reaction mixture was stirred for 20 min at −78 °C and at 0 °C for 20 min. The resulting suspension was dissolved in a mixture of dry THF (8 mL) and dry TMEDA (16 mL) and after 5 min a solution of **35** (2.04 g, 4 mmol) in dry THF (8 mL) was added at 0 °C. The reaction mixture was stirred at this temperature for 3 h, quenched with water, and extracted with ether. The combined extracts were washed with water, dried, concentrated, and purified by silica gel chromatography (elution with 0.5% methanol and 25% ether in petroleum ether up to 2% methanol in ether) to give **36a** (1.15 g, 62%) as a light yellow gum: IR (neat, cm^{-1}) 3417 (br), 1660; ^1H NMR (300 MHz, C_6D_6) δ 7.67–7.60 (m, 2 H), 7.03–6.95 (m, 3 H), 6.73–6.65 (m, 2 H), 6.60–6.55 (m, 2 H), 6.30 (d, J = 6.9 Hz, 1 H), 5.58 (br s, 1 H), 5.51 (d, J = 6.9 Hz, 1 H), 5.47 (t, J = 2.5 Hz, 1 H), 4.65 (br d, J = 11.0 Hz, 1 H), 4.60 (d, J = 6.2 Hz, 1 H), 4.35 (br s, 1 H), 4.20 (t, J = 9.3 Hz, 2 H), 3.24 (s, 3 H), 2.55–2.33 (m, 2 H), 2.08 (ddd, J = 13.5, 10.9, 6.2 Hz, 1 H), 1.67 (dd, J = 13.5, 3.9 Hz, 1 H), 1.46 (s, 3 H); ^{13}C NMR (75 MHz, C_6D_6) ppm 156.5, 151.0, 143.3, 138.1 (2 C), 135.0, 128.9, 128.8 (2 C), 128.7, 118.4 (2 C), 115.0 (2 C), 109.6, 99.3, 88.6, 85.7, 84.8, 80.5, 69.6, 64.3, 55.1, 35.0, 30.2, 21.7; MS m/z (M^+) calcd 468.1607, obsd 468.1607.

(1*Z*,2-*endo*,3-*exo*,6-*endo*)-6-[[(1,1-Dimethylethyl)diphenylsilyl]oxy]-2-(4,5-dihydro-2-furanyl)-1-[2-(4-methoxyphenoxy)ethenyl]-3-methyl-3-(phenylthio)-7-oxabicyclo[2.2.1]heptan-2-ol (36b). ***tert*-Butylchlorodiphenylsilane** (1.10 g, 4 mmol) was added in one portion to a stirred solution of **36a** (0.94 g, 2 mmol) and imidazole (340 mg, 5 mmol) in dry DMF (1.0 mL) at rt. The mixture was stirred under N_2 for 16 h, poured into water, and extracted with ether. The combined extracts were washed with brine, dried, concentrated, and purified by silica gel chromatography (elution with 0.25% methanol and 12% ether in petroleum ether up to 1% methanol and 50% ether in petroleum ether) to give **36b** (0.42 g, 30%) as a colorless oil; IR (neat, cm^{-1}) 3390 (br), 1670; ^1H NMR (300 MHz, C_6D_6) δ 7.77–7.67 (m, 2 H), 7.65–7.60 (m, 4 H), 7.20–7.05 (m, 6 H), 7.03–6.95 (m, 3 H), 6.65–6.55 (m, 4 H), 6.34 (s, 1 H), 6.20 (d, J = 6.9 Hz, 1 H), 5.60 (t, J = 2.4 Hz, 1 H), 5.34 (d, J = 6.9 Hz, 1 H), 5.04 (dd, J = 10.2, 3.5 Hz, 1 H), 4.50 (d, J = 5.9 Hz, 1 H), 4.45–4.27 (m, 2 H), 3.25 (s, 3 H), 2.53–2.45 (m, 2 H), 1.67–1.57 (m, 1 H), 1.57 (s, 3 H), 1.39 (dd, J = 13.0, 3.9 Hz, 1 H), 1.09 (s, 9 H); ^{13}C NMR (75 MHz, C_6D_6) ppm 159.5, 156.0, 151.9, 144.5, 138.1 (2 C), 136.6 (2 C), 136.4 (2 C), 135.4, 132.7, 132.6, 130.39, 130.37, 129.8 (2 C), 128.5, 128.1 (4 C), 118.4 (2 C), 114.8 (2 C), 107.5, 99.3, 88.5, 85.2, 84.8, 81.6, 69.6, 63.9, 55.1, 36.0, 30.0, 27.0 (3 C), 22.2, 19.1; MS m/z (M^+) calcd 706.2784, obsd 706.2775.

(3a*α*,4*α*,7*β*,9*α*,10*α*,11a*β*)-7-[[(1,1-Dimethylethyl)diphenylsilyl]oxy]-2,3,3a,4,7,8,9,10,11,11a-decahydro-4-(4-methoxyphenoxy)-10-methyl-10-(phenylthio)-6,9-epoxycyclodeca[*b*]furan-11-one (37). A stirred mixture of **36b** (184 mg, 0.26 mmol) and anhydrous K_2CO_3 (180 mg, 1.3 mmol) in degassed anhydrous decalin (5.2 mL) was heated at gentle reflux under N_2 for 1 h. The total reaction mixture was purified by alumina chromatography (activity III, elution with 5–80% ether in petroleum ether) to give **37** (113 mg, 61%) as a colorless gum: IR ($CHCl_3$, cm^{-1}) 1716; ^1H NMR (300 MHz, C_6D_6) δ 7.62–7.58 (m, 4 H), 7.55–7.53 (m, 2 H), 7.23–7.10 (m, 6 H), 7.00–6.95 (m, 3 H), 6.90–6.85 (m, 2 H), 6.80–6.73 (m, 2 H), 5.42 (dd, J = 6.6, 1.6 Hz, 1 H), 4.93 (quintet, J = 8.6 Hz, 1 H), 4.47 (d, J = 7.9 Hz, 1 H), 4.33 (ddd, J = 9.3, 7.6, 1.7 Hz, 1 H), 4.30–4.21 (m, 2 H), 4.20 (dd, J = 7.8, 5.9 Hz, 1 H), 3.87 (td, J = 8.0, 2.7 Hz, 1 H), 3.37 (s, 3 H), 2.44 (dddd, J = 12.0, 7.6, 6.0, 2.6 Hz, 1 H), 1.70 (ddd, J = 13.1, 7.3, 5.9 Hz, 1 H), 1.69–1.59 (m, 1 H), 1.55 (ddd, J = 12.9, 9.3, 8.0 Hz, 1 H), 1.25 (s, 3 H), 1.09 (s, 9 H); ^{13}C NMR (75 MHz, $CDCl_3$) ppm 205.9, 160.0, 154.8, 152.7, 137.3 (2 C), 136.0 (2 C), 135.8 (2 C), 133.6, 133.3, 131.3, 130.3 (2 C), 129.1 (2 C), 129.0, 128.2 (2 C), 128.1 (2 C), 118.4 (2 C), 114.9 (2 C), 99.7, 86.2, 83.2, 78.8, 71.0, 69.4, 64.1, 55.2, 47.3, 33.8, 33.0, 27.0 (3 C), 21.2, 19.3; MS m/z (M^+) calcd 706.2784, obsd 706.2771.

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Supplementary Material Available: 300-MHz ^1H NMR spectra of **23**, **24**, **27**, and **30–37**, as well as the final calculated (MM3) atomic coordinates for A–D as they appear in Figure 2 (16 pages). This material is contained in many libraries on microfiche, immediately follows this article in the microfilm version of the journal, and can be ordered from the ACS; see any current masthead page for ordering information.

Tertiary Carbinamines by Addition of Organocerium Reagents to Nitriles and Ketimines

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Organocerium reagents, prepared by reaction of aromatic and primary and secondary alkyllithium reagents with anhydrous cerium chloride, add to nitriles twice to give tertiary carbinamines in often excellent yields. Addition of *n*-$BuCeCl_2$ to acetophenone is about 4 times faster than addition to benzonitrile. Only 1,2-diaddition is observed in the reaction of $MeCeCl_2$ with cinnamonitrile. The species formed in the double addition of organocerium reagents to nitriles are sufficiently basic to generate a benzyne intermediate by abstraction of an aromatic proton and nucleophilic enough to undergo an intramolecular Chichibabin reaction. Reaction of N-unsubstituted ketimines or their lithium salts with organocerium reagents permits the synthesis of tertiary carbinamines with three different groups on the tertiary carbon center.

Introduction

Tertiary carbinamines (amines in which one bond from nitrogen is to a tertiary carbon atom) are usually prepared by addition of carbocations to nitriles (the Ritter reaction[1]). This reaction requires strongly acidic conditions which may cause skeletal rearrangements and which may not be compatible with other groups present in the substrate. Hydrolysis of the initially formed acyl derivatives of tertiary carbinamines is often difficult, necessitating strongly acidic or basic conditions. Another route to these amines is the reduction of tertiary nitro compounds.[2] Treatment

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0022-3263/92/1957-4521$03.00/0

of diaryl ketoximes with sodium in liquid ammonia followed by alkylation gives tertiary carbinamines, but the reaction is limited in scope.[3] Reaction of organometallic species, such as organolithium compounds and Grignard reagents, with nitriles usually gives imines.[4] Double addition of these reagents to nitriles to give tertiary carbinamines has been reported in only a few isolated or special cases. Thus some Grignard reagents add twice to nitriles in refluxing toluene, but imines are usually the major products and the reaction fails with benzonitrile and phenylacetonitrile.[5] Allylmagnesium halides add twice to nitriles[6] as do Grignard reagents to α-alkoxy nitriles,[6c,7] 2-hydroxybenzonitrile,[8] and cyanogen.[9] α,α-Dibutylbenzylamine is formed in low yield in the reaction of *n*-butyllithium with benzonitrile at room temperature.[10]

Organometallic reagents such as organolithium compounds and Grignard reagents do not normally add to N-unsubstituted ketimines. Tertiary carbinamines have been obtained in such reactions by replacing the hydrogen atom in the imines by groups such arylsulfenyl,[11] acyl,[12] or trimethylsilyl.[13] The imine salts obtained on addition of Grignard reagents to α-alkoxy nitriles react with alkyl- and aryllithium compounds to give tertiary carbamines in addition to other products, but the reaction fails with other nitriles.[14] The products obtained on addition of methyl- or ethylmagnesium iodide to benzoylacetonitrile react with allylmagnesium bromide to give the corresponding tertiary carbinamines.[15]

The reaction of nitriles with organolanthanide reagents[16] has received little attention, possibly because of the report[17] that the reagent prepared from anhydrous cerium chloride and *n*-butyllithium reacts with 4-cyanobenzophenone to give, after 3 h at −65 °C, only the adduct to the carbonyl group [2-(4-cyanophenyl)-2-hexanol] in 48% yield. The reagent prepared from *n*-butylmagnesium chloride and anhydrous cerium chloride adds to phenylacetonitrile to give the imine in low yield.[18,19] Derivatives of *secondary* carbinamines have been prepared by addition of organocerium reagents to *N*-benzylaldimines,[19,20] *N,N*-disubstituted hydrazones,[21] and oxime ethers.[22]

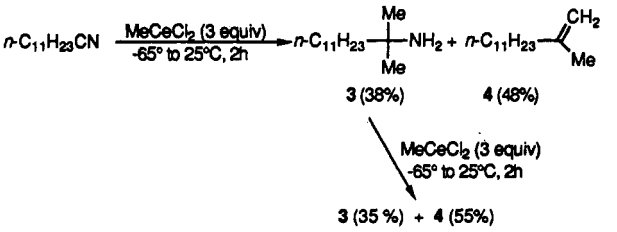
Table I. Double Addition of Organocerium Reagents to Nitriles

$R^1CN + R^2CeCl_2$ (3 equiv) → $R^1R^2R^2CNH_2$

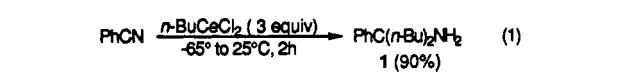
entry	R^1	R^2	conditions	product	yield (%)
1	*n*-$C_{11}H_{23}$	Me	−65 °C, 5 h	3	64[a]
2	*i*-Pr	*i*-Pr	25 °C, 20 h	5	32
3	*t*-Bu	*n*-Bu	25 °C, 2.5 h	6	82
4	cycloheptyl	Me	25 °C, 20 h	7	42
5	1-adamantyl	Me	25 °C, 20 h	8	75
6	Ph	*i*-Pr	25 °C, 20 h	9	50
7	Ph	*s*-Bu	25 °C, 5 h	10	64
8	$MeC_6H_4CH_2$	*n*-Bu	25 °C, 20 h	11	16
9	Ph	Ph	25 °C, 20 h	12	98
10	4-PhC_6H_4	*i*-Pr	25 °C, 2 h	13	47
11	2-furyl	2-furyl	25 °C, 2 h	14	89
12	*i*-Pr	2-thienyl	25 °C, 2 h	15	14
13	1-naphtyl	Me	25 °C, 2 h	16	41[b]

[a] The conversion was 94%; unreacted *n*-$C_{11}H_{23}CN$ was recovered in 31% yield. [b] In addition, naphthalene was isolated in 32% yield.

Scheme I



Double Additions of Organocerium Reagents to Nitriles. Organocerium reagents prepared[17] from anhydrous cerium chloride and primary and secondary alkyllithium and aromatic lithium reagents were found to add to nitriles twice to give tertiary carbinamines in often excellent yields. Thus reaction of 3 equiv of n-$BuCeCl_2$[23] with benzonitrile at −65 °C and stirring the mixture at 25 °C for 2 h gave α,α-dibutylbenzenemethanamine (1) in 90% yield (eq 1). The same yield was obtained when the



(1)

reaction was carried out at −65 °C for 5 h. Reagents prepared from other anhydrous lanthanide chlorides gave the following yields in the reaction of eq 1: $PrCl_3$, 74%; $NdCl_3$, 86%; $YbCl_3$, 74%; $LaCl_3$, 20%.[24] Yttrium chloride

(3) Gautier, J. A.; Miocque, M.; Fauran, C.; Le Cloarec, A. Y. *Bull. Soc. Chim. Fr.* **1968**, 2916.

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(14) Gauthier, R.; Axiotis, G. P.; Chastrette, M. *J. Organomet. Chem.* **1977**, *140*, 245.

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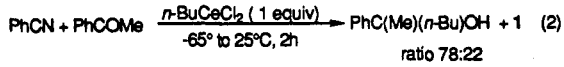
(23) The notation $RCeCl_2$ is used throughout this paper; the exact nature of these reagents has not yet been determined.[16]

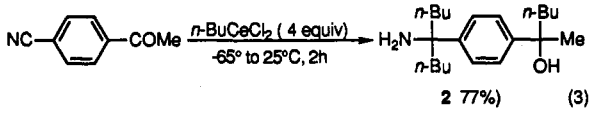
(24) The yield was identical whether $LaCl_3 \cdot 7H_2O$, dried at 140–150 °C under vacuum, or commercially available anhydrous $LaCl_3$ was employed. However, the possibility exists that some of the other lanthanide chlorides that failed to react cannot be dehydrated cleanly by simple vacuum drying.

produced the amine 1 in 3% yield. The chlorides of the following lanthanides failed to react under the conditions of eq 1: Sm, Eu, Gd, Tb, Dy, Ho, Er.[24] Because $CeCl_3$ is the cheapest of the rare earth chlorides, it was used exclusively in all subsequent reactions. When the ratio of C_6H_5CN:$CeCl_3$:*n*-BuLi was 1.3:2:4 (1.5 equiv of "*n*-Bu_2CeCl") the yield of 1 was 60%, and when the ratio was 1:1:3 (1 equiv of "*n*-Bu_3Ce") the yield was 44%. Therefore, an RLi:$CeCl_3$ ratio of 1:1 was adopted for further investigations of this reaction. Employing an equimolar ratio of benzonitrile and *n*-$BuCeCl_2$ gave amine 1 in 33% yield in addition to unreacted benzonitrile; the monoadduct, valerophenone imine was formed in only 0.4% yield. The second addition of *n*-$BuCeCl_2$ to benzonitrile is thus considerably faster than the first. As shown below, such a rate difference is not always observed. Competition of benzonitrile and acetophenone for a limited amount of *n*-$BuCeCl_2$ (eq 2) showed that addition to the cyano group in



(2)

this system is about 4 times slower than addition to the carbonyl group. Reaction of 4-cyanoacetophenone with 4 equiv of *n*-$BuCeCl_2$ at room temperature gave the triadduct 2 in 77% yield (eq 3). When this reaction was

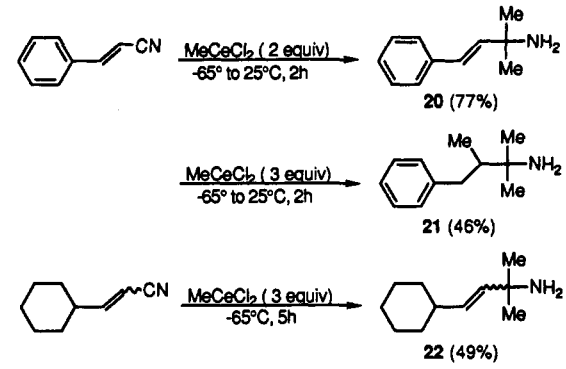


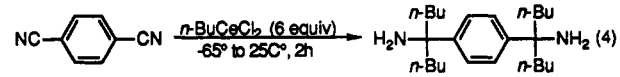
2 77%) (3)

carried out under the conditions described by Imamoto et al. (1.3 equiv of *n*-$BuCeCl_2$, −70 °C, 5 h),[17] the triadduct 2 was isolated in 10% yield.

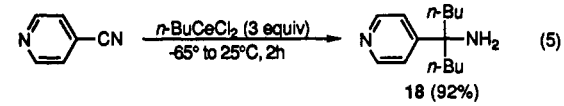
Additional examples of the double addition of organocerium reagents to nitriles are listed in Table I. Many of these reactions have not been optimized. The yields can probably be increased in some cases by carrying out the reactions at −65 °C to suppress olefin formation, a commone side reaction with aliphatic nitriles. Thus when the reaction mixture of entry 1 was warmed to room temperature before workup, 2-methyl-1-tridecene (4) was formed in 48% yield (Scheme I). The internal olefin was absent within detectability by ^1H NMR spectroscopy. Olefin 4 was also formed when amine 3 was treated with 3 equiv of $MeCeCl_2$ (but not with anhydrous $CeCl_3$ alone) at 25 °C (Scheme I). The mechanism of this conversion of a primary amine into an olefin is unknown.[25] It appears to be limited in scope since neither 1-decylamine nor 4-phenylpiperidine gave olefins with $MeCeCl_2$. The low yield in the reaction of *n*-$BuCeCl_2$ with 4-tolylacetonitrile (entry 8) was not unexpected because of the presence of acidic α-protons in the substrate. α,α-Bis(2-furanyl)-2-furanmethanamine (14), the product in entry 11, proved to be rather unstable, decomposing slowly at room temperature and quickly on attempted molecular distillation; it was characterized as the 4-tolyurea. When the reaction of $MeCeCl_2$ with 1-naphthalenecarbonitrile (entry 13) was carried out at −65 °C for 6 h, the diadduct 16 and the imine of 1-acetylnaphthalene were formed in a ratio of 1:3; the starting material was completely absent. Thus in this reaction the first addition is somewhat faster than the second. The naphthalene formed in the room temperature reaction appears to be the result of a base-catalyzed elimination of acetone imine from the diadduct 16. The reactions of *n*-$BuCeCl_2$ with 1,4-dicyanobenzene (eq 4), 4-pyridinecarbonitrile (eq 5), and 1-phenethylpiperidine-4-carbonitrile (eq 6) further demonstrate the versatility of this transformation.

Scheme II

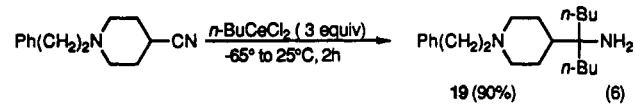




(4)



(5)



(6)

Reaction of 2 equiv of $MeCeCl_2$ with cinnamonitrile gave the 1,2-diadduct 20 exclusively.[26] When 3 equiv was employed, the triadduct 21 was obtained (Scheme II). A similar reaction has been observed in the addition of $PhYbCl_2$ to benzalacetophenone to give 2,2,3,4-tetraphenylpropanol, and a mechanism involving a metallocycle intermediate has been proposed.[27] Addition of the third methyl group requires the presence of a phenyl group in the β position: when it was replaced by a cyclohexyl group, the diadduct 22 was formed exclusively even with 3 equiv of the reagent (Scheme II). To avoid olefin formation, the reaction was carried out at low temperatures, but no triadduct was detected in a second experiment in which the temperature was raised to 25 °C for 2 h.

The reagents formed by reaction of lithium phenylacetylide and *t*-BuLi with $CeCl_3$ did not add to nitriles at room temperature. The lack of reactivity of *t*-$BuCeCl_2$ was surprising since reaction of this species with N,N-disubstituted hydrazones has been reported to proceed at or below room temperature.[21a] On the other hand, the uncatalyzed addition of bulky Grignard reagents to nitriles requires elevated reaction temperatures.[28] The species obtained from Grignard reagents and anhydrous cerium chloride[18] also did not furnish tertiary carbinamines on reaction with nitriles.

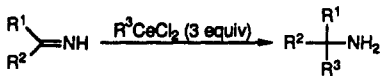
(25) The formation of olefins in the reaction of lithium tetraalkyl ate complexes with epoxides has been postulated to proceed by elimination of "cerium oxide" as the final step: (a) Ukaji, I.; Fujisawa, T. *Tetrahedron Lett.* **1988**, *29*, 5165. (b) Ukaji, Y.; Yoshida, A.; Fujisawa, T. *Chem. Lett.* **1990**, 157.

(26) Exclusive 1,2-addition has been reported in the reaction of organocerium reagents with 1,3-oxazolidines (masked N-substituted imines): Pridgen, L. N., Mokhallalati, M. K., Wu, M.-J. *J. Org. Chem.* **1992**, *57*, 1237 and references cited therein.

(27) Hou, Z.; Fujiwara, T.; Jintoku, N.; Mine, K.; Yokoo, K.; Taniguchi, H. *J. Org. Chem.* **1987**, *52*, 3524.

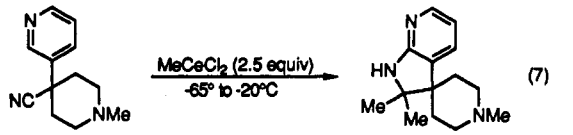
(28) Weiberth, F. J.; Hall, S. S. *J. Org. Chem.* **1987**, *52*, 3901 and references cited therein.

Table II. Addition of Organocerium Reagents to Imines



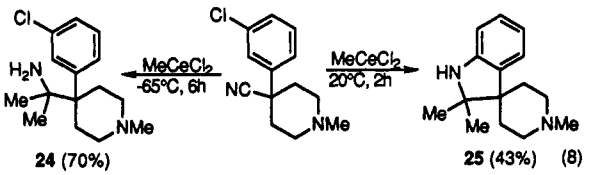
R^1	R^2	R^3	conditions	product	yield (%)
n-Bu	*t*-Bu	Me	25 °C, 2 h	**27**	62
Ph	*n*-Bu	Me	−65 °C, 5 h	**28**	71
Ph	Ph	*n*-Bu	25 °C, 2 h	**29**	79

The species generated in the diaddition of organocerium reagents to nitriles are strongly nucleophilic as evidenced by the intramolecular Chichibabin reaction[29] depicted in eq 7. They are also sufficiently basic to abstract an aromatic proton to generate a benzyne intermediate[30] with the ultimate formation of the spiroindoline **25** (eq 8).



(7)

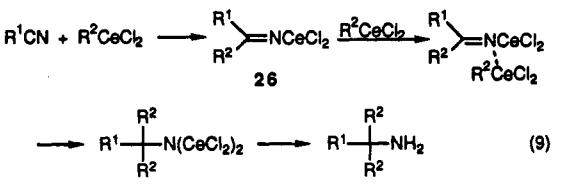
23 (45%)



24 (70%) **25** (43%) (8)

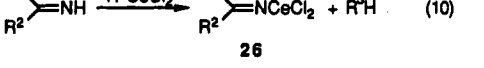
When this reaction was carried out at −65 °C for 6 h, only the diadduct **24** was observed; oddly, when the mixture was then stirred at room temperature for 16 h, no further reaction occurred and no spiropiperidine **25** was isolated under these conditions.

The mechanism of the double addition of organocerium reagents to nitriles is open to speculation. The first step is presumably formation of an adduct resembling **26** (eq 9). Coordination of another molecule of R^2CeCl_2 with the imine nitrogen and intramolecular transfer of the second R^2 group is not unreasonable in view of the high electrophilicity of cerium. The involvement of ate complexes such as $Li^+(CeCl_4)^-$ and the role of the solvent, THF, must be also considered. Transmetalation to give $R^1R^2C{=}NCeR^2Cl$ may occur as well.

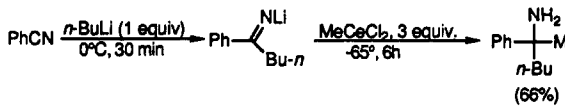


(9)

Addition of Organocerium Reagents to Ketimines. N-Unsubstituted ketimines react with organocerium reagents to give tertiary carbinamines (Table II). This transformation permits the synthesis of tertiary carbinamines with three different groups on the tertiary carbon center. The first step is presumably formation of the imine salt **26** (eq 10) which is a likely intermediate in the addition to nitriles as well (eq 9). As in the latter reaction, *t*-BuCeCl$_2$ failed to add to ketimines. The ketimines were prepared by addition of organolithium reagents to nitriles followed by hydrolysis. Alternatively, the lithium salt of the ketimine may be allowed to react with the organocerium reagent directly (eq 11); under these conditions, 12% of valerophenone imine was also isolated, and the conversion was thus 78%.



26 (10)



(66%) (11)

Experimental Section

General. ^1H (300 MHz) and ^{13}C (75 MHz) NMR spectra were determined in $CDCl_3$ unless otherwise specified. Melting points were measured in an unsealed capillary tube and are uncorrected. HRMS were determined by chemical ionization (NH_3) or by electron ionization.

Materials. Starting materials and reagents were obtained from Aldrich Chemical Co., Milwaukee, WI, unless stated otherwise. The THF used was EM Science anhydrous grade (stored over 4A sieves).

α,α-Dibutylbenzenemethanamine (1). General Procedure for the Generation and Addition of Organocerium Reagents to Nitriles and Ketimines. $CeCl_3{\cdot}7H_2O$ (15.0 g, 40.2 mmol) was dried with magnetic stirring at 140–150 °C (0.1 mm) for 2 h. A glass wool plug was inserted into the adapter connecting the flask to the vacuum source, and entrained solids were returned into the flask by frequent tapping. Nitrogen was added slowly, and the flask was cooled in an ice bath. THF (80 mL) was added, and the suspension was stirred at 25 °C for 2 h. *n*-BuLi (16 mL of a 2.5 M solution in hexanes, 40 mmol) was added, keeping the temperature below −50 °C. The mixture was stirred in a dry ice/acetone bath for 30 min, and benzonitrile (1.34 g, 13 mmol) in 2 mL of THF was added. Stirring at −65 °C was continued for 5 h. Concentrated NH_4OH (25 mL) was added at less than −40 °C, and the mixture was brought to 25 °C and filtered with the aid of Celite. The solids were washed several times with CH_2Cl_2, and the aqueous layer of the filtrates was extracted twice with CH_2Cl_2. The combined organic phases were dried and concentrated. The residue was taken up in 30 mL of toluene and stirred with 30 mL of 3% H_3PO_4 for 15 min. The toluene layer was extracted with two 10-mL portions of water, and the combined aqueous phases were washed once with toluene and made basic with concd NH_4OH. The mixture was extracted several times with CH_2Cl_2, and the residue obtained on removal of the solvent from the dried ($MgSO_4$) extracts was short-path distilled to give 2.53 g (90%) of **1**, boiling at a bath temperature of 80–130 °C (0.003 mm) [lit.[10] bp 152 °C (15 mm)]: ^1H NMR δ 7.2–7.4 (m, 5 H), 1.8 (m, 2 H), 1.6 (m, 2 H), 1.4 (br, 2 H), 1.2 (m, 6 H), 1.0 (m, 2 H), 0.8 (t, J = 6 Hz, 6 H); ^{13}C NMR δ 13.892, 23.102, 25.776, 43.858, 57.518, 125.580, 125.599, 127.823, 147.535. Anal. Calcd for $C_{15}H_{25}N$: C, 82.13; H, 11.49; N, 6.39. Found: C, 81.80; H, 11.52; N, 6.14. The hydrochloride of **1** had mp 209–216 °C after crystallization from water. Anal. Calcd for $C_{15}H_{26}ClN$: C, 70.42; H, 10.24; N, 5.48. Found: C, 70.27; H, 10.34; N, 5.45.

Competition Experiment. A suspension of 20 mmol of *n*-BuCeCl$_2$ in 40 mL of THF was prepared as described above, and a solution of 2.40 g (20 mmol) of acetophenone and 2.06 g (20 mmol) of benzonitrile in 4 mL of THF was added below −50 °C. The cooling bath was removed, and the reaction was quenched after 2 h. The ^1H NMR of the crude product showed the presence of PhC(Me)(*n*-Bu)OH[17] and **1** in a ratio of 78:22.

4-(1-Amino-1-butylpentyl)-α-butyl-α-methylbenzenemethanol (2). The reaction shown in eq 3 was carried out with 1.45 g (10 mmol) of 4-cyanobenzophenone to give 2.45 g (77%) of **2**, bp 180–200 °C bath temperature (0.003 mm): ^1H NMR δ 7.3–7.4 (AB q, J = 8 Hz, 4 H), 0.9–1.8 (m, 21 H), 1.6 (s, 3 H), 0.8

(29) For a review of the Chichibabin reaction, see: Pozharski, A. F.; Simonov, A. M.; Doron'kin, V. N. *Usp. Khim.* **1978**, *47*, 1933; *Russ. Chem. Rev. (Engl. Transl.)* **1978**, *47*, 1042. For examples of intramolecular Chichiban reactions, see: (a) Hawes, E. M.; Wibberley, D. G. *J. Chem. Soc. C* **1966**, 315. (b) Hawes, E. M.; Davies, H. L. *J. Heterocycl. Chem.* **1973**, *10*, 39.

(30) The formation of indolines by intramolecular cyclization of (3-chlorophenyl)alkylamines under the influence of strong bases has been shown to proceed by a benzyne mechanism: (a) Huisgen, R.; Koenig, H. *Chem. Ber.* **1959**, *92*, 203. (b) Huisgen, R.; Koenig, H.; Bleeker, N. *Ibid.* **1959**, *92*, 424. (c) Fleming, I.; Woolias, M. *J. Chem. Soc., Perkin Trans. 1* **1979**, 827.

(t, J = 6 Hz, 9 H); HRMS calcd for $C_{21}H_{38}NO$ [(M + H)$^+$] 320.29534, measured 320.29612. Anal. Calcd for $C_{21}H_{37}NO$: C, 78.94; H, 11.67; N, 4.38. Found: C, 78.77; H, 11.81; N, 4.36.

2-Methyl-2-tridecanamine (3). The crude product was dissolved in hexanes and stirred with excess 10% HCl. The precipitate was collected, washed with hexanes, and reconverted into the free base, 1.58 g (64%), bp 100–120 °C bath temperature (0.1 mm): ^{1}H NMR δ 1.2–1.4 (narrow m, 22 H), 1.1 (s, 6 H), 0.9 (t, J = 6 Hz, 3 H); ^{13}C NMR δ 13.873, 22.489, 24.366, 29.163, 29.493, 30.198, 30.234, 31.745, 45.066, 49.177 (some signals were not completely resolved); HRMS calcd for $C_{14}H_{32}N$ [(M + H)$^+$] 214.2535, measured 214.2542. The hydrochloride had mp 118–119 °C after crystallization from i-PrOH. Anal. Calcd for $C_{14}H_{32}ClN$: C, 67.30; H, 12.91; N, 5.61. Found: C, 67.54; H, 13.03; N, 5.54. Unreacted dodecyl cyanide (0.75 g, 31%) was isolated from the hexane layer.

2-Methyl-1-tridecene (4). The hexane phases from the experiment carried out at 25 °C (Scheme I) were dried, the solvent was removed, and the residue was short-path distilled (110 °C bath temperature, 5 mm) to give 4: ^{1}H NMR δ 4.7 (2 s, 2 H), 2.0 (t, J = 7 Hz, 2 H), 1.7 (s, 3 H), 1.2–1.4 (m, 18 H), 0.9 (t, J = 6 Hz, 3 H); ^{13}C NMR δ 13.892, 22.177, 22.525, 27.552, 29.200, 29.410, 29.493, 31.872, 109.347, 146.089 (some of the signals were not completely resolved); HRMS calcd for $C_{14}H_{28}$ 196.21910, measured 196.21967. An authentic sample of 4 was prepared as follows: to a suspension of 7.1 g (20 mmol) of methyltriphenylphosphonium bromide in 20 mL of dry THF was added at 0 °C 8.3 mL (21 mmol) of 2.5 M n-BuLi in hexanes, the mixture was stirred in an ice bath for 2 h, and 2-tridecanone (3.0 g, 15.1 mmol) in 2 mL of THF was added. After stirring at 25 °C for 18 h, water was added and the mixture was extracted several times with hexanes. Removal of the solvents and short-path distillation of the residue gave 2.41 g (81%) of 4, bp 100–130 °C bath temperature (1 mm), identical by ^{1}H and ^{13}C NMR with the sample described above. Treatment of 0.5 g of 4 with 0.2 g of p-toluenesulfonic acid in 5 mL of acetic acid at 25 °C overnight resulted in a ca. 1:4 mixture of 4 and the internal olefin 2-methyl-2-tridecene. The ^{1}H NMR of the latter had δ 5.1 (t, 1 H), 1.6 (s, 3 H), 1.7 (s, 3 H) among others.

2,4-Dimethyl-3-(1-methylethyl)-3-pentanamine (5): bp 90–110 °C bath temperature (5 mm); ^{1}H NMR δ 2.0 (septet, J = 7 Hz, 3 H), 0.9 (d, J = 7 Hz + br, 20 H); ^{13}C NMR δ 18.877, 33.078, 58.096. The hydrochloride had mp >320 °C after crystallization from 2-propanol. Anal. Calcd for $C_{10}H_{24}ClN$: C, 61.99; H, 12.49; N, 7.23. Found: C, 62.19; H, 12.75; N, 7.08.

5-(1,1-Dimethylethyl)-5-nonanamine (6): bp 90–110 °C bath temperature (5 mm); ^{1}H NMR δ 1.2–1.6 (m, 12 H), 1.0 (t + s + br, 17 H); ^{13}C NMR δ 14.098, 23.922, 26.122, 27.533, 35.976, 38.115, 56.913; HRMS calcd for $C_{13}H_{30}N$ [(M + H)$^+$] 200.2378, measured 200.2383.

α,α-Dimethylcycloheptanemethanamine (7): bp 100 °C bath temperature (10 mm); ^{1}H NMR δ 1.2–1.8 (m, 15 H), 1.0 (s, 6 H); ^{13}C NMR δ 27.707, 27.845, 28.074, 28.797, 50.578, 52.327; HRMS calcd for $C_{10}H_{22}N$ [(M + H)$^+$] 156.17452, measured 156.1743.

α,α-Dimethyltricyclo[3.3.1.1^{3,7}]decane-1-methanamine (8): ^{1}H NMR δ 2.0 (m, 3 H), 1.5–1.9 (m, 12 H), 1.2 (br, 2 H), 1.0 (s 6 H); ^{13}C NMR δ 25.061, 28.669, 36.011, 37.028, 37.897, 53.306. The hydrochloride had mp >320 °C (lit.[31] no mp or analysis given). Anal. Calcd for $C_{13}H_{24}ClN$: C, 67.95; H, 10.53; N, 6.10. Found: C, 67.79; H, 10.76; N, 6.03.

α,α-Bis(1-methylethyl)benzenemethanamine (9): bp 100 °C bath temperature (0.003 mm); ^{1}H NMR δ 7.1–7.5 (m, 5 H), 2.2 (septet, J = 7 Hz, 2 H), 1.1 (br, 2 H), 0.8 (d, J = 7 Hz, 6 H), 0.7 (d, J = 7 Hz, 6 H); ^{13}C NMR δ 16.730, 17.462, 33.658, 62.379, 125.663, 127.128, 127.329, 143.626. The hydrochloride had mp >320 °C after crystallization from DMF. Anal. Calcd for $C_{13}H_{22}ClN$: C, 68.55; H, 9.74; N, 6.15. Found: C, 68.55; H, 9.77; N, 6.03.

α,α-Bis(1-methylpropyl)benzenemethanamine (10): mixture of two diastereomers; bp 120 °C bath temperature (0.003 mm); ^{1}H NMR δ 7.2–7.5 (m, 5 H), 1.6–2.0 (m, 3 H), 1.0–1.4 (m, 3 H), 0.6–1.0 (m, 14 H); HRMS calcd for $C_{15}H_{26}N$ [(M + H)$^+$] 220.2065, measured 220.2081. Anal. Calcd for $C_{15}H_{25}N$: C, 82.13; H, 11.49; N, 6.39. Found: C, 81.93; H, 11.67; N, 6.23. The hydrochloride had mp >320 °C after crystallization from 90% 1-butanol. Anal. Calcd for $C_{15}H_{26}ClN$: C, 70.42; H, 10.24; N, 5.48. Found: C, 70.47; H, 10.38; N, 5.34.

α,α-Dibutyl-4-methylbenzeneethanamine (11): bp 90 °C bath temperature (0.001 mm); ^{1}H NMR δ 7.1 (AB q, J = 8 Hz, split further, 4 H), 2.6 (s, 2 H), 2.3 (s, 3 H), 1.3 (m, 12 H), 0.9 (t, J = 7 Hz, split further, 6 H); ^{13}C NMR δ 14.029, 20.859, 23.239, 25.867, 39.234, 46.101, 53.727, 128.547, 130.369, 134.891, 135.477; HRMS calcd for $C_{17}H_{30}N$ [(M + H)$^+$] 248.2378, measured 248.2376.

α,α-Diphenylbenzenemethanamine (12). The product was identical by IR and ^{1}H and ^{13}C NMR spectroscopy with an authentic sample (Lancaster Synthesis).

α,α-Bis(1-methylethyl)-1,1′-biphenyl-4-methanamine (13): bp 180–195 °C bath temperature (0.002 mm); ^{1}H NMR δ 7.3–7.6 (m, 9 H), 2.3 (septet, J = 7 Hz, 2 H), 1.4 (br, 2 H), 0.9 (d, J = 7 Hz, 6 H), 0.8 (d, J = 7 Hz, 6 H); ^{13}C NMR δ 16.844, 17.618, 33.814, 62.485, 125.777, 126.862, 126.923, 127.871, 128.622, 138.354, 140.881, 142.929. Anal. Calcd for $C_{19}H_{25}N$: C, 85.38; H, 9.42; N, 5.24. Found: C, 85.48; H, 9.60; N, 5.15. The hydrochloride had mp >320 °C after crystallization from 85% aqueous 1-BuOH. Anal. Calcd for $C_{19}H_{26}ClN$: C, 75.10; H, 8.62; N, 4.61. Found: 74.94; H, 8.74; N, 4.44.

α,α-Bis(2-furanyl)-2-furanmethanamine (14). To 3.40 g (50 mmol) of furan in 20 mL of THF was added below −10 °C 16 mL (40 mmol) of 2.5 M n-BuLi in hexanes. After 4 h at 25 °C the mixture was cannulated below −40 °C into a stirred suspension of $CeCl_3$ prepared from 15.0 g (40 mmol) of $CeCl_3 \cdot 7H_2O$ as described for the synthesis of 1. After 30 min at −65 °C, 2-furancarbonitrile (1.23 g, 1.3 mmol) in 3 mL of THF was added, and the mixture was stirred without cooling for 4 h and worked up to give 3.05 g of 14 of about 89% purity as determined by ^{1}H NMR: yield 2.71 g (89%); ^{1}H NMR δ 7.4 (s, 3 H), 6.3 (narrow m, 3 H), 6.1 (narrow m, 3 H), 2.5 (br, 2 H); ^{13}C NMR δ 56.080, 107.141, 110.181, 142.133, 155.180; HRMS calcd for $C_{13}H_{12}NO_3$[(M + H)$^+$] 230.08172, measured 230.08062. The 4-tolylurea of 14 was crystallized from DMF; it turned dark at ca. 160 °C but had no definite mp: ^{1}H NMR (in DMSO-d_6) δ 8.6 (s, 1 H), 7.6 (s, 3 H), 7.2 (s + d, J = 8 Hz, 3 H), 7.0 (d, J = 8 Hz, 2 H), 6.4 (narrow m, 3 H), 6.2 (narrow m, 3 H), 2.2 (s, 3 H). Anal. Calcd for $C_{21}H_{18}N_2O_4$: C, 69.60; H, 5.01; N, 7.73. Found: C, 69.71; H, 5.00; N, 7.68.

α-(1-Methylethyl)-α-(2-thienyl)-2-thiophenemethanamine (15). To a solution of 6.72 g (41 mmol) of 2-bromothiophene in 30 mL of THF was added below −50 °C 16 mL (40 mmol) of 2.5 M n-BuLi in hexanes. After 10 min at −60 °C the mixture was cannulated into a stirred suspension of 40 mmol of anhydrous $CeCl_3$ in 40 mL of THF prepared as described for the synthesis of 1. After 30 min at −65 °C 2-methylpropanenitrile (0.92 g, 1.3 mmol) in 2 mL of THF was added, and the mixture was stirred for 2 h without cooling and worked up. The basic fraction (0.90 g) was short-path distilled (130–145 °C bath temperature, 0.002 mm) to give 0.55 g of 15 of ca. 80% purity (0.44 g, 14%): ^{1}H NMR δ 7.2 (d, 2 H), 7.0 (d, 2 H), 6.9 (t, 2 H), 2.6 (septet, J = 7 Hz, 1 H), 2.0 (br, 2 H), 0.9 (d, J = 7 Hz, 6 H); ^{13}C NMR δ 17.571, 39.700, 62.534, 123.144, 123.501, 126.532, 153.705; HRMS calcd for $C_{12}H_{16}NS_2$ [(M + H)$^+$] 238.07241, measured 238.07365. The phenylurea of 15 had mp 228 °C after crystallization from DMF: ^{1}H NMR (in DMSO-d_6) δ 8.6 (s 1 H), 6.9–7.4 (m, 15 H), 2.8 (septet, J = 7 Hz, 1 H), 0.8 (d, J = 7 Hz, 6 H). Anal. Calcd for $C_{19}H_{20}N_2OS_2$: C, 64.01; H, 5.65; N, 7.86. Found: C, 63.70; H, 5.37; N, 7.91.

α,α-Dimethyl-1-naphthalenemethanamine (16): ^{1}H NMR δ 8.9 (d, J = 8 Hz, 1 H), 7.9 (d, J = 8 Hz, 1 H), 7.8 (d, J = 8 Hz, 1 H), 7.6 (d, J = 8 Hz, 1 H), 7.3–7.5 (m, 3 H), 1.8 (2 s, 8 H); ^{13}C NMR δ 33.265, 53.865, 122.760, 124.811, 124.894, 125.132, 127.565, 128.107, 129.224, 131.220, 135.010, 144.956; HRMS calcd for $C_{13}H_{16}N$ [(M + H)$^+$] 186.1283, measured 186.1292.

$\alpha,\alpha,\alpha',\alpha'$-Tetrabutyl-1,4-benzenedimethanamine (17): bp 175–190 °C bath temperature (0.001 mm); ^{1}H NMR δ 7.2 (s, 4 H), 0.9–1.8 (m, 28 H), 0.8 (t, J = 6 Hz, 12 H); ^{13}C NMR δ 13.962, 23.156, 25.909, 43.660, 57.337, 125.208, 144.939. Anal. Calcd for $C_{24}H_{46}N_2$: C, 79.73; H, 12.30; N, 7.77. Found: C, 79.91; H, 12.42; N, 7.68. The hydrochloride had mp 297–302 °C after crystallization from EtOH. Anal. Calcd for $C_{24}H_{46}Cl_2N_2$: C, 66.49; H,

(31) Aldrich, P. E.; Hermann, E. C.; Meier, W. E.; Paulshock, M.; Prichard, W. W.; Snyder, J. A.; Watts, J. C. *J. Med. Chem.* **1971**, *14*, 535.

10.69; N, 6.46. Found: C, 66.04, H, 10.90; N, 6.29.

α,α-Dibutyl-4-pyridinemethanamine (18): bp 130–150 °C bath temperature (0.003 mm); ^{1}H NMR δ 8.6 (d, J = 6 Hz, split further, 2 H), 7.3 (d, J = 6 Hz, 2 H), 1.4–1.8 (m + br, 6 H), 1.2 (m, 6 H), 0.8–1.0 (m, + t, J = 7 Hz, 8 H); ^{13}C NMR δ 13.727, 22.892, 25.537, 43.299, 57.408, 121.030, 149.421, 156.727; HRMS calcd for $C_{14}H_{25}N_2$ [(M + H)$^+$] 221.2015, measured 221.2018. The dihydrochloride had mp 218–222 °C dec after crystallization from 2-propanol. Anal. Calcd for $C_{14}H_{26}Cl_2N_2$: C, 57.34; H, 8.94; N, 9.55. Found: C, 57.27; H, 9.02; N, 9.55.

α,α-Dibutyl-1-(2-phenylethyl)-4-piperidinemethanamine (19): bp 180–205 °C bath temperature (0.001 mm); ^{1}H NMR δ 7.2–7.3 (m, 5 H), 3.1 (d, J = 11 Hz, 2 H), 2.8 (m, 2 H), 2.6 (m, 2 H), 2.0 (t, J = 11 Hz, 2 H), 0.9–2.7 (m, 19 H), 0.9 (t, J = 7 Hz, 6 H); ^{13}C NMR δ 13.992, 23.413, 25.364, 25.858, 33.695, 36.982, 43.665, 54.213, 54.432, 60.614, 125.827, 128.226, 128.556, 140.485. Anal. Calcd for $C_{22}H_{38}N_2$: C, 79.94, H, 11.59; N, 8.47. Found: C, 79.69 H, 11.62; N, 8.06. The dihydrochloride crystallized from 95% aqueous 2-propanol as the monohydrate, mp 270–272 °C dec. Anal. Calcd for $C_{22}H_{42}Cl_2N_2O$: C, 62.69; H, 10.04; N, 6.65. Found: C, 62.75; H, 10.19; N, 6.50.

***trans*-2-Methyl-4-phenyl-3-buten-2-amine (20)**: bp 110–140 °C bath temperature (5 mm); ^{1}H NMR δ 7.2–7.4 (m, 5 H), 6.4 (d, J = 16 Hz, 1 H), 6.3 (d, J = 16 Hz, 1 H), 1.4 (br, 2 H), 1.3 (s, 6 H). ^{13}C NMR δ 30.601, 50.697, 124.958, 126.166, 127.036, 128.437, 137.281, 140.128. The hydrochloride had mp 218–219 °C after crystallization from 2-propanol. Anal. Calcd for $C_{11}H_{16}ClN$: C, 66.83; H, 8.16; N, 7.08. Found: C, 66.77; H, 8.20; N, 7.03.

α,α,β-Trimethylbenzenepropanamine (21): bp 110–130 °C bath temperature (3 mm); ^{1}H NMR δ 7.1–7.3 (m, 5 H), 3.0 (d/d, J = 13/3 Hz, 1 H), 2.1 (d/d, J = 13/11 Hz, 1 H), 1.6 (m, 1 H), 1.3 (br, 2 H), 1.1 (s, 6 H), 0.8 (d, J = 7 Hz, 3 H); ^{13}C NMR δ 27.688, 28.457, 38.025, 46.576, 51.685, 125.506, 128.070, 128.985, 142.041. The hydrochloride had mp 192–193 °C after crystallization from EtOH. Anal. Calcd for $C_{12}H_{20}ClN$: C, 67.47; H, 9.43; N, 6.55. Found: C, 67.40; H, 9.51; N, 6.51.

4-Cyclohexyl-2-methyl-3-buten-2-amine (22). The starting material, 3-cyclohexane-2-propenenitrile, was prepared as follows: a mixture of 3.36 g (30 mmol) of cyclohexanecarboxaldehyde, 10.0 g (33 mmol) of (cyanomethylene)triphenylphosphorane (K and K), and 20 mL of THF was heated under reflux for 18 h, the solvent was removed, the residue was stirred with 20 mL of ether, and the mixture was filtered. Removal of the solvent from the filtrate and short-path distillation of the residue at 120–140 °C bath temperature (5 mm) gave 2.95 g (72%) of 3-cyclohexane-2-propenenitrile as a 77:23 mixture of trans and cis isomers. Treatment with $MeCeCl_2$ afforded **22** as a ca. 80:20 mixture of trans and cis isomers, bp 90–115 °C bath temperature (10 mm). *trans*-**22**: ^{1}H NMR δ 5.5 (d, J = 16 Hz, 1 H), 5.4 (d/d, J = 16/6 Hz, 1 H), 1.9 (m, 1 H), 1.6–1.8 (m, 4 H), 1.2 (s, 6 H), 1.0–1.2 (m, 8 H); ^{13}C NMR olefinic C at δ 135.624, 136.796, *cis*-**22**: ^{1}H NMR δ 5.4 (d, J = 12 Hz, 1 H), 5.0 (d/d, J = 12/11 Hz, 1 H), 2.6 (m, 1 H), 2.6 (s, 3 H) among others. ^{13}C NMR olefinic C at δ 131.156, 137.675. The hydrochloride of *cis* + *trans*-**22** had mp 133–134 °C after crystallization from MeCN. Anal. Calcd for $C_{11}H_{22}ClN$: C, 64.84; H, 10.88; N, 6.87. Found: C, 64.65; H, 11.04; N, 6.80.

1′,2′-Dihydro-1,2′,2′-trimethylspiro[piperidine-4,3′(3*H*)-pyrrolo[2,3-*b*]pyridine] (23). A suspension of 10 mmol of $MeCeCl_2$ was prepared as described for the synthesis of 1, and 0.81 g (4 mmol) of 1-methyl-4-(3-pyridyl)-4-piperidinecarbonitrile[32] in 4 mL of THF was added. The mixture was stirred at −20 °C for 30 min and then worked up. The crude product was crystallized from ethyl acetate to give 0.42 g (45%) of **23**: mp 153.5–155 °C; ^{1}H NMR δ 7.8 (d, J = 7 Hz, 1 H); 7.6 (d, J = 7 Hz, 1 H), 6.5 (d/d, J = 7/8 Hz, 1 H), 4.5 (br s, 1 H), 2.8 (m, 2 H), 2.4 (m + s, 5 H), 1.7–2.0 (m, 4 H), 1.2 (s, 6 H); ^{13}C NMR δ 23.960, 30.666, 46.133, 46.323, 52.240, 64.931, 112.965, 128.963, 133.059, 145.796, 162.068. Anal. Calcd for $C_{14}H_{21}N_3$: C, 72.68; H, 9.15; N, 18.16. Found: C, 72.59; H, 9.05; N, 18.15.

4-(3-Chlorophenyl)-α,α,1-trimethyl-4-piperidinemethanamine (24). A suspension of 40 mmol of $MeCeCl_2$ prepared as described for the synthesis of 1 was treated at −60 °C with a solution of 3.12 g (13.3 mmol) of 1-methyl-4-(3-chlorophenyl)-4-piperidinecarbonitrile[33] in 5 mL of THF, and the mixture was stirred at −65 °C for 6 h. Isolation as described above and crystallization of the crude product from 1-propanol gave 2.56 g (70%) of **24** in two crops: mp 92–93 °C; ^{1}H NMR δ 7.2–7.3 (m, 4 H), 2.7 (m, 2 H), 2.3 (m, 2 H), 2.1 (s, 3 H), 2.0 (m, 2 H), 1.8 (m, 2 H), 1.2 (very broad, 2 H), 1.0 (s, 6 H); ^{13}C NMR δ 25.657, 29.328, 45.854, 48.069, 52.107, 73.925, 126.130, 127.842, 128.931, 129.838, 133.958, 142.884. Anal. Calcd for $C_{15}H_{23}ClN_2$: C, 67.52; H, 8.69; N, 10.50. Found: C, 67.46; H, 8.67; N, 10.47.

1′,2,2-Trimethyl-1,2-dihydrospiro[3*H*-indole-3,4′-piperidine] (25). The reaction was carried out as described for **24** above except that 2.80 g (11.9 mmol) of 1-methyl-4-(3-chlorophenyl)-4-piperidinecarbonitrile was used, and the reaction mixture was stirred at 25 °C for 2 h. Chromatography of the crude product (silica, EtOAc/Et_3N, 97:3) gave 0.69 g (27%) of 4-(3-chlorophenyl)-1-methylpiperidine followed by 1.19 g (43%) of **25**: ^{1}H NMR δ 7.6 (d, J = 7 Hz, 1 H), 7.1 (t/d, J = 7/1 Hz, 1 H), 6.8 (t/d, J = 8/1 Hz, 1 H), 6.7 (d, J = 8 Hz, 1 H), 3.6 (br, 1 H), 2.8 (d/t, J = 12/3.5 Hz, 2 H), 2.6 (t/d, J = 12/3.5 Hz, 2 H), 2.5 (s, 3 H), 1.9 (t/d, J = 12/4.5 Hz, 2 H), 1.8 (d, J = 13 Hz, split further, 2 H), 1.3 (s, 6 H); ^{13}C NMR δ 24.043, 30.931, 46.338, 46.550, 52.331, 66.956, 109.498, 117.607, 126.065, 127.021, 135.124, 149.081. The fumarate had mp 193–194 °C after crystallization from 9:1 1-propanol/H_2O. Anal. Calcd for $C_{19}H_{26}N_2O_4$: C, 65.88; H, 7.57; N, 8.09. Found: C, 65.97; H, 7.57; N, 7.98.

2-(1,1-Dimethylethyl)-2-hexanamine (27). The starting material, 2,2-dimethyl-3-heptanimine, was prepared as follows: to 32 mL (80 mmol) of 2.5 M *n*-BuLi in hexanes and 30 mL of THF was added at −10 °C 5.0 g (60 mmol) of 2,2-dimethylpropanenitrile. The mixture was stirred at 0 °C for 30 min and treated with H_2O, and the product was extracted into ether. Short-path distillation (100 °C bath temperature, 15 mm) gave 7.27 g (90%) of the imine: ^{1}H NMR δ 9.0 (br s, 1 H), 2.2 (t, J = 6 Hz, 2 H), 1.5 (br m, 2 H), 1.4 (m, 2 H), 1.1 (s, 9 H), 0.9 (t, J = 7 Hz, 3 H); ca. 5% of the geometrical isomer was present (δ 2.5, t). **27** had bp 80–100 °C bath temperature (10 mm): ^{1}H NMR δ 1.2–1.5 (m, 6 H), 0.9–1.0 (2 s + t + br, 17 H); ^{13}C NMR δ 14.056, 21.747, 23.569, 25.190, 26.407, 36.442, 37.330, 55.266. Anal. Calcd for $C_{10}H_{23}N$: C, 76.36; H, 14.74; N, 8.90. Found: C, 75.95; H, 14.64; N, 8.95.

α-Butyl-α-methylbenzenemethanamine (28). (a) From Valerophenone Imine. Valerophenone imine (α-butylbenzenemethanimine) was prepared from benzonitrile and *n*-BuLi as described under **27**. Reaction under the conditions given in Table II gave **28**: bp 80 °C bath temperature (0.002 mm); ^{1}H NMR δ 7.2–7.5 (m, 5 H), 1.6–1.8 (m, 2 H), 1.5 (br s, 2 H), 1.4 (s, 3 H), 1.0–1.3 (m, 4 H), 0.8 (t, J = 7 Hz, 3 H); ^{13}C NMR δ 13.892, 23.038, 26.435, 31.056, 44.966, 54.808, 125.049, 125.846, 127.961, 149.055. The hydrochloride had mp 153–156 °C after crystallization from acetonitrile. Anal. Calcd for $C_{12}H_{20}ClN$: C, 67.43; H, 9.43; N, 6.55. Found: C, 67.40; H, 9.55; N, 6.49.

(b) Via *N*-Lithiovalerophenone Imine. Benzonitrile (0.69 g, 6.7 mmol) in 2 mL of THF was added at 0 °C to 2.7 mL (6.7 mmol) of 2.5 M *n*-BuLi in hexanes and 3 mL of THF. The mixture was stirred at 0 °C for 30 min and cannulated into a stirred suspension of 20 mmol of $MeCeCl_2$ (prepared as described for the synthesis of 1), keeping the temperature below −60 °C. Isolation after 6 h at −65 °C gave 0.78 g (66%) of **28**, identical with the product obtained above. The neutral product was valerophenone imine (12%).

α-Butyl-α-phenylbenzenemethanamine (29). Benzophenone imine (2.37 g, 1.31 mmol) was treated with *n*-$BuCeCl_2$ under the conditions give in Table II. The crude product was dissolved in ether and treated with a solution of HCl in ether to give 2.86 g (79%) of the hydrochloride of **29**, mp 237–239 °C. Anal. Calcd for $C_{17}H_{22}ClN$: C, 74.03; H, 8.04; N, 5.08. Found: C, 73.88; H, 8.10; N, 5.02. The free base had ^{1}H NMR δ 7.2–7.4 (m, 10 H), 2.2 (m, 2 H), 1.8 (br s, 2 H), 1.1–1.4 (m, 4 H), 0.8 (t, J = 7 Hz, 3 H); ^{13}C NMR δ 13.983, 23.166, 26.288, 42.375, 60.905, 126.093, 126.514, 127.952, 148.945.

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(32) This compound was prepared from 3-pyridineacetonitrile by the method of ref 33a.

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on lanthanide chemistry, and Professors R. H. Grubbs and B. M. Trost for helpful discussions.

Registry No. 1, 41718-44-9; 2, 141983-52-0; 3, 32836-50-3; 3·HCl, 141983-74-6; 4, 18094-01-4; 5, 141983-53-1; 5·HCl, 141983-77-9; 6, 141983-54-2; 7, 141983-55-3; 8, 3433-03-2; 8·HCl, 1660-17-9; 9, 42044-72-4; 9·HCl, 141983-78-0; 10, 141983-56-4; 10·HCl, 141983-79-1; 11, 141983-57-5; 12, 5824-40-8; 13, 141983-58-6; 13·HCl, 141983-80-4; 14, 141983-59-7; 14 *p*-tolylurea derivative, 141983-81-5; 15, 141983-60-0; 15 phenylurea derivative, 141983-82-6; 16, 141983-61-1; 17, 141983-62-2; 17·2HCl, 141983-91-7; 18, 141983-63-3; 18·2HCl, 141983-83-7; 19, 141983-64-4; 19·2HCl, 141983-84-8; 20, 141983-65-5; 20·HCl, 141983-85-9; 21, 141983-66-6; 21·HCl, 141983-86-0; *cis*-22, 141983-71-3; *cis*-22·HCl, 141983-72-4; *trans*-22, 141983-67-7; *trans*-22·HCl, 141983-73-5; 23, 141983-68-8; 24, 141983-69-9; 25, 141983-70-2; 25·fumarate, 141983-87-1; 27, 99868-56-1; 28, 33083-81-7; 28·HCl, 141983-88-2; 29, 22308-24-3; 29·HCl, 19274-92-1; $CeCl_3$, 7790-86-5; $BuCeCl_2$, 94616-73-6; $MeCeCl_2$, 94616-84-9; *i*-$PrCeCl_2$, 119021-56-6; *s*-$BuCeCl_2$, 141983-75-7; $PhCeCl_2$, 99354-16-2; benzonitrile, 100-47-0; acetophenone, 98-86-2; α-butyl-α-methylbenzenemethanol, 4396-98-9; 4-cyanobenzophenone, 1503-49-7; dodecanenitrile, 2437-25-4; 2-methylpropionitrile, 78-82-0; 2,2-dimethylpropionitrile, 630-18-2; cycloheptanecarbonitrile, 32730-85-1; 1-adamantanecarbonitrile, 23074-42-2; *p*-tolylacetonitrile, 2947-61-7; 4-phenylbenzonitrile, 2920-38-9; 2-furancarbonitrile, 617-90-3; 1-naphthalenecarbonitrile, 86-53-3; 2-furanylcerium dichloride, 141983-76-8; 2-thienylcerium dichloride, 138769-83-2; 2-tridecanone, 593-08-8; 2-methyl-2-tridecene, 62060-10-0; naphthalene, 91-20-3; furan, 110-00-9; 2-bromothiophene, 1003-09-4; *p*-phenylenedicarbonitrile, 623-26-7; 4-pyridinecarbonitrile, 100-48-1; 1-phenethyl-4-piperidinecarbonitrile, 23793-56-8; (*E*)-cinnamonitrile, 1885-38-7; (*Z*)-3-cyclohexylacrylonitrile, 78978-70-8; (*E*)-3-cyclohexylacrylonitrile, 22031-57-8; 1-methyl-4-(3-pyridyl)-4-piperidinecarbonitrile, 104742-20-3; 1-methyl-4-(3-chlorophenyl)-4-piperidinecarbonitrile, 126555-97-3; (*E*)-2,2-dimethyl-3-heptanimine, 141983-89-3; valerophenone imine, 16659-09-9; benzophenone imine, 1013-88-3; (*Z*)-2,2-dimethyl-3-heptanimine, 141983-90-6.

Supplementary Material Available: ^{13}C NMR spectra of 4, 6, 7, 11, and 16 for which elemental analyses were not obtained (5 pages). This material is contained in many libraries on microfiche, immediately follows this article in the microfilm version of the journal, and can be ordered from the ACS; see any current masthead page for ordering information.

Calixarenes. 27. Synthesis, Characterization, and Complexation Studies of Double-Cavity Calix[4]arenes

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The ease with which calix[4]arenes can be selectively substituted at the distal phenolic oxygens is employed to advantage to build a second cavity and create two classes of "double-cavity calixarenes". Through the use of 3,5-dinitrobenzoyl chloride, 3-nitro-5-carbomethoxybenzoyl chloride, 3,5-dinitrobenzyl chloride, or 3-nitro-5-carbomethoxybenzyl chloride the diesters 2 and 16, diethers 3 and 17, and ether–ester 10 have been prepared. The second cavity is built by reduction of the nitro groups to amino groups to give compounds 4, 5, 13, 18, and 19 followed by treatment with a diacyl chloride. The products obtained from 4, 5, and 13 are double-spanned double-cavity calix[4]arenes; those from 18 and 19 are single-spanned double-cavity calix[4]arenes. A study of the complexation characteristics of the double-spanned double-cavity calixarenes (6, 7, and 14) shows the diester double-cavity calix[4]arene 6 to be the most effective of the three in forming complexes with acidic compounds (i.e., phenols and carboxylic acids) as well as basic compounds (i.e., pyridines, imidazoles, aliphatic amines). The K_{assoc} values range from < 5 to 55 M^{-1} and are dependent both on the shape and the acidity or basicity of the guest. Several lines of evidence, including molecular modeling studies, indicate that complexation occurs at the side rather than the bottom of the host molecule, providing an explanation for the differences in K_{assoc} for various pairs of guests and also establishing the rationale for the synthesis of the single-spanned double-cavity calix[4]arenes (20, 21) which form quite strong complexes ($K_{assoc} > 10^3$) with certain guests such as resorcinol.

The calix[4]arenes[1] are easily synthesized cavity-containing molecules possessing hydroxyl groups on the "lower rim" and potentially free para positions on the "upper rim". Several of the methods for achieving upper rim functionalization have been developed in this laboratory,[2] our major attention in the past having been devoted to the cavity on which these introduced functions reside. The hydroxyl groups, however, also provide convenient points for attachment of various moieties, as numerous other workers have actively demonstrated.[3] The present paper deals with this latter aspect of calixarene functionalization and describes methods whereby a second cavity is introduced into the calix[4]arenes. The program had its inception in the discovery that calix[4]arenes can be converted in good yield to compounds containing a pair of 3,5-dinitrobenzoyl moieties attached in a 1,3-fashion to oxygens on the lower rim (i.e., positions 25 and 27).[4]

Synthesis of Double-Spanned Double-Cavity Calix[4]arenes

The three double-spanned double-cavity calix[4]arenes that have been synthesized for a comparison of their complexing abilities are designated as the diester double-spanned double-cavity calix[4]arene 6, the ester–ether double-spanned double-cavity calix[4]arene 14, and the diether double-spanned double-cavity calix[4]arene 7. They are prepared as described below.

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