that of picoline (entry 12). According to data in the entries 13-15 Me_2-TPDM and *t*-Bu_2-TPDM, ligands were obtained in good or high yields under conditions similar to those for Me-TPDM.

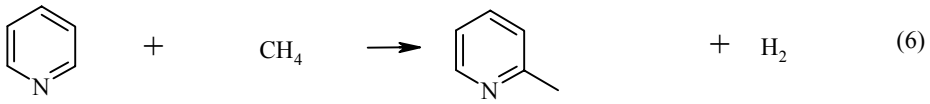
Thus, reactions (1), (2) can be a general route for synthesis of dipyridinemethanes and tripyridinedimethanes from the correspondingly substituted simplest pyridines. In order to learn more about the scope and limitations of this method, we have studied a more complicated nucleophile, 2-pyridyl-2-propyllithium, and a more complicated electrophile, 2,2-bis(2-pyridyl)propane (DPP). The latter was obtained by one-pot four-step synthesis by two stepwise deprotonations of DPM with butyllithium in glyme solution and methylation of each carbanion formed with methyl iodide. It turned out that lithiated isopropylpyridine, which can be effectively prepared in glyme but not in ether solution, does not react with isopropylpyridine even in 2 h at 190°C:

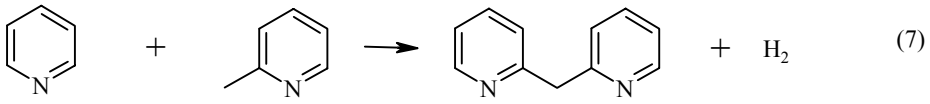


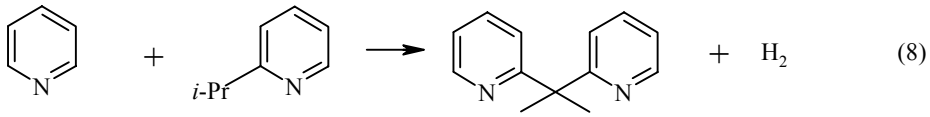
Moreover, treatment of DPP with LiPic at ambient temperature overnight leads to complete conversion of DPP with destruction of its skeleton and formation of products of condensation of 2-isopropylpyridine and dipyridylmethane. This result is consistent with the scheme of nucleophilic substitution at the second *ortho* carbon atom of the pyridine ring of DPP being an unusual example of aromatic nucleophilic substitution with carbanion as a leaving group:



In order to understand the driving force of the reactions studied in this work, we have conducted DFT calculations for three model transformations (Eq. (6)-(8)). Standard Gibbs free energies for each of the reaction are indicated:

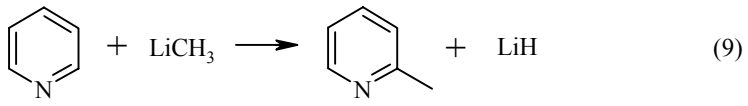






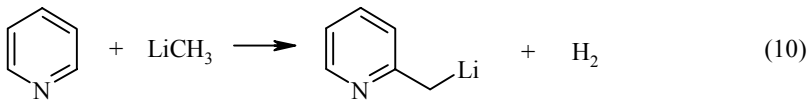
ΔG^0_{298} = 11.2 (6), 11.0 (7), 14.4 kcal/mol (8)

According to these results, pyridine alkylations with methane, 2-pyridylmethane, and 2-(2-pyridyl)-propane are almost equally unfavorable. Calculation of Gibbs free energy changes for reactions involving the corresponding organolithium compounds, methyllithium, 2-pyridylmethyllithium, and 2-pyridyl-2-propyllithium, can be done by the combination of these values with the pK_a values of the alkylating reagent from one side and the reaction product from the other (Eq. (9)):



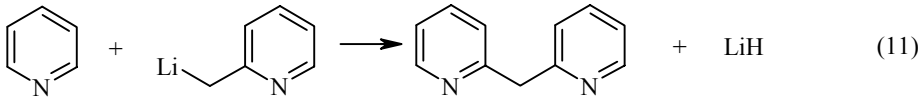
ΔG^0_{298} (9) = ΔG^0_{298} (6) + 1.36 [pK_a(H_2) – pK_a(CH_4)] = 11.2 – 27.2 = – 16.0 kcal/mol

Here the values pK_a(H_2) = 35 for KH–18-crown-6 system in THF solution [16] and pK_a(CH_4) = 55 for DMSO solution [17] were used. In fact, due to the lower solubility of LiH in most solvents as compared with that of KH in the presence of 18-crown-6, dihydrogen can behave as a stronger acid and ΔG^0_{298} (9) will be more negative. So, increased acidity by going from methane to dihydrogen makes this reaction possible in accordance with experimental observations [13] and can be considered as its main driving force. Another combination of the reaction products is favorable but slightly less than in the case of LiH as a reaction product, again, in accordance with experimental observations (Eq. (10)):



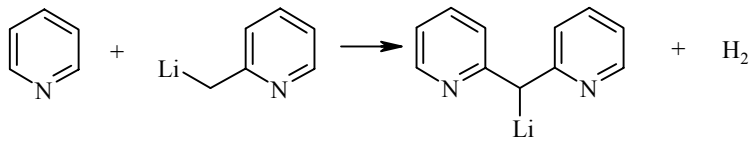
ΔG^0_{298} (10) = ΔG^0_{298} (6) + 1.36 [pK_a(PicH) – pK_a(CH_4)] = 11.2 – 28.6 = – 17.4 kcal/mol

The value pK_a(PicH) = 34 [18] for lithium salt scale in THF solution was used.
In a similar way, Gibbs free energy changes for reactions (11) and (12) can be calculated:



ΔG^0_{298} (11) = ΔG^0_{298} (7) + 1.36 [pK_a(H_2) – pK_a(PicH)] = 11.0 + 1.4 = 12.4 kcal/mol

According to this result, no gain in acidity is observed here and the reactions are unfavorable almost to the same degree as reaction (7). But in the case of the reaction products being dipyridylmethyllithium and dihydrogen, this condensation can proceed in accordance with our observations:

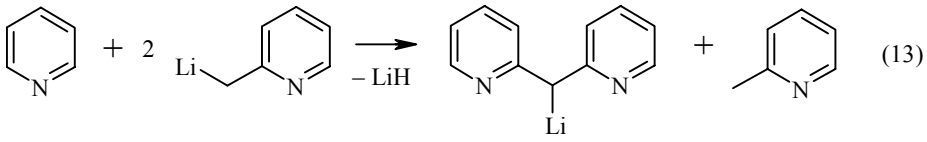


(12)

$$\Delta G^0_{298}\,(12) = \Delta G^0_{298}\,(7) + 1.36\,[pK_a(\mathrm{DPM}) - pK_a(\mathrm{PicH})] = 11.0 - 21.8 = -10.8\ \mathrm{kcal/mol}$$

Here we have assumed that the influence of the 2-pyridyl substituents on methane acidity is additive and the pK_a difference for the pair PicH–DPM is almost the same as for methane–2-picoline, pK_a(DPM) = 18.

It is important to mention here that when the LiPic-to-pyridine ratio is 2:1, the condensation can be even more favorable due to product stabilization *via* protonation of a second mole of LiPic with DPM produced (Eq. (13)):

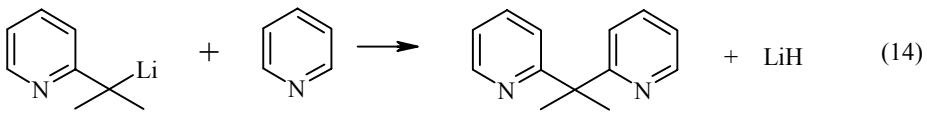


(13)

$$\Delta G^0_{298}\,(13) = \Delta G^0_{298}\,(7) + 1.36\,[pK_a(\mathrm{DPM}) + pK_a(\mathrm{H_2}) - 2\,pK_a(\mathrm{PicH})] = -9.4\ \mathrm{kcal/mol}$$

This provides a possible explanation to the highly effective use of a 2:1 ratio of LiPic to electrophile which has been found experimentally and which leads to the best results for Me-DPM and Me_2-DPM (Table 1, Entries 4, 6).

Finally, considering pyridine condensation with 2-pyridyl-2-propyllithium, since no acidic hydrogens are present at the bridging carbon of DPP, we can calculate the Gibbs free energy change only for the case where LiH and DPP are the condensation products (Eq. (14)):

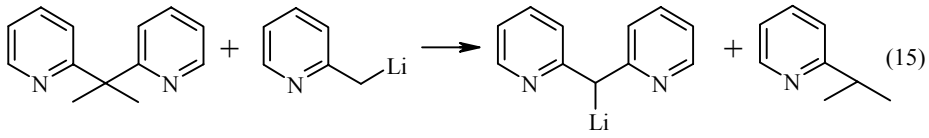


(14)

$$\Delta G^0_{298}\,(14) = \Delta G^0_{298}\,(8) + 1.36\,[pK_a(\mathrm{H_2}) - pK_a(i\text{-PrPy})] = 14.4 - 1.4 = 13.0\ \mathrm{kcal/mol}$$

In this calculation it is assumed that each methyl group at the acidic α-carbon atom increases the pK_a value of PicH by 1 unit [19], and thus we obtain an estimate of the pK_a of 2-isopropylpyridine, pK_a(*i*-PrPy) ~ 36.

In accordance with this calculated result and with our experimental observation, no condensation of 2-pyridyl-2-propyllithium with 2-isopropylpyridine is possible. *Vice versa*, nucleophilic cleavage of the C(propanediyl)–C(pyridyl) bond in DPP with LiPic is very favorable due to the formation of the lithium salt of DPM, which is more acidic than PicH:



$$\Delta G^0_{298}(15) = \Delta G^0_{298}(7) - \Delta G^0_{298}(8) + 1.36\,[pK_a(\mathrm{DPM}) - pK_a(\mathrm{PicH})] =$$
$$= -3.4 - 21.8 = -25.2 \text{ kcal/mol}$$

This is in full agreement with our experiment.

EXPERIMENTAL

All manipulations were carried out under purified argon using the standard Schlenk technique. Diethyl ether, glyme, and toluene from Aldrich were distilled under argon over sodium – benzophenone. Pyridine, 2-picoline, 2,6-lutidine, and 4-*tert*-butylpyridine from Aldrich were distilled under argon atmosphere over calcium hydride. All the liquids were stored in gas-tight bulbs. All other reagents, 10 M butyllithium solution in hexane, and methyl iodide were used as purchased from Aldrich. 2-Isopropylpyridine was synthesized according to a slightly modified procedure [20]. ^{1}H NMR spectra were recorded on a Varian Gemini 300 spectrometer (^{1}H 300 MHz). ^{1}H NMR chemical shifts are relative to the residual solvent resonance as internal standard. High-resolution mass spectra were obtained on a Kratos MS80 RFAQQ instrument.

The theoretical calculations in this work were performed using the density functional theory (DFT) method [21], specifically functional PBE [22], implemented in an original program package "Priroda" [23]. In the PBE calculations, relativistic Stevens–Bash–Krauss (SBK) effective core potentials (ECP) [24-26] optimized for DFT calculations were used. The basis set was the 311-split for main group elements with one additional polarization p-function for hydrogen, and an additional two polarization d-functions for elements of higher periods. Full geometry optimization was performed without constraints on symmetry. For all the species under investigation, frequency analysis was carried out. All minima were checked in the absence of imaginary frequencies.

Preparation of 2-Pyridylmethyllithium and 6-Methyl-2-pyridylmethyllithium. A flame-dried 300 ml Schlenk flask connected to a vacuum-argon line and equipped with a Teflon valve was filled with purified argon and the teflon stopcock was replaced by a rubber septum. In the flask 30 ml of diethyl ether or glyme per each 0.1 mol of pyridine derivative to be lithiated was added through a Teflon cannula. Then 2-picoline or 2,6-lutidine (0.1 or 0.2 mol) was introduced with a syringe. The flask was placed then into an ice bath and 10 M butyllithium solution in hexane (10.0 ml, 0.1 mol per each 0.1 mol of 2-picoline or 2,6-lutidine to be metallated) was added dropwise with stirring by hand. After the addition of butyllithium was complete, the flask with the dark red solution has been removed from the bath. The rubber septum was replaced by the teflon stopcock and the flask left to stay at ambient temperature for 1 h. Diethyl ether (or glyme) was removed in vacuum and the yellow crystalline residue was dried at 0.1 Torr during 1 h.

Condensation of 2-Pyridylmethyllithium, (6-Methyl-2-pyridyl)methyllithium, and 2-Pyridyl-2-propyllithium with either Pyridine, 2-Picoline, 4-*tert*-Butylpyridine, or 2,2-Bis(2-pyridyl)propane (General Procedure). Into a Schlenk flask containing 0.1 or 0.2 mol of the appropriate 2-pyridylmethyllithium nucleophile suitable pyridine derivatives in amounts indicated in Table 1 were introduced with a syringe. Toluene (30 ml per each 0.1 mol of butyllithium used) was added, then *via* cannula if necessary. The rubber septum was replaced by a Teflon stopcock and the flask was either left to stay at room temperature or connected to a condenser with receiver and immersed for 20 min into silicon oil bath heated to 110°C to distill the residual ether off and to let the greater part of the dihydrogen evolve. Usually 10-20 ml of liquid was collected. Then if heating at higher temperatures was needed, the Teflon valve was closed and the temperature of the silicone oil bath was raised. At the end of the synthesis, the reaction mixture turned purple-red. It was cooled in an ice bath

and methanol (8 ml per each 0.1 mol of organolithiums used) was added with a syringe dropwise to decompose the lithium hydride precipitated. After addition of water (8-9 ml per each 0.1 mol of organolithiums used), the yellow liquid could be easily separated by filtration from the white precipitate of hydrated lithium hydroxide. The liquid was dried over solid potassium hydroxide and fractionally distilled first at ambient temperature to recover the excess of pyridine compound if it was used and then under vacuum.

Condensation of 2,2-Bis(2-pyridyl)propane with 2-pyridylmethyllithium. The amounts of the reagents were tenfold less as compared with those given in the general procedure above; 0.01 mol of 2-pyridylmethyllithium and 0.01 mol of 2,2-bis(2-pyridyl)propane were used. The reaction mixture was left to stay for 10 h at ambient temperature. After the usual work-up procedure, according to NMR analysis, it contained no starting DPP but some amounts of DPM (see below) and 2-isopropyl-substituted DPM derivatives (the resonance of the *i*-Pr group was not equivalent to that of free 2-isopropylpyridine [20]).

Condensation of 2-Pyridyl-2-propyllithium with 2-Isopropylpyridine. The amounts of the reagents were tenfold less as compared with those given in the general procedure above; 0.01 mol of 2-pyridyl-2-propyllithium and 0.01 mol of 2-isopropylpyridine were used. The reaction mixture was heated 2 h at 190°C. According to NMR analysis, after the usual work-up it contained the starting 2-isopropylpyridine only.

2,2'-Dipyridylmethane, DPM (1). The reagent ratio and yield of the condensation product are indicated in Table 1. Bp 95-98°C at 0.7 Torr (cf. 104-106°C/0.2 Torr [27]). ^{1}H NMR (25°C, $CDCl_3$), δ, ppm: 4.31 (2H, s, CH_2); 7.10 (2H, dd, *J* = 7.5, 5.0, C(5)H); 7.24 (2H, d, *J* = 7.8, C(3)H); 7.58 (2H, dt, *J* = 1.8, 7.6, C(4)H); 8.50-8.56 (2H, m, C(6)H).

6-Methyl-2,2'-dipyridylmethane, Me-DPM (2). The reagent ratio and yield of the condensation product are indicated in Table 1. Bp 97-102°C at 0.7 Torr (cf. 114-116°C/0.5 Torr [27]). ^{1}H NMR (25°C, $CDCl_3$), δ, ppm: 2.51 (3H, s, CH_3); 4.29 (2H, s, CH_2); 6.96 (1H, d, *J* = 7.6, C(5)H); 6.97 (1H, d, *J* = 7.6, C(3)H); 7.11 (1H, d, *J* = 7.6, C(2)terminal-H); 7.21 (1H, d, *J* = 7.6, C(5)terminal-H); 7.45 (1H, t, *J* = 7.6, C(4)H); 7.56 (1H, dt, *J* = 1.8, 7.6, C(4)terminal-H); 8.49-8.55 (1H, m, C(6)terminal-H).

6,6'-Dimethyl-2,2'-dipyridylmethane, Me_2-DPM (3). The reagent ratio and yield of the condensation product are indicated in Table 1. Bp 117-121°C at 0.7 Torr. ^{1}H NMR (25°C, $CDCl_3$), δ, ppm: 2.51 (6H, s, CH_3); 4.26 (2H, s, CH_2); 6.95 (4H, d, *J* = 7.6, C(3)H, C(5)H); 7.43 (2H, t, *J* = 7.6, C(4)H). High-resolution mass spectrum, *m/z:* M = 198.11611. $C_{13}H_{14}N_2$. Calculated 198.11570

2,6-Bis(2-pyridylmethyl)pyridine, Tripyridinedimethane, TPDM (4). The reagent ratio and yield of the condensation product are indicated in Table 1. Bp 165-168°C at 0.1 Torr. ^{1}H NMR (25°C, $CDCl_3$), δ, ppm: 4.31 (4H, s, CH_2); 7.03 (2H, d, *J* = 7.7, C(3)central-H, C(5)central-H); 7.10 (2H, dd, *J* = 7.6, 4.9, C(5)terminal-H); 7.21 (2H, d, *J* = 7.7, C(3)terminal-H); 7.48 (1H, t, *J* = 7.7, C(4)central-H); 7.55 (2H, dt, *J* = 1.8, 7.7, C(4)terminal-H); 8.49-8.54 (2H, m, C(6)terminal-H). High-resolution mass spectrum, *m/z*: found 261.12730. $C_{17}H_{15}N_3$. Calculated 261.12660.

2-(6-Methyl-2-pyridylmethyl)-6-(2-pyridylmethyl)pyridine, 6-Methyltripyridinedimethane, Me-TPDM (5). The reagent ratio and yield of the condensation product are indicated in Table 1. Bp 169-171°C at 0.7 Torr. ^{1}H NMR (25°C, $CDCl_3$), δ, ppm: 2.51 (3H, s, CH_3); 4.28 (2H, s, CH_2); 4.31 (2H, s, CH_2); 6.95 (2H, d, *J* = 7.7, C(3)H, C(5)H); 7.00 (1H, d, *J* = 7.7, C(3)central-H); 7.02 (1H, d, *J* = 7.7, C(5)central-H); 7.09 (1H, dd, *J* = 7.7, 4.8, C(5)terminal-H); 7.22 (1H, dd, *J* = 7.7, 0.9, C(3)terminal-H); 7.42 (1H, t, *J* = 7.7, C(4)H); 7.46 (1H, t, *J* = 7.7, C(4)central-H); 7.55 (1H, dt, *J* = 1.8, 7.7, C(4)terminal-H); 8.48-8.54 (1H, m, C(6)terminal-H). High-resolution mass spectrum, *m/z*: found 275.13685. $C_{18}H_{17}N_3$. Calculated 275.142247.

2,6-Bis(6-methyl-2-pyridylmethyl)pyridine, 6,6'-Dimethyltripyridinedimethane, Me_2-TPDM (6). The reagent ratio and yield of the condensation product are indicated in Table 1. Bp 173-178°C at 0.15 Torr. ^{1}H NMR (25°C, $CDCl_3$), δ, ppm: 2.51 (6H, s, CH_3); 4.29 (4H, s, CH_2); 6.95 (2H, d, *J* = 7.5, C(5)terminal-H); 6.96 (2H, d, *J* = 7.5, C(3)terminal-H); 6.99 (2H, d, *J* = 7.2, C(3)central-H, C(5)central-H); 7.42 (2H, t, *J* = 7.5, C(4)terminal-H); 7.45 (1H, t, *J* = 7.2, C(4)central-H). High-resolution mass spectrum, *m/z*: found 289.15664. $C_{19}H_{19}N_3$. Calculated 289.15790.

2,6-Bis(4-*tert*-butyl-2-pyridylmethyl)pyridine, 4,4'-Bis(*tert*-butyl)tripyridinedimethane, (*tert*-Bu)$_2$-TPDM (7). The reagent ratio and yield of the condensation product are indicated in Table 1. Bp 195-200°C at 0.1 Torr. ^{1}H NMR (25°C, $CDCl_3$), δ, ppm: 1.23 (18H, s, CH_3); 4.30 (4H, s, CH_2); 7.02 (2H, d, J = 7.7, C(3)central-H, C(5)central-H); 7.09 (2H, dd, J = 1.8, 5.4, C(5)terminal-H); 7.22-7.25 (2H, m, C(3)terminal-H); 7.47 (1H, t, J = 7.7, C(4)central-H), 8.39-8.43 (2H, m, C(6)terminal-H). High-resolution mass spectrum, *m/z*: found 373.25083. $C_{25}H_{31}N_3$. Calculated 373.25180.

Synthesis of 2,2-Bis(2-pyridyl)propane, 2,2'-Dipyridine-2,2-propane, DPP, $C_{13}H_{14}N_2$ by Methylation of Dipyridylmethane, DPM. A flame-dried 300 ml Schlenk flask connected to a vacuum-argon line and equipped with a stirring bar was filled with purified argon. In the flask 50 ml of glyme was added through a Teflon cannula. Then DPM (5.8 g, 34 mmol) was introduced with a syringe. The flask was placed then into an ice bath and 10 M butyllithium solution in hexane (3.5 ml, 35 mmol) was added dropwise with stirring. After the addition of butyllithium was complete, the flask with the dark red solution was left for 15 min. Then methyl iodide (2.25 ml, 4.83 g, 34 mmol) was added dropwise with syringe with intense stirring. With the last drops of methyl iodide the reaction mixture became almost colorless. These treatments of the solution with butyllithium and then with methyl iodide have been repeated one time more. To the resulting yellow solution with some precipitated lithium iodide, potassium hydroxide (4.3 g, 66 mmol) dissolved in 3 ml of water was added with intense stirring. Then the liquid phase was separated by filtration from the inorganic salts precipitated and dried over solid potassium hydroxide, and the solvent was distilled off. The oily residue was then distilled under vacuum to give pure DPP. Yield 6.7 g (90 %); bp 90-95°C at 0.7 Torr. ^{1}H NMR (25°C, $CDCl_3$), δ, ppm: 1.78 (6H, s, CH_3); 7.03-7.08 (2H, m, C(5)H); 7.13-7.18 (2H, m, C(3)H); 7.52-7.57 (2H, m, C(4)H); 8.51-8.55 (2H, m, C(6)H). High-resolution mass spectrum, *m/z*: found 198.11647. $C_{13}H_{14}N_2$. Calculated 198.11570.

CONCLUSION

We conclude that a Chichibabin-like condensation (Eqs. (1), (2)) is a convenient synthetic route to dipyridinemethanes and tripyridinemethanes driven by a large (not less than 10 pK_a units) gain in the acidity of its participants. This statement is the basis for understanding its limitations when planning the synthesis of alkyl-substituted pyridines and, in particular, polypyridine- polyalkanes according to these schemes. In turn, polypyridinepolyalkanes can be easily cleaved at the bridging carbon–pyridine carbon bond with carbanionic nucleophiles even if only a small gain in acidity can be reached when going from reactants to the cleavage products.

Synthetic application of the method described here for the synthesis of macrocyclic polypyridinepolyalkanes (pyridinophanes or calixpyridines) is now under way.

A.N.V. is grateful to Prof. Kenneth G. Caulton for a post-doctoral Fellowship at Indiana University. S.V.B. thanks BRHE REC-007 for support of his participation in this work. This work was made possible in part due to funding from the Russian Foundation for Basic Research (grant No 01-03-32692a).

REFERENCES

1. J. Canty, A. Dedieu, H. Jin, A. Milet, and M. K. Richmond, *Organometallics*, **15**, 2845 (1996).
2. D. D. Wick and K. I. Goldberg, *J. Am. Chem. Soc.*, **119**, 10235 (1997).
3. S. A. O'Reilly, P.S. White, and J. L. Templeton, *J. Am. Chem. Soc*., **118**, 5684 (1996).
4. C. M. Wang, J. W. Ziller, and T. C. Flood, *J. Am. Chem. Soc*., **117**, 1647 (1995).

5. G. Wilkinson (editor), *Comprehensive Coordination Chemistry. The Synthesis, Reactions, Properties, and Applications of Coordination Compounds,* Pergamon Press, Oxford; New York; Toronto, 1987, Vol. 2, 73.
6. L. F. Szczepura, L. M. Witham, and K. J. Takeuchi, *Coord. Chem. Rev*., **174**, 5 (1998).
7. J. Canty, N. J. Minchin, B. W. Skelton, and A. H. White, *J. Chem. Soc., Dalton Trans*., 2201 (1986).
8. J. Manzur, *Transit. Met. Chem*., **11**, 220 (1986).
9. A. Meister, N. Takano, T. Chuard, M. Graf, K. Bernauer, H. Stoeckli-Evans, and G. Suess-Fink, *Z. Anorg. Allgem. Chem*., **621**, 117 (1995).
10. M. T. Garland and D. Grandjean, *Acta Crystallogr.*, C**43**, 643 (1987).
11. A. M. Garcia and J. Manzur, *Acta Crystallogr.*, C**50**, 1882 (1994).
12. E. Spodine, J. Manzur, M. T. Garland, J. P. Fackler, Jr., R. J. Staples, and B. Trzcinska-Bancroft, *Inorg. Chim. Acta*, **203**, 73 (1993).
13. H. Vorbrueggen and M. Maas, *Heterocycles*, **27**, 2659 (1988).
14. C. Osuch and R. Levine, *J. Am. Chem. Soc*., **78**, 1723 (1956).
15. F. P. Schmitz, H. Hilgers, and B. Gemmel, *Makromol. Chem*., **191**, 1033 (1990).
16. E. Buncel and B. Menon, *J. Am. Chem. Soc.*, **99**, 4457 (1977).
17. D. Algrim, J. E. Bares, J. C. Branca, and F. G. Bordwell, *J. Org. Chem.*, **43**, 5024 (1978).
18. R. R. Fraser, T. S. Mansour, and S. Savard, *J. Org. Chem.*, **50**, 3232 (1985).
19. F. G. Bordwell, J. E. Bartmess, and J. A. Hautala, *J. Org. Chem*. **43**, 3095 (1978).
20. E. Pasquinet, P. Rocca, F. Marsais, A. Goddard, and G. Queguiner, *Tetrahedron*, **54**, 8771 (1998).
21. R. G. Parr and W. Yang, *Density-functional Theory of Atoms and Molecules*, Oxford, 1989.
22. J. P. Perdew, K. Burke, and M. Ernzerhof, *Phys. Rev. Lett.*, **77**, 3865 (1996).
23. Yu. A. Ustynyuk, L.Yu. Ustynyuk, D.N. Laikov, and V.V. Lunin, *J. Organomet. Chem*., **597**, 182 (2000).
24. W. J. Stevens, H. Bash, and M. Krauss, *J. Chem. Phys*., **81**, 6026 (1984).
25. W. J. Stevens, H. Bash, M. Krauss, and P. Jasien, *Can. J. Chem*., **70**, 612 (1992).
26. T. R. Cundari and W. J. Stevens, *J. Chem. Phys*., **98,** 5555 (1993).
27. P. J. Chivers and T. A. Crabb, *Tetrahedron,* **26**, 3369 (1970).