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Reductive Generation of Aldehyde Metal Enolate from Ketene. A One-Flask Process to 1,1,2- and 1,2,2-Trisubstituted Dihydronaphthalenes from 1- and 2-Naphthalenecarboxylates

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Summary: Successive treatment of 2,6-di-*tert*-butyl-4-(methoxyphenyl)-1- and -2-naphthalenecarboxylates (BHA esters) (**1**, **2**) with organolithium in THF, lithium triethylborohydride in refluxing THF, methyl iodide–HMPA, and finally sodium borohydride in MeOH provided regio- and stereoselectively 1,1,2- and 1,2,2-trisubstituted dihydronaphthalenes (**3**, **4**), respectively, in good yields. This one-flask process is constituted from a sequence of five reactions involving reductive generation of aldehyde metal enolate from ketene as a key step.

Carbon–carbon bond forming reaction of a metal enolate has become a versatile and powerful methodology in synthetic organic chemistry.[1] This relies on an efficient generation of a metal enolate from carbonyl compounds, for example, by deprotonation of esters or ketones with strong metal amide bases[2,3] or by conjugate addition of α,β-unsaturated esters or ketones with carbon or hydride nucleophiles.[4,5] However, only very few methods have been developed for generation of aldehyde metal enolate.[3,6]

The thermally induced cleavage of ester lithium enolates to ketenes followed by in situ trapping with organolithiums has been reported to provide the corresponding ketone lithium enolates.[7,8] We describe generation and alkylation of aldehyde metal enolate by way of hydride reduction of ketene with lithium triethylborohydride[8] for the first time in a one-flask process to 1,1,2- and 1,2,2-trisubstituted dihydronaphthalenes (**3**, **4**) from 2,6-di-*tert*-butyl-4-(methoxyphenyl)-1- and -2-naphthalenecarboxylates (BHA esters) (**1**, **2**).

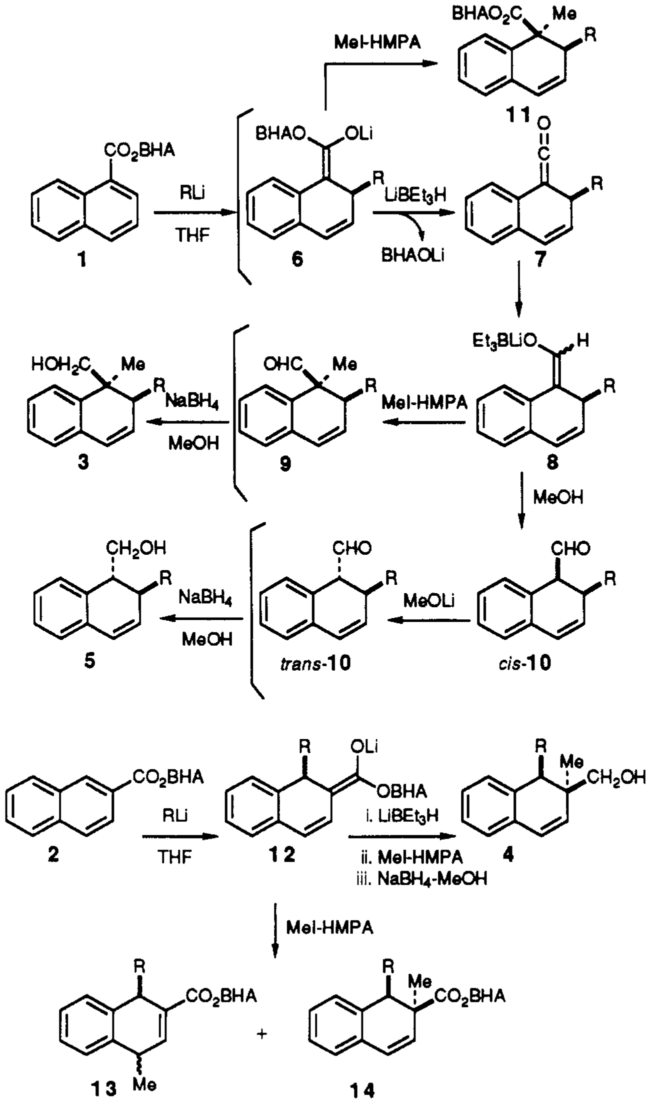
A one-flask process is exemplified by the conversion of BHA ester of 1-naphthalenecarboxylic acid (**1**) to *cis*-2-butyl-1-(hydroxymethyl)-1-methyl-1,2-dihydronaphthalene (**3a**).[9,10] A solution of butyllithium (1.2 mmol, 1.5 M in hexane) was added to a solution of **1** (1.0 mmol) in THF (10 mL) at −78 °C. After the mixture was stirred at −78 °C for 20 min, a solution of lithium triethylborohydride (3.0 mmol, 1 M in THF) was added, and the mixture was stirred under reflux for 1.5 h to generate aldehyde metal enolate.[11] The mixture was then treated with HMPA (20 mmol) and methyl iodide (20 mmol) at −78 °C and stirred

Table I. One-Flask Synthesis of Dihydronaphthalenes (**3**, **4**, **5**) from **1** and **2**[a]

entry	1 or 2	RLi	electrophile	product[b]	yield,[c] %
1	1	Bu	MeI	**3a**	75
2	1	vinyl	MeI	**3b**	42
3	1	Ph	MeI	**3c**	65
4	1	Bu	MeOH	**5a**	81
5	1	vinyl	MeOH	**5b**	61
6	1	Ph	MeOH	**5c**	85
7	2	Bu	MeI	**4a**	93
8	2	vinyl	MeI	**4b**	52
9	2	Ph	MeI	**4c**	66

[a] Reaction was carried out according to the procedure described in the text. [b] Oxidation of alcohol (**3**, **4**) with PCC/CH_2Cl_2 afforded the corresponding aldehyde (**9** and oxidation product of **4**) of which NMR showed the reasonable agreement with those reported.[12,18,19] [c] Yields referred to purified isolated compounds.

Scheme I



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(1) For examples, see: *Asymmetric Synthesis*; Morrison, J. D., Ed.; Academic Press: New York, 1983–1985; Vols. 1–5. *Carbon-Carbon Bond Formation*; Augustin, R. L., Ed.; Marcel Dekker, Inc.: New York, 1979. Stowell, J. C. *Carbanions in Organic Synthesis*; John Wiley & Sons: New York, 1979.

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(7) Häner, R.; Laube, T.; Seebach, D. *J. Am. Chem. Soc.* **1985**, *107*, 5396 and references cited therein.

(8) To our knowledge no efficient reductive generation of aldehyde metal enolate has been reported. *The Chemistry of Ketenes, Allenes and Related Compounds*; Patai, S., Ed.; John Wiley & Sons: New York, 1980; Part 1 and 2.

(9) Prepared by treating acid chloride with lithiated BHA. (a) Heathcock, C. H.; Pirrung, M. C.; Montgomery, S. H.; Lampe, J. *Tetrahedron* **1981**, *37*, 4087; (b) Cook, M. P., Jr. *J. Org. Chem.* **1986**, *51*, 1637.

(10) Compounds **1**–**5**, **11**, **13**, and **14** provided satisfactory spectroscopic and analytical data.

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at 0 °C for 2 h. The mixture was diluted with methanol (5 mL) at −78 °C and then treated with sodium borohydride (6.0 mmol) at 0 °C for 30 min. The mixture was then quenched with 10% aqueous HCl (50 mL) and extracted with benzene. The extracts were washed with brine and dried. Concentration and purification by silica gel column chromatography (hexane–ether, 5:1) afforded **3a** in 75% yield. The structure of **3a** was supported by spectroscopic[12] and analytical data.

Some of the reaction results are summarized in Table I. It is noteworthy that 1- and 2-naphthalenecarboxylates (**1**, **2**) were equally well converted to the corresponding dihydronaphthalenes (**3**, **4**, **5**) in good yields.

The one-flask process is constituted from a sequence of five chemical reactions: (1) addition of organolithium to naphthalene nucleus (**6**), (2) ketene formation (**7**) from BHA ester lithium enolate (**6**),[7] (3) in situ reduction of ketene with lithium triethylborohydride to aldehyde metal enolate (**8**),[13] (4) methylation of enolate with methyl iodide in the presence of HMPA (**9**), and finally (5) reduction of aldehyde with sodium borohydride in methanol to alcohol (**3**).[14]

Reductive generation of aldehyde metal enolate (**8**)[13] is apparent judging from the following results. Reduction of ester (**11**; R = Bu), prepared in 95% yield by treating **1** successively with butyllithium and methyl iodide–HMPA, afforded a mixture of complex products, being absent of alcohol **3**.[15] During the reduction of ester lithium enolate (**6**), disappearance of *cis*- and *trans*-esters[16] and at the same time appearance of BHA were detected by TLC analysis. Protonation of aldehyde metal enolate **8** with methanol and subsequent sodium borohydride reduction provided *trans*-1,2-disubstituted-1,2-dihydronaphthalenes (**5**) in high yields.[17] It is also important to note that although direct methylation of BHA ester enolate (**12**) generated from **2** provided a mixture of products (**13**, **14**), alkylated at the 4- and 2-positions, in a ratio of 2:1, probably due to the steric hindrance exhibited by BHA portion, methylation of aldehyde enolate afforded regio- and stereoselectively *cis*-alcohol (**4**).

In conclusion, we have developed for the first time a methodology for reductive generation and subsequent alkylation of aldehyde metal enolate. Since the present one-flask process to 1,2-disubstituted and 1,1,2- and 1,2,2-trisubstituted dihydronaphthalenes is an alternative to the elegant reaction scheme developed by Meyers based on the oxazoline[12,18] and imine chemistry,[19] our next goal is the development of an enantioselective one-flask process.[20,21]

Supplementary Material Available: Spectral and analytical data for **3–5**, **9**, **11a,c**, **13a**, and **14a** (6 pages). Ordering information is given on any current masthead page.

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[11] Reduction with diisobutyl aluminum hydride in place of super hydride provided **3a** in 30% yield.

[12] Meyers, A. I.; Lutomski, K. A.; Laucher, D. T. *Tetrahedron* **1988**, *110*, 3107.

[13] Actual metal species, lithium or borane enolate, or ate complexes shown in **8**, are not clear at the present time. Lithium enolates have been proposed not to form the corresponding enoxytrialkylborates. Negishi, E.; Idacavage, M. J. *Tetrahedron Lett.* **1979**, 845.

[14] Isolation of aldehyde caused a decreased yield, probably due to instability.

[15] Attempted oxidative removal of BHA of **11** with ceric ammonium nitrate (CAN)[9b] provided a mixture of coomplex products. However, catalytic hydrogenation of **11** and subsequent oxidative removal of BHA with CAN afforded the corresponding tetrahydronaphthalenecarboxylic acid.

[16] Addition reaction of organolithium with BHA naphthalenecarboxylate followed by aqueous workup provided the corresponding *cis*- and *trans*-dihydronaphthalenes in quantitative yield.

[17] After addition of methanol (5 mL) in the reaction at the stage of **8**, the whole mixture was warmed up to room temperature and then reduced with sodium borohydride to afford *trans*-**5** stereoselectively. Concomitant addition of methanol and sodium borohydride provided a mixture of *cis*- and *trans*-alcohols, indicating that initial protonation product is *cis*-aldehyde **10**.

[18] Meyers, A. I.; Roth, G. P.; Hoyer, D.; Barner, B. A.; Laucher, D. *J. Am. Chem. Soc.* **1988**, *110*, 4611. Andrews, R. C.; Teague, S. J.; Meyers, A. I. *Ibid.* **1988**, *110*, 7854 and references cited therein.

[19] Meyers, A. I.; Brown, J.; Laucher, D. *Tetrahedron Lett.* **1987**, *28*, 5283 and 5297.

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Carbon–Carbon Bond Cleavage by the Dianion Mechanism. Small Kinetic Advantage over the Radical Anion Cleavage

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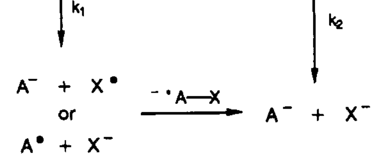
Summary: Carbon–carbon bond cleavage in dianions is faster than in radical anions as expected from thermodynamic considerations. However, in contrast to the radical anion fragmentation, where $\Delta G^{\ddagger} \cong \Delta G$, the dianion scission has a much larger intrinsic barrier ($\Delta G^{\ddagger} \gg \Delta G$).

Reductive cleavage of single C–C bonds by alkali metals has been postulated to involve radical anions, dianions, or even polyanions.[2,3] There are, however, only a few mechanistic studies published so far which provide data concerning the identity of the reactive species undergoing bond scission.[4-7] Two of these studies provided evidence

Scheme I



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[1] On leave from the Technical University of Łódź (Poland).

[2] For a summary of the relevant literature, see: (a) Grovenstein, E., Jr.; Bhatti, A. M.; Quest, D. E.; Sengupta, D.; VanDerveer, D. *J. Am. Chem. Soc.* **1983**, *105*, 6290 and references therein. (b) Staley, S. W. In *Selective Organic Transformations*; Thyagarajan, B. S., Ed.; Wiley Interscience: New York, 1972; Vol. 2, p 309. (c) Holy, N. L. *Chem. Rev.* **1974**, *74*, 243.

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