A Novel Tandem [2 + 2] Cycloaddition−Dieckmann Condensation with Ynolate Anions. Efficient Synthesis of Substituted Cycloalkenones and Naphthalenes via Formal [*n* + 1] Cycloaddition

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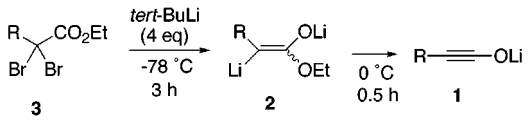
A novel tandem [2 + 2] cycloaddition−Dieckmann condensation via ynolate anions is described. Ynolate anions are useful for the formation of reactive β-lactone enolates via a pathway not involving the enolization of the corresponding β-lactones. The [2 + 2] cycloaddition of ynolate anions with δ- or γ-keto esters, followed by Dieckmann condensation, gives bicyclic β-lactones, which are easily decarboxylated to produce synthetically useful 2,3-disubstituted cyclopentenones and cyclohexenones in one pot. This tandem reaction was applied to a novel, one-pot synthesis of highly substituted naphthalenes.

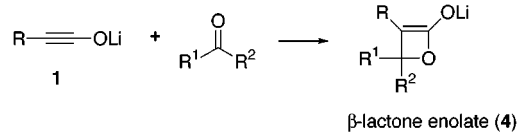
Introduction

Stabilized carbanions, like enolate anions, are fundamental reactive species that are widely used in synthetic organic chemistry. Ynolate anions[1] with a triple bond in place of the double bond of enolate anions are ketene anion equivalents and, as such, are expected to act as multifunctional carbanions for ketenes which are also highly reactive species.[2] Since Schöllkopf first succeeded in generating lithium ynolates and found that their cycloaddition with aldehydes and ketones gave β-lactone enolates,[3] there have been many published reports on the synthesis of ynolates and their reactions.[4−10] However, studies on the versatility of ynolate anions have remained at a rather basic level. To advance ynolate chemistry, it would be useful if one could develop a general and convenient methodology for the preparation of ynolates (**1**). Recently, we reported a new method for the generation of lithium ynolates via the cleavage of ester dianions (**2**) prepared from readily available α,α-dibromoesters (**3**) (Scheme 1).[11]

Scheme 1



Scheme 2



This finding has led to our present investigation of ynolate chemistry.[12] First, we focused on the β-lactone enolates (**4**) generated by the cycloaddition of ynolate anions with carbonyl compounds (Scheme 2).[3,5,11] It occurred to us that a well-designed reaction using ynolates could make possible one-pot multistep syntheses involving tandem reactions[13] via intermediate β-lactone enolates. If the β-lactone enolates could be produced via a method not involving enolization of the corresponding β-lactones, these reactions would be of greater utility. Since modern synthetic organic chemistry demands high

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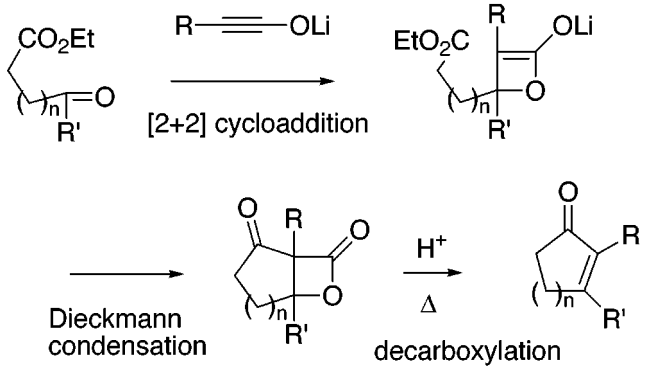
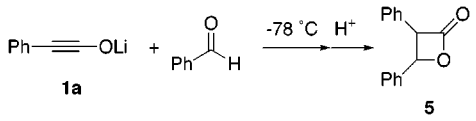
Scheme 3



Scheme 4



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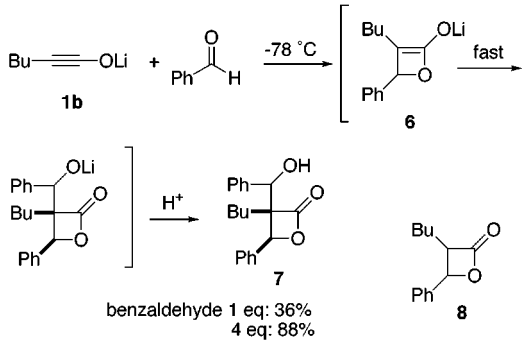


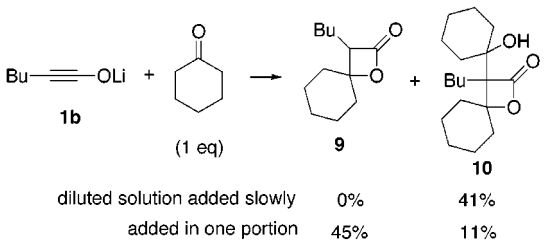
efficiency, ynolate anions are promising reagents in minimizing synthetic steps as well as in providing new chemistry.

We describe herein the full details, including scope and limitations, of a novel tandem [2 + 2] cycloaddition−Dieckmann condensation via ynolate anions to provide 2,3-disubstituted cycloalkenones (Scheme 3).[14] A one-pot synthesis of highly substituted naphthalenes is also included as an application of this tandem reaction.

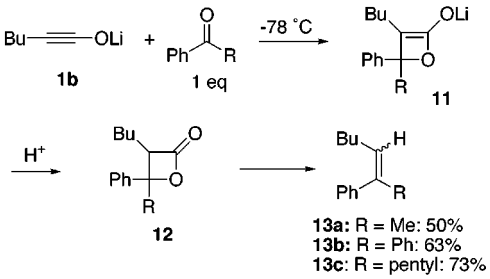
Results and Discussion

Cycloaddition of Ynolates with Carbonyl Compounds. Schöllkopf has reported that the ynolate anion (**1a**) bearing a phenyl substituent reacts with benzaldehyde to give the 3,4-disubstituted *β*-lactone (**5**) (Scheme 4).[3] We have found, however, that the alkyl-substituted ynolates (e.g., **1b**) reacted with an excess of benzaldehyde to afford the 3,3,4-trisubstituted *β*-lactone (**7**, 2:1 adducts) (Scheme 5). Even when only 1 equiv of the aldehyde was added, none of the 3,4-disubstituted *β*-lactone (**8**) was

Scheme 6



Scheme 7



observed. This is due to the much higher nucleophilicity of the intermediate enolate (**6**). The ynolate (**1a**), by comparison, has lower nucleophilicity because of the stabilization of the anion by the phenyl group. This result illustrates the apparent difficulty of tandem reactions utilizing aldehydes; namely, the *β*-lactone enolates generated would be immediately trapped by the aldehydes. To realize a tandem reaction of *β*-lactone enolates derived from ynolates, the nucleophilicity of the enolates should be less than that of the ynolates themselves.

Next, we examined reactions of ynolates with ketones. A diluted THF solution of cyclohexanone was slowly added to a solution of the ynolates at −78 °C to give only the 2:1 adduct (**10**). However, when cyclohexanone was added in one portion, the desired *β*-lactone (**9**) was isolated in 45% yield (Scheme 6). These results suggest that the difference in reactivity between the enolate and the ynolate is smaller than that for benzaldehyde. Encouraged by these results, we then tried to use more sterically hindered ketones. Not unexpectedly, reactions of the ynolate anion (**1b**) with acetophenone and benzophenone at −78 °C provided the desired 1:1 adducts (**12**) without generation of the 2:1 adducts, suggesting that the nucleophilicity of the ynolate (**1b**) was higher than that of the enolates (**11**) (Scheme 7). The *β*-lactones (**12**) were decarboxylated during workup to give the olefins (**13a**,**b**). Pentyl phenyl ketone also provided the *β*-lactone, which was decarboxylated by refluxing in benzene in the presence of silica gel to give **13c** in good overall yield.[15]

Tandem [2 + 2] Cycloaddition−Dieckmann Condensation. In the cycloaddition described above, if the ketone possesses another electrophilic center in the molecule, an intramolecular cyclization might proceed sequentially to provide bicyclic *β*-lactones, leading to the formation of synthetically useful disubstituted cycloalkenes. Based on this idea, we selected *δ*-keto esters as the substrate, expecting the tandem [2 + 2] cycloaddition−Dieckmann condensation to take place (Scheme 8). The keto ester **14** (0.8 mmol) was added at −78 °C to a solution of the ynolate (**1b**), prepared from the α,α-

(13) For recent reviews on tandem reactions, see: Chapdelaine, M. J.; Hulce, M. In *Organic Reactions*; Paquette, L. A., Ed.; Wiley: New York, 1990; pp 225−653. Ho, T.-L. *Tandem Organic Reactions*; Wiley: New York, 1992. Bunce, R. A. *Tetrahedron* **1995**, *51*, 13103−13159. Tietze, L. F. *Chem. Rev.* **1996**, *96*, 115−136. Denmark, S. E.; Thrarensen, A. *Chem. Rev.* **1996**, *96*, 137−165. Winkler, J. D. *Chem Rev.* **1996**, *96*, 167−176. Ryu, I.; Sonoda, N.; Curran, D. *Chem. Rev.* **1996**, *96*, 177−194. Parsons, P. J.; Penkett, C. S.; Shell, A. J. *Chem Rev.* **1996**, *96*, 195−206.

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Scheme 8

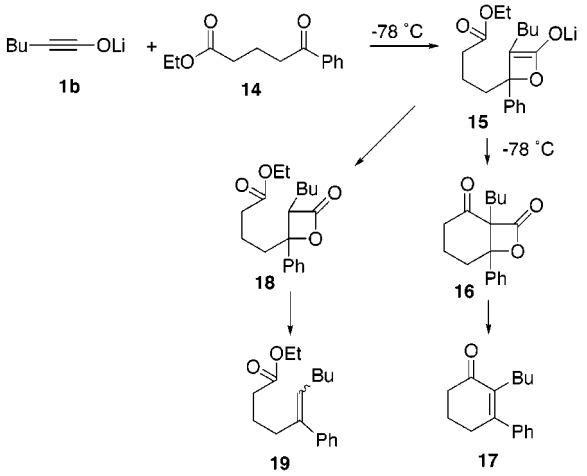
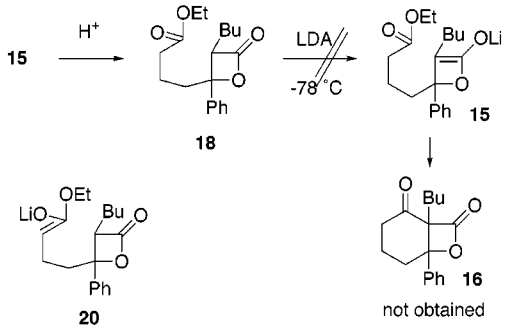


Table 1. Tandem [2 + 2] Cycloaddition−Dieckmann Condensation

reaction time (h)	**19** (%)	**17** (%)	total (%)
0.5	46	26	72
1.5	36	46	82
3.0	17	66	83
5.0	6	74	80

dibromoester (1.0 mmol) and *t*-BuLi (4.0 mmol) according to the usual procedure. TLC showed that the starting ester had immediately disappeared and that two spots had appeared simultaneously. After 5 h at −78 °C, the crude mixture seemed to contain the desired bicyclic *β*-lactone (**16**). Since the products did not respond to purification with silica gel column chromatography, they were treated with Danheiser's method of decarboxylation (method A: refluxing in benzene for several hours in the presence of a catalytic amount of silica gel)[15] without purification. After filtration and concentration, 2-butyl-3-phenyl-2-cyclohexenone (**17**) was isolated in 74% overall yield along with ethyl 5-phenyl-5-decenoate (**19**), which was derived from the uncyclized *β*-lactone (**18**). When the reaction was quenched after a shorter time, the uncyclized product (**19**) was obtained in higher yield, as shown in Table 1. These results show that the *β*-lactone enolates (**15**) are actually the intermediates and that the rate-determining step is the Dieckmann condensation. This is the first example of a tandem [2 + 2] cycloaddition−Dieckmann condensation, although tandem reactions using Dieckmann condensation, such as the Michael−Dieckmann reaction, are well known.[16] Unlike conventional Dieckmann condensations in which reactions are thermodynamically controlled to provide cyclic enolized *β*-ketoesters, ours is a kinetically controlled reaction affording nonenolizable keto lactones bearing quaternary carbons.[17] As far as we know, there are few reports of this type of Dieckmann condensation.

Scheme 9



We next attempted the direct generation of the reactive intermediate, the *β*-lactone enolate, from the corresponding *β*-lactone (Scheme 9). The *β*-lactone **18**, obtained by protonation of the lactone enolate **15**, was treated with LDA at −78 °C. When TLC showed that nothing had occurred, the mixture was then warmed to 0 °C, resulting in decomposition and recovery of **18**. It is possible that the less-hindered ester, and not the *β*-lactone (**16),** was converted into the enolate (**20**). This result indicates the difficulty in directly generating the enolate **15** from the *β*-lactone **18**. However, using the ynolate anion solved this problem by allowing the regioselective formation of the enolate via [2 + 2] cycloaddition prior to Dieckmann condensation.

To establish the generality of the tandem methodology, reactions using a variety of *δ*-keto esters[18] were examined. As shown in Table 2, these esters can serve as substrates and furnish 2,3-disubstituted cyclohexenones in good yields (entries 1−5). Primary carbon substituted ynolates (R = Me, Bu) afforded the desired products; however, when the cyclohexyl-substituted ynolate was used, the uncyclized *β*-lactone was obtained because the Dieckmann condensation did not proceed, probably due to steric hindrance (entry 6).

γ-Keto esters are also suitable substrates for this tandem reaction to provide synthetically useful 2,3-disubstituted cyclopentenones (entries 7−11). A keto diester (**24**) also gave the desired cyclopentenone (**33**), which demonstrates that the method will work with substrates having other ester functions. A keto ester (**25**) did not afford the seven-membered ring, probably due to the steric strain in the transition state of Dieckmann condensation. In some cases (e.g., entries 10, 11), the bicyclic intermediates decomposed during workup. Presumably, the *β*-lactones were opened at room temperature by the attack of water or hydroxide, followed by a retroaldol reaction. To avoid the possibility of decomposition, decarboxylation catalyzed by acid should proceed prior to the ring opening of the *β*-lactones. Thus, the reaction mixture of the Dieckmann condensation was quenched with 3% HCl−EtOH, followed by immediate refluxing (decarboxylation method B). As a result, the desired cycloalkenones were successfully obtained in higher yields (entries 4, 8, 10, 11). With this improved

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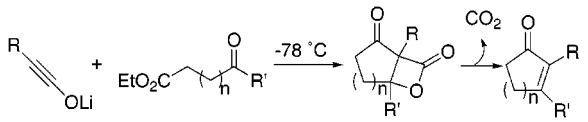
(17) In this case, the kinetically generated *β*-lactone enolates reacted with the ester irreversibly without proton exchange. See also House, H. O. *Modern Synthetic Reactions*, 2nd edition; W. A. Benjamin, Inc.: Menlo Park, 1972; p 740.

(18) Most of the starting keto esters or the corresponding carboxylic acids are commercially available.

Table 2. Synthesis of 2,3-Disubstituted-2-cycloalkenones via the Tandem Reaction



entry	ynolate	R	keto ester	R′	*n*	time (h)[a]	decarboxylation[b]	cycloalkenone	yield (%)
1	**1b**	Bu	**14**	Ph	2	5	A	**17**	74
2	**1c**	Me	**14**	Ph	2	1.5	A	**26**	89
3	**1b**	Bu	**21**	Me	2	1.5	A	**27**	78
4	**1b**	Bu	**21**	Me	2	1.5	B	**27**	89
5	**1c**	Me	**21**	Me	2	1.5	A	**28**	54
6	**1d**	c-Hex	**14**	Ph	2	48	A	**29**	0[c]
7	**1b**	Bu	**22**	Ph	1	1.5[d]	A	**30**	63
8	**1b**	Bu	**22**	Ph	1	1.5	B	**30**	89
9	**1b**	Bu	**23**	Me	1	1.5	A	**31**	83
10	**1c**	Me	**22**	Ph	1	1.5	B	**32**	84
11	**1c**	Me	**24**	$EtO_2C(CH_2)_2-$	1	2	B	**33**	60
12	**1c**	Me	**25**	Ph	3	2	A	**34**	0

[a] Time of the tandem reaction at −78 °C. [b] Method A: A solution of the β-lactone in benzene was refluxed in the presence of silica gel. Method B: The tandem reaction mixture was quenched with 3% HCl−EtOH, and the resulting solution was refluxed. [c] The uncyclized olefin was obtained in 85% yield. [d] −40 °C.

decarboxylation procedure, a facile one-pot synthesis of 2,3-disubstituted cycloalkenones was achieved.

Using this transformation, we carried out, in good yield, concise syntheses of both dihydrojasmone (**35**),[19] by the reaction of the pentyl-substituted ynolate with ethyl 4-oxopentanoate, and a potential intermediate (**36**) for α-cuparenone (**37**), by the one-pot reaction of the methyl-substituted ynolate with ethyl 4-oxo-4-(4-methylphenyl)butanoate (Scheme 10).[20]

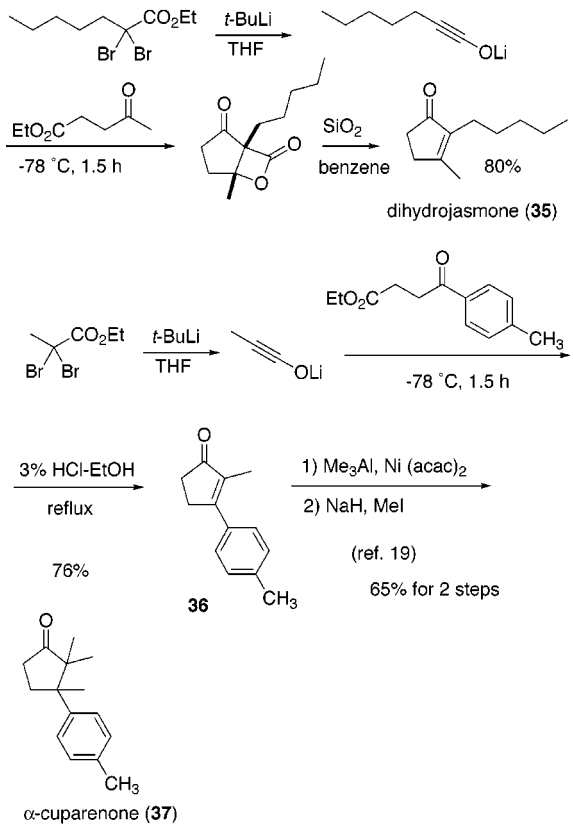
This process can also be applied to the synthesis of fused rings. The cyclic keto ester **38** reacts with the ynolate to afford, in good yield, 1-methylhexahydronaphthalen-2-one (**39**), the Robinson annulation product (Scheme 11). This tandem process is an efficient alternative to the classical annulation.

The bicyclic β-lactones (e.g., **40**) possess contiguous quaternary carbons, of which the stereochemistry is strictly defined. To exploit the stereocenters, we tried to convert the β-lactone into other functionalities without losing the stereochemistry (Scheme 12). Attempts at direct methanolysis and aminolysis resulted in generation of the diketo ester **41** and the diketo amide **42**, respectively. These products, which lost their stereocenters at the angular positions of the β-lactone, are thought to arise from nucleophilic addition of methanol and benzylamine followed by a retroaldol reaction.

To prevent the retroaldol reaction, the ketone was reduced by $NaBH_4$ to give the alcohol **43**, then subjected to aminolysis by benzylamine. As expected, the compound (**44**) bearing the two quaternary stereogenic centers derived from the β-lactone (**40**) was generated in good yield. These results clearly demonstrate the synthetic utility of the bicyclic β-lactones (e.g., **40**).

One-Pot Synthesis of Highly Substituted Naphthalenes by Tandem Reaction. The naphthalene nucleus is an important skeleton in organic chemistry because it is not only found in biologically active natural products,[21] but is also frequently used as a stereocontrol unit.[22] However, the regioselective synthesis of highly substituted naphthalenes is not easily accomplished using conventional approaches.[23] On the basis of the results described above, we envisioned preparing naphthalenes (**46**) via the tandem reaction of ynolate anions

Scheme 10



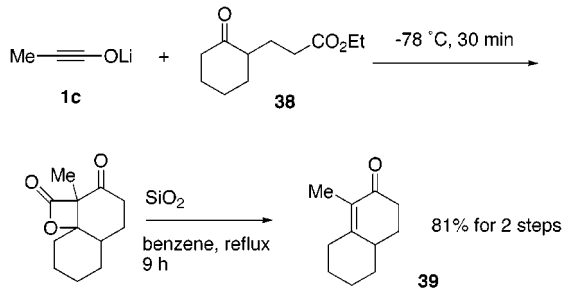
(19) For recent examples of syntheses of dihydrojasmone: Bellina, F.; Ciucci, D.; Rossi, R.; Vergamini, O. *Tetrahedron* **1999**, *55*, 2103-2112. Shono, T.; Yamamoto, Y.; Takigawa, K.; Maekawa, H.; Ishifune, M.; Kashimura, S. *Chem. Lett.* **1994**, 1045−1048. Solrokin, V. L.; Kulinkovich, O. G. *Zh. Org. Khim.* **1993**, *29*, 1119−1121. Mathew, J. *J. Org. Chem.* **1990**, *55*, 5294−5297. Ho, T.-L. *Chem. Ind.* **1988**, 762 and references cited in these papers.

(20) Cossy, J.; Gille, B.; BouzBouz, S.; Bellosta, V. *Tetrahedron Lett.* **1997**, *38*, 4069−4070. Recent examples of syntheses of α-cuparenones: Nakashima, H.; Sato, M.; Taniguchi, T.; Ogasawara, K. *Tetrahedron Lett.* **2000**, *41*, 2639−2642. Avila-Zarraga, J. G.; Maldonado, L. A. *Chem. Lett.* **2000**, 512−513 and references cited in these papers.

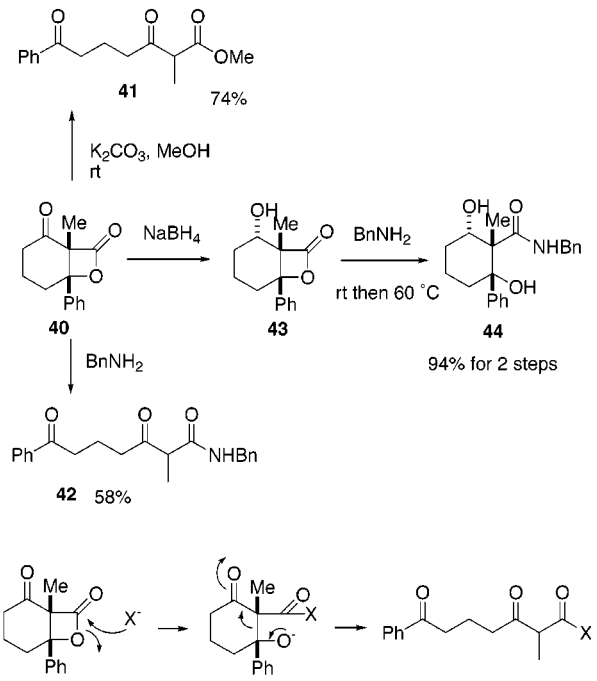
(21) For examples, see: Deshpande, A. M.; Argade, N. P.; Natu, A. A.; Eckman, *J. Bioorg. Med. Chem.* **1999**, *7*, 1237−1240. Mathe-Allainmat, M.; Gall, M. L.; Jellimann, C.; Andrieux, J.; Langlois, M. J. *Bioorg. Med. Chem.* **1999**, *7*, 2945−2952. Also see ref 3e.

(22) For examples of binaphthyls, see: Shibasaki, M.; Sasai, H.; Arai, T. *Angew. Chem., Int. Ed. Engl.* **1997**, *36*, 1236−1256. Pu, L. *Chem. Rev.* **1998**, *98*, 2405−2494.

Scheme 11



Scheme 12

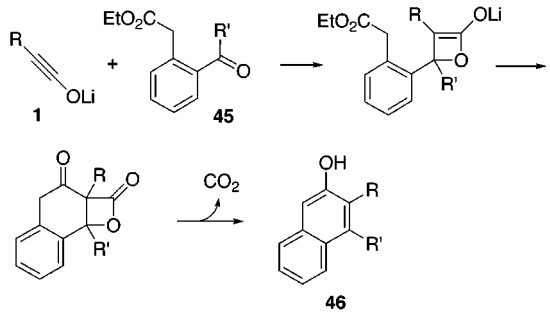


(**1**) with 2-acylphenylacetates (**45**) as the δ-keto esters (Scheme 13).

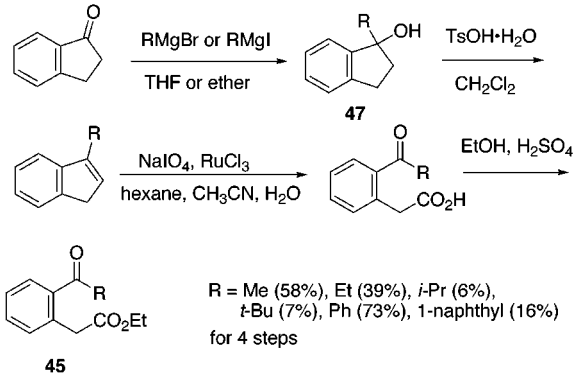
The substrate (**45**) was prepared according to Meyers' improved procedure,[24] as shown in Scheme 14. 1-Indanone was reacted with MeMgBr in ether to give the adduct (**47**), which was dehydrated (catalytic TsOH, CH_2Cl_2), oxidized (catalytic $RuCl_3$, $NaIO_4$ in hexane, acetonitrile, and H_2O),[25] and esterified (EtOH, catalytic H_2SO_4) to afford (**45**) in good to moderate overall yields.

The substrates having the sterically hindered substituents R, however, were obtained in only moderate yields because of the difficulty in adding the Grignard reagents to indanone in the first step. As a result, they were

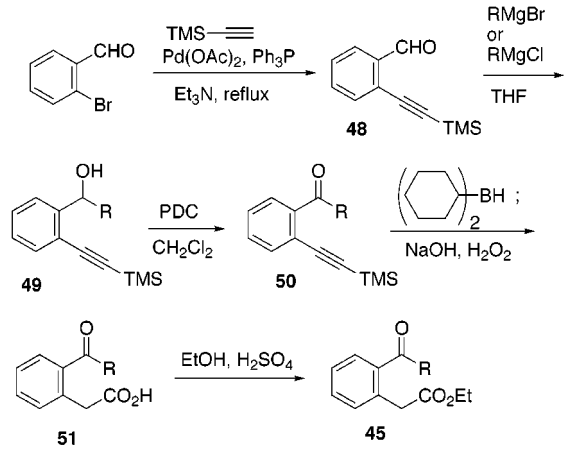
Scheme 13



Scheme 14



Scheme 15



synthesized via another route, as shown in Scheme 15. 2-Bromobenzaldehyde was coupled with trimethylsilylacetylene via the Sonogashira reaction to give the product (**48**),[26] which was reacted with the Grignard reagent to afford the secondary alcohol (**49**). The alcohol was oxidized by PDC to produce the ketone (**50**), which was hydroborated, and upon oxidation,[27] gave the keto carboxylic acid (**51**) without reduction of the ketone. Finally, the desired substrate (**45**) was synthesized by esterification in better overall yields.

The ynolate (**1**), prepared from the α,α-dibromoester (1.0 mmol) and *t*-BuLi (4.0 mmol), was reacted with ethyl

(23) For recent examples of the construction of naphthalenes: (a) Padwa, A.; Austin, D. J.; Chiacchio, U.; Kassir, J. M.; Rescifina, A.; Xu, S. L. *Tetrahedron Lett.* **1991**, *32*, 5923−5926. (b) Nishi, Y.; Tanabe, Y. *Tetrahedron Lett.* **1995**, *36*, 8803−8806. (c) Turnbull, P.; Moor, H. W. *J. Org. Chem.* **1995**, *60*, 644−649. (d) Yadav, K. M.; Mohanta, P. K.; Ila, H.; Junjappa, H. *Tetrahedron* **1996**, *52*, 14049−14056. (e) Andersen, N. G.; Maddaford, S. P.; Keay, B. A. *J. Org. Chem.* **1996**, *61*, 2885−2887. (e) Cotelle, P.; Catteau, J. P. *Tetrahedron Lett.* **1997**, *38*, 2969−2972. (f) Koning, C. B.; Michael, J. P.; Rousseau, A. L. *Tetrahedron Lett.* **1997**, *38*, 893−896. (g) Koning, C. B.; Michael, J. P.; Rousseau, A. L. *J. Chem. Soc., Perkin Trans. 1* **2000**, 787−797. (h) Kao, C.-L.; Yen, S. Y.; Chern, J.-W. *Tetrahedron Lett.* **2000**, *41*, 2207−2210. (i) Iwasawa, N.; Shido, M.; Maeyama, K.; Kusama, H. *J. Am. Chem. Soc.* **2000**, *122*, 10226−10227. (j) Kiselyov, A. S. *Tetrahedron Lett.* **2001**, *42*, 3053−3056. (k) Kajikawa, S.; Nishino, H.; Kurosawa, K. *Tetrahedron Lett.* **2001**, *42*, 3351−3354.

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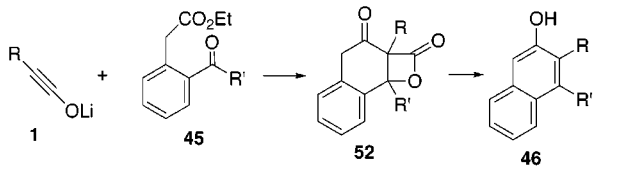
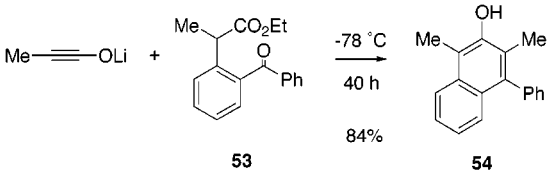
Table 3. One-Pot Synthesis of 3,4-Disubstituted-2-naphthols



entry	R	R′	conditions	yield (%)
1	Me	Me	−78 °C, 0.5 h	76
2	Me	Et	−78 °C, 0.5 h	85
3	Me	i-Pr	−78 °C, 42 h	88
4	Me	Ph	−78 °C, 2 h	72
5	Me	1-naphthyl	−78 °C then rt, 18 h	82
6	Bu	Me	−78 °C, 0.5 h	93
7	Bu	Ph	−78 °C, 43 h	72
8	c-Hex	Me	rt, 1.5 h	57

Scheme 16



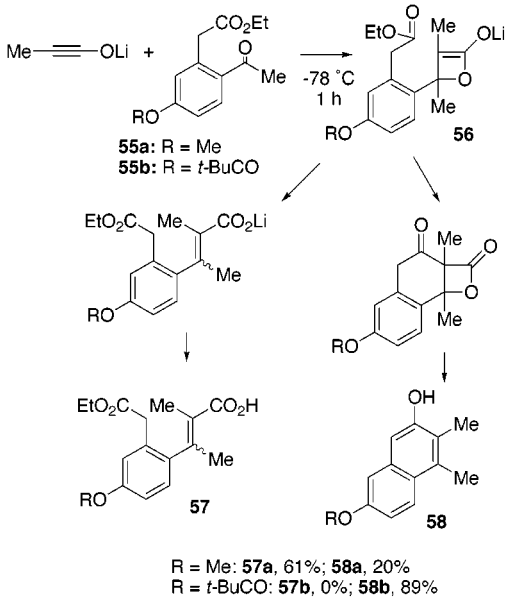
(2-acetylphenyl)acetate (**45**, R′ = Me, 0.8 mmol) in THF, and the mixture was stirred for 30 min at −78 °C. After the usual workup and purification, 3,4-dimethyl-2-naphthol (**46**, R, R′ = Me) was isolated in 76% yield. Since no β-lactone (**52**) was detected in the NMR and IR spectra of the crude mixture, decarboxylation of the β-lactone and subsequent enolization must have proceeded during the workup. This is a novel methodology for the synthesis of substituted naphthalenes.

To establish the generality of this process, we examined reactions using several kinds of 2-acylphenylacetates. As shown in Table 3, the desired 3,4-disubstituted 2-naphthols were successfully obtained in good yields. The ynolates can also react with sterically hindered ketones to afford the corresponding sterically congested naphthols, although they required longer reaction times and/or higher temperatures (entries 2, 3, 8). Judging from TLC analysis, the rate-determining step seems to be the Dieckmann condensation. A 1,1′-binaphthyl compound was also efficiently synthesized (entry 5).

The synthesis of the highly substituted naphthalenes was more challenging. As shown in Scheme 16, ethyl 2-(2-benzoylphenyl)propionate (**53**) proved to be a good substrate for this one-pot process and gave 1,3,4-trisubstituted-2-naphthol (**54**) in good yield.

2-Acetyl-5-methoxyphenylacetate (**55**), easily prepared by Friedel−Crafts acylation of ethyl 3-methoxyphenylacetate, afforded the desired trisubstituted 2-naphthol (**58**) in only 20% yield, along with 61% of the olefin (**57**). This is probably due to ring opening of the β-lactone enolate (**56**) accelerated by the electron-donating group in the para position, since it is known that at a higher temperature (e.g., at room temperature), enolates are easily converted into olefins via electrocyclic reactions.[28] Thus, the substrate **55b** having a pivaloyloxy group in place of the methoxy group was used to decrease the

Scheme 17



electron density of the phenyl ring. As expected, the desired 2-naphthol (**58b**) was produced exclusively in 89% yield (Scheme 17).

Next, a one-pot methyl etherification of the naphthols was attempted because of the instability of some of the naphthols. Initially, MeI and HMPA were added to the basic reaction mixture at −78 °C, and it was allowed to warm to room temperature over 18 h for decarboxylation. The desired methyl ether (**61a**) was isolated, along with the olefin (**63**, R = Me), in 46% and 26% yield, respectively. The side product was thought to arise from a retro-Dieckmann condensation induced by lithium ethoxide at room temperature, followed by ring opening of the resulting β-lactone enolate (**62**). To prevent the competitive, undesired retro-Dieckmann condensation, the reaction was quenched and acidified with acetic acid at −78 °C and allowed to warm to room temperature. Then, an excess of dimethyl sulfate, potassium carbonate, and DMF was added. As expected, the desired methyl ether (**61a**) was isolated in 76% yield. Using this procedure, trisubstituted naphthalene ethers (**61**) were obtained in good yields (Scheme 18).

Conclusion

We have developed a novel tandem [2 + 2] cycloaddition−Dieckmann condensation of ynolates to efficiently synthesize 2,3-disubstituted cyclopentenones and cyclohexenones. This tandem reaction can be formally regarded as an [n + 1] cycloaddition (n = 4, 5). Moreover, this tandem reaction was applied to one-pot syntheses of highly substituted naphthalenes. Since these products, especially sterically hindered naphthalenes, are difficult to synthesize via short routes using conventional methods, this approach should be useful for organic synthesis. We also demonstrated that the β-lactone enolates, generated by cycloaddition of ynolates with ketones, are useful reactive intermediates. Additionally, this result also shows the high versatility of ynolates.

Experimental Section

General. ^{1}H NMR were measured in $CDCl_3$ solution and referenced to TMS (0.00 ppm). ^{13}C NMR were measured in $CDCl_3$ solution and referenced to $CDCl_3$ (77.0 ppm). All

(28) Pioneering work of this type of reaction: Mulzer, J.; Kerkmann, T. *J. Am. Chem. Soc.* **1980**, *102*, 3620−3622. See also refs 5a, 12a, and 12e.

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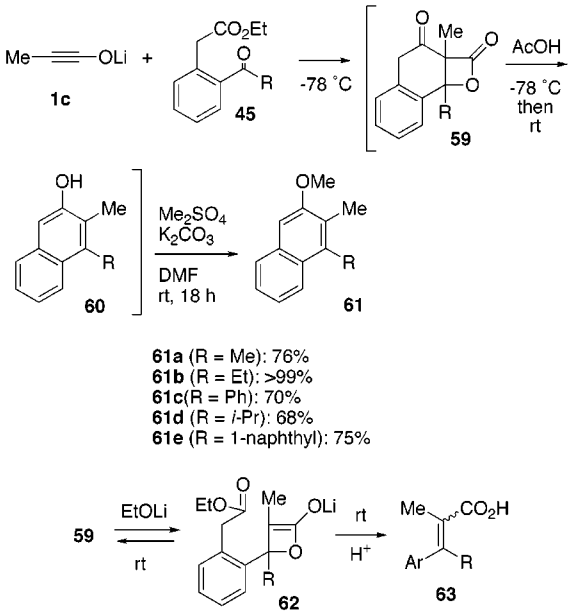
Scheme 18



reactions were performed in oven-dried glassware under a positive pressure of argon, unless otherwise noted. Reaction mixtures were stirred magnetically. Solutions of alkyllithium reagents were transferred by syringe or cannula and were introduced into reaction vessels through rubber septa.

Representative Procedure (Method A). Synthesis of 2-Butyl-3-phenyl-2-cyclohexenone (17)[29] from Butyl-Substituted Lithium Ynolate (Table 2, Entry 1). To a solution of ethyl 2,2-dibromohexanoate (302 mg, 1.0 mmol)[11b] in 6 mL of dry THF, cooled to −78 °C under argon, was added dropwise a solution of *tert*-butyllithium (2.70 mL, 4.0 mmol, 1.48 M in pentane). The yellow solution was stirred for 3 h at −78 °C and allowed to warm to 0 °C. After 30 min, the resulting colorless reaction mixture was cooled to −78 °C, and a solution of ethyl 5-oxo-5-phenylpentanoate (**14**) (176 mg, 0.80 mmol) in THF (2 mL) was added dropwise. After 5 h at −78 °C, a saturated NH_4Cl solution was added, and the resulting mixture was extracted with ethyl acetate. The organic phase was successively washed with saturated solutions of $NaHCO_3$ and NaCl, dried over $MgSO_4$, filtered, and concentrated to afford a yellow oil. This crude mixture was dissolved in benzene (10 mL), and 100 mg of 100−270 mesh chromatographic silica gel was added. The reaction mixture was heated at reflux for 10 h and then allowed to cool to room temperature before filtering. The filtrate was concentrated to afford a yellow oil, which was chromatographed over silica gel (2−5% ethyl acetate in hexane) to yield 136 mg (74%) of **17** as a colorless oil and 13 mg (6%) of **19** as a colorless oil.

17. ^{1}H NMR ($CDCl_3$, 400 MHz) δ: 0.74 (t, J = 7.3 Hz, 3H), 1.14 (tq, J = 7.3 Hz, 7.3 Hz, 2H), 1.21−1.29 (m, 2H), 2.04−2.15 (m, 4H), 2.51 (t, J = 6.4 Hz, 2H), 2.59 (t, J = 6.4 Hz, 2H), 7.17 (d, J = 6.8 Hz, 2H), 7.30−7.40 (3H, m). IR (neat): 1668, 1616 cm^{-1}. MS m/z: 228 (M^+, 100%), 229 (M + 1).

Ethyl 5-Phenyl-5-decenoate (19). ^{1}H NMR ($CDCl_3$, 400 MHz) δ: 0.82 (t, J = 7.0 Hz, 2.5H), 0.88−0.98 (m, 0.5H), 1.21−1.32 (m, 7H, including t, J = 7.0 Hz, 2.5H), 1.57−1.72 (m, 2.3H), 1.92 (dt, J = 7.3 Hz, 7.3 Hz, 1.7H), 2.26 (t, J = 7.5 Hz, 2H), 2.36 (t, J = 7.5 Hz, 2H), 4.10 (q, J = 7.0 Hz, 2H), 5.44 (t, J = 7.3 Hz, 0.83H), 5.69 (t, J = 7.3 Hz, 0.17H), 7.12 (d, J = 7.0 Hz, 1H), 7.20−7.46 (m, 4H). IR (neat): 1736 cm^{-1}. MS m/z: 274 (M^+), 129 (100%). HRMS (EI): calcd for $C_{18}H_{26}O_2$ (MH^+), 274.1933; found, 274.1906.

Representative Procedure (Method B). Synthesis of 2-Butyl-3-phenyl-2-cyclopentenone (30) from Lithium Ynolate (1b) (Table 2, Entry 8). To a solution of ethyl 2,2-dibromohexanoate (302 mg, 1.0 mmol) in 6 mL of dry THF at −78 °C under argon was added dropwise a solution of *tert*-butyllithium (2.72 mL, 4.0 mmol, 1.47 M in pentane). The yellow solution was stirred for 3 h at −78 °C and allowed to warm to 0 °C. After 30 min, the resulting colorless reaction mixture was cooled to −78 °C. Then a solution of ethyl 4-oxo-4-phenylbutanoate (**22**) (165 mg, 0.80 mmol) in THF (2 mL) was added to the reaction mixture. After stirring for 1.5 h at −78 °C, 3% HCl in ethanol (5 mL) was added, and the mixture was refluxed. After 2 h, the reaction mixture was cooled to room temperature and concentrated. The residue was diluted with ethyl acetate and neutralized with saturated $NaHCO_3$ solution. The resulting mixture was extracted with ethyl acetate. The organic phase was washed with saturated NaCl solution, dried over $MgSO_4$, filtered, and concentrated to afford a yellow oil, which was chromatographed over silica gel (2−5% ethyl acetate in hexane) to yield 153 mg (89%) of **30** as a colorless oil. ^{1}H NMR (300 MHz, $CDCl_3$) δ: 0.74 (t, J = 7.2 Hz, 3H), 1.25−1.50 (m, 4H), 2.37 (t, J = 7.2 Hz, 2H), 2.52 (t, J = 4.8 Hz, 2H), 2.88−2.91 (t, J = 4.8 Hz, 2H), 7.45−7.47 (m, 5H). ^{13}C NMR (75 MHz, $CDCl_3$) δ: 13.6 (q), 22.8 (t), 23.6 (t), 29.6 (t), 30.3 (t), 34.0 (t), 127.0 (d), 128.5 (d), 129.1 (d), 136.5 (s), 141.1 (s), 166.8 (s), 209.4 (s). IR (neat): 1696, 1624 cm^{-1}. MS m/z: 214 (M^+), 128 (100%). HRMS (EI): calcd for $C_{15}H_{18}O$ (M^+), 214.1358; found, 214.1323.

Representative Procedure for the Synthesis of 2-Naphthol (46, R, R′ = Me) from Lithium Ynolate (1c) (Table 3, Entry 1). To a solution of ethyl 2,2-dibromohexanoate (260 mg, 1.0 mmol) in 6 mL of dry THF at −78 °C under argon was added dropwise a solution of *tert*-butyllithium (2.80 mL, 4.0 mmol, 1.43 M in pentane). The yellow solution was stirred for 3 h at −78 °C and allowed to warm to 0 °C. After 30 min, the resulting colorless reaction mixture was cooled to −78 °C. Then a solution of ethyl 2-acetylphenylacetate (**45**, R′ = Me) (165 mg, 0.80 mmol) in THF (2 mL) was added to the reaction mixture. After stirring for 0.5 h at −78 °C, a solution of saturated aqueous NH_4Cl was added, and the mixture was extracted with ethyl acetate. The organic phase was successively washed with saturated solutions of $NaHCO_3$ and NaCl, dried over $MgSO_4$, filtered, and concentrated to afford a yellow oil, which was chromatographed over silica gel (2−5% ethyl acetate in hexane) to yield 105 mg (76%) of **46** (R, R′ = Me) as a yellow solid, which was recrystallized from a mixture of ethyl acetate and hexane to give brown prisms (mp 114.2−115.0 °C). ^{1}H NMR (300 MHz, $CDCl_3$) δ: 2.40 (3H, s), 2.61 (3H, s), 4.94 (1H, s), 6.98 (1H, s), 7.35 (2H, m), 7.62 (1H, dd, J = 2.1, 7.2 Hz), 7.95 (1H, dd, J = 2.1, 7.2 Hz). ^{13}C NMR (75 MHz, $CDCl_3$) δ: 12.6 (q), 14.8 (q), 107.2 (d), 123.3 (d), 123.9 (d), 124.4 (s), 125.2 (d), 126.5 (d), 128.4 (s), 132.9 (s), 133.5 (s), 152.2 (s). IR ($CHCl_3$): 3598, 1176 cm^{-1}. MS m/z: 172 (M^+, 100%), 173 (M + 1), 157 ($M^+ - CH_3$). Anal. Calcd for $C_{12}H_{12}O$: C, 83.69; H, 7.02. Found: C, 83.49; H, 7.19.

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Supporting Information Available: Synthetic procedures and characterization. This material is available free of charge via the Internet at http://pubs.acs.org.

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