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Cycloaddition Reactions of 1-Lithio-1,3-dienes with Aromatic Nitriles Affording Multiply Substituted Pyridines, Pyrroles, and Linear Butadienylimines

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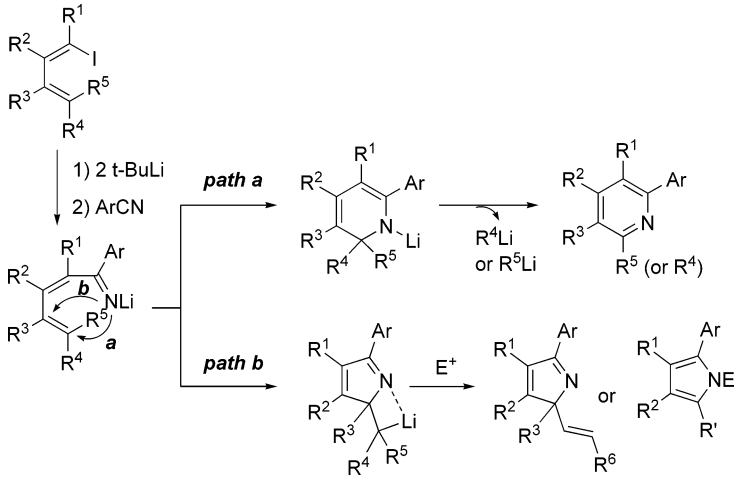

Fully or partially substituted 1-iodo- or 1-bromo-1,3-dienes could be readily lithiated using *t*-BuLi or *n*-BuLi to afford their corresponding 1-lithio-1,3-diene derivatives in quantitative yields. When these in situ generated lithium reagents were treated with organonitriles, depending on the substitution patterns of the butadienyl skeletons, substituted pyridines, pyrroles, and/or linear butadienyl imines were formed in good to excellent yields via *N*-lithioketimine intermediates. In the cases of 1,2,3,4-tetrasubstituted and 2,3-disubstituted 1-lithio-1,3-dienes, pyridine derivatives or linear butadienyl imines were generally formed depending on the reaction temperatures. When 1,2,3,4-tetrasubstituted 4-halo-1-lithio-1,3-dienes and 1,2-disubstituted 1-lithio-1,3-dienes were treated with organonitriles, pyrrole derivatives or linear butadienyl imines were obtained. Competition between 5-exo and 6-endo cyclization was found to be responsible for the formation of either pyrroles or pyridines. Selective elimination of RLi from the lithiated cyclic N-containing intermediates was observed. The order of elimination was found to be LiCl > Me_3SiLi > LiH.

Introduction

The development of synthetically useful methods for the preparation of N-containing heterocycles such as pyridine and pyrrole derivatives has continuously been a major research topic in synthetic chemistry,[1,2] because these N-containing heterocycles, especially pyridine and pyrrole derivatives, are of great importance in many areas including natural products synthesis, materials chemistry, coordination chemistry, pharmaceutical chemistry, and the agrochemical industry.[1−4] Among the many synthetic methods for pyridine and pyrrole derivatives with a

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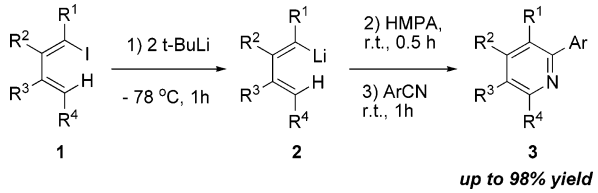
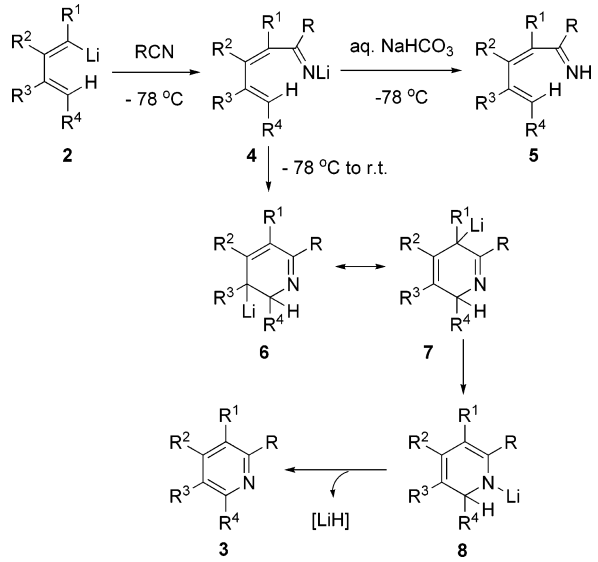
wide diverse of substitution patterns,[1−4] the addition reaction of organolithium reagents to organonitriles, which is fundamental in organometallic chemistry,[5−7] provides an alternative synthetic method.[5−9]

Conventionally, the addition intermediates, *N*-lithioketimines, are intramolecularly trapped by organohalides via nucleophilic substitution to generate N-containing heterocycles such as pyridines.[8,9] We have recently communicated a novel synthetic method for the preparation of pyridines from the cycloaddition of organonitriles with 1-lithio-1,3-dienes (Scheme 1).[10] On the basis of the experimental observations, we have proposed a reaction mechanism for this addition reaction leading to pyridine

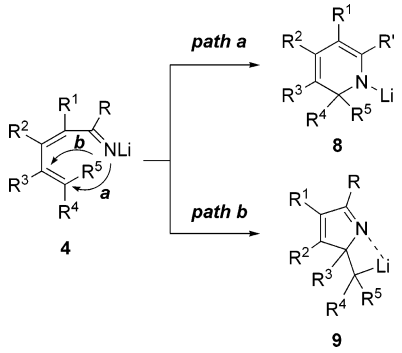
SCHEME 1. Generation and Reaction of 1,2,3,4-Tetrasubstituted 1-Lithio-1,3-dienes with Organonitriles Affording Multiply Substituted Pyridine Derivatives



SCHEME 2. A Proposed Reaction Mechanism for the Reaction of 1-Lithio-1,3-dienes with Organonitriles Leading to Pyridine Derivatives



SCHEME 3. 6-Endo-trig versus 5-Exo-trig



derivatives. As illustrated in Scheme 2, the *N*-lithioketimines **4** must be formed as the reactive addition intermediates at −78 °C, because hydrolysis of the reaction mixture at −78 °C afforded the linear imines **5** in high yields.[10] With reaction temperature increasing, intramolecular lithiation-cyclization took place to form cyclic intermediates **6**−**8**, which afforded pyridine derivatives via elimination of LiH.

As described above, the reaction of 1,2,3,4-tetrasubstituted 1-lithio-1,3-dienes **2** with organonitriles afforded pyridine derivatives exclusively as the final products at room temperature.[10] However, in principle, a five-membered N-containing heterocycle such as a pyrrole derivative **9** might be also formed (Scheme 3). In addition, aromatization via elimination of a lithium salt from **8** is the driving force. It could be expected that, as illustrated in Scheme 4, either LiR^4 or LiR^5 might be

(1) For recent reviews on the synthesis of pyridine derivatives, see: (a) Varela, J. A.; Saa, C. *Chem. Rev.* **2003**, *103*, 3787−3901. (b) Jones, G. In *Comprehensive Heterocyclic Chemistry*; Katritzky, A. R., Rees, C. W., Scriven, V. F. V., Eds.; Pergamon: Oxford, 1996; Vol. 5, pp 167−243. (c) Grotjahn, D. B. Transition Metal Alkyne Complexes: Transition Metal-Catalyzed Cyclotrimerization. In *Comprehensive Organometallic Chemistry II*; Abel, E. W., Stone, F. G. A., Wilkinson, G., Eds.; Hegedus, L. S., Vol. Ed.; Pergamon: Oxford, 1995; Vol. 12, p 741. (d) Henry, G. D. *Tetrahedron* **2004**, *60*, 6043−6061. (e) Newkome, G. R.; Patri, A. K.; Holder, F.; Schubert, U. S. *Eur. J. Org. Chem.* **2004**, 235−254. (f) Xi, Z.; Li, Z. *Top. Organomet. Chem.* **2004**, *8*, 27−56.

(2) For recent reviews on the synthesis of pyrrole derivatives, see: (a) Luh, T. Y.; Lee, C. F. *Eur. J. Org. Chem.* **2005**, 3875−3885. (b) Sundberg, R. J. In *Comprehensive Heterocyclic Chemistry*; Katritzky, A. R., Rees, C. W., Scriven, V. F. V., Eds.; Pergamon: Oxford, 1996; Vol. 2, p 119. (c) Gribble, G. W. In *Comprehensive Heterocyclic Chemistry*; Katritzky, A. R., Rees, C. W., Scriven, E. F. V., Eds.; Pergamon: Oxford, 1996; Vol. 2, p 207. (d) Jones, R. A. *Pyrroles, Part II, The Synthesis, Reactivity and Physical Properties of Substituted Pyrroles*; Wiley: New York, 1992. See also: (e) Mathew, P.; Asokan, C. V. *Tetrahedron* **2006**, *62*, 1708−1716. (f) Lu, L.; Chen, G.; Ma, S. *Org. Lett.* **2006**, *8*, 835−838 and references therein.

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(4) For reviews on the bioactivity and physical properties of pyrrole derivatives, see: (a) Furstner, A. *Angew. Chem., Int. Ed.* **2003**, *42*, 3582−3603. (b) Hoffmann, H.; Lindel, T. *Synthesis* **2003**, 1753−1783. (c) Balme, G. *Angew. Chem., Int. Ed.* **2004**, *43*, 6238−6241. (d) Yamaguchi, S.; Tamao, K. *J. Organomet. Chem.* **2002**, *653*, 223−228. (e) Guernion, N. J. L.; Hayes, W. *Curr. Org. Chem.* **2004**, *8*, 637−651.

(5) Wakefield, B. J. *Organolithium Methods*; Academic Press: San Diego, CA, 1988; p 62.

(6) For recent reviews on the reaction of organolithium reagents with organonitriles affording pyridine derivatives and related compounds, see: (a) Foubelo, F.; Yus, M. *Curr. Org. Chem.* **2005**, *9*, 459−490. (b) Langer, P.; Freiberg, W. *Chem. Rev.* **2004**, *104*, 4125−4149. (c) Xi, Z. *Eur. J. Org. Chem.* **2004**, 2773−2781. (d) Najera, C.; Sansano, J. M.; Yus, M. *Tetrahedron* **2003**, *59*, 9255−9303.

(7) Reactions of mono organolithium compounds with nitriles: (a) Anker, R. M.; Cook, A. H. *J. Chem. Soc.* **1941**, 323−331. (b) Scala, A. A.; Bikales, N. M.; Becker, E. I. *J. Org. Chem.* **1965**, *30*, 303−304. (c) Berry, D. J.; Wakefield, B. J. *J. Chem. Soc. C* **1971**, 642−645. (d) Berry, D. J.; Cook, J. D.; Wakefield, B. J. *J. Chem. Soc., Perkin Trans. 1* **1972**, 2190−2192. (e) Cook, L. S.; Wakefield, B. J. *Tetrahedron Lett.* **1976**, 147−150. (f) Cook, L. S.; Wakefield, B. J. *J. Chem. Soc., Perkin Trans. 1* **1980**, 2392−2397. (g) Seyferth, D.; Hui, R. C.; Wang, W. *J. Org. Chem.* **1993**, *58*, 5843−5845. (h) Armstrong, D. R.; Clegg, W.; MacGregor, M.; Mulvey, R. E.; O'Neil, P. A. *J. Chem. Soc., Chem. Commun.* **1993**, 608−610. (i) Armstrong, D. R.; Henderson, K. W.; MacGregor, M.; Mulvey, R. E.; Ross, M. J.; Clegg, W.; O'Neil, P. A. *J. Organomet. Chem.* **1995**, *486*, 79−93. (j) Ball, S. C.; Davies, R. P.; Raithby, P. R.; Shields, G. P.; Snaith, R. *J. Organomet. Chem.* **1998**, *550*, 457−461. (k) Coleman, C. M.; O'Shea, D. F. *J. Am. Chem. Soc.* **2003**, *125*, 5054−5055.

(8) Recent references on the reaction of organolithium reagents with organonitriles leading to pyridine formation, see: (a) Hansen, H. M.; Lysen, M.; Begtrup, M.; Kristensen, J. K. *Tetrahedron* **2005**, *61*, 9955−9960. (b) Kristensen, J. K.; Vedso, P.; Begtrup, M. *J. Org. Chem.* **2003**, *68*, 4091−4092. (c) Pawlas, J.; Begtrup, M. *Org. Lett.* **2002**, *4*, 2687−2690. (d) Lysen, M.; Kristensen, J. L.; Vedso, P.; Begtrup, M. *Org. Lett.* **2002**, *4*, 257−259. (e) Pawlas, J.; Vedso, P.; Jakobsen, P.; Huusfeldt, P. O.; Begtrup, M. *J. Org. Chem.* **2001**, *66*, 4214−4219.

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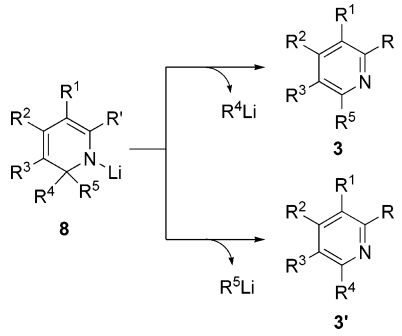
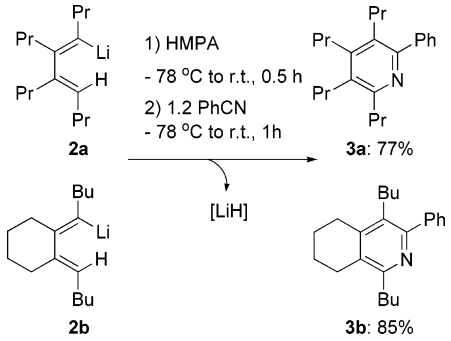
(10) Chen, J.; Song, Q.; Wang, C.; Xi, Z. *J. Am. Chem. Soc.* **2002**, *124*, 6238−6239.

SCHEME 4. Elimination of R^4Li versus Elimination of R^5Li



SCHEME 5. Elimination of LiH To Afford Pyridine Derivatives



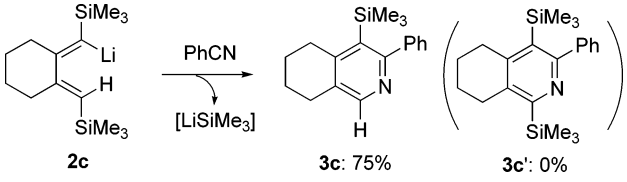
eliminated from **8** and both types of elimination could lead to the formation of pyridine derivatives **3** or **3′**. Therefore, during our systematic investigation into this synthetically useful reaction, we envisioned that not only pyridine derivatives but also pyrrole derivatives of diversified structures could be prepared following the above novel cycloaddition reaction. In this paper, we report the scope and limitations of the cycloaddition reactions of substituted 1-lithio-1,3-dienes with organonitriles. A wide variety of pyridine derivatives, pyrrole derivatives, and linear butadienyl imines of diversified substitution patterns could be prepared following this method.

Results and Discussion

Reaction of 1,2,3,4-Tetrasubstituted 1-Lithio-1,3-dienes 2 with Organonitriles. Formation of Multi-Substituted Pyridines and/or Pyrroles. 1,2,3,4-Tetrasubstituted 1-lithio-1,3-dienes reacted cleanly with aromatic organonitriles (ArCN) to afford multiply substituted pyridines and tetrahydroisoquinolines in high isolated yields.[10] For example (Scheme 5), 1,2,3,4-tetrapropyl 1-lithio-1,3-diene **2a** reacted with PhCN affording the pyridine derivative **3a** in 77% isolated yield, and the tetrahydroisoquinoline **3b** was obtained in 85% isolated yield from **2b** and PhCN. When aliphatic organonitriles were used, messy mixtures were obtained probably due to the relatively acidic nature of α-hydrogen of aliphatic organonitriles.

In the above-mentioned reactions,[10] elimination of LiH rather than PrLi or BuLi took place, leading to the aromatic rings of pyridine derivatives (Scheme 5). However, interestingly, when trimethylsilyl-substituted 1-lithio-1,3-diene **2c** was used, unlike the reaction of **2a**,**b**, elimination of $LiSiMe_3$ rather than LiH took place (Scheme 6). The tetrahydroisoquinoline **3c** was obtained solely in 75% isolated yield, obviously via elimination of $LiSiMe_3$. The product **3c′** via elimination of LiH was not formed at all.

SCHEME 6. Elimination of $LiSiMe_3$ versus Elimination of LiH



With the above results in hand, we tried to investigate reactions of other types of 1-lithio-1,3-dienes with organonitriles. First, 1,2,3,4-tetraethyl 1-iodo-4-chloro-1,3-diene **10a** was prepared.[11,12] Selective lithiation of **10a** afforded 1-lithio-1,3-diene **11a** in a quantitative yield as followed by GC measurement. Reactions of **11a** with organonitriles afforded the linear imines **12** in high isolated yields upon hydrolysis at −78 °C after the reaction mixture was stirred at −78 °C for 1 h, as expected (Scheme 7). It is noteworthy that these linear imines were stable in air and could tolerate the normal workup procedures and purification process using column chromatography. The reaction temperature was then increased. After 3 h at 0 °C, the linear imine **12a** decreased to 50% yield, while the pyridine derivative **3d** appeared and was obtained in 39% isolated yield. The linear imines disappeared completely after 3 h at room temperature. Hydrolysis of the reaction mixtures afforded the pyridine derivatives **3d** and **3e** in 47% and 56% isolated yields, respectively. Surprisingly, along with formation of the expected pyridines derivatives **3d** and **3e**, unexpected pyrrole derivatives **13a** and **13b** were also obtained. If the reaction temperature was increased to 50 °C immediately from −78 °C, the pyridines derivatives **3** were not obtained at all in most cases, while the pyrrole derivatives **13** were obtained as the only final products in high isolated yields. To further study the reaction mechanism, we treated the isolated linear imine **12a** with *n*-BuLi. At this treatment, the *N*-lithioketimine **14a** should be formed. As expected, a mixture of **3d** and **13a** was obtained (Scheme 8).

As shown in Scheme 9, a competition between path a and path b is operating in this reaction. The involvement of path b in this reaction may be due to the steric hindrance of the chlorinated carbon center and the electro-withdrawing effect of the chlorine atom. These results show that path b is thermodynamically favored, affording the five-membered intermediates **9**. For the formation of pyrrole derivatives, although we were not successful in trapping the intermediates **9**, a carbene-like intermediate **16** must be generated and followed by a 1,2-H shift (Scheme 9) to afford the pyrrole derivatives **13**.[13]

It is interesting to note that the intermediate **8** underwent elimination of LiCl rather than EtLi (Scheme 9) to afford pyridine derivatives **3**. Product **15** via elimination of EtLi was not

(11) Preparative methods for 1-iodo-1,3-diene derivatives, see: (a) Takahashi, T.; Kondakov, D. Y.; Xi, Z.; Suzuki, N. *J. Am. Chem. Soc.* **1995**, *117*, 5871−5872. (b) Takahashi, T.; Sun, W.; Xi, C.; Ubayama, H.; Xi, Z. *Tetrahedron* **1998**, *54*, 715−726. (c) Ubayama, H.; Sun, W.; Xi, Z.; Takahashi, T. *Chem. Commun.* **1998**, 1931−1932. (d) Xi, Z.; Liu, X.; Lu, J.; Bao, F.; Fan, H.; Li, Z.; Takahashi, T. *J. Org. Chem.* **2004**, *69*, 8547−8549.

(12) Reactions of 1-lithio-1,3-dienes with unsaturated organic substrates, see: (a) Song, Q.; Li, Z.; Chen, J.; Wang, C.; Xi, Z. *Org. Lett.* **2002**, *4*, 4627−4629. (b) Fang, H.; Song, Q.; Wang, Z.; Xi, Z. *Tetrahedron Lett.* **2004**, *45*, 5159−5162. (c) Wang, C.; Song, Q.; Xi, Z. *Tetrahedron* **2004**, *60*, 5207−5214. (d) Wang, C.; Lu, J.; Mao, G.; Xi, Z. *J. Org. Chem.* **2005**, *70*, 5150−5156. See also: (e) Shirley, D. A.; Cameron, M. D. *J. Am. Chem. Soc.* **1952**, *74*, 664−665. (f) Fitt, J. J.; Gschwend, H. W. *J. Org. Chem.* **1979**, *44*, 303−305.

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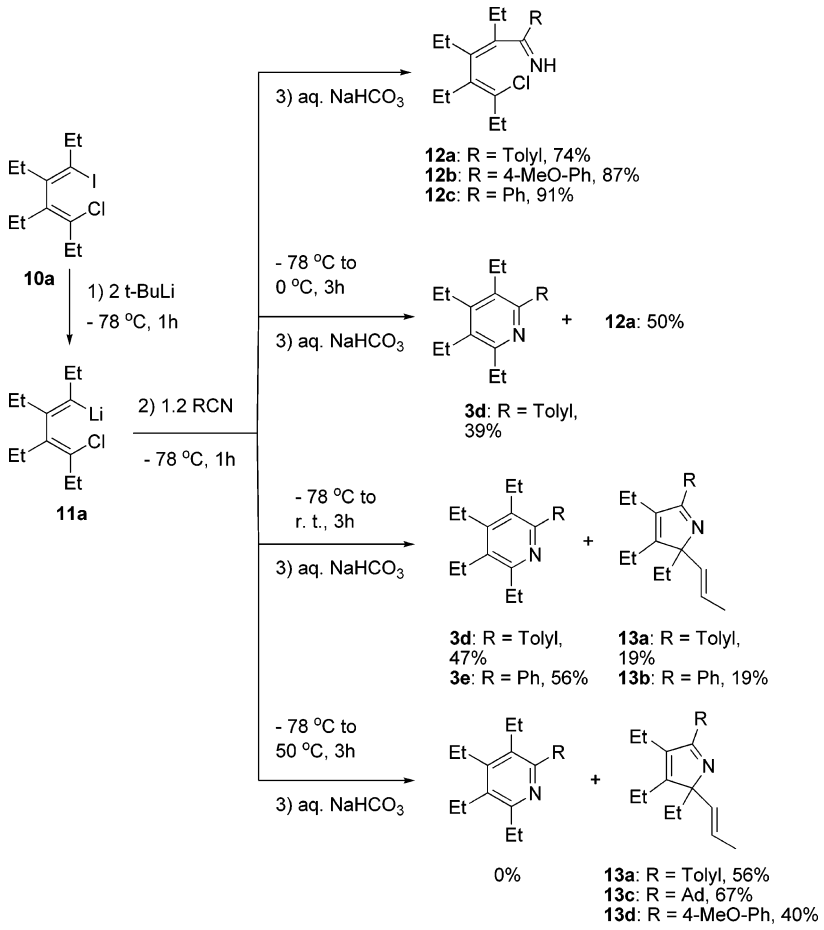
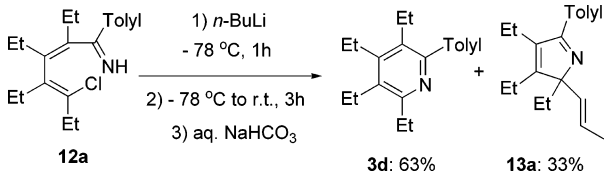
SCHEME 7. Reaction of 4-Chloro-1-lithio-1,3-diene 11a with Organonitriles Affording Pyridines and Pyrroles



SCHEME 8. Treatment of Linear Imine 12a with *n*-BuLi



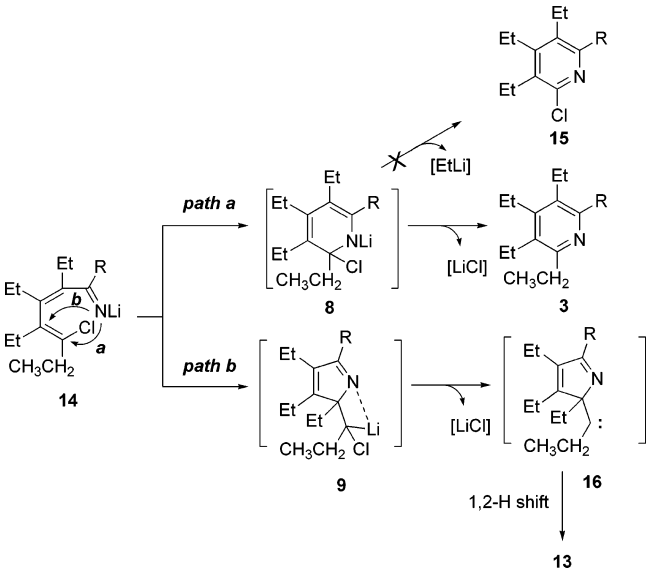
observed. Further, to know whether $LiSiMe_3$ or LiCl is eliminated when both are present in the intermediate, we prepared the monolithio reagent **11b**. Interestingly, as shown in Scheme 10, LiCl was selectively eliminated, affording the pyridine derivative **3f** in 68% isolated yield as the only final product.

We also prepared the lithium reagents **17** possessing a methyl group at position 4 (Scheme 11). We found the procedure reported recently by Hudrilik was very effective for preparation of this type of monolithium reagent.[14] However, no intramolecular lithiation-cyclization of **18** took place even at elevated reaction temperatures. The linear butadienyl imines were not stable in these cases. Trap of **18** with PhCOCl gave a stable product **19** in 74% yield.

Reaction of Disubstituted 1-Lithio-1,3-dienes with Organonitriles. To further investigate the effect of substitution patterns on the butadienyl skeletons of these mono lithium reagents, we prepared the 1,2-dibutyl monoiodobutadiene **20**,[11a] which could be also readily lithiated to afford its corresponding

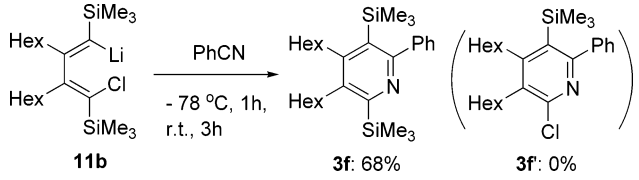
(14) Hudrilik, P. F.; Dai, D.; Hudrilik, A. M. *Tetrahedron Lett.* **2006**, *47*, 3427−3430.

SCHEME 9. Proposed Reaction Mechanisms for the Formation of Pyridines and Pyrroles from 4-Chloro-1-lithio-1,3-dienes and Organonitriles

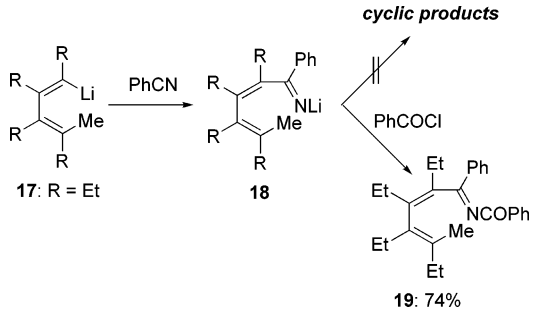


1,2-dibutyl 1-lithio-1,3-butadiene **21**. Reaction of **21** with organonitriles at −78 °C generated the linear butadienyl imines **22** upon quenching with aqueous $NaHCO_3$ (Scheme 12). When the temperature was increased to a higher temperature, in addition to linear butadienyl imines **22**, the pyrrole derivatives **23** appeared. If the reaction was carried out at reflux, the pyrrole

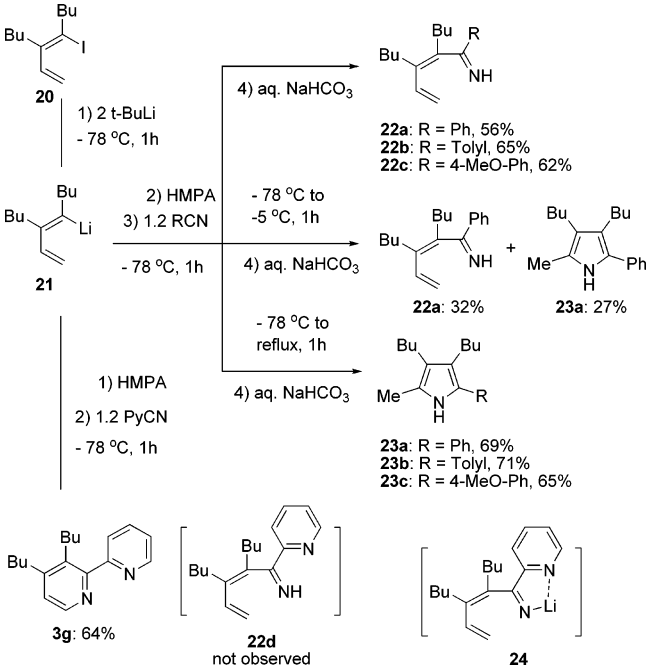
SCHEME 10. Elimination of LiCl versus Elimination of $LiSiMe_3$



SCHEME 11. Reaction of 4-Methyl-Substituted Mono Lithio Reagents with ArCN



SCHEME 12. Reaction of 1,2-Disubstituted 1-Lithio Reagents with Organonitriles

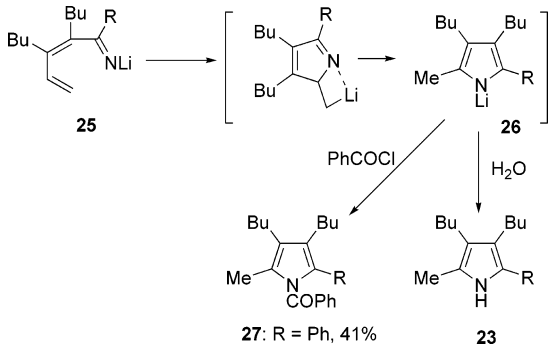


derivatives **23** were obtained as the sole products in high isolated yields. No pyridines were formed, except in the case of PyCN. When PyCN was used, the bipyridine derivative **3g** was obtained in 64% isolated yield even at −78 °C (Scheme 12). No linear imine **22d** was observed. The coordination of the nitrogen atom to the Li atom (intermediate **24**) is assumed to be essential for this special reactivity.

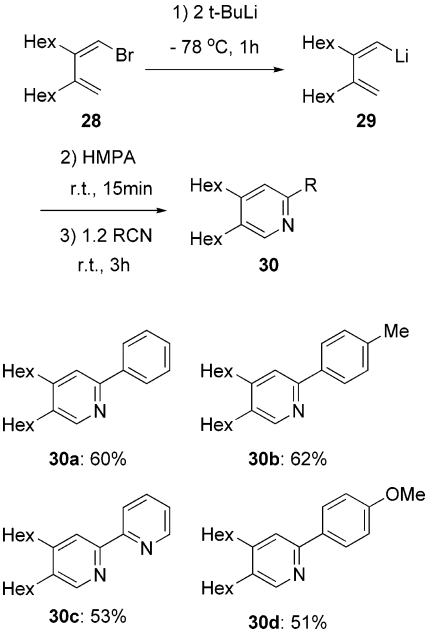
A proposed mechanism for the formation of pyrrole derivatives **23** from **21** is given in Scheme 13. The 5-exo intramolecular lithiation-cyclization of **25** took place to afford the lithio pyrrole intermediates **26**. Indeed, when the reaction mixture was further trapped with PhCOCl, acylated product **27** was formed in 41% isolated yield (Scheme 13).

Interestingly, when the substitution pattern on the butadienyl skeletons of monolithio reagents was changed to 2,3-disubstituted patterns, for example, 2,3-dihexyl-1-lithio-1,3-diene **29**,[15] its reaction with organonitriles afforded pyridine derivatives **30** as the only products (Scheme 14). No pyrrole derivatives were formed in these cases.

SCHEME 13. Proposed Mechanism for the Formation of 23 from 21



SCHEME 14. Reaction of 2,3-Disubstituted 1-Lithio Reagents with Organonitriles



Conclusions

The above results clearly demonstrate that the substitution patterns on the butadienyl skeletons of the monolithio reagents remarkably influence the reactivity of these lithium reagents. Substituents at positions 3 and 4 of the skeleton of 1-lithio-1,3-butadienes play an important role in the reaction paths, leading to either 5-exo or 6-endo cyclization. As summarized in Figure 1, *N*-lithioketimines Type I (from 1,2,3,4-tetrasubstituted lithium reagents) and Type II (from 2,3-disubstituted lithium reagents) undergo 6-endo cyclization to give pyridine derivatives, while *N*-lithioketimines Type III (with a chlorine atom at position 4) and Type IV (from 1,2-disubstituted lithium reagents) undergo 6-endo and 5-exo competitive cyclization to give either pyridine derivatives or pyrrole derivatives, depending on the reaction conditions. The order of elimination of RLi from

(15) Xi, Z.; Song, Z.; Liu, G.; Liu, X.; Takahashi, T. *J. Org. Chem.* **2006**, *71*, 3154−3158.

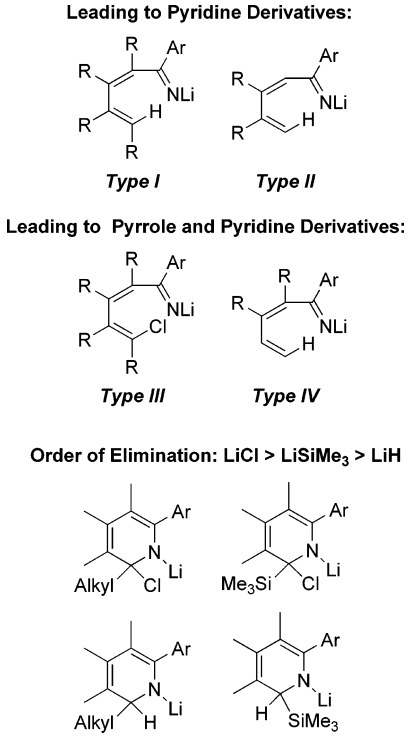


FIGURE 1. Summary of reactivities of cycloaddition intermediates of 1-lithio-1,3-dienes with organonitriles.

the lithiated cyclic N-containing intermediates was found to be LiCl > $LiSiMe_3$ > LiH. No elimination of alkyllithium salts was observed.

Experimental Section

Typical Procedure for the Preparation of Linear Butadienyl Imines 12a−c, Pyridine 3d−e, and Pyrroles 13a−d from 1,2,3,4-Tetraethyl 1-Iodo-4-chloro-1,3-diene 10a. To a diethyl ether (5 mL) solution of 1,2,3,4-tetraethyl 1-iodo-4-chloro-1,3-diene **10a** (1.0 mmol) at −78 °C was added *t*-BuLi (2.0 mmol, 1.5 M in pentane). The above reaction mixture was then stirred at −78 °C for 1 h to generate 1-lithio-1,3-diene **11a**, which was monitored by GC analysis or by TLC. After addition of organonitriles (1.2 mmol) at −78 °C, the mixture was stirred at −78 °C for 1 h. If the mixture was not quenched at −78 °C, then it was stirred at 0 °C, room temperature, or 50 °C for 3 h, respectively. The above reaction mixture was then quenched with saturated aqueous $NaHCO_3$ at −78 °C and extracted with diethyl ether. The extract was washed with brine and dried over $MgSO_4$. The solvent was evaporated in vacuo to give a yellow oil, which was purified by column chromatography to afford **12a−c** (silica, treated by Et_3N, hexane:Et_2O = 10:1), pyridines **3d**,**e** (silica, hexane:Et_2O = 30:1), and pyrroles **13a−d** (silica, hexane:Et_2O = 10:1), respectively.

12a. Colorless liquid, isolated yield 74% (235 mg). ^{1}H NMR (C_6D_6, TMS): δ 0.80 (t, J = 7.5 Hz, 3H), 0.91−0.97 (m, 6H), 1.09 (t, J = 7.8 Hz, 3H), 1.84−2.40 (m, 11H), 6.99−7.02 (m, 2H), 7.16 (s, 1H), 7.92−7.95 (m, 2H). ^{13}C NMR (C_6D_6, TMS): δ 12.6, 13.1, 13.3, 13.9, 21.3, 24.1, 25.6, 27.2, 28.8, 128.5, 129.1, 133.8, 136.4, 138.0, 138.9, 140.3, 140.5, 177.06. HRMS calcd for $C_{20}H_{28}N^{35}Cl$ 317.1910, found 317.1911.

3d. Colorless liquid, isolated yield 47% (132 mg). ^{1}H NMR ($CDCl_3$, TMS): δ 1.00 (t, J = 7.5 Hz, 3H), 1.18−1.31 (m, 9H), 2.38 (s, 3H), 2.58 (q, J = 7.5 Hz, 2H), 2.67−2.75 (m, 4H), 2.82 (q, J = 7.5 Hz, 2H), 7.18−7.31 (m, 4H). ^{13}C NMR ($CDCl_3$, TMS): δ 14.6, 15.3, 15.4, 15.6, 21.2, 21.3, 21.7, 22.0, 28.3, 128.6, 128.7, 132.4, 133.1, 136.6, 139.5, 149.1, 156.6, 158.1. HRMS calcd for $C_{20}H_{27}N$ 281.2143, found 281.2132.

13a. Colorless liquid, isolated yield 56% (157 mg). ^{1}H NMR ($CDCl_3$, TMS): δ 0.58 (t, J = 7.5 Hz, 3H), 0.93 (t, J = 7.5 Hz, 3H), 1.11 (t, J = 7.5 Hz, 3H), 1.68 (dd, J = 6.3, 1.5 Hz, 3H), 1.77−2.47 (m, 9H), 5.28 (dq, J = 15.6, 1.5 Hz, 1H), 5.69 (dq, J = 15.6, 6.3 Hz, 1H), 7.19−7.56 (m, 4H). ^{13}C NMR ($CDCl_3$, TMS): δ 7.5, 13.2, 14.3, 18.1, 18.6, 19.5, 21.3, 27.1, 83.9, 124.3, 127.6, 128.8, 131.1, 133.4, 137.1, 138.8, 166.0, 174.4. HRMS calcd for $C_{20}H_{27}N$ 281.2144, found 281.2147.

Typical Procedure for the Preparation of Pyridine 3f. To a diethyl ether (5 mL) solution of 2,3-dihexyl-1,4-di(trimethylsilyl) 1-iodo-4-chloro-1,3-diene (1.0 mmol) at −78 °C was added *t*-BuLi (2.0 mmol, 1.5 M in pentane). The above reaction mixture was then stirred at −78 °C for 1 h to generate its corresponding 1-lithio-1,3-diene **11b**, which was monitored by GC analysis or by TLC. After addition of PhCN (1.2 mmol) at −78 °C, the mixture was stirred at −78 °C for 1 h. The mixture was then stirred at room temperature for 3 h. The above reaction mixture was then quenched with saturated aqueous $NaHCO_3$ and extracted with diethyl ether. The extract was washed with brine and dried over $MgSO_4$. The solvent was evaporated in vacuo to give a yellow oil, which was purified by column chromatography (silica, hexane:Et_2O = 30:1) to afford **3f**.

3f. Colorless liquid, isolated yield 68% (318 mg). ^{1}H NMR ($CDCl_3$, TMS): δ −0.01 (s, 9H), 0.45 (s, 9H), 0.85−0.92 (m, 6H), 1.28−2.91 (m, 20H), 7.35−7.47 (m, 5H). ^{13}C NMR ($CDCl_3$, TMS): δ 2.8, 3.7, 14.0, 14.0, 22.5, 22.6, 29.5, 29.6, 30.7, 31.9, 32.0, 35.7, 37.8, 39.4, 127.4, 127.8, 127.9, 128.0, 129.8, 145.0, 165.1, 166.3, 167.3. HRMS calcd for $C_{29}H_{49}NSi_2$ 467.3404, found 467.3401.

Typical Procedure for the Preparation of Compound 19. To a diethyl ether (5 mL) solution of 1,2,3,4-tetraethyl 1-iodo-4-methyl-1,3-diene (1.0 mmol) at −78 °C was added *t*-BuLi (2.0 mmol, 1.5 M in pentane). The above reaction mixture was then stirred at −78 °C for 1 h to generate its corresponding 1-lithio-1,3-diene **17**, which was monitored by GC analysis or by TLC. After addition of PhCN (1.2 mmol) at −78 °C, the mixture was stirred at −50 °C for 1 h. PhCOCl (1.5 mmol) was added at −50 °C, and the mixture was stirred at room temperature for 1 h. The above reaction mixture was then quenched with saturated aqueous $NaHCO_3$ and extracted with diethyl ether. The extract was washed with brine and dried over $MgSO_4$. The solvent was evaporated in vacuo to give a yellow oil, which was purified by column chromatography (silica, hexane:Et_2O = 30:1) to afford **19**.

19. Colorless liquid, isolated yield 74% (286 mg). ^{1}H NMR ($CDCl_3$, TMS): δ 0.47−0.57 (m, 3H), 0.72−0.78 (m, 3H), 0.84−1.01 (m, 6H), 1.51 (s, 1.85H), 1.66 (s, 1.15H), 1.79−2.34 (m, 8H), 7.37−7.55 (m, 6H), 7.96−8.07 (m, 4H). ^{13}C NMR ($CDCl_3$, TMS): δ 11.0, 11.5, 12.1, 12.2, 12.3, 12.9, 13.2, 13.6, 15.7, 19.4, 23.6, 24.6, 26.0, 26.4, 26.6, 27.08, 27.13, 28.3, 128.3, 128.6, 128.76, 128.79, 129.2, 131.5, 131.6, 131.7, 132.1, 132.2, 132.7, 133.1, 134.1, 134.3, 134.3, 137.4, 137.5, 141.3, 141.6, 170.3, 170.4, 179.8, 180.0. HRMS calcd for $C_{27}H_{33}NO$ 387.2562, found 387.2556.

Typical Procedure for the Preparation of Linear Butadienyl Imines 22a−c, Pyridine 3g, and Pyrroles 23a−c from 1,2-Dibutyl 1-Iodo-1,3-diene 20. To a diethyl ether (5 mL) solution of 1,2-dibutyl 1-iodo-1,3-diene **20** (1.0 mmol) at −78 °C was added *t*-BuLi (2.0 mmol, 1.5 M in pentane). The above reaction mixture was then stirred at −78 °C for 1 h to generate its corresponding 1-lithio-1,3-diene **21**, which was monitored by GC analysis or by TLC. HMPA (1.0 mmol) was then added, and the reaction mixture was stirred at room temperature for 15 min. After addition of organonitriles (1.2 mmol) at −78 °C, the mixture was stirred at −78 °C for 1 h. If the mixture was not quenched at −78 °C, it was then stirred at −5 °C or refluxed for 1 h, respectively. The above reaction mixture was then quenched with saturated aqueous $NaHCO_3$ and extracted with diethyl ether. The extract was washed with brine and dried over $MgSO_4$. The solvent was evaporated in vacuo to give a yellow oil, which was purified by column chromatography to afford **22a−c** (silica, treated by Et_3N before

used, hexane:Et_2O = 10:1), pyridines **3g** (silica, treated by Et_3N, hexane: Et_2O = 30:1), and pyrroles **23a**−**c** (silica, treated by Et_3N, hexane:Et_2O = 30:1), respectively.

22a. Colorless liquid, isolated yield 56% (151 mg). ^{1}H NMR ($CDCl_3$, TMS): δ 0.82−1.01 (m, 6H), 1.29−1.52 (m, 8H), 2.22−2.40 (m, 4H), 4.96−5.00 (m, 1H), 5.22−5.28 (m, 1H), 6.30−6.39 (m, 1H), 7.37−7.44 (m, 3H), 7.75−7.77 (m, 2H), 9.20 (br, 1H). ^{13}C NMR ($CDCl_3$, TMS): δ 13.9, 14.0, 22.8, 23.2, 26.7, 30.8, 30.9, 31.6, 113.8, 127.9, 128.5, 130.8, 135.5, 136.2, 137.4, 141.2, 179.4. HRMS calcd for $C_{19}H_{27}N$ 269.2144, found 269.2137.

3g. Colorless liquid, isolated yield 64% (172 mg). ^{1}H NMR ($CDCl_3$, TMS): δ 0.76 (t, J = 7.2 Hz, 3H), 0.97 (t, J = 7.2 Hz, 3H), 1.15−1.68 (m, 8H), 2.66−2.83 (m, 4H), 7.11 (d, J = 4.8 Hz, 1H), 7.26−7.30 (m, 1H), 7.60−7.63 (m, 1H), 7.76−7.82 (m, 1H), 8.39 (d, J = 4.8 Hz, 1H), 8.64−8.66 (m, 1H). ^{13}C NMR ($CDCl_3$, TMS): δ 13.6, 14.0, 22.8, 22.9, 27.5, 32.0, 32.7, 32.8, 122.4, 124.0, 124.3, 135.1, 136.5, 146.2, 148.4, 151.0, 157.3, 159.9. HRMS calcd for $C_{18}H_{24}N_2$ 268.1940, found 268.1937.

23a. Colorless liquid, isolated yield 69% (186 mg). ^{1}H NMR ($CDCl_3$, TMS): δ 0.89−0.97 (m, 6H), 1.34−1.58 (m, 8H), 2.19 (s, 3H), 2.37−2.42 (m, 2H), 2.52−2.58 (m, 2H), 7.13−7.58 (m, 6H). ^{13}C NMR ($CDCl_3$, TMS): δ 11.4, 14.0, 14.1, 23.0, 23.1, 24.3, 24.7, 34.0, 34.0, 120.7, 120.8, 124.0, 125.4, 125.7, 126.2, 128.6, 134.3. HRMS calcd for $C_{19}H_{27}N$ 269.2144, found 269.2141.

Typical Procedure for the Preparation of Acylated Pyrrole 27. To a diethyl ether (5 mL) solution of 1,2-dibutyl 1-iodo-1,3-diene **20** (1.0 mmol) at −78 °C was added *t*-BuLi (2.0 mmol, 1.5 M in pentane). The above reaction mixture was then stirred at −78 °C for 1 h to generate 1-lithio-1,3-diene **21**, which was monitored by GC analysis or by TLC. HMPA (1.0 mmol) was then added, and the reaction mixture was stirred at room temperature for 15 min. After addition of organonitriles (1.2 mmol) at −78 °C, the mixture was stirred at −78 °C for 1 h. It was then stirred refluxing for 1 h. PhCOCl (1.5 mmol) was added, and the reaction mixture was stirred at room temperature for 1 h. The above reaction mixture was then quenched with saturated aqueous $NaHCO_3$ and extracted with diethyl ether. The extract was washed with brine and dried over $MgSO_4$. The solvent was evaporated in vacuo to give a yellow oil, which was purified by column chromatography (silica, hexane: Et_2O = 10:1) to afford **27**.

27. Colorless liquid, isolated yield 41% (153 mg). ^{1}H NMR ($CDCl_3$, TMS): δ 0.83 (t, J = 7.2 Hz, 3H), 0.97 (t, J = 7.2 Hz, 3H), 1.22−1.57 (m, 8H), 2.24 (s, 3H), 2.34−2.47 (m, 4H), 6.96−7.48 (m, 10H). ^{13}C NMR ($CDCl_3$, TMS): δ 11.9, 13.9, 14.1, 22.8, 22.9, 24.2, 24.2, 33.5, 33.7, 123.2, 125.0, 126.1, 127.7, 127.75, 127.83, 129.5, 123.0, 130.2, 132.4, 133.7, 136.0, 171.2. HRMS calcd for $C_{26}H_{31}NO$ 373.2406, found 373.2406.

Typical Procedure for the Preparation of Pyridines 30a−d. To a THF (5 mL) solution of 2,3-dihexyl 1-bromo-1,3-diene **28** (1.0 mmol) at −78 °C was added *t*-BuLi (2.0 mmol, 1.5 M in pentane). The above reaction mixture was then stirred at −78 °C for 1 h to generate its corresponding 1-lithio-1,3-diene **29**, which was monitored by GC analysis or by TLC. HMPA (1.0 mmol) was then added, and the reaction mixture was stirred at room temperature for 15 min. After addition of organonitriles (1.2 mmol), the mixture was stirred at room temperature for 3 h. The above reaction mixture was then quenched with saturated aqueous $NaHCO_3$ and extracted with diethyl ether. The extract was washed with brine and dried over $MgSO_4$. The solvent was evaporated in vacuo to give a yellow oil, which was purified by column chromatography (silica, hexane: Et_2O = 30:1) to afford **30a**−**d**.

30a. Colorless liquid, isolated yield 60% (194 mg). ^{1}H NMR ($CDCl_3$, TMS): δ 0.88−0.92 (m, 6H), 1.32−1.67 (m, 16H), 2.60−2.66 (m, 4H), 7.24−7.49 (m, 4H), 7.94−7.98 (m, 2H), 8.42 (s, 1H). ^{13}C NMR ($CDCl_3$, TMS): δ 14.1, 22.61, 22.64, 29.3, 29.4, 29.8, 30.4, 31.0, 31.7, 32.2, 120.7, 126.7, 128.4, 128.6, 134.6, 139.7, 150.0, 150.3, 155.0. HRMS calcd for $C_{23}H_{33}N$ 323.2613, found 323.2608.

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Supporting Information Available: Characterization data for all products except for an illustrative example; copies of ^{1}H and ^{13}C NMR spectra for all isolated compounds. This material is available free of charge via the Internet at http://pubs.acs.org.

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