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Reactions via Carbonyl Anions. [4 + 1] Cyclocoupling of the Azadienyllithium with Carbon Monoxide

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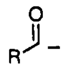
Generation and reactions of carbonyl anions, relatively unknown species, have been studied. The reaction of β-phenyl-2-azaethenyllithium **13**, generated from aryl isocyanides **12** and *t*-BuLi, with carbon monoxide gives 3*H*-indole derivatives **18** in 42–44% yields after quenching with methyl iodide. Similarly, β-phenyl-1-azaethenyllithium **21**, obtainable by the addition of alkyllithium to benzonitriles **20**, reacts with carbon monoxide and methyl iodide to afford 1*H*-isoindole derivatives **27** in 73–81% yields. A 1,4-diazabutadienyl anion **35** gives a cyclic urea **39** on reacting with carbon monoxide and methyl iodide. These reactions represent novel [4 + 1] cyclocoupling reactions of dienyl anions with carbon monoxide via carbonyl anions **14**, **23**, and **36** as the intermediates.

Introduction

The chemical species having a negatively charged carbonyl group is called carbonyl anion or acyllithium and represented by the structure **1** or **2**, respectively. These species appear rarely in chemical literatures and not at all in organic chemistry textbooks, since they are too reactive to be characterized or to undergo selective and meaningful reactions. It has long been suggested that usually very complex reaction of organolithium compounds with carbon monoxide might proceed via acyllithium as the initial intermediate.[1] Recently, two research directions have met success in realizing highly selective reactions via otherwise almost uncontrollable reaction of an acyllithium. One is trapping of acyllithium, generated from alkyllithium and carbon monoxide, by electrophiles present in situ under very careful reaction conditions.[2] This methodology reported by Seyferth may be referred to as the *intermolecular* version. The other methodology developed by us has been based on the *intramolecular* reactions, which enables the immediate conversion of an acyllithium generated to other still-reactive species such as lithium enolates.[3]



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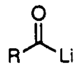

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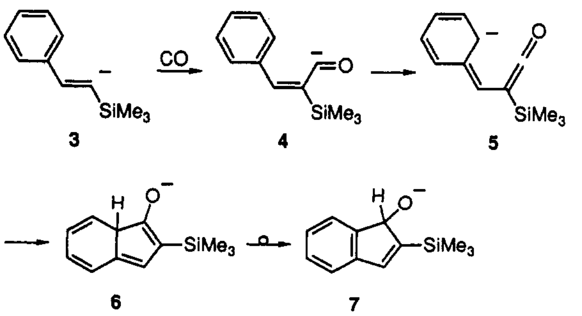
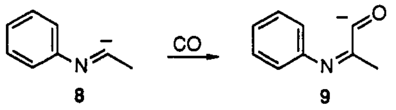
In our previous study on cyclization via an acyllithium, we reported formal [4 + 1] cyclocoupling of (β-phenylvinyl)lithium **3** with carbon monoxide (eq 1).[3b]



(1)

We have now found that the unique [4 + 1] cyclocoupling is not limited to the reported example of **3** but can be extended to nitrogen-containing analogues **8** and **10** (eqs 2 and 3). The results of the study on these new *intramolecular* reactions via carbonyl anions **9** and **11** are described below.



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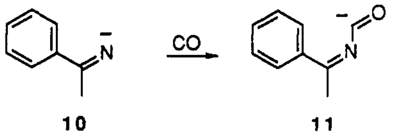

(3)

Results and Discussion

For vinyl anions such as (β-phenylvinyl)lithium **3**, a variety of methods are available for their generation. For the anions **8** (*C*-lithioaldimine) in which the β-carbon atom is replaced with a nitrogen atom in **3**, conventional methods of lithiation such as metal–halogen exchange or hydrogen abstraction can not be applied. We have prepared the *C*-lithioaldimines **8** by α-addition of alkyllithium to isocyanides.[4] The anions **10** (*N*-lithioketimine) can be easily prepared from alkyllithium and nitriles. The lithio compounds **8** and **10** were prepared generally in the range of 50–90% yields[5] and subjected to the reaction with carbon monoxide in situ. One of the double bonds

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(1) (a) Ryan, M.; Tsutsumi, S. *Bull. Chem. Soc. Jpn.* **1962**, *35*, 1121. (b) Jutzi, P.; Schöder, F.-W. *J. Organomet. Chem.* **1970**, *24*, 1. (c) Trzupek, L. S.; Newirth, T. L.; Kelly, E. G.; Sbarbati, N. E.; Whitesides, G. M. *J. Am. Chem. Soc.* **1973**, *95*, 8118. (d) Nudelman, N. S.; Vitale, A. A. *J. Org. Chem.* **1981**, *46*, 4626.

(2) (a) Seyferth, D.; Weinstein, R. M. *J. Am. Chem. Soc.* **1982**, *104*, 5534. (b) Seyferth, D.; Hui, R. C. *Organometallics* **1984**, *3*, 327. (c) Seyferth, D.; Hui, R. C. *Tetrahedron Lett.* **1984**, *25*, 5251. (d) Seyferth, D.; Weinstein, R. M.; Hui, R. C.; Wang, W.-L.; Archer, C. M. *J. Org. Chem.* **1991**, *56*, 5768. (e) Seyferth, D.; Weinstein, R. M.; Hui, R. C.; Wang, W.-L.; Archer, C. M. *J. Org. Chem.* **1992**, *57*, 5620.

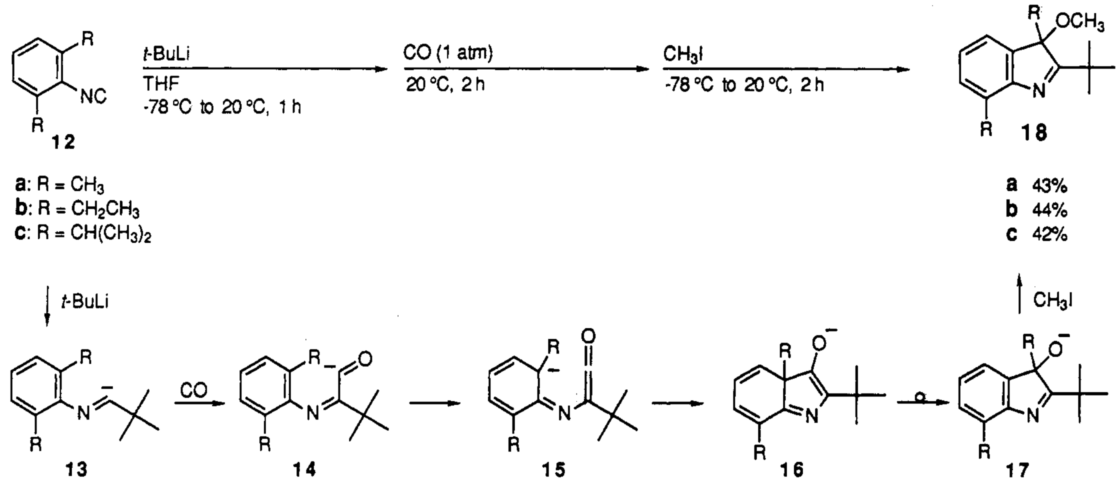
(3) (a) Murai, S.; Ryu, I.; Iriguchi, J.; Sonoda, N. *J. Am. Chem. Soc.* **1984**, *106*, 2440. (b) Ryu, I.; Hayama, Y.; Hirai, A.; Sonoda, N.; Orita, A.; Ohe, K.; Murai, S. *J. Am. Chem. Soc.* **1990**, *112*, 7061. See also: (c) Smith, K.; Pritchard, G. J. *Angew. Chem., Int. Ed. Engl.* **1990**, *29*, 282.

(4) (a) Walborsky, H. M.; Niznik, G. E. *J. Am. Chem. Soc.* **1969**, *91*, 7778. (b) Walborsky, H. M.; Ronman, P. *J. Org. Chem.* **1978**, *43*, 731. (c) Ito, Y.; Kobayashi, K.; Saegusa, T. *J. Am. Chem. Soc.* **1977**, *99*, 3532. (d) Ito, Y.; Kobayashi, K.; Seko, N.; Saegusa, T. *Bull. Chem. Soc. Jpn.* **1984**, *57*, 73.

(5) As confirmed by quenching with methyl iodide or aqueous NH_4Cl.

0022-3263/94/1959-0477$04.50/0

Scheme 1

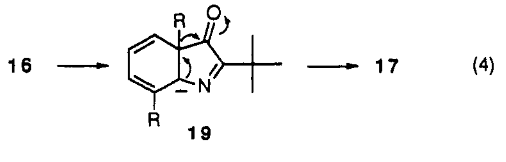


in aryl groups in **8** and **10** worked as a part of the azabutadienyl unit in the cyclocoupling described below.

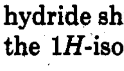
Reaction of *C*-Lithioaldimines 13 with Carbon Monoxide. When reacted with carbon monoxide, *C*-lithioaldimines **13** having a dialkylphenyl group underwent [4 + 1] cyclocoupling similar to that of eq 1, interestingly, with alkyl migration (Scheme 1).

We were obliged to use the 2,6-dialkylphenyl group as in **12**, since unsubstituted phenyl isocyanide suffered from ortho lithiation.[6] To the THF solution of 2,6-dimethylphenyl isocyanide (**12a**) was added a pentane solution of *t*-BuLi (1.2 equiv) at −78 °C. The mixture was exposed to carbon monoxide of an atmospheric pressure at 20 °C for 2 h, wherein 0.5–1.3 equiv of carbon monoxide was absorbed. After quenching with methyl iodide (10 equiv) at −78 °C, the mixture was allowed to warm up to 20 °C. The standard workup gave a 3*H*-indole derivative **18a** in 43% yield. Similarly, **18b** and **18c** were obtained in the yields of 44 and 42% from the corresponding isocyanides **12b** and **12c**, respectively.

The cyclization may have proceeded according to the steps shown in Scheme 1. The carbonyl anion **14** cyclizes from the structure of **15** to give **16**. This *intramolecular* process seems successfully fast enough to compete with *intermolecular* reactions which take place usually giving very complex results. The rearrangement of an alkyl group in **16** is interesting. The driving force would certainly be aromatization energy. In addition, the negative charge in **19** forces the alkyl group to migrate onto the electron deficient adjacent carbonyl atom (eq 4). There have been scattered precedents of the rearrangement of an alkyl group wherein it is pushed by a negative charge, and an adjacent electrophilic center can accommodate the migrating alkyl group.[7,8] It is important for realizing selective reactions via carbonyl anions which are usually too reactive to discriminate electrophiles that the generated product should not possess any electrophilic centers such as a carbonyl group. The intermediate **17** no longer has a carbonyl function and has only an imino group sterically protected by a bulky *tert*-butyl group.



Reaction of *N*-Lithioketimines 21 with Carbon Monoxide. Encouraged by the results described above, we examined the reaction of *C*-aryl-*N*-lithioketimines **21** with carbon monoxide. In this case the expected carbonyl anion is of the type of **11**. Although such a carbonyl anion is not known to our knowledge, this species such as carbamoyllithium **22** seems to be less reactive than acyllithium **2**.[9] We thought this stability would lead to satisfied results. As shown in Scheme 2, the [4 + 1] cyclocoupling proceeded nicely with *N*-lithioketimines **21** and carbon monoxide. Interestingly, the results imply that the cyclization takes place also through isocyanate intermediate **24**. The hydride shift in **25**, similar to that from **6** to **7**, afforded the 1*H*-isoindole derivatives **26**.[10]



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The *N*-lithioketimine **21** was prepared from an aryl cyanide and alkyllithium as shown in Scheme 2. A similar *N*-lithioketimine can also be prepared from an alkyl cyanide and aryllithium. Thus, *tert*-butyl cyanide reacted with 2-lithiofuran to give **28**. The anion **28** then reacted with carbon monoxide and methyl iodide successively to

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[6] See ref 4b.

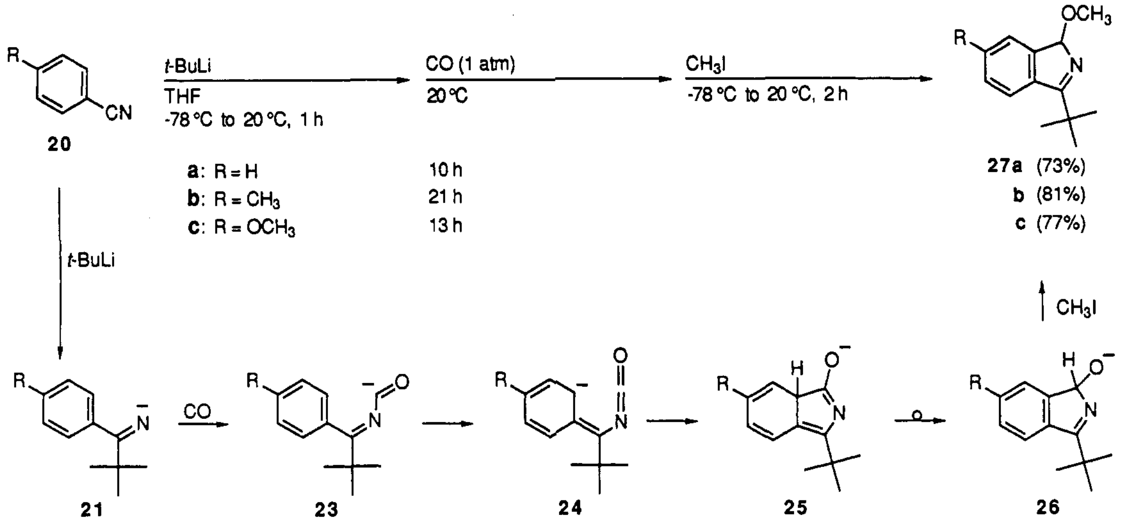
[7] For examples in boronate complexes: (a) Levy, A. B.; Schwartz, S. J. *Tetrahedron Lett.* **1976**, 2201. (b) Danheiser, R. L.; Savoca, A. C. *J. Org. Chem.* **1985**, *50*, 2401. In cuprate complexes: (c) Kitatani, K.; Hiyama, T.; Nozaki, H. *Bull. Chem. Soc. Jpn.* **1977**, *50*, 1600. (d) Kocienski, P.; Wadman, S. *J. Am. Chem. Soc.* **1989**, *111*, 2363. In zincate complexes: (e) Harada, T.; Hattori, K.; Katsuhira, T.; Oku, A. *Tetrahedron Lett.* **1989**, *30*, 6035. (f) Harada, T.; Katsuhira, T.; Hattori, K.; Oku, A. *J. Org. Chem.* **1993**, *58*, 2958. In (α-haloacyl)silanes: (g) Sato, T.; Abe, T.; Kuwajima, I. *Tetrahedron Lett.* **1978**, 259. (h) Kuwajima, I.; Matsumoto, K. *Tetrahedron Lett.* **1979**, 4095. (i) Sato, T.; Matsumoto, K, Abe, T.; Kuwajima, I. *Bull. Chem. Soc. Jpn.* **1984**, *57*, 2167.

[8] Smith has reported topologically similar migration of *tert*-butyl group in the reaction involving an aroyllithuim, see ref 3c.

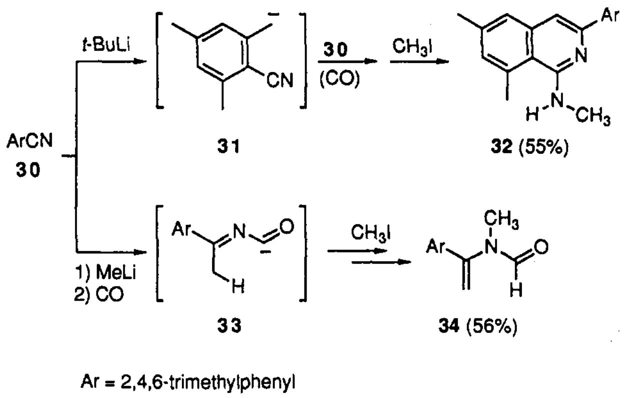
[9] (a) Jutzi, P.; Schröder, F.-W. *Angew. Chem., Int. Ed. Engl.* **1971**, *10*, 339. (b) Rautenstrauch, V.; Joyeux, M. *Angew. Chem., Int. Ed. Engl.* **1979**, *18*, 83. (c) Rautenstrauch, V.; Joyeux, M. *Angew. Chem., Int. Ed. Engl.* **1979**, *18*, 85. (d) Narayana, C.; Periasamy, M. *Synthesis* **1985**, 253. (e) Lindsay, C. M.; Widdowson, D. A. *J. Chem. Soc., Perkin Trans. 1* **1988**, 569. (f) Peretz, D. G.; Nudelman, N. S. *J. Org. Chem.* **1988**, *53*, 408. (g) Mizuno, T.; Nishiguchi, I.; Okushi, T.; Hirashima, T. *Tetrahedron Lett.* **1991**, *32*, 6867.

[10] An alternative mechanism for this step, i.e., a [1,5] hydrogen sigmatropic shift in **25**, remains.

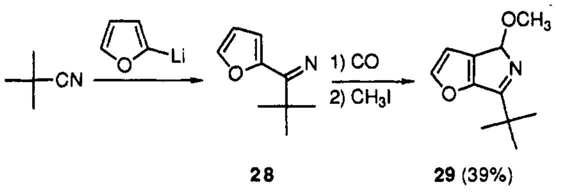
Scheme 2



Scheme 3



afford an interesting heterocycle **29** (eq 5). The result

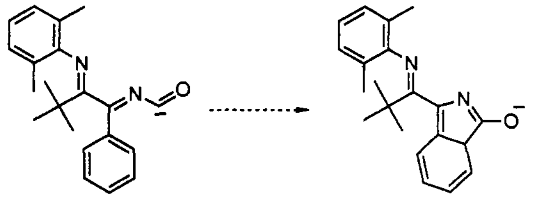
 (5)

indicates that a furan ring can be a component of [4 + 1] cyclocoupling with carbon monoxide.

We have attempted the reaction using 2,6-dialkyl-substituted benzonitriles. However, we could not observe the cyclization similar to that shown in Scheme 1, instead, undesired reactions took place (Scheme 3). Nitrile **30** reacted with *t*-BuLi but gave a benzyl anion **31**, which reacted with another molecule of **30**, leading to **32** without reacting with carbon monoxide. The same nitrile **30** reacted with MeLi and then carbon monoxide to afford an carbonyl anion **33**, in which intramolecular proton abstraction altered the course of the reaction to afford **34**.

Reaction of 1,4-Diazabutadienyllithium 35 with Carbon Monoxide. In the [4 + 1] cyclocoupling described above, one unsaturated bond in the phenyl group participated in the reaction as a part of the 4π component in conjugation with a carbon–nitrogen double bond. It seemed important and interesting to find a [4 + 1] cyclocoupling reaction not involving a phenyl ring as the part of the 4π component. After various attempts, we have succeeded in generation of a suitable anion for this purpose, i.e., 1,4-diazabutadienyllithium **35**, and found another new [4 + 1] cyclocoupling as illustrated in Scheme 4.

Isocyanide **12a** was converted by successively reacting with four reagents (*t*-BuLi, RCN, CO, and CH_3I) to urea derivatives **39** in the yields of 49% for R = Ph and 44% for R = *t*-Bu in one pot under the conditions shown in Scheme 4. The 1,4-diazabutadienyllithium **35** underwent [4 + 1] cyclocoupling with carbon monoxide via the carbonyl anions **36** and the isocyanates **37**.

 (6)

36a

It was interesting to note that the carbonyl anion **36a** did not cyclize according to the course of eq 6, in correspondence to the transformation of **23** to **25** in Scheme 2. The intermediate **37a** in which the negative charge is largely localized on the electronegative nitrogen atom should be more stable than the structure required for the reaction of eq 6 (not shown but similar to **24**), destroying aromatic stabilization.

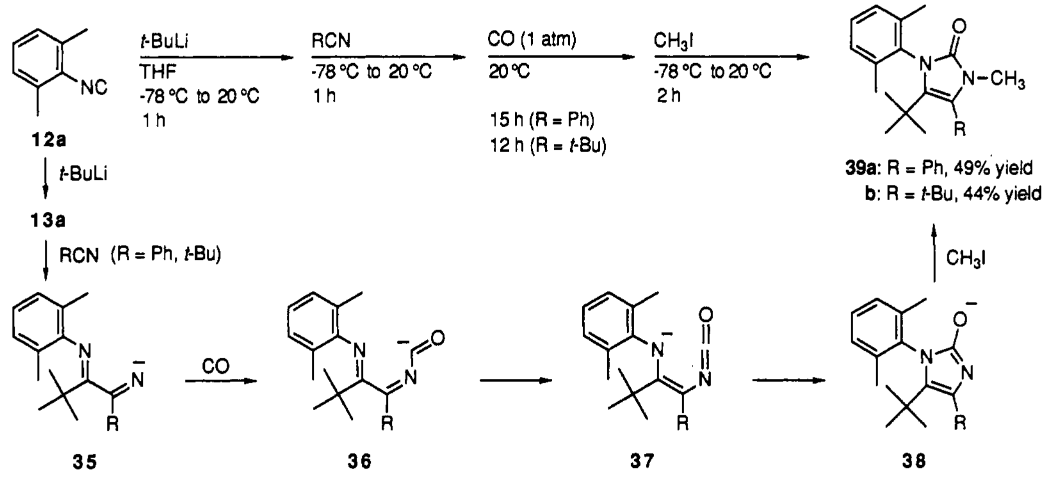
Conclusion

It has been demonstrated that the strategy of *intramolecular* conversion is effective for realizing selective reactions of very reactive carbonyl anions. The [4 + 1] cyclocoupling proceeds when azabutadienyllithium compounds are reacted with carbon monoxide. The examples of [4 + 1] cyclocoupling have been found for 2-azabutadienyl (Scheme 1), 1-azabutadienyl (Scheme 2), and 1,4-diazabutadienyl (Scheme 4) systems. The new [4 + 1] cyclocoupling reaction, in addition to the one previous reported (eq 1),[3b] seems to have considerable generality and should find further applications.

Experimental Section

All glassware was flame-dried prior to use under a stream of dried nitrogen. Tetrahydrofuran (THF) was distilled from sodium benzophenone ketyl. A 1.7 M pentane solution of *t*-BuLi

Scheme 4



(Aldrich Chemical Co.) and a 1.2 M ether solution of MeLi (Tokyo Kasei Kogyo Co.) were purchased and used without titration. A hexane solution of *n*-BuLi (Nacalai Tesque, Inc.) was purchased and titrated prior to use by the Gilman method.[11] ^{1}H NMR and ^{13}C NMR spectra were recorded on a JEOL GSX 270 (^{1}H at 270 MHz, ^{13}C at 68 MHz) spectrometer as solutions in $CDCl_3$. Mass spectra were recorded on a Shimadzu GCMS-QP1000 spectrometer. IR spectra were recorded on a Hitachi 270-50 infrared spectrophotometer as KBr pellets or neat. Melting points were determined on a Mitamura Riken Kogyo micro melting point apparatus and were uncorrected.

The isocyanides 12[12] and nitrile 30[13] were prepared according to the literature. Others were commercially available.

Reaction of 2,6-Dimethylphenyl Isocyanide (12a) with *t*-BuLi and Carbon Monoxide. A 100-mL round-bottomed flask equipped with a magnetic stirrer bar, a three-way stopcock, and a nitrogen line was flame-dried under a stream of nitrogen. In the reaction flask were placed 20 mL of anhydrous THF and 0.524 g (4.0 mmol) of 2,6-dimethylphenyl isocyanide (**12a**), and the solution was cooled to -78 °C with a dry ice/MeOH bath. To the stirred solution was added dropwise 2.8 mL of a pentane solution of *t*-BuLi (1.7 M, 4.8 mmol) by a syringe, and the mixture was allowed to warm up gradually to 20 °C over 1 h. The three-way stopcock was then connected to a vacuum line (20 mmHg) and also to a balloon filled with carbon monoxide through a glass column packed with soda lime and anhydrous calcium sulfate. After two cycles of evacuation of nitrogen and filling with carbon monoxide, the reaction mixture was stirred under the atmosphere of carbon monoxide for 2 h, wherein 58 mL (0.60 equiv) of carbon monoxide was absorbed. To the reaction mixture was added 2.48 mL (40 mmol) of methyl iodide at -78 °C and the mixture was allowed to warm up gradually to 20 °C. To the mixture were added 20 mL of ether and 20 mL of water, and the organic layer was separated. The aqueous layer was extracted with ether (15 mL × 3). The organic layers were combined and dried over magnesium sulfate. The solvents were removed under reduced pressure to provide a brown liquid, which was subjected to column chromatography on silica gel (hexane/CH_2Cl_2 3:2) and Kugelrohr distillation (160 °C/7 Torr) to give pure 3,7-dimethyl-2-(1,1-dimethylethyl)-3-methoxy-3*H*-indole (**18a**, 0.399 g, 43% yield).

3,7-Dimethyl-2-(1,1-dimethylethyl)-3-methoxy-3*H*-indole (18a): 43% yield; white solid, mp 54-56 °C; ^{1}H NMR ($CDCl_3$) δ 1.42 (s, 9H, *t*-Bu), 1.64 (s, 3H, CH_3), 2.52 (s, 3H, CH_3), 2.86 (s, 3H, CH_3O), 7.03 (dd, J = 6.8, 2.2 Hz, 1H, ArH), 7.09 (dd, J = 7.6, 6.8 Hz, 1H, ArH), 7.13 (dd, J = 7.6, 2.2 Hz, ArH); ^{13}C NMR ($CDCl_3$) δ 16.3 (CH_3), 24.2 (CH_3), 29.4 ($(CH_3)_3C$), 37.3 ($(CH_3)_3C$), 53.0 (CH_3O), 91.0 (CH_3OC), 119.2 (Ar), 125.6 (Ar), 130.2 (Ar), 130.8 (Ar), 138.5 (Ar), 150.1 (Ar), 189.9 (C=N); IR (KBr) 1558 (C=N) cm^{-1}; MS m/z (rel inten) 216 (M^+ - 15, 6), 175 (26), 174 (11), 161 (11), 160 (100), 57 (30). Anal. Calcd for $C_{15}H_{21}NO$: C, 77.88; H, 9.15; N, 6.05. Found: C, 77.80; H, 9.17; N, 6.02.

3,7-Diethyl-2-(1,1-dimethylethyl)-3-methoxy-3*H*-indole (18b): 44% yield; colorless liquid, bp 206 °C/7 Torr; ^{1}H NMR ($CDCl_3$) δ 0.52 (t, J = 7.6 Hz, 3H, CH_3), 1.28 (t, J = 7.6 Hz, 3H, CH_3), 1.42 (s, 9H, *t*-Bu), 2.12 (q, J = 7.6 Hz, 2H, CH_2), 2.90 (s, 3H, CH_3O), 2.94 (td, J = 7.6, 2.7 Hz, 2H, CH_2), 7.00 (dd, J = 6.6, 1.9 Hz, 1H, ArH), 7.10 (dd, J = 7.6, 6.6 Hz, 1H, ArH), 7.15 (dd, J = 7.6, 1.9 Hz, 1H, ArH); ^{13}C NMR ($CDCl_3$) δ 7.6 (CH_3), 15.2 (CH_3), 23.8 (CH_2), 29.4 (CH_2), 29.8 ($(CH_3)_3C$), 37.2 ($(CH_3)_3C$), 53.2 (CH_3O), 96.1 (CH_3OC), 119.8 (Ar), 125.5 (Ar), 128.9 (Ar), 136.3 (Ar), 136.6 (Ar), 151.4 (Ar), 189.1 (C=N); IR (neat) 1564 (C=N) cm^{-1}; MS m/z (rel inten) 259 (M^+, 3), 244 (36), 203 (39), 202 (30), 189 (15), 188 (100), 115 (10), 77 (11), 57 (35). Anal. Calcd for $C_{17}H_{25}NO$: C, 78.72; H, 9.71; N, 5.40. Found: C, 78.76; H, 9.79; N, 5.48.

2-(1,1-Dimethylethyl)-3-methoxy-3,7-bis(1-methylethyl)-3*H*-indole (18c): 42% yield; colorless liquid, bp 182 °C/5 Torr; ^{1}H NMR ($CDCl_3$) δ 0.34 (d, J = 6.8 Hz, 3H, CH_3), 1.20 (d, J = 6.8 Hz, 3H, CH_3), 1.29 (d, J = 6.8 Hz, 3H, CH_3), 1.31 (d, J = 6.7 Hz, 3H, CH_3), 1.42 (s, 9H, *t*-Bu), 2.58 (hept, J = 6.8 Hz, 1H, CH), 2.92 (s, 3H, CH_3O), 3.63 (hept, J = 6.8 Hz, 1H, CH), 7.06 (dd, J = 6.8, 2.7 Hz, 1H, ArH), 7.08 (t, J = 6.8 Hz, 1H, Ar), 7.19 (dd, J = 6.8, 2.7 Hz, 1H, ArH); ^{13}C NMR ($CDCl_3$) δ 16.4 (CH_3), 16.8 (CH_3), 22.8 (CH_3), 23.6 (CH_3), 28.7 (CH), 29.6 ($(CH_3)_3C$), 32.2 (CH), 37.2 ($(CH_3)_3C$), 53.6 (CH_3O), 99.0 (CH_3OC), 121.3 (Ar), 124.8 (Ar), 126.0 (Ar), 134.5 (Ar), 140.6 (Ar), 151.3 (Ar), 189.8 (C=N); IR (KBr) 1566 (C=N) cm^{-1}; MS m/z (rel inten) 287 (M^+, 3), 272 (60), 244 (26), 231 (52), 230 (100), 217 (14), 216 (93), 198 (24), 188 (15), 183 (17), 182 (10), 168 (11), 158 (10), 156 (10), 144 (10), 115 (14), 91 (14), 77 (11), 57 (48). Anal. Calcd for $C_{19}H_{29}NO$: C, 79.39; H, 10.17; N, 4.87. Found: C, 79.12; H, 10.28; N, 4.96.

Reaction of Benzonitrile (20a) with *t*-BuLi and Carbon Monoxide. In the similar manner as described for **12a**, 0.206 g (2.0 mmol) of benzonitrile (**20a**) in 20 mL of THF was reacted with *t*-BuLi (1.7 M in pentane, 2.4 mmol, 1.4 mL) at -78 °C and then warmed to 20 °C (over 1 h), carbon monoxide (54 mL, 1.1 equiv absorbed during 10 h) at 20 °C, and methyl iodide (20 mmol) at -78 °C then warmed to 20 °C. Kugelrohr distillation (110 °C/6 Torr) of the product mixture gave pure 3-(1,1-dimethylethyl)-1-methoxy-1*H*-isoindole (**27a**, 0.301 g, 73% yield).

3-(1,1-Dimethylethyl)-1-methoxy-1*H*-isoindole (27a): 73% yield; white solid, mp 82-85 °C; ^{1}H NMR ($CDCl_3$) δ 1.03 (s, 9H, *t*-Bu), 3.24 (s, 3H, CH_3O), 4.18 (s, 1H, CH), 7.4-7.5 (m, 3H, ArH), 7.8-7.9 (m, 1H, ArH); ^{13}C NMR δ 27.4 ($(CH_3)_3C$), 33.0 (CH_3O), 36.3 ($(CH_3)_3C$), 72.3 (CH), 123.3 (Ar), 124.1 (Ar), 127.9 (Ar), 130.4 (Ar), 133.0 (Ar), 144.8 (Ar), 170.1 (C=N); IR (KBr) 1684 (C=N) cm^{-1}; MS, m/z (rel inten) 203 (M^+, 0.2), 148 (11), 147 (100), 146 (69), 91 (15). Anal. Calcd for $C_{13}H_{17}NO$: C, 76.81; H, 8.43; N, 6.89. Found: C, 76.56; H, 8.37; N, 6.82.

3-(1,1-Dimethylethyl)-1-methoxy-6-methyl-1*H*-isoindole (27b): 81% yield; white solid, mp 88-90 °C; ^{1}H NMR ($CDCl_3$)

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δ 1.02 (s, 9H, *t*-Bu), 2.42 (s, 3H, CH_3), 3.23 (s, 3H, CH_3O), 4.09 (s, 1H, CH), 7.27 (d, J = 7.8 Hz, 1H, ArH), 7.36 (d, J = 7.8 Hz, 1H, ArH), 7.63 (s, 1H, ArH); ^{13}C NMR ($CDCl_3$) δ 21.0 (CH_3), 27.2 ($(CH_3)_3C$), 32.8 (CH_3O), 36.1 ($(CH_3)_3C$), 72.0 (CH), 123.4 (Ar), 123.7 (Ar), 131.2 (Ar), 133.0 (Ar), 137.7 (Ar), 141.8 (Ar), 170.1 (C=N); IR (KBr) 1678 (C=N) cm^{-1}; MS m/z (rel inten) 217 (M^+, 0.1), 162 (10), 161 (90), 160 (100), 105 (12). Anal. Calcd for $C_{14}H_{19}NO$: C, 77.38; H, 8.81; N, 6.45. Found: C, 77.36; H, 8.90; N, 6.41.

1,6-Dimethoxy-3-(1,1-dimethylethyl)-1*H*-isoindole (27c): 77% yield; white solid, mp 104–106 °C; ^{1}H NMR ($CDCl_3$) δ 1.02 (s, 9H, *t*-Bu), 3.23 (s, 3H, CH_3O), 3.86 (s, 3H, CH_3O), 4.08 (s, 1H, CH), 7.02 (dd, J = 8.3, 2.4 Hz, 1H, ArH), 7.32 (d, 1H, J = 2.44 Hz, ArH), 7.37 (d, 1H, J = 8.3 Hz, ArH); ^{13}C NMR ($CDCl_3$) δ 27.2 ($(CH_3)_3C$), 32.9 (CH_3O), 36.2 ($(CH_3)_3C$), 55.5 (CH_3O), 71.9 (CH), 106.0 (Ar), 118.4 (Ar), 124.9 (Ar), 134.3 (Ar), 136.9 (Ar), 159.7 (Ar), 169.9 (C=N); IR (KBr) 1680 (C=N) cm^{-1}; MS m/z (rel inten) 233 (M^+, 0.2), 177 (51), 176 (100). Anal. Calcd for $C_{14}H_{19}NO_2$: C, 72.07; H, 8.21; N, 6.00. Found: C, 72.10; H, 8.25; N, 5.95.

Reaction of *tert*-Butyl Cyanide with 2-Lithiofuran and Carbon Monoxide. A THF solution of 2-lithiofuran was prepared from 0.190 g (2.8 mmol) of furan and 2.0 mL of a hexane solution of *n*-BuLi (1.4 M, 2.8 mmol) in 5 mL of anhydrous THF at −20 °C over 1 h.[14] The solution was added dropwise with a canula to 5 mL of a THF solution of 0.172 g (2.1 mmol) of *tert*-butyl cyanide at −78 °C. The mixture was allowed to warm up to 20 °C and exposed to an atmosphere of carbon monoxide for 24 h, wherein 36 mL of carbon monoxide (0.71 equiv) was absorbed. Quenching with methyl iodide (20 mmol) at 20 °C and usual workup followed by gradient elution chromatography on silica gel (1:0, 1:1 CH_2Cl_2/ether) gave pure 2-(1,1-dimethylethyl)-4-methoxy-4*H*-pyrrolo[4,3-*b*]furan (**29**, 0.156 g, 39% yield).

2-(1,1-Dimethylethyl)-4-methoxy-4*H*-pyrrolo[4,3-*b*]furan (29): 39% yield; white solid, mp 106–108 °C; ^{1}H NMR ($CDCl_3$) δ 1.03 (s, 9H, *t*-Bu), 3.14 (s, 3H, CH_3O), 3.96 (s, 1H, CH), 6.59 (d, J = 2.0 Hz, 1H, CH), 7.47 (d, J = 2.0 Hz, 1H, CH); ^{13}C NMR ($CDCl_3$) δ 26.4 ($(CH_3)_3C$), 32.0 (CH_3O), 35.5 ($(CH_3)_3C$), 69.7 (CH), 105.3 (Ar), 121.4 (Ar), 147.5 (Ar), 166.8 (Ar), 169.5 (C=N); IR (KBr) 1682 (C=N) cm^{-1}; MS m/z (rel inten) 193 (M^+, 2), 137 (100), 136 (15), 109 (12), 57 (16). Anal. Calcd for $C_{11}H_{15}NO_2$: C, 68.37; H, 7.82; N, 7.25. Found: C, 68.36; H, 7.82; N, 7.22.

Reaction of 2,4,6-Trimethylbenzonitrile (30) with *t*-BuLi and Carbon Monoxide. In the similar manner as described for **12a**, 0.870 g (6.0 mmol) of 2,4,6-trimethylbenzonitrile (**30**) in 30 mL of THF was reacted with *t*-BuLi (1.7 M in pentane, 7.1 mmol, 4.2 mL) at −78 °C and then warmed to 20 °C over 1 h. The reaction mixture was stirred under the atmosphere of carbon monoxide for 15 h and 3.72 mL (60 mmol) of methyl iodide was added to the mixture at −78 °C. After 1 h at 20 °C and usual workup, gradient elution chromatography on silica gel (8:1, 2:1 hexane/ether) of the product mixture gave pure 6,8-dimethyl-1-(methylamino)-3-(2,4,6-trimethylphenyl)isoquinoline (**32**, 0.267 g, 55% yield).

6,8-Dimethyl-1-(methylamino)-3-(2,4,6-trimethylphenyl)isoquinoline (32): 55% yield; white solid, mp 168–170 °C; ^{1}H NMR ($CDCl_3$) δ 2.16 (s, 6H, CH_3), 2.33 (s, 3H, CH_3), 2.40 (s, 3H, CH_3), 2.91 (s, 3H, CH_3), 3.05 (d, J = 4.9 Hz, 3H, CH_3), 5.52 (br, 1H, NH), 6.70 (s, 1H, ArH), 6.93 (s, 3H, ArH), 7.01 (s, 1H, ArH), 7.26 (s, 1H, ArH); ^{13}C NMR ($CDCl_3$) δ 20.3 (CH_3), 21.1 (CH_3), 21.2 (CH_3), 24.7 (CH_3), 29.5 (CH_3), 111.4 (Ar), 115.8 (Ar), 125.0 (Ar), 128.1 (Ar), 130.9 (Ar), 133.0 (Ar), 136.3 (Ar), 136.6 (Ar), 138.7 (Ar), 139.6 (Ar), 150.7 (Ar), 156.8 (Ar); IR (KBr) 3508 (NH), 2968, 1623, 1575, 1521 cm^{-1}; MS m/z (rel inten) 305 (25), 304 (M^+, 100), 303 (69), 290 (17), 289 (68), 275 (13); HRMS calcd for $C_{21}H_{24}N_2$ 304.1932, found 304.1932.

Reaction of 2,4,6-Trimethylbenzonitrile (30) with MeLi and Carbon Monoxide. In the similar manner as described for **12a**, 0.290 g (2.0 mmol) of 2,4,6-trimethylbenzonitrile (**30**) in 10 mL of THF was reacted with MeLi (1.2 M in ether, 2.5 mmol, 2.1 mL) at −78 °C and then warmed to 20 °C (over 1 h), carbon monoxide (38 mL, 0.79 equiv absorbed during 15 h) at 20 °C, and methyl iodide (20 mmol) at −78 °C and then warmed to 20 °C. Column chromatography on silica gel (hexane/AcOEt 4:1) gave pure *N*-methyl-1-(2,4,6-trimethylphenyl)ethenylformamide (**34**, 0.234 g, 56% yield).

***N*-Methyl-*N*-[1-(2,4,6-trimethylphenyl)ethenyl]formamide (34):** 56% yield; colorless liquid, bp 152 °C/1 Torr; ^{1}H NMR ($CDCl_3$) δ 2.17 (s, 6H, CH_3), 2.29 (s, 3H, CH_3), 3.17 (s, 3H, CH_3N), 4.37 (s, 1H, CH), 4.91 (s, 1H, CH), 6.89 (s, 2H, ArH), 8.02 (s, 1H, CHO); ^{13}C NMR ($CDCl_3$) δ 19.3 (CH_3), 20.8 (CH_3), 28.0 (CH_3N), 97.8 (CH_2), 128.3 (Ar), 131.9 (CH_2C), 136.2 (Ar), 138.1 (Ar), 144.4 (Ar), 161.2 (C=O); IR (neat) 1686 (C=O) cm^{-1}; MS m/z (rel inten) 203 (M^+, 48), 188 (10), 176 (15), 175 (13), 174 (51), 161 (13), 160 (100), 159 (22), 158 (13), 145 (28), 144 (27), 143 (11), 133 (11), 130 (19), 129 (42), 128 (27), 127 (12), 115 (20), 105 (10). Anal. Calcd for $C_{13}H_{17}NO$: C, 76.81; H, 8.43; N, 6.89. Found: C, 76.57; H, 8.46; N, 6.90.

Reaction of *C*-Lithioaldimine 13a with Benzonitrile (20a) and Carbon Monoxide. A THF solution of *C*-lithioaldimine **13a** was prepared from 0.288 g (2.2 mmol) of 2,6-dimethylphenyl isocyanide (**12a**) and 1.6 mL of a pentane solution of *t*-BuLi (1.7 M, 2.7 mmol) in 5 mL of anhydrous THF as described above. The solution was added dropwise with a cannula to a solution of 0.208 g (2.0 mmol) of benzonitrile (**20a**) in 5 mL of THF at −78 °C and then warmed to 20 °C. The mixture was exposed to an atmosphere of carbon monoxide for 12 h, wherein 44 mL of carbon monoxide (0.92 equiv) was absorbed. Quenching with methyl iodide (20 mmol) at 20 °C and usual workup followed by Kugelrohr distillation (150 °C/8 Torr) gave yellow solids which were subjected to gradient elution chromatography on silica gel (5:1, 0:1 CH_2Cl_2/AcOEt) to afford pure 4-(1,1-dimethylethyl)-3-(2,6-dimethylphenyl)-1-methyl-5-phenylimidazol-2(1*H*)-one (**39a**, 0.329 g, 49% yield).

4-(1,1-Dimethylethyl)-3-(2,6-dimethylphenyl)-1-methyl-5-phenylimidazol-2(1*H*)-one (39a): 49% yield; white solid, mp 149–152 °C; ^{1}H NMR ($CDCl_3$) δ 0.90 (s, 9H, *t*-Bu), 2.22 (s, 6H, CH_3), 2.91 (s, 3H, CH_3N), 7.13 (d, J = 6.4 Hz, 1H, ArH), 7.13 (d, J = 8.6 Hz, 1H, ArH), 7.22 (dd, J = 6.4, 8.6 Hz, 1H, ArH), 7.3–7.6 (m, 5H, ArH); ^{13}C NMR ($CDCl_3$) δ 18.4 (CH_3), 28.2 (CH_3N), 31.2 ($(CH_3)_3C$), 32.9 ($(CH_3)_3C$), 120.7 (Ar), 126.4 (Ar), 128.2 (Ar), 128.5 (Ar), 128.6 (Ar), 131.9 (Ar), 132.4 (Ar), 136.3 (Ar), 138.0 (Ar), 152.3 (C=O); IR (KBr) 1692 (C=O) cm^{-1}; MS m/z (rel inten) 334 (M^+, 52), 320 (23), 319 (100), 277 (11), 77(15). Anal. Calcd for $C_{22}H_{26}N_2O$: C, 79.01; H, 7.84; N, 8.38. Found: C, 78.84; H, 7.86; N, 8.34.

4,5-Bis(1,1-dimethylethyl)-3-(2,6-dimethylphenyl)-1-methylimidazol-2(1*H*)-one (39b): 44% yield; white solid, mp 137–140 °C; ^{1}H NMR ($CDCl_3$) δ 1.25 (s, 9H, *t*-Bu), 1.61 (s, 9H, *t*-Bu), 2.18 (s, 6H, CH_3), 3.52 (s, 3H, CH_3N), 7.11 (d, J = 6.4 Hz, 1H, ArH), 7.11 (d, J = 8.6 Hz, 1H, ArH), 7.21 (dd, J = 6.4, 8.6 Hz, 1H, ArH); ^{13}C NMR ($CDCl_3$) δ 18.3 (CH_3), 32.6 ($(CH_3)_3C$), 33.2 ($(CH_3)_3C$, CH_3N), 33.5 ($(CH_3)_3C$), 33.7 ($(CH_3)_3C$), 127.8 (Ar), 128.3 (Ar), 129.9 (Ar), 137.1 (Ar), 138.5 (Ar), 153.8 (C=O); IR (KBr) 1694 (C=N) cm^{-1}; MS m/z (rel inten) 315 (10), 314 (M^+, 46), 300 (23), 299 (100), 257 (13), 243 (39), 201 (15), 105 (12), 79 (14), 77 (18), 57 (49). Anal. Calcd for $C_{20}H_{30}N_2O$: C, 76.39; H, 9.62; N, 8.91. Found: C, 76.33; H, 9.91; N, 8.81.

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