of **16**, bp 55–57 °C (3 mm): IR 3000, 1710 cm^{-1}; ^1H NMR δ 1.0 (d, J = 7 Hz, 6 H), 2.5 (septet, J = 7 Hz, 1 H), 3.0 (t, J = 8 Hz, 2 H), 3.95 (q, J = 8, 2 H); ^{19}F NMR −71.6 (t, J = 8 Hz, 2 F), −74.8 (t, J = 8 Hz, 3 F). Anal. Calcd for $C_8H_{11}F_5O_2$: C, 41.03; H, 4.73; F, 40.57. Found: C, 41.05; H, 4.90; F, 40.68.

1-Azido-1,1-difluoro-4-methyl-3-pentanone (17). A mixture of **1** (1.7 g, 0.01 mol) and sodium azide (0.8 g, 0.011 mol) in acetone (10 mL) was stirred at 25 °C for 1 h, after which time ^{19}F NMR analysis showed the absence of starting ketone. The solvent was evaporated and the residual oil distilled to give 1.2 g (67%) of **17**, bp 30–31 °C (0.5 mm): IR 3000, 2190, 1710 cm^{-1}; ^1H NMR δ 1.0 (d, J = 7 Hz, 6 H), 2.6 (septet, J = 7 Hz, 1 H), 3.1 (t, J = 11 Hz, 2 H); ^{19}F NMR −70.4 (t, J = 11 Hz). Anal. Calcd for $C_6H_9F_2N_3O$: C, 40.67; H, 5.12; N, 23.70. Found: C, 40.57; H, 5.01; N, 23.65.

Isopropyl 3-Azido-3,3-difluoropropionate (18). Similar reaction of **2** (2.0 g, 0.011 mol) and sodium azide (1.2 g, 0.017 mol) for 16 h gave 1.1 g (53%) of **18**, bp 55–58 °C (20 mm): IR 3000, 2190, 1760 cm^{-1}; ^1H NMR δ 1.05 (d, J = 7 Hz, 6 H), 3.0 (t, J = 12 Hz, 2 H), 5.05 (septet, J = 7 Hz, 1 H); ^{19}F NMR −70.4 (t, J = 12 Hz). Anal. Calcd for $C_6H_9F_2N_3O_2$: C, 37.30; H, 4.69; N, 21.75. Found: C, 37.09; H, 4.87; N, 22.06.

2-Azido-2,2-difluoroacetophenone (19). A mixture of chlorodifluoroacetophenone (1.8 g, 0.01 mol) and sodium azide (1.0 g, 0.014 mol) in dimethyl sulfoxide (5 mL) was heated at 100 °C for 5 min and then cooled to ambient temperature and diluted with water (50 mL). The mixture was extracted with CH_2Cl_2 (20 mL) and the organic layer washed with water (2 × 20 mL), dried ($MgSO_4$), and evaporated. The residue was distilled to give 1.5 g (81%) of **19**, bp 75–76 °C (1.0 mm): IR 3050, 2200, 1720 cm^{-1}; ^1H NMR δ 7.0–7.5 (m); ^{19}F NMR −78.4 (s). Anal. Calcd for $C_8H_5F_2N_3O$: C, 48.74; H, 2.56; N, 21.31. Found: C, 48.67; H, 2.81; N, 21.02.

Acknowledgment. This work was supported by the Office of Naval Research.

Additions of Alkyllanthanum Triflates to Carbonyl Compounds: Reactive Organometallic Nucleophiles

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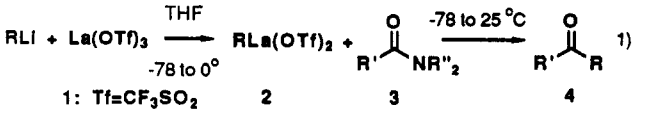
Received November 30, 1989

Addition of alkyl- or aryllithium compounds to lanthanum(III) triflate [$La(OSO_2CF_3)_3$, **1**] in ethereal solvents produces the title reagents **2** that undergo nucleophilic addition to carbonyl compounds under mild conditions. These reagents resemble alkylcerium halides in their reactions with enolizable carbonyl compounds but are more reactive. In particular, they are useful for the conversion of hindered, tertiary amides to ketones. ^1H NMR spectroscopy was employed to clarify mechanistic aspects of this addition process. The title reagents actually appear to be a mixture of several species; formulation of their structure has proven elusive. However, in the presence of a tertiary amide, these species react to give a single, tetrahedral intermediate, which is quite stable in solution.

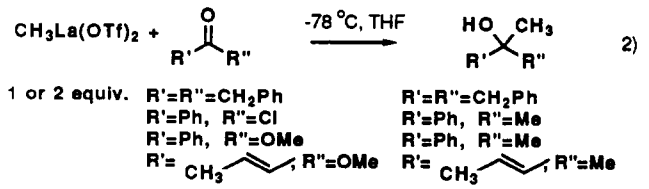
Introduction

There has been considerable recent interest in the chemistry of organolanthanide compounds and their application as reagents for organic synthesis.[2] In particular, organometallic compounds derived from cerium halides and related compounds undergo chemoselective additions to carbonyl compounds, even with easily enolizable systems.[3] We recently discovered that organolanthanum triflates **2**, derived from the reaction of organolithium compounds with lanthanum(III) triflate **1**,[4] undergo smooth addition–elimination reactions with tertiary amides **3** to provide ketones **4** (eq 1).[5] We report here full details of this work and describe further results concerning the reactivity of these reagents.



Results and Discussion

Reactions of $RLa(OTf)_2$ with Carbonyl Compounds. The reactions of reagents **2** with aldehydes and ketones parallel those described for organocerium chlorides ($RCeCl_2$), i.e. enolizable systems such as 1,3-diphenylacetone react cleanly, affording the expected addition product in very high yields (Table I, entry 1, and eq 2).



We do note, however, that reagents **2** appear to be more reactive than organocerium halides; the addition reactions employing **2** are practically complete within minutes of mixing at −78 °C whereas those involving $RCeCl_2$ require

(1) (a) Ontario Postgraduate Scholar, 1989. (b) Watsearch Summer Student.

(2) For a review of the use of organolanthanides in organic synthesis, see: Long, J. R. In *Handbook on the Physics and Chemistry of the Rare Earths*; North Holland Publishing Co.: Amsterdam, 1986; Chapter 57.

(3) For the use of organocerium(III) reagents in synthesis, see: (a) Imamoto, T.; Takiyama, N.; Nakamura, K.; Hatajima, T.; Kamiya, Y. *J. Am. Chem. Soc.* **1989**, *111*, 4392 and references cited therein.

(4) (a) Forsberg, J. A.; Spaziano, V. T.; Balasubramanian, T. M.; Liu, G. K.; Kinsely, S. A.; Duckworth, C. A.; Poteruca, J. J.; Brown, P. S.; Miller, J. L. *J. Org. Chem.* **1987**, *52*, 1017. (b) Almasio, M.-C.; Arnaud-Neu, F.; Schwing-Weill, M.-J. *Helv. Chim. Acta* **1983**, *66*, 1296.

(5) Preliminary communication: Collins, S.; Hong, Y. *Tetrahedron Lett.* **1987**, *28*, 4391.

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Table I. Additions of Organolanthanum Triflates to Carbonyl Compounds[a]

entry	R (equiv)	R′	R″	solvent	T, °C	time, min	% yield[b]
1	Me (1.0)	$PhCH_2$	$PhCH_2$	THF	−78	10	98
2	Me (1.0)	Ph	OMe	THF	−78	30	25[c]
3	Me (2.0)	(*E*)-CH_3CH=CH	OMe	THF	−78	30	95[d]
4	Me (1.0)	Ph	Cl	THF	−78	5	48[c]
5	Me (2.0)	Ph	Cl	THF	−78	30	98[c]
6	Me (1.2)	Ph	Et	THF	−78	30	95
7	Ph (2.0)	Ph	Et	THF	−78	30	98
8	*n*-Bu (1.2)	Ph	Et	Et_2O	−30	30	94
9	Me (1.2)	*m*-MePh	Et	Et_2O	0	30	92
10	Me (2.0)	*p*-MePh	Et	THF	−78	20	98
11	Me (2.0)	*m*-ClPh	Et	THF	−78	20	95
12	Me (3.0)	*m*-MeOPh	Et	THF	−78	20	96
13	Me (3.0)	*o*-MeOPh	Et	Et_2O	25	20	91
14	Me (1.0)	Ph	*i*-Pr	Et_2O	−78 to 25	30	80[e]
15	Me (3.0)	*p*-$MeOPhCH_2$	Et	THF	−78	20	82[f]
16	Ph (2.0)	3-pentyl	Et	Et_2O	−30	30	81[g]
17	Me (1.5)	3-pyridyl	Et	THF	−78	30	92
18	Me (1.5)	4-pyridyl	Et	THF	−78	30	90
19	Me (2.0)	2-thienyl	Et	THF	−100 to 25	30	85
20	Me (2.5)	3-thienyl	Et	THF	−78 to 0	30	91
21	Me (3.0)	2-furyl	Et	THF	−78 to 0	30	88
22	Me (3.0)	3-furyl	Et	THF	−78 to 0	30	93

[a] For typical procedure, see the Experimental Section. For the structures of the products, see eq 1 (entries 6–22) and eq 2 (entries 1–5). [b] Isolated yields of homogeneous material. All compounds prepared are known and were characterized by their IR and ^1H NMR spectra. [c] Yield of 2-phenyl-2-propanol. No ketone was produced. [d] Yield of (*E*)-2-methylpent-3-en-2-ol. [e] 2-Phenyl-2-propanol was also produced in 10% yield. [f] Dimethyl-*p*-methoxybenzyl carbinol was also produced (16% yield). [g] Diphenyl-1-ethylpropyl carbinol was also isolated (12% yield).

longer reaction times at this temperature.

The reactions of compounds **2** with carboxylic acid esters and acid chlorides was briefly examined (Table I, entries 2–5, and eq 2). It was not possible to cleanly add 1 equiv of compound **2** to these substrates to provide ketones. In all cases, the products formed were the corresponding tertiary alcohol and recovered starting material (entries 2 and 4). Of course, quantitative conversion to the tertiary alcohol could be achieved using 2 equiv of reagent **2** (Table I, entries 3 and 5). Clean 1,2-addition to methyl crotonate was observed, producing the dimethyl carbinol in high yield as a single isomer (entry 3). The behavior of esters and acid chlorides toward reagent **2** is quite different than that observed for tertiary amides.

The reactions of compound **2** with tertiary aromatic (entries 6–14, Table I), aliphatic (entries 15–16), and heterocyclic (entries 17–22) amides **3** proceed cleanly, providing ketones **4** in excellent yields (Table I, eq1). A large excess of reagent **2** can be employed with only occasional complications arising from further reaction of compound **2** with the product (Table I, entries 13–15). In certain cases, an excess of reagent **2** is required for complete conversion, particularly if the amide contains additional donor functionality (e.g. entries 11, 12, and 16–21).

One should note that all of the amides studied here are somewhat hindered, i.e. the alkyl group on nitrogen is either ethyl or isopropyl. Organolithium compounds or Grignard reagents in the presence of cerium trichloride[3a,6] will convert unhindered *N,N*-dimethylamides to ketones, but, in general (vide infra), organolithium compounds do not *efficiently* effect this transformation with the more hindered systems studied here due to competing metalation.[7] Since the *N,N*-diethyl- or *N,N*-diisopropylamide moiety is a very useful directing group for ortho–metalation of aromatic and heterocyclic compounds,[7] the conversion described here allows efficient transformation of these somewhat inert functional groups under mild conditions to one that can be further elaborated once the amide has served its purpose.

Metalation of tertiary amides can be suppressed by use of nonpolar solvents; under these conditions *N,N*-diethylbenzamides are converted to ketones with organolithium compounds at room temperatuare.[8a] However, the synthetic yields are lower than reported here. A variety of methods, which employ amides with additional ligating groups bonded to nitrogen and organolithium or Grignard reagents, have been developed for the conversion of tertiary amides to ketones.[8]

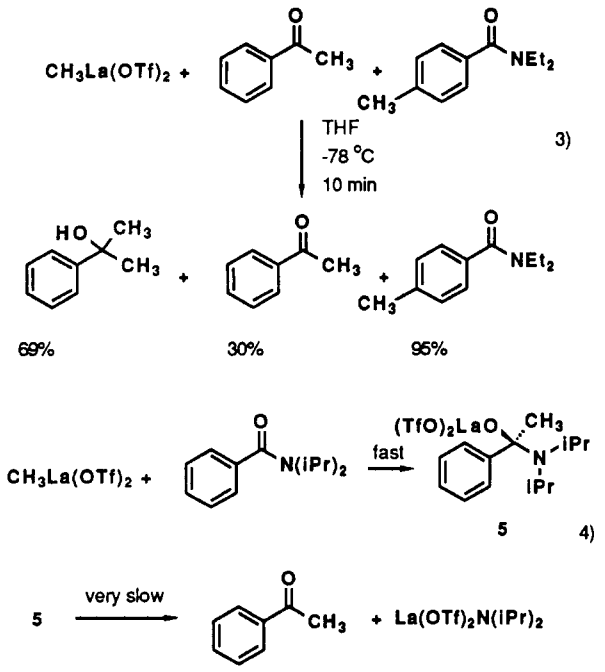
Mechanism of the Addition Process. The fact that tertiary amides can be cleanly converted to ketones in the presence of a large excess of compound **2** suggests that the ketone is not present in detectable amounts prior to workup. A competition experiment established a ketone would react preferentially with reagent **2** under these conditions. An equimolar mixture of acetophenone and *N,N*-diethyl-*p*-toluamide on treatment with 1 equiv of compound **2** (R = Me) provided dimethylphenyl carbinol (69%), acetophenone (30%), and recovered toluamide (95%) as the sole products (eq 3). This result suggests that the collapse of the putative tetrahedral addition product **5** to the ketone is much slower than the rate of its formation from reagent **2** and the amide (eq 4).

We have attempted to obtain spectroscopic evidence to the existence of intermediate **5**. The addition of compound **2** (R = Me) to *N,N*-diisopropylbenzamide was selected for study, since this reaction proceeds at a convenient rate to allow monitoring by ^1H NMR (Table I, entry 14). the reaction of compound **2** (R = Me, 1.0 equiv) with this amide (0.5 equiv) in THF-d_8 was monitored by variable-

(6) Organocerium(III) chlorides derived from organolithium compounds and $CeCl_3$ react sluggishly with the amides studied here and provide a mixture of alcohols and ketones: Collins, S., Hong, Y., unpublished results.

(7) For reviews on directed metalation, see, inter alia: (a) Snieckus, V. *Lectures in Heterocyclic Chemistry, Suppl. J. Heterocycl. Chem.* **1984**, *21*, 95. (b) Beak, P.; Snieckus, V. *Acc. Chem. Res.* **1982**, *15*, 306. (c) Snieckus, V. *Heterocycles* **1980**, *14*, 1649. (d) Gschwend, H. W.; Rodriquez, H. R. *Org. React.* **1979**, *26*, 1.

(8) (a) Comins, D. L.; Brown, J. D. *J. Org. Chem.* **1986**, *51*, 3566. (b) Nahm S.; Weinreb, S. M. *Tetrahedron Lett.* **1981**, 3815. (c) Meyers, A. I.; Comins, D. L. *Ibid.* **1978**, 5179. For a recent synthetic application of the Weinreb procedure,[8b] see: (d) Evans, D. A.; Bender, S. L.; Morris, J. *J. Am. Chem. Soc.* **1988**, *110*, 2506.



temperature ^{1}H NMR (see the Experimental Section). At low temperatures one observes, in addition to signals due to the tertiary amide and reagent **2** (vide infra), resonances at δ 3.18 [multiplet, C*H*(CH$_3$)$_2$], 1.66 (singlet), 1.4 [doublet, J = 7.2 Hz, CH(C*H*$_3$)$_2$], and 1.0 [doublet, J = 7.2 Hz, CH(C*H*$_3$)$_2$] in an integrated ratio of 2:3:6:6, as well as additional signals in the aromatic region. At higher temperatures the intensities of these signals increase at the expense of those due to the amide and "reagent" **2**. At no time during this experiment were resonances due to the expected product, acetophenone, observed, even at room temperature. We suggest that the spectral characteristics of the major, observed product are consistent with the formation of the tetrahedral intermediate **5**. In particular, the singlet at 1.66 ppm is in the region expected for a methyl group β to oxygen, nitrogen, and an aromatic ring (calculated 1.68 ppm[9]), and the isopropyl methyl groups are diastereotopic as expected for intermediate **5**, which contains a chiral center. Under these conditions and on a preparative scale, a small amount of dimethylphenyl carbinol is also produced (e.g. Table I, entry 14; in THF the ratio of ketone:alcohol is roughly 15:1).[10] Thus, the adduct **5** appears to be relatively stable; decomposition to the ketone must occur slowly, but the latter compound quickly reacts with reagent **2** to form the tertiary alcohol and is therefore not detected in the mixture prior to workup.

A few final comments regarding the nature of "compounds" **2** are in order. Addition of a slight excess of methyllithium (prepared by the reaction of *n*-BuLi with methyl iodide in hexane) to a THF suspension of La(OTf)$_3$ results in complete dissolution (even at −78 °C) at a concentration of 0.1 M. The ^{1}H NMR spectrum of this solution reveals the presence of broad resonances at ca. −0.01, −0.5, and −0.9 ppm, which differ in intensity depending on the source of methyllithium (i.e. halide free or containing lithium halide) and the temperature of the addition. There is no evidence for the existence of free methylithium (at δ −2.1) in these solutions, although we cannot rule out rapid equilibration of free methyllithium with soluble "ate" species[11] or compounds exemplified by structure **2**. It appears that several species are present depending on conditions—a feature which, fortunately, does not detract from the synthetic utility of the addition process discussed here. All such species appear capable of reacting with a teritary amide, either directly or by equilibration, to provide very high yields of ketones via a stable, tetrahedral intermediate.

Experimental Section

All solvents and reagents wer reagent grade and purified as required. Diethyl ether and tetrahydrofuran were dried and deoxygenated by distillation from benzophenone ketyl under nitrogen. Alkyllithium compounds were purchased from commercial sources (Aldrich) and titrated before use. Lanthanum(III) triflate was prepared from La$_2$O$_3$ and trifluoromethanesulfonic acid as described in the literature[4] and dried at 0.1 mmHg and 140 °C for 16 h. It was stored in a Vacuum Atmospheres glovebox prior to use and weighed out as required. Infrared spectra were obtained on a Perkin-Elmer 983 spectrometer in chloroform solution or as thin films. Polystyrene film was used for calibration. Routine ^{1}H NMR and ^{13}C NMR spectra were acquired on a Bruker AC-200 instrument at 200 and 50 MHz, respectively, in CDCl$_3$ solution. Spectral data are referenced to internal tetramethylsilane. Low-temperature ^{1}H NMR spectra were obtained on a Bruker AM-250 instrument in THF-d_8 solution, and chemical shifts are referenced to THF-d_8 (1.73 ppm). Methanol was used for temperature calibration. Mass spectra were obtained on a VG7077 instrument at the University of Guelph. Elemental analyses were performed at Guelph Chemical Laboratories.

The amides used in this work, which, with the exception of *N*,*N*-diethyl-*p*-methoxyphenylacetamide, were all known compounds, were prepared from the corresponding carboxylic acids, via the acid chlorides, as exemplified by the following procedure.

Preparation of *N*,*N*-Diethyl-*p*-methoxyphenylacetamide. Diethylamine (11.0 g, 15 mmol) was added to a solution of *p*-methoxyphenylacetyl chloride, prepared from *p*-methoxyphenylacetic acid (5.0 g, 30.1 mmol) and excess SOCl$_2$ (1 h, reflux), in dry toluene (20 mL) at 0 °C over 10–15 min. The mixture was stirred at room temperature for 30 min and then diluted with ether (100 mL) and 2.0 M HCl (100 mL). The organic phase was separated, washed with saturated NaHCO$_3$ solution, dried (MgSO$_4$), filtered, and concentrated in vacuo to provide crude amide (6.0 g, 90%) which was further purified by Kugelrohr distillation (bp 128–130 °C, 0.05 mmHg): ^{1}H NMR (200 MHz) δ 7.16 (d, J = 7.6 Hz, 2 H), 6.82 (d, J = 7.6 Hz, 2 H), 3.72 (s, 3 H), 3.59 (s, 2 H), 3.34 and 3.26 (two overlapping q, J = 7.4 Hz, total 4 H), 1.08 and 1.05 (two overlapping t, J = 7.4 Hz, total 6 H) ppm; ^{13}C NMR (50 MHz) δ 169.6, 157.7, 129.0, 126.9, 113.3, 54.5, 41.6, 39.4, 13.6, 12.3 ppm; IR (thin film) 3062, 1635, 1582, 1457 cm^{-1}. Anal. Calcd for C$_{13}$H$_{19}$NO$_2$: C, 70.56; H, 8.65; N, 6.30. Found: C, 70.65; H, 8.80; N, 6.36

Reaction of Compounds 2 with Carbonyl Compounds: General Procedure. Lanthanum triflate (703.2 mg, 1.2 mmol) was weighed into a dry, two-necked round-bottom flask in a glovebox. The salt was suspended in 10 mL of dry solvent (see Table I) and stirred at room temperature for 15 min under argon. The suspension was cooled to −78 °C (acetone–dry ice bath), and the alkyllithium compound (1.2 mmol) was added via syringe over 2 min. The suspension was warmed to 0 °C at which time a colorless or pale yellow solution was obtained. After the solution was recooled to −78 °C, the carbonyl compound (1.0 mmol), dissolved in 2 mL of solvent, was added via syringe. Three additional 1-mL portions of solvent were used to complete this transfer. The reactions were monitored by TLC (silica gel) until the carbonyl compound had been consumed (for times and temperatures see Table I). The reaction was quenched by the addition of saturated, aqueous ammonium chloride solution (2.0 mL) and

(9) This value was calculated using data in Williams, D. H.; Fleming, I. *Spectroscopic Methods in Organic Chemistry*, 4th ed.; McGraw-Hill Ltd.: London, 1987; Chapter 3.

(10) Note that the singlet at 1.66 ppm is not due to the methyl groups of this alcohol which appear at 1.59 ppm in this solvent.

(11) We note that the ^{1}H NMR chemical shifts observed for reagent **2** are similar to those observed for methyllanthanum "ate" complexes that have been previously characterized; see: Schumann, H.; Muller, J.; Bruncks, N.; Lauke, H.; Pickardt, J. *Organometallics* **1984**, *3*, 69 and references cited therein.

allowed to warm to room temperature. The mixture was diluted with ether (20 mL), and the organic phase was washed with water (10 mL) and saturated brine (10 mL). The organic phase was dried ($MgSO_4$), filtered, and concentrated to dryness in vacuo. The product could be further purified, if desired, by crystallization or by passage through a short pad of silica gel eluting with hexane–ethyl acetate, 5:1.

NMR Reaction of Methyllanthanum Triflate with *N,N*-Diisopropylbenzamide. A 5-mm NMR tube, sealed to a glass tube equipped with a male 14/20 joint and a stopcock inlet, was charged with 29.3 mg (0.05 mmol) of $La(OTf)_3$. The apparatus was connected to vacuum transfer manifold also connected to a Schlenk tube containing previously dried and degassed THF-d_8. A 1.0 M solution of methyllithium (prepared by reaction of *n*-butyllithium with methyl iodide in hexane followed by filtration) in THF-d_8 and a 1.0 M solution of *N,N*-diisopropylbenzamide in THF-d_8 were also separately prepared. Approximately 0.4 mL of THF-d_8 was considered onto the $La(OTf)_3$ in the NMR tube under vacuum. After refilling the apparatus with nitrogen, 50 μL of the methyllithium solution was added via syringe through the stopcock inlet to the suspension of $La(OTf)_3$ at −78 °C. The suspension was degassed by three, freeze–pump–thaw cycles, the contents of the NMR tube being mixed by warming the base of the tube during the thawing process. The apparatus was refilled with nitrogen, and 100 μL of the amide solution was added in the NMR tube at −78 °C through the stopcock. The solution was then frozen in liquid nitrogen, the apparatus was evacuated, and the NMR tube was sealed off. The tube was then quickly transferred to a NMR probe, previously equilibrated at 220 K. ^1H NMR spectra were recorded at the following temperatures: 220, 240, 260, 280, and 298 K.

Acknowledgment. We would like to thank the Natural Sciences and Engineering Research Council for generous financial support of this work.

Registry No. 1, 52093-26-2; 3 (R′ = $PhCH_2$, R″ = $PhCH_2$), 102459-18-7; 3 (R′ = Ph, R″ = OMe), 126328-28-7; 3 (R′ = (*E*)-CH_3CH = CH, R″ = OMe), 126328-29-8; 3 (R′ = Ph, R″ = Cl), 22180-78-5; 3 (R′ = Ph, R″ = Et), 1696-17-9; 3 (R′ = *m*-MePh, R″ = Et), 134-62-3; 3 (R′ = *p*-MePh, R″ = Et), 2728-05-4; 3 (R′ = *m*-ClPh, R″ = Et, 15952-65-5; 3 (R′ = *m*-MeOPh, R″ = Et), 62924-93-0; 3 (R′ = *o*-MeOPh, R″ = Et), 51674-10-3; 3 (R′ = Ph, R″ = *i*-Pr), 20383-28-2; 3 (R′ = *p*-$MeOPhCH_2$, R″ = Et), 115348-15-7; 3 (R′ = 3-pentyl, R″ = Et), 79868-38-5; 3 (R′ = 3-pyridyl, R″ = Et), 59-26-7; 3 (R′ = 4-pyridyl, R″ = Et), 530-40-5; 3 (R′ = 2-thienyl, R″ = Et), 14313-93-0; 3 (R′ = 3-thienyl, R″ = Et), 73540-75-7; 3 (R′ = 2-furyl, R″ = Et), 32488-17-8; 3 (R′ = 3-furyl, R″ = Et), 73540-76-8; 4 (R = Me, R′ = $PhCH_2$), 103-79-7; 4 (R = Me, R′ = (*E*)-CH_3CH = CH), 3102-33-8; 4 (R = Me, R′ = Ph), 98-86-2; 4 (R = Ph, R′ = Ph), 119-61-9; 4 (R = Bu, R′ = Ph), 1009-14-9; 4 (R = Me, R′ = *m*-MePh), 585-74-0; 4 (R = Me, R′ = *p*-MePh), 122-00-9; 4 (R = Me, R′ = *m*-ClPh), 99-02-5; 4 (R = Me, R′ = *m*-MeOPh), 586-37-8; 4 (R = Me, R′ = *o*-MeOPh), 579-74-8; 4 (R = Me, R′ = *p*-$MeOPhCH_2$), 122-84-9; 4 (R = Ph, R′ = 3-pentyl), 5682-46-2; 4 (R = Me, R′ = 3-pyridyl), 350-03-8; 4 (R = Me, R′ = 4-pyridyl), 1122-54-9; 4 (R = Me, R′ = 2-thienyl), 88-15-3; 4 (R = Me, R′ = 3-thienyl), 1468-83-3; 4 (R = Me, R′ = 2-furyl), 1192-62-7; 4 (R = Me, R′ = 3-furyl), 14313-09-8; 5, 126375-09-5; MeLi, 917-54-4; PhLi, 591-51-5; BuLi, 109-72-8; MeC(Ph)(OH)Me, 617-94-7; $MeOC_6H_4$-*p*-$CH_2C(Me)_2OH$, 35144-39-9; $Et_2CHC(Ph)_2OH$, 126328-30-1; $MeOC_6H_4$-*p*-$CH_2C(O)Cl$, 4693-91-8; $MeOC_6H_4$-*p*-CH_2CO_2H, 104-01-8.

Synthetic Studies toward the Novel Tetracyclic Diterpene Longipenol: Construction of the ABD Tricarbocyclic Framework

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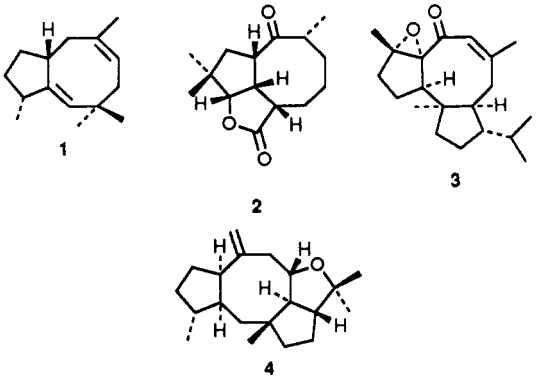
Received August 22, 1989

An approach (AB → ABD → ABCD) for the synthesis of tetracyclic diterpene longipenol **5** of insect origin has been conceived employing a 5-5-5 → 5-8 strategy for the construction of the highly functionalized bicyclo[6.3.0]undecanedione derivatives **18** and **19** from the readily available triquinane precursor **12**. An intramolecular Mukaiyama reaction (**22** → **23**) has been successfully effected to generate the tricyclic ABD ring system **23**.

In the past few years, several C_{15}-sesqui-, C_{20}-di-, and C_{25}-sesterterpene natural products embodying an eight-membered ring have been isolated and characterized from terrestrial plants, marine organisms, phytopathogenic fungi, and insects.[1,2] Among the more interesting carbocyclic variations present in them are the uncommon 5-8 and 5-8-5 fused ring systems represented here by precapnelladiene **1**,[3] asteriscanolide **2**,[2c] basmenone **3**,[2h] and epoxydictymene **4**.[2f] In view of the structural novelty of these cyclooctanoid terpenes, considerable synthetic activity has been witnessed in this area in the recent past.[4,5]



(1) (a) Devon, T. K.; Scott, A. I. *Handbook of Naturally Occuring compounds*; Academic Press: New York, 1972; Vol. II. (b) Glasby, J. S. *Enclyclopaedia of the Terpenoids*; Wiley-Interscience: New York, 1982.

(2) Some of the recently isolated cyclooctanoid natural products are (a) Crenulide: Midland S. L.; Wing, R. W.; Sims, J. J. *J. Org. Chem.* **1983**, *48*, 1906. (b) *Pachylactone*: Ishitsuka, M.; Kusumi, T.; Kakisawa, H.; Kawakami, Y.; Nagai, Y.; Sato, T. *Tetrahedron Lett.* **1983**, *24*, 5117. (c) Asteris Canolide: San Feliciano, A.; Barrero, A. F.; Medarde, M.; Miguel del Corral, J. M.; Arumbinu, A. *Ibid.* **1985**, *26*, 2369. (d) Neolamnanyl acetate: Izac, R. R.; Fenical, W.; Tagle, B.; Clardy, J. *Tetrahedron* **1981**, *37*, 2569. (e) Roseadione: Adesomoju, A. A.; Okogun, J. I.; Cava, M. P.; Carroll, P. J. *Phytochemistry* **1983**, *22*, 2535. (f) Epoxydictymene: Enoki, N.; Fusysaki, A.; Suchiro, K.; Ishida, R.; Matsumoto, T. *Tetrahedron Lett.* **1983**, *24*, 4341. (g) Anadensin: Huneck, S.; Baxter, G.; Cameron, A. F.; Connolly, J. D.; Rycroft, D. S. *Ibid.* **1983**, *24*, 3787. (h) Basmenone: Wahlberg, I.; Exlund, A. M.; Nishid, J.; Enzell, C. R.; Berg, J. E. *Ibid.* **1983**, *24*, 843. (i) Longipenol: Prestwitch, G. D.; Tempesta, M. S.; Turner, C. *Ibid.* **1984**, *25*, 1531. (j) Cystoseirol: Francisco, A. C.; Banaigs, B.; Codimier, L.; Cave, A. *Ibid.* **1985**, *26*, 4919.

(3) Ayanoglu, E.; Gebreyesus, T.; Beechan, C. M.; Djerassi, C. *Tetrahedron* **1979**, *35*, 1035.

0022-3263/90/1955-3568$02.50/0