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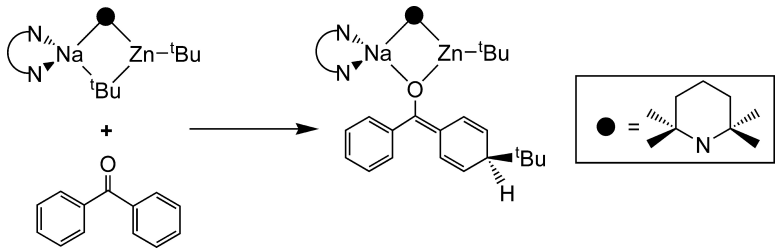

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Trapping, Stabilization, and Characterization of an Enolate Anion of a 1,6-Adduct of Benzophenone Chelated by a Sodium Alkylamidozincate Cation

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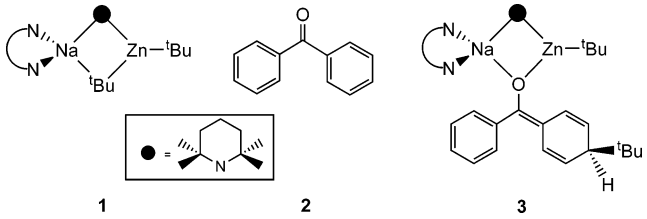
Though they represent one of the oldest classes of -ate compounds in history, dating back to 1858,[1] alkali metal zincates have been underemployed for long periods and only now are beginning to realize their potential as versatile tools of the synthetic chemist. Studied both experimentally and to a lesser extent theoretically,[2] these bimetallic reagents have been utilized effectively in deprotonative metalation,[3] halogen−metal exchange,[4] nucleophilic addition,[5] and ring-opening[6] methodologies. While this work has been mainly performed stoichiometrically, recent reports[7,8] reveal that alkali metal zincates can also be employed catalytically in iodine−zinc exchange reactions. Heteroleptic zincates of general formula $[M^+ZnR_1R_2(X)^-]$ are particularly attractive to study, as they offer either (or both) R^- ligand or X^- ligand reactivity toward a substrate, and especially so, now as compounds of this class are implicated in the catalytic cycle of the above iodine−zinc exchange reactions. In that connection, a recent paper[2] notes that, in general, dialkylhydridozincates $[M^+Zn(R)_2H^-]$, dialkylsilylzincates $[M^+Zn(R)_2(SiR'_3)^-]$, and most germanely to the present study, dialkylamidozincates $[M^+Zn(R)_2(NR'_2)^-]$ transfer selectively the non-carbon ligand to electrophiles. Here, in this paper, we present a reaction that bucks this trend and in which the sodium dialkylamidozincate [TMEDA·Na(μ-^{t}Bu)(μ-TMP)Zn^{t}Bu)], **1** (Scheme 1) (TMEDA is *N*,*N*,*N*′,*N*′-tetramethylethylenediamine; TMP is 2,2,6,6-tetramethylpiperidide), is established as a new, selective alkylating agent. Thus, benzophenone **2** is converted to the mono-*tert*-butylated 1,6-adduct **3**, which remarkably, due to stabilization of the dearomatized enolato anion by coordination to the bulky sodium alkylamidozincate cation left following alkyl transfer, has been obtained in an isolable crystalline form, permitting its crystallographic as well as spectroscopic characterization.

Previously, **1** had only been investigated in the context of deprotonative metalation, which found that it behaves as a selective alkyl base toward benzene.[9] How would it behave as a nucleophile? Diaryl ketone **2** seemed to be an ideal co-reactant with which to probe this question since it lacks acidic H atoms and a previous study by Uchiyama et al.[10] ascertained that it is reduced nonselectively by a NaH/$ZnCl_2$/2^{t}BuLi mixture [a solution synthon of the zincate, Zn(^{t}Bu)$_2$H$^-$] to give both ^{t}Bu$^-$ and H$^-$ 1,2-addition products in poor yield (18 and 4%, respectively). Note that no metallo intermediates were isolated nor characterized in this earlier study as the reaction solutions were worked-up to completion giving the corresponding alcohols. In the present study, a hexane solution of **1** was treated with an equimolar amount of **2** at room temperature.[11] A yellow to celtic green color change accompanied the reaction. Freezer cooling of this solution afforded green crystals of **3**, which are stable indefinitely when stored under argon in a drybox.

Comparing the molecular structure of product **3** (Figure 1)[12] with the known structure of reactant **1**[9] reveals that the ^{t}Bu exits and enolato entry occurs with retention of connectivity within the remaining backbone of the structure. Thus, joined by a TMP−N bridge, the Na and Zn atoms also carry terminal TMEDA (N,N′-

Scheme 1. Structural Formulas of Compounds **1**−**3**



attached) and ^{t}Bu (C-attached) ligands, respectively. Completing an essentially planar NaOZnN1 ring (sum of endocyclic angles, 359.24°), the enolato O-attached anion occupies the second bridge position in **3** vacated by the ^{t}Bu ligand in **1**. Examining dimensions, the O atom approaches Na more closely [length = 2.2214(19) Å] than the ^{t}Bu bridge does in **1** [the closest C−Na contact at 2.750(10) Å involves a Me group, not the tertiary C].[9] This is also the case for Zn but to a much more limited extent [i.e., O−Zn in **3**, 2.0138(17) Å; μC−Zn in **1**, 2.149(9) Å]. Corresponding bonds within the Na−μN−Zn bridges show much less deviation from each other [i.e., N−Na in **3**, 2.441(2) Å; in **1**, 2.412(6) Å; N−Zn in **3**, 1.9519(19) Å; in **1**, 2.034(6) Å]. The monatomic nature of the O also results in sharpening of the Na−μN−Zn bond angle from 98.6(2)° in **1** to 89.47(7)° in **3**. Significantly, the substituted Ph ring lies toward the Zn−O quadrant of the central (NaOZnN) ring, which is more sterically accessible than the alternative TMEDA-filled Na−O quadrant that accommodates the unsubstituted Ph ring. This key distinction exemplifies the attraction (possible advantage) of bimetallic reagents over monometallic analogues as the participation of two distinct metals leads naturally to an asymmetry[13] within structures/transition states that can influence (at best, dictate) the selectivity of nucleophilic addition. The dihedral angle between the two faces of the Ph rings is 56.5(3)°. C−C bond lengths involving the butylated Ph ring reflect the loss of aromaticity and resulting

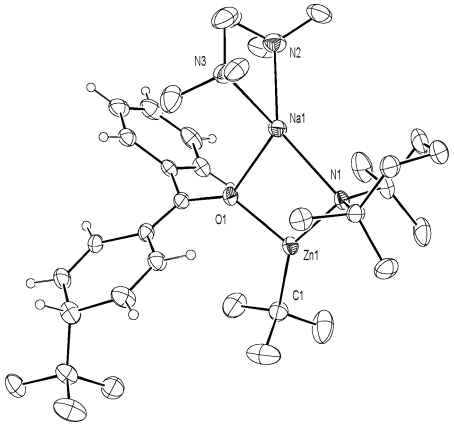


Figure 1. Molecular structure of **3** with 30% probability displacement ellipsoids. Disorder in the TMEDA ligand and alkyl H atoms have been omitted for clarity.

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more localized double/single bond pattern [ipso-benzylic, 1.361-(4) Å; ipso-ortho, 1.458(4)/1.455(4) Å; ortho-meta, 1.334(4)/1.331-(4) Å; meta-para, 1.507(4)/1.506(4) Å; cf. in the unsubstituted Ph ring, ipso-benzylic 1.493(4) Å; range of others, 1.379(5)−1.395-(4) Å].

There is no precedent in the Cambridge Structural Database[14] for an alkylated benzophenone enolate structure of zinc or sodium or indeed of any metal comparable to **3**. Moreover, structures of 1,6-addition adducts of benzophenone with any kind of substituent are also extremely rare. There are lanthanide complexes of Sm[15] and Yb[16] having two H atoms at the para Ph position, though these are not products of nucleophilic addition but of alcohol-promoted protonation of metal benzophenone dianion species. Extending the search further than benzophenone reveals a general paucity of organometallic structures with disubstitution at the para position of a Ph-type ring. One example is an osmium vinylidene complex with Me/H substitution,[17] though again it is synthesized in a different way, namely, by hydride addition to a para-tolyl substituent of an osmium carbyne complex.

Olah previously reported[18] that benzophenone could be efficiently *tert*-butylated to 4-*tert*-butylbenzophenone (yield, 52%) with *tert*-butyllithium and oxidizing thionyl chloride, though the intermediate lithium enolates were not observed in this study.[19] The work disclosed here introduces the sodium zincate **1** as a novel, alternative, *tert*-butylating agent having the added attractions that it permits isolation/crystallization/characterization of the reactive enolate and can generate the 1,6-adduct **3** in bulk hydrocarbon solvent (in the lithium case, reaction in such nonpolar media gives primarily carbonyl addition). Another major advantage is that the zincate reagent cleanly butylates benzophenone at room temperature, whereas the more aggressive lithium reagent has to be employed at −100 °C. This promising result, which demands that a systematic study of zincates in addition reactions now be conducted, adds to the growing body of evidence concerning the "synergic reactivity" of such bimetallic reagents as on its own ^{t}Bu$_2$Zn is passive toward benzophenone.

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Supporting Information Available: Full experimental details and crystallographic data of **1** and **3**. This material is available free of charge via the Internet at http://pubs.acs.org.

References

(1) Wanklyn, J. A. *Liebigs Ann. Chem*. **1858**, *107*, 125.
(2) Uchiyama, M.; Nakamura, S.; Ohwada, T.; Nakamura, M.; Nakamura, E. *J. Am. Chem. Soc.* **2004**, *126*, 10897.
(3) (a) Uchiyama, M.; Miyoshi, T.; Kajihara, Y.; Sakamoto, T.; Otani Y.; Ohwada, T.; Kondo, Y. *J. Am. Chem. Soc.* **2002**, *124*, 8514. (b) Imahori, T.; Uchiyama, M.; Sakamoto, T.; Kondo, Y. *Chem. Commun.* **2001**, 2450. (c) Kondo, Y.; Shilai, M.; Uchiyama, M.; Sakamoto, T. *J. Am. Chem. Soc.* **1999**, *121*, 3539.
(4) (a) Harada, T.; Katsuhira, K.; Hara, D.; Kotani, Y.; Maejima, K.; Kaji, R.; Oku, A. *J. Org. Chem.* **1993**, *58*, 4897. (b) Kondo, Y.; Takazawa, N.; Yamazaki, C.; Sakamoto, T. *J. Org. Chem.* **1994**, *59*, 4717.
(5) (a) Tückmantel, W.; Oshima, K.; Nozaki, H. *Chem. Ber*. **1986**, *119*, 1581. (b) Uchiyama, M.; Kameda, M.; Mishima, O.; Yokoyama, N.; Koike, M.; Kondo, Y.; Sakamoto, T. *J. Am. Chem. Soc.* **1998**, *120*, 4934.
(6) Uchiyama, M.; Koike, M.; Kameda, M.; Kondo, Y.; Sakamoto, T. *J. Am. Chem. Soc*. **1996**, *118*, 8733.
(7) Kneisel, F. F.; Dochnahl, M.; Knochel, P. *Angew. Chem., Int. Ed.* **2004**, *43*, 1017.
(8) Gong, L.-Z.; Knochel, P. *Synlett* **2005**, 267.
(9) Andrikopoulos, P. C.; Armstrong, D. R.; Barley, H. R. L.; Clegg, W.; Dale, S. H.; Hevia, E.; Honeyman, G. W.; Kennedy, A. R.; Mulvey, R. E. *J. Am. Chem. Soc*. **2005**, *127*, 6184.
(10) Uchiyama, M.; Furumoto, S.; Saito, M.; Kondo, Y.; Sakamoto, T. *J. Am. Chem. Soc*. **1997**, *119*, 11425.
(11) Preparation of [TMEDA·Na{μ-OC(Ph)(4-^{t}Bu-C$_6$H$_5$)}(μ-TMP)Zn(^{t}Bu)] (**3**): A Schlenk tube was charged with 2 mmol (0.358 g) of ^{t}Bu$_2$Zn, which was dissolved in 10 mL of hexane. In a separate Schlenk tube, 2 mmol of BuNa (0.16 g) was suspended in 10 mL of hexane and a molar equivalent of (H)TMP (2 mmol, 0.34 mL) added via syringe. The resultant creamy white suspension was allowed to stir for an hour, after which, the hexane solution containing ^{t}Bu$_2$Zn was added via a syringe. The suspension color changed from creamy white to a yellow hue (seemed to be less solid, but requires TMEDA for it all to go into solution). This was followed by the addition of a molar equivalent of TMEDA (2 mmol, 0.30 mL). The resultant suspension was heated gently to form a yellow solution, which was allowed to cool to ambient temperature; 2 mmol (0.36 g) of benzophenone was added via a solids addition tube, and the solution changed color immediately from yellow to dark green. This green solution was placed in a freezer operating at −26 °C to aid the crystallization. A large crop (1.54 g, 60%) of green crystals formed in solution, which were suitable for X-ray crystallographic analysis.
(12) Crystal data for (**3**): $C_{36}H_{62}N_3NaOZn$, $M = 641.25$, orthorhombic, *Pbcn*, $a = 20.2268(3)$, $b = 20.8583(5)$, $c = 19.3017(4)$ Å, $V = 8143.3(3)$ Å^3, $Z = 8$, $T = 123$ K; 82 015 reflections collected, 8980 were unique, $R_{int} = 0.070$; data were collected on a Nonius KappaCCD diffractometer with Mo Kα radiation ($\lambda = 0.71073$ Å). The TMEDA ligand was modeled as disordered over two sites. Final refinement (*SHELXL-97*; G. M. Sheldrick, University of Göttingen, Germany) to convergence on F^2 gave $R = 0.0502$ (F, 5379 obs. data only) and $R_w = 0.1469$, all data), GOF = 1.085, 430 refined parameters, residual electron density max. and min. 0.509 and −0.243 e Å^{-3}.
(13) The asymmetry of the structure of **3** is retained in cyclohexane-d_{12} solution as can be discerned from the two distinct ^{13}C NMR resonances each for the Me-, α-, and β-C atoms of TMP. ^{1}H NMR (400.13 MHz, cyclohexane-d_{12}, 300 K): δ 0.81 [9H, s, CH_3-^{t}Bu on Ph ring], 1.10 [6H, s, CH_3-TMP], 1.29 [9H, s, CH_3-^{t}Bu], 1.68 [6H, m, β- and γ-TMP], 2.13 [12H, s, CH_3-TMEDA], 2.23 [4H, s, CH_2-TMEDA], 2.82 [1H, s, H_5 of Ar], 4.95 [1H, d, H_2 of Ar], 5.37 [1H, d, H_4 of Ar], 6.05 [1H, d, H_3 of Ar], 6.39 [1H, d, H_1 of Ar], 7.031 [5H, s, H_{8-10} of Ar]. ^{13}C{H} NMR (100.63 MHz, cyclohexane-d_{12}, 300 K): δ 11.76 [C(CH$_3$)$_3$-^{t}Bu on Ph ring], 14.44 [C(CH$_3$)$_3$ of ^{t}Bu], 19.13 [γ-TMP], 27.69 [CH$_3$ of ^{t}Bu on ring], 30.59 [CH$_3$ of ^{t}Bu], 34.12, 34.19 [CH$_3$-TMP], 36.43, 36.56 [β-TMP], 46.29 [CH$_3$-TMEDA], 50.29 [C_5 of Ar], 54.01 and 52.88 [α-TMP], 58.38 [CH$_3$-TMEDA], 106.77 [C_6 of Ar], 115.99 [C_2 of Ar], 121.33 [C_4 of Ar], 125.72 [C_1 of Ar], 127.07, 127.85 [C_{8-10} of Ar], 129.17 [C_3 of Ar], 129.41 [C_{8-10} of Ar], 129.93 [C_7 of Ar], 146.59 [C_{11} of Ar]. For labeling atom scheme, see Supporting Information.
(14) (a)Allen, F. H. *Acta Crystallogr. Sect. B* **2002**, *58*, 380. (b) Cambridge Structural Database, version 5.26 with May 2005 update.
(15) Hou, Z.; Yoshimura, T.; Watatsuki, Y. *J. Am. Chem. Soc.* **1994**, *116*, 11169.
(16) Yoshimura, T.; Hou, Z.; Watatsuki, Y. *Organometallics* **1995**, *14*, 5382.
(17) Roper, W. R.; Waters, J. M.; Wright, L. J.; Van Meurs, F. *J. Organomet. Chem*. **1980**, *201*, C27.
(18) Olah, G. A.; Wu, A.-H.; Farooq, O. *Synthesis* **1991**, 1179.
(19) For mechanistic studies of addition reactions of organolithium and organomagnesium compounds to benzophenone, see: (a) Ashby, E. C.; Bowers, J. R., Jr. *J. Am. Chem. Soc*. **1981**, *103*, 2242. (b) Yamataka, H.; Kawafuji, Y.; Nagareda, K.; Miyano, N.; Hanafusa, T. *J. Org. Chem.* **1989**, *54*, 4706.

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