2 H, J = 1.5 Hz), 7.23 (s, 5 H); IR (CCl_4) 3100–2780, 1720, 1555, 1230, 1070 cm^{-1}.

2-Benzyl-3-oxo-2-azabicyclo[2.2.1]heptane (15). A solution of 0.337 g (0.0017 mol) of cured **14** in 150 mL of ethyl acetate was reduced in a Parr apparatus at 2 atm in the presence of 200 mg of 10% Pd/C for 3 h. After removal of the catalyst and the solvent, the oily residue was purified by bulb-to-bulb distillation at 130 °C (4 mm) to give a light yellowish oil (0.340 g, 99% yield). This oil was further purified by preparative TLC (silica gel GF, ethyl acetate) and then by preparative gas chromatography on an 6 ft × $^1/_4$ in. column packed with 3% SE-30 on 60/80 Chromosorb W at 190 °C: NMR ($CDCl_3$) δ 1.33–2.10 (m, 6 H), 2.83 (m, 1 H), 3.64 (m, 1 H), 3.89 (d, 1 H, J = 15 Hz), 4.66 (d, 1 H, J = 15 Hz), 7.25 (s, 5 H); IR (CCl_4) 3100–2820, 1720, 1240, 1070 cm^{-1}. Anal. C, H, N.

Acknowledgment. We thank the NIH for their generous support of this research through Grant AM17458.

Registry No. **1a**, 5906-38-7; **1b**, 7421-56-9; **1c**, 5906-39-8; **1d**, 60511-87-7; **1e**, 78805-41-1; **1f**, 78805-42-2; **1g**, 78805-43-3; **2d**, 78805-44-4; **3a**, 38318-60-4; **3b**, 75409-90-4; **3c**, 60494-12-4; **3d**, 75409-92-6; **3e**, 75422-81-0; **3f**, 78805-45-5; **3g**, 78805-46-6; **3h**, 78805-47-7; **3i**, 78805-48-8; **3j**, 78805-49-9; **3k**, 78805-50-2; **3l**, 78805-51-3; **3m**, 78822-62-5; **3n**, 78805-52-4; **3o**, 78805-53-5; **3q**, 78805-54-6; **6c**, 78805-55-7; **6d**, 67809-25-0; **8a**, 150-76-5; **8b**, 15174-02-4; **8c**, 14786-82-4; **8d**, 13523-62-1; **8e**, 88-32-4; **8f**, 78805-56-8; **8g**, 13522-79-7; **9a**, 78805-57-9; **9b**, 78805-58-0; **9c**, 78805-59-1; **9d**, 78805-60-4; **9e**, 78805-61-5; **9f**, 78805-62-6; **9g**, 78805-63-7; **10h**, 67809-27-2; **10i**, 78805-64-8; **10j**, 78805-65-9; **10k**, 78805-66-0; **10l**, 78805-67-1; **10m**, 78805-68-2; **10n**, 78805-69-3; **10o**, 78805-70-6; **12**, 78805-71-7; **13d**, 67809-30-7; **13h**, 57864-15-0; **13i**, 57864-14-9; **13j**, 78805-72-8; **13k**, 78805-73-9; **13l**, 78805-74-0; **13m**, 78805-75-1; **13n**, 78805-76-2; **13o**, 78805-77-3; **13p**, 78805-78-4; **13q**, 78805-79-5; **14**, 78805-80-8; **15**, 78805-81-9; phenol·Na, 139-02-6; 4-phenoxyphenol·Na, 73355-29-0; benzyl bromide, 100-39-0; 4-(4-methylphenoxy)benzyl bromide, 78805-82-0; *p*-cresol·K, 1192-96-7; 4-bromo-2-nitroanisole, 33696-00-3; 2,6-dinitro-4-methylphenol, 609-93-8; *p*-toluenesulfonyl chloride, 98-59-9; 3,5-diiodo-4-(4-methoxybenzyl)benzyl chloride, 40279-83-2; 1-propanethiol, 107-03-9; 2-azabicylo[2.2.2]octan-3-one, 3306-69-2.

Supplementary Material Available: Tables IV–VII giving yields and physical and spectral data for compounds **3**, **9**, **10**, and **13** (5 pages). Ordering information is given on any current masthead page.

β-Amino Ester Enolate as an Acrylate Anion Equivalent for the Synthesis of α-Methylene Esters, Acids, and Lactones[1,2]

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The lithium enolate (**18**) of methyl 3-(dimethylamino)propionate (**17**) has been developed as a synthetic equivalent of the α-anion (**15**) of acrylic acid. The enolate, obtained by treatment of the free ester (**17**) with lithium diisopropylamide, may be alkylated with a variety of alkyl halides to give products which may be considered to be protected acrylate esters. Unmasking is accomplished by quaternization with methyl iodide followed by DBN-induced elimination to give the free acrylates. The products derived from allylic halides may conveniently be converted into α-methylene lactones.

The acrylate unit and related groups (**1**, Chart I) are found as structural features of a very large number of naturally occurring compounds, many of which possess useful biological activity. Included among these compounds are several classes of unsaturated carboxylic acids, esters, and lactones. Some specific examples of the acids are ambrosic acid (**2**),[3] the eremophildienoic acid (**3**),[4] the fatty acid derivatives (**4**) of β-alanine,[5] conocandin (**5**),[6] and several other closely related compounds.[7] Simple ester derivatives of some of these and similar acids are also known.[8] In addition, unsaturated ester groups such as angelates and tiglates occur as appendages of several physiologically active compounds.[9] Furthermore, acrylates are observed in reduced forms as unsaturated aldehydes (e.g., **6**–**8**)[10] and alcohols (e.g., **9** and **10**).[10c,e,11] However,

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(2) For preliminary communications describing portions of this investigation see: (a) Yu, L.-C.; Helquist, P. *Tetrahedron Lett.* **1978**, 3423–3426. (b) Yu, L.-C.; Helquist, P. *Synth. Commun.*, in press.

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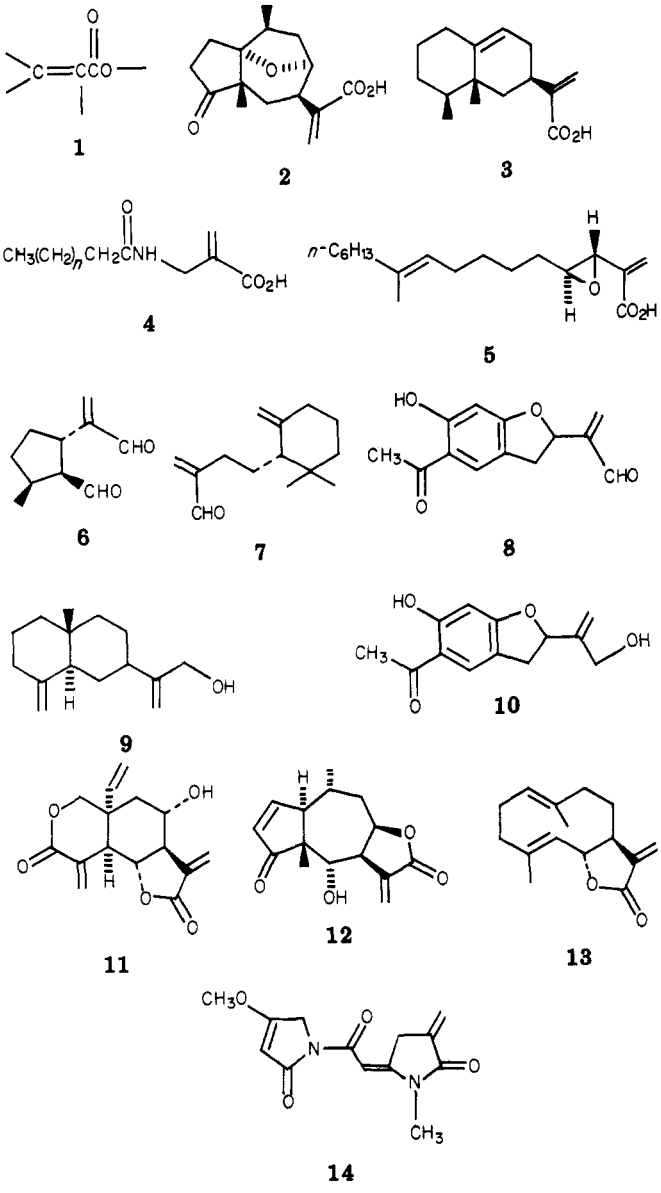
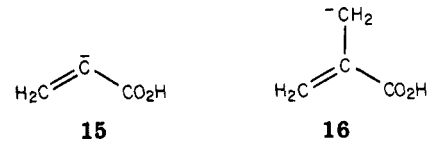
0022-3263/81/1946-4536$01.25/0

Chart I



the most commonly occurring acrylate derivatives are the very well-known α-methylene lactones, many of which possess anticancer activity.[9a,12] A few of the more important examples of these compounds are vernolepin (11),[13] helenalin (12),[14] and costunolide (13).[15] Finally, a few α-methylene lactams such as pukeleimide E (14) have been reported.[16]

Because of the importance of acrylate derivatives and, in particular, the α-methylene lactones, many methods have been developed for the synthesis of these classes of compounds.[17-19] Indeed, these methods have been employed in the total synthesis of several natural products. Most of the methods that have been developed can be classified according to two general approaches: (1) α-methylenation of preexisting carbonyl systems and (2) direct introduction of intact acrylate units. Of these two strategies, the latter is inherently the more attractive because of the greater degree of convergency associated with this approach. Conceptually, one of the most direct approaches for the introduction of the acrylate group would be reactions of appropriate electrophilic reagents with, formally speaking, the α-anion 15 of acrylic acid. However,



various species related to this anion (e.g., the dianion, esters, etc.) have proven to be rather elusive. As a result, synthetic equivalents of this acrylic acid anion have been developed.[20] A related approach has been the use of intermediates that are equivalent to the allylic anion derivative (16) of methacrylic acid.[21]

In this paper we give a detailed account of our investigations of an acrylate synthon which, in addition to the inherent advantages discussed above for this basic approach, permits the introduction of the acrylate unit in a conveniently protected form. This latter feature is an important consideration in multistep synthesis of complex natural products, especially in light of the high reactivity

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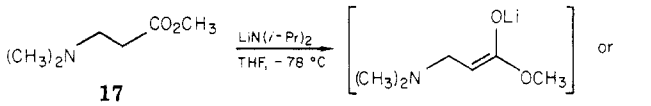
of α,β-unsaturated acid derivatives.

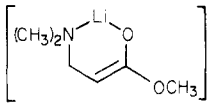
Results and Discussion

Our underlying strategy was to develop a method based upon the use of an acrylate synthon of the general structure $ZCH_2CH_2CO_2R$ in which the group Z, after appropriate modification, may ultimately serve as a leaving group in an elimination reaction to unmask the acrylate system. However, reagents of this type would need to meet the requirement of undergoing conversion to the corresponding enolates which could be alkylated with various reagents but which would not undergo spontaneous, premature elimination. The use of methyl hydracrylate was developed previously in accord with these same basic principles.[20a] In preliminary studies, we had attempted to employ 3-mercaptopropionic acid and several derivatives as acrylate synthons, but all of these attempts were frustrated by undesired selective alkylations at sulfur or elimination reactions. Fortunately, the use of a reagent bearing a nitrogen-containing leaving group has proven to be much more successful.[2,20d]

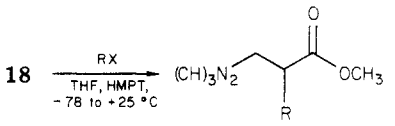
Our reagent, methyl 3-(dimethylamino)propionate (17), is conveniently obtained in large, preparative-scale quantities from the simply performed reaction[22] of dimethyl amine with methyl acrylate, two widely available, inexpensive starting materials. Under the usual conditions for the generation of enolates from esters,[23] 17 reacts with lithium diisopropylamide to give the intermediate 18 (eq 1) which appears to be quite stable. Even after prolonged



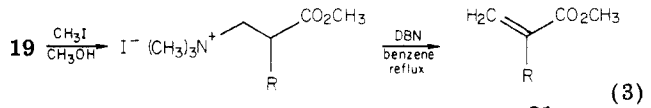
17 18



18a (1)



19 (2)



20 21 (3)

periods of time at room temperature, solutions of 18 undergo subsequent reactions with no significant loss in yields of the resulting products. The existence of the enolate as a chelated species (18a) may possibly account for this stability. Furthermore, we have not observed an exchange of dialkylamide groups between our reagent and the amide base employed in formation of the enolate.

Relative to earlier work of others, enolates of β-amino esters have been generated as intermediates in pathways reported by Still[20d] and by Hase.[20f] In the former case, this type of enolate was trapped with triethylsilyl chloride, and the resulting ketene acetal participated in a subsequent Claisen rearrangement.[20d] In the latter case, the enolates were formed by 1,4-addition of lithium diisopropylamide to acrylates followed by trapping with benzeneselenenyl bromide in most cases, although a few examples of alkylation with methyl iodide were also reported.[20f] In neither one of these studies was a thorough investigation of the reactivity of the enolates with other electrophiles reported.

Table I. Synthesis of Acrylates

RX	compd	yield,[a,d] % 19	21
CH_3I	a	(88)[b]	(84)[b]
CH_3CH_2I	b	(69)[b]	
n-C_4H_9I	c	63 (67)[b]	81 (85)[b]
n-C_4H_9Br		(57)[c]	
CH_2=$CHCH_2Br$	d	83	(87)[b]
	e	78	74
	f	78 (80)[b]	87
	g	82	78

[a] The yields are given for isolated products unless otherwise noted. [b] Yields determined by GLC calibrated with a pure sample of the product and an internal standard are given in parentheses. [c] Yield determined by ^1H NMR integration with an internal standard. [d] The yield of 20 was 100% in all cases.

The intermediate (18) reacts with alkyl halides to produce the corresponding 2-substituted propionates (19) which are actually Mannich base derivatives, a very useful class of compounds (eq 2).[24] Although the reactions with primary alkyl iodides and allylic bromides in the presence of hexamethylphosphoric triamide (HMPT) proceed efficiently (see Table I), 18 is apparently not sufficiently nucleophilic to give good yields of products from reactions with other alkyl halides and epoxides. The use of the potassium enolate (from potassium hydride,[25] potassium diisopropylamide,[26] or potassium hexamethyldisilazide[27]) does not lead to any significant improvements in these reactions.

The alkylation products 19 are actually masked acrylates, in fulfillment of one of the goals of our work outlined above. Deprotection is accomplished in two straightforward steps: quaternization of methyl iodide occurs quantitatively in all cases studied, and elimination is performed by treatment of the salts 20 with 1,5-diazabicyclo[4.3.0]non-5-ene (DBN) in benzene at reflux to give the 2-substituted acrylates (21, eq 3). These conversions are summarized in Table I.

Conceptually, a very direct route to α-methylene γ-butyrolactones would involve the reaction of the enolate 18 with epoxides, but as noted above, 18 is not sufficiently nucleophilic to react with these less reactive alkylating agents. However, a quite useful, alternative route is based

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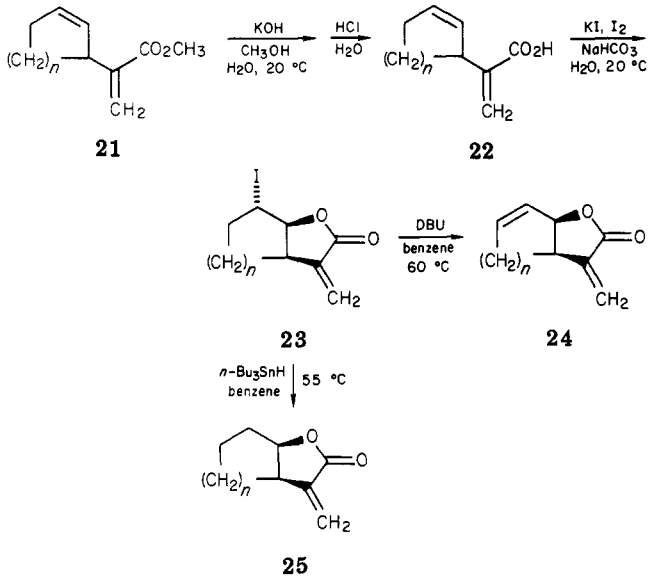
Table II. Synthesis of α-Methylene γ-Butyrolactones

	yield,[a] %			
n	22	23	24	25
1 (e)	100	100	88	68
2 (f)	90	95	94	60
3 (g)	99	100	78	80

[a] All yields are reported for isolated products except for compound 25e for which the yield was determined by GLC with an internal standard.

Scheme I[a]



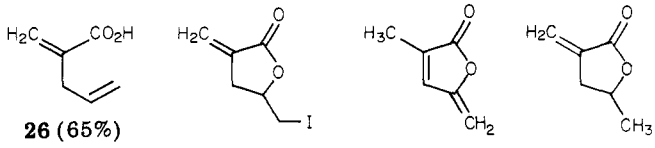
21 22 23 24 25

[a] e, n = 1; f, n = 2; g, n = 3.

upon the use of the products (21e–g) derived from allylic halides. These particular acrylates are hydrolyzed to the acids (22) which are then subjected to iodolactonization.[28] Finally, the lactones (23) may be treated with 1,8-diazabicyclo[5.4.0]undec-7-ene (DBU) to give the elimination products 24 or with tri-n-butyltin hydride[20c,29] to produce the reductive deiodination products 25. These transformations are summarized in Scheme I and Table II.

Of special note is that the more highly unsaturated products (24), with respect to arrangement of functionality and the nature of the fused ring systems, resemble a number of naturally occurring lactones. Also, this approach is well suited to the synthesis of these natural products in that the masked acrylate group as in 19 could be carried through several steps of a synthesis while other structural features of these often complex systems are elaborated.

An exactly analogous sequence of reactions may be performed by starting with the alkylation product (21d) derived from allyl bromide itself. The following products are obtained in the yields indicated. Note that the dehydroiodination of 27 produces a γ-methylene-2-butenolide rather than an α-methylene-γ-butyrolactone.



26 (65%) 27 (100%) 28 (26%) 29 (18%)

Conclusion

The work described in this paper provides a very practical route to acrylate derivatives. The principal reagent is especially readily available compared to the compounds used in several of the previously developed methods. With respect to applying this approach to the synthesis of important lactone systems, a key consideration is the availability of the appropriate allylic halides, compounds which are generally obtainable by a number of straightforward procedures.

Experimental Section

General Procedures. All reactions of organolithium reagents and other air-sensitive materials were performed under nitrogen. Solutions of these materials were transferred with hypodermic needles. Tetrahydrofuran (THF) was distilled from dark blue or dark purple solutions of sodium benzophenone radical anion or dianion under nitrogen. Hexamethylphosphoric triamide (HMPT) was distilled under vacuum from calcium hydride. The organolithium reagents were stored at 0 °C under nitrogen and were titrated prior to use by the method of Watson and Eastham[30] or Kofron and Baclawski.[31] All other reagents were distilled or recrystallized prior to use. Low temperatures were maintained through use of dry ice–acetone (−78 °C) or ice–water baths.

The ^{1}H NMR spectra were recorded at 60 MHz with a Varian EM-360 spectrometer or at 80 MHz with a Varian HFT-80 spectrometer. The NMR spectra were obtained from CCl_4 or $CDCl_3$ solutions containing tetramethylsilane (Me_4Si) as the internal standard. The chemical shifts are expressed in parts per million (γ) downfield from Me_4Si, and the ^{1}H NMR peak areas are expressed as the number of hydrogen atoms (H). Mass spectra were recorded with Hewlett-Packard Model 2982A and AEI Model MS-30 mass spectrometers by using electron-impact ionization at 70 eV. The IR spectra were obtained with a Pye-Unicam Model SP-1000 or a Perkin-Elmer Model 727 spectrophotometer as neat liquid films, as solutions in chloroform, or as KBr wafers and were calibrated with a polystyrene standard. Elemental analyses were performed by Galbraith Laboratories, Inc. The analytical results are given only when they agree with the calculated values within ±0.3%. In all other cases, the homogeneity of the compounds was demonstrated by careful GLC and TLC, and molecular formulas were determined by high-resolution mass spectroscopy. Preparative GLC was performed with a Varian Aerograph Model 900 gas chromatograph using a 6 ft × $^1/_2$ in. 5% SE-30 column. Analytical GLC was performed with a Hewlett-Packard Model 5711 gas chromatograph equipped with a flame-ionization detector, a linear temperature programmer, a Hewlett-Packard Model 3380A electronic integrator, and a 6 ft × $^1/_8$ in. 5% OV-1 column. Crude products were generally prepurified by bulb-to-bulb distillation at reduced pressure.

Methyl 2-[(Dimethylamino)methyl]hexanoate (19c). Methyl 2-(dimethylamino)propanoate (17) was prepared according to the procedure of Rouvier.[22] Then, to a solution of lithium diisopropylamide (76 mmol)[23] in THF (180 mL) at −78 °C under nitrogen was added 17 (12.3 mL, 72 mmol). After 30 min, a solution of 1-iodobutane (8.6 mL, 76 mmol) and HMPT (13 mL, 76 mmol) was added slowly. The mixture was stirred at 25 °C for 1 h, quenched by the addition of saturated aqueous ammonium chloride (30 mL), and partitioned between ether and water. The aqueous layer was extracted with additional ether, and the combined ether extracts were washed with water and saturated aqueous sodium chloride, dried (anhydrous magnesium sulfate), and concentrated by rotary evaporation. Distillation of the residue afforded 8.42 g (63%) of pure 19c as a clear, colorless oil: bp 50–52 °C (0.1 torr); IR (neat) 1740 cm^{-1}; ^{1}H NMR ($CDCl_3$) 3.70 (s, 3 H), 2.32–2.78 (m, 3 H), 2.23 (s, 6 H), 0.6–1.8 (m, 9 H); mass spectrum, m/e 187.1586 (M^+; 187.1572 calcd for $C_{10}H_{21}NO_2$). Similar procedures were employed for the remaining compounds of this series for which the following data are reported.

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19a: prepared from iodomethane (0.78 mL, 12.6 mmol); 88% yield (GLC with *n*-decane as the internal standard); bp 60 °C (15 torr); IR (neat) 1735 cm^{-1}; ^1H NMR (CCl_4) 3.60 (s, 3 H), 2.30 (m, 3 H), 2.12 (s, 6 H), 1.08 (d, J = 6 Hz, 3 H).[22]

19b: prepared from iodoethane (0.34 mL, 4.2 mmol); 69% yield (GLC with *n*-undecane as the internal standard); bp 85 °C (16 torr); IR (neat) 1740 cm^{-1}; ^1H NMR ($CDCl_3$) 3.70 (s, 3 H), 2.57 (m, 3 H), 2.23 (s, 6 H), 1.53 (m, 2 H), 0.90 (t, J = 7 Hz, 3 H); mass spectrum, m/e 159.1236 (M^+; 159.1259 calcd for $C_8H_{17}NO_2$).

19d: prepared from allyl bromide (21 mL, 240 mmol); 83% yield (isolated); bp 78–80 °C (15 torr); IR (neat) 3080, 3010, 1737, 1631, 990, 913 cm^{-1}; ^1H NMR ($CDCl_3$) 5.40–6.10 (m, 1 H), 4.70–5.23 (m, 2 H), 3.63 (s, 3 H), 1.87–2.83 (m, overlapping a singlet at 2.18, 11 H).

Anal. Calcd for $C_9H_{17}NO_2$: C, 63.13; H, 10.00; N, 8.18. Found: C, 62.88; H, 10.06; N, 8.15.

19e: prepared from 3-bromocyclopentene (7.0 g, 55 mmol); 78% yield (isolated); bp 64–66 °C (1 torr); IR (neat) 3050, 1737, 1612 cm^{-1}; ^1H NMR ($CDCl_3$) 5.40–5.60 (m, 2 H), 3.69 (s, 3 H), 1.15–3.05 (m, overlapping a singlet a 2.20, 14 H); mass spectrum, m/e 197.1393 (M^+; 197.1416 calcd for $C_{11}H_{19}NO_2$).

19f: prepared from 3-bromocyclohexene (1.46 mL, 12.6 mmol); 78% yield (isolated); bp 82–84 °C (1 torr); IR (neat) 3020, 1740, 1640 cm^{-1}; ^1H NMR ($CDCl_3$) 5.17–5.83 (m, 2 H), 3.62 (s, 3 H), 0.83–2.83 (m, overlapping a singlet at 2.17, 16 H); mass spectrum, m/e 211.1563 (M^+; 211.1572 calcd for $C_{12}H_{21}NO_2$).

19g: prepared from 3-bromocycloheptene (8.2 mL, 58 mmol); 82% yield (isolated); bulb-to-bulb distillation performed at oven temperature of 142 °C (0.02 torr); IR (neat) 3020, 1740, 1647 cm^{-1}; ^1H NMR ($CDCl_3$) 5.50–5.97 (m, 2 H), 3.67 (s, 3 H), 0.67–2.87 (m overlapping a singlet at 2.33, 18 H); mass spectrum, m/e 225.1733 (M^+; 225.1729 calcd for $C_{13}H_{23}NO_2$).

Methyl 2-(Dimethylamino)hexanoate Methiodide (20c). To a solution of **19c** (2.94 g, 15.7 mmol) and methanol (50 mL) at 25 °C was added iodomethane (11.7 mL, 188 mmol). After being allowed to stand in the dark for 18 h, the mixture was concentrated in vacuo, and the residue was washed with ether, leaving 6.81 g of solid **20c** which was used directly in the next step of the transformation. Analogous procedures were employed for quarternization of the remaining compounds of this series.

Methyl 2-*n*-Butylacrylate (21c). The crude **20c** (6.81 g) was suspended in a solution of DBN 4.3 mL, 35 mmol) and benzene (30 mL). The mixture was heated at reflux under nitrogen for 2.3 h, cooled to 25 °C, washed with 1 N hydrochloric acid, water, and saturated aqueous sodium chloride, dried (anhydrous magnesium sulfate), and concentrated by rotary evaporation. Distillation of the residue gave 1.80 g (81% overall from **19c**) of pure **20c** as a clear, colorless liquid: bp 85 °C (32 torr); IR (neat)[32] 1727, 1635 cm^{-1}; ^1H NMR ($CDCl_3$) 6.15 (br s, 1 H), 5.53 (m, 1 H), 3.76 (s, 3 H), 2.03–2.53 (m, 2 H), 0.67–1.60 (m, 7 H). Similar procedures were employed for the following acrylates with exceptions as indicated.

Compound **21a** was prepared in 84% yield (glc with *n*-undecane as the internal standard) by shaking the salt **20a** with a mixture of 5% aqueous sodium bicarbonate (1.1 equiv) and methylene chloride for 24 h at 25 °C. The resulting methyl methacrylate (**21a**) was identical with a commercial sample by GLC.

21d: prepared from the salt **20d** and DBN; 87% yield (GLC with *n*-undecane as the internal standard); IR (neat) 1728, 1635 cm^{-1}; ^1H NMR ($CDCl_3$) 5.45–6.31 (m, overlapping broad singlets at 5.56 and 6.18, 3 H), 5.15 (m, 1 H), 4.97 (m, 1 H), 3.75 (s, 3 H), 3.05 (br d, J = 6.4 Hz, 2 H).

Anal. Calcd for $C_7H_{10}O_2$: C, 66.65; H, 7.99. Found: C, 66.57; H, 7.91.

21e: prepared from crude **20e** and DBN; 74% yield isolated by bulb-to-bulb distillation (oven temperature 70 °C, 0.016 torr); IR (neat) 3050, 1720, 1625 cm^{-1}; ^1H NMR ($CDCl_3$) 5.20–6.40 (m, overlapping a broad singlet at 5.50 and a doublet at 6.11, J = 1.2 Hz, 4 H), 3.50–4.05 (m, overlapping a singlet at 3.76, 4 H), 2.32 (m, 3 H), 1.60 (m, 1 H); mass spectrum, m/e 152.0829 (M^+; 152.0837 calcd for $C_9H_{12}O_2$).

21f: prepared from crude **20f** and DBN; 87% yield after isolation by bulb-to-bulb distillation (oven temperature 30 °C, 0.046 torr); IR (neat) 3020, 1720, 1625 cm^{-1}; ^1H NMR ($CDCl_3$) 6.21 (d, J = 1.3 Hz, 1 H), 5.3–6.0 (m, overlapping a broad singlet at 5.54, 3 H), 3.75 (s, 3 H), 3.34 (m, 1 H), 1.18–2.23 (m, 6 H).

Anal. Calcd for $C_{10}H_{14}O_2$: C, 72.26; H, 8.49. Found: C, 71.96; H, 8.40.

21g: prepared from **20g** and DBN; 78% yield after distillation; bp 33 °C (0.01 torr); IR (neat) 3015, 1720, 1625 cm^{-1}; ^1H NMR ($CDCl_3$) 5.35–6.35 (m, overlapping a doublet at 6.19, J = 1 Hz, and a broad singlet at 5.61, 4 H), 3.50–3.89 (m, overlapping a singlet at 3.75, 4 H), 1.10–2.35 (m, 8 H).

Anal. Calcd for $C_{11}H_{16}O_2$: C, 73.30; H, 8.95. Found: C, 73.07; H, 9.12.

2-(2-Cyclohepten-1-yl)-2-propenoic Acid (22 g). To a solution of potassium hydroxide (2.44 g, 43.5 mmol), methanol (7 mL), and water (20 mL) at 20 °C was added **21g** (4.40 g, 24.0 mmol). The mixture was stirred at 20 °C for 24 h, acidified with 0.5 N hydrochloric acid, and concentrated in vacuo to remove methanol. The remaining mixture was extracted with ether. The extracts were washed with water and saturated aqueous sodium chloride, dried (anhydrous magnesium sulfate), and concentrated by rotary evaporation, leaving 4.01 g (99%) of **22g** as a colorless oil which was sufficiently pure for further use but which could be purified by bulb-to-bulb distillation (oven temperature 100 °C, 0.02 torr): IR (neat) 3015, 1691, 1624 cm^{-1}; ^1H NMR ($CDCl_3$) 11.0 (br s, 1 H), 6.38 (d, J = 0.9 Hz, 1 H), 5.56–6.20 (m, 3 H), 3.49 (m, 1 H), 1.16–2.45 (m, 8 H).

Anal. Calcd for $C_{10}H_{14}O_2$: C, 72.26; H, 8.49. Found: C, 72.25; H, 8.33.

Analogous procedures were used for the following cases.

22e: prepared from **21e** (4.70 g, 39.2 mmol); 100% yield (isolated); bp 77 °C (0.03 torr); IR (neat) 1685, 1625 cm^{-1}; ^1H NMR ($CDCl_3$) 11.31 (br s, 1 H), 6.28 (d, J = 0.9 Hz, 1 H), 5.50–6.17 (m, 3 H), 3.75 (m, 1 H), 1.07–2.70 (m, 4 H); mass spectrum, m/e 138.0697 (M^+; 138.0681 calcd for $C_8H_{10}O_2$).

Anal. Calcd for $C_8H_{10}O_2$: C, 69.55; H, 7.29. Found: C, 69.70; H, 7.27.

22f: prepared from **21f** (1.12 g, 6.76 mmol); 90% yield (isolated); IR (neat) 3020, 1690, 1620 cm^{-1}; ^1H NMR ($CDCl_3$) 11.35 (br s, 1 H), 6.40 (d, J = 1.1 Hz, 1 H), 5.33–6.30 (m, 3 H), 3.35 (br s, 1 H), 1.07–2.27 (m, 6 H).[20d]

26: prepared from **21d** (5.04 g, 39.7 mmol); 65% crude yield; purified by bulb-to-bulb distillation (oven temperature 40 °C, 0.02 torr); IR (neat) 3080, 1700, 1693, 1630 cm^{-1}; ^1H NMR ($CDCl_3$) 12.0 (br s, 1 H), 6.38 (br s, 1 H), 5.32–6.18 (m, overlapping a doublet at 5.70, J = 1 Hz, 2 H), 5.20 (br s, 1 H), 4.92 (m, 1 H), 3.0 (br d, J = 6 Hz, 2 H).

Anal. Calcd for $C_6H_8O_2$: C, 64.27; H, 7.19 Found: C, 64.17; H, 7.11.

2-Iodo-10-oxa-8-methylenebicyclo[5.3.0]decan-9-one (23g). To a clear solution of **22g** (3.41 g, 20.5 mmol), sodium bicarbonate (2.80 g, 33.3 mmol), and water (130 mL) at 25 °C was added a solution of potassium iodide (34.8 g, 210 mmol), iodine (11.14 g, 43.86 mmol), and water (140 mL). After being stirred in the dark for 30 h, the mixture was diluted with aqueous sodium sulfite and extracted with chloroform. Obtained from the extracts was 6.00 g (100%) of **23g** as a viscous yellow oil for which further purification was not necessary: IR (neat) 3120, 1787, 1675 cm^{-1}; ^1H NMR ($CDCl_3$) 6.27 (d, J = 2.5 Hz, 1 H), 5.60 (d, J = 2.1 Hz, 1 H), 4.85 (dd, J = 8.5, 8.0 Hz, 1 H), 4.34 (dt, J = 8.8, 1.7 Hz, 1 H), 3.0–3.5 (m, 1 H), 1.1–2.7 (m, 8 H).

Anal. Calcd for $C_{10}H_{13}IO_2$: C, 41.12; H, 4.49. Found: C, 41.14; H, 4.24.

Similar procedures were employed for the following compounds.

23e: prepared in 100% yield (isolated as a solid) from **22e** (4.61 g, 33.4 mmol); IR ($CHCl_3$) 1765, 1660 cm^{-1}; ^1H NMR ($CDCl_3$) 6.25 (d, J = 2.4 Hz, 1 H), 5.73 (d, J = 2.1 Hz, 1 H), 5.22 (d, J = 6.5 Hz, 1 H), 4.46 (br s, 1 H), 3.61 (m, 1 H), 1.45–2.90 (m, 4 H); mass spectrum, m/e 263.9676 (M^+; 263.9647 calcd for $C_8H_9IO_2$).

23f: prepared in 95% yield (isolated as a crystalline solid) from **22f** (0.922 g, 6.06 mmol); mp 80–80.5 °C (lit.[20d] mp 79–81 °C); IR (KBr) 3080, 1780, 1672 cm^{-1}; ^1H NMR ($CDCl_3$) 6.24 (d, J = 2.7 Hz, 1 H), 5.56 (d, J = 2.5 Hz, 1 H), 4.75 (t, J = 6.9 Hz, 1 H), 4.0 (m, 1 H), 3.0–3.45 (m, 1 H), 1.05–2.40 (m, 6 H).[20d]

27: prepared in 100% yield (isolated) from **26** (1.01 g, 9.02 mmol); bp 75 °C (0.02 torr); IR (neat) 1770, 1653 cm^{-1}; ^1H NMR ($CDCl_3$) 6.18 (dd, J = 3.5, 2.0 Hz, 1 H), 5.67 (dd, J = 3.5, 2.0 Hz,

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1 H), 4.20–4.92 (m, 1 H), 2.38–3.68 (m, overlapping a doublet at 3.38, J = 6 Hz, 4 H).

Anal. Calcd for $C_6H_7IO_2$: C, 30.28; H, 2.96. Found: C, 30.49; H, 2.91.

10-Oxa-8-methylenebicyclo[5.3.0]dec-2-en-9-one (24g). To a solution of **23g** (0.394 g, 1.35 mmol) in benzene (2.5 mL) at 25 °C under nitrogen was added DBU (0.27 mL, 1.8 mmol). After being stirred at 62 °C for 9 h, the mixture was filtered to remove white solid, and the filtrate was washed with 0.5 N hydrochloric acid, dried (anhydrous magnesium sulfate), and concentrated by rotary evaporation. Bulb-to-bulb distillation (oven temperature 160 °C, 0.02 torr) of the residue afforded 0.172 g (78%) of **24g** as a clear, colorless liquid: IR (neat) 3060, 1765, 1660 cm^{-1}; ^1H NMR ($CDCl_3$) 6.24 (d, J = 2.6 Hz, 1 H), 5.0–5.9 (m, 4 H), 3.18 (m, 1 H), 1.2–2.5 (m, 6 H); mass spectrum, m/e 164.0842 (M^+; 164.0837 calcd for $C_{10}H_{12}O_2$). The following compounds were obtained by similar procedures.

24e: prepared from **23e** (3.54 g, 13.4 mmol); 88% yield (isolated); IR (neat) 3058, 1755, 1658, 1615 cm^{-1}; ^1H NMR ($CDCl_3$) 5.33–6.71 (m, overlapping doublets at 6.29, J = 2.9 Hz, and 5.66, J = 2.5 Hz, 5 H), 3.58 (m, 1 H), 2.13–3.33 (m, 2 H); mass spectrum, m/e 136.0546 (M^+; 136.0524 calcd for $C_8H_8O_2$).

Anal. Calcd for $C_8H_8O_2$: C, 70.58; H, 5.92. Found: C, 69.64; H, 5.94.

24f: prepared from **23f** (0.476 g, 1.72 mmol); 94% yield (isolated); IR (neat) 3040, 1765, 1650 cm^{-1}; ^1H NMR ($CDCl_3$) 5.67–6.43 (m, overlapping doublets at 6.25, J = 2.6 Hz, 5.60 J = 2.2 Hz, 4 H), 4.87 (dd, J = 7.2, 2.2 Hz, 1 H), 2.93–3.83 (m, 1 H), 1.34–2.37 (m, 4 H).[33]

Anal. Calcd for $C_9H_{10}O_2$: C, 71.98; H, 6.71. Found: C, 71.80; H, 6.85.

28: prepared from **27** (0.407 g, 1.71 mmol); 26% yield (isolated by bulb-to-bulb distillation; oven temperature 25 °C, 0.005 torr); IR (neat) 1770, 1652, 1612 cm^{-1}; ^1H NMR ($CDCl_3$) 7.17 (m, 1 H), 5.15 (d, J = 2.5 Hz, 1 H), 4.82 (d, J = 2.5 Hz, 1 H), 2.07 (s, 3 H); mass spectrum, m/e 110.0379 (M^+; 110.0368 calcd for $C_6H_6O_2$).

8-Oxa-10-methylenebicyclo[5.3.0]decan-9-one (25g). To a solution of **23g** (0.894 g, 3.10 mmol) and benzene (15 mL) at 20 °C under nitrogen was added tri-n-butyltin hydride (0.83 mL, 3.14 mmol). After being stirred at 55 °C for 15 h, the solution was concentrated by rotary evaporation, and the residue was chromatographed on alumina (methylene chloride) to give 0.40 g (80%) of **25g** as a clear, colorless oil: IR (neat) 3100, 1760, 1660 cm^{-1}; ^1H NMR ($CDCl_3$) 6.28 (d, J = 3.5 Hz, 1 H), 5.53 (d, J = 3.5 Hz, 1 H), 4.67 (dt, J = 9, 2 Hz, 1 H), 2.9–3.5 (m, 1 H), 0.9–2.3 (m, 10 H); mass spectrum, m/e 166.0976 (M^+; 166.0994 calcd for $C_{10}H_{14}O_2$).[34]

The following compounds were similarly obtained.

25e: prepared from **23e** (0.498 g, 1.88 mmol); 68% yield (GLC with n-pentadecane as the internal standard); purified by chromatography on silica gel (35% ethyl acetate/hexane, R_f 0.35); IR (neat) 1760, 1658 cm^{-1}; ^1H NMR ($CDCl_3$) 6.24 (d, J = 2.5 Hz, 1 H), 5.64 (d, J = 2.2 Hz, 1 H), 4.99 (m, 1 H), 3.41 (m, 1 H), 1.00–2.25 (m, 6 H).

Anal. Calcd for $C_8H_{10}O_2$: C, 69.55; H, 7.29. Found: C, 69.49; H, 7.31.

25f: prepared from **23f** (0.347 g, 1.25 mmol); 60% yield (isolated by chromatography on silica gel, 1:1 hexane–ether); IR (neat) 1767, 1655 cm^{-1}; ^1H NMR ($CDCl_3$) 6.18 (d, J = 2.5 Hz, 1 H), 5.53 (d, J = 2.5 Hz, 1 H), 4.53 (q, J = 5.5 Hz, 1 H), 3.02 (m, 1 H), 0.7–2.3 (m, 8 H).[20d,35]

29: prepared from **27** (0.778 g, 3.27 mmol); 18% yield (GLC); purified by preparative GLC; IR (neat) 1770, 1670 cm^{-1}; ^1H NMR ($CDCl_3$) 6.30 (t, J = 2 Hz, 1 H), 5.73 (t, J = 2 Hz, 1 H), 4.73 (sextet, J = 7 Hz, 1 H), 2.17–3.40 (m, 2 H), 1.47 (d, J = 7 Hz, 3 H); mass spectrum, m/e 112.0524 (M^+; 112.0524 calcd for $C_6H_8O_2$).

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Registry No. 17, 3853-06-3; 18, 78804-62-3; **19a**, 10205-34-2; **19b**, 69637-59-8; **19c**, 69637-60-1; **19d**, 69637-61-2; **19e**, 78804-63-4; **19f**, 69637-62-3; **19g**, 78804-64-5; **20a**, 33016-24-9; **20c**, 69637-63-4; **20d**, 78804-65-6; **20e**, 78804-66-7; **20f**, 69637-65-6; **20g**, 78822-60-3; **21a**, 80-62-6; **21c**, 3070-68-6; **21d**, 51122-89-5; **21e**, 78804-67-8; **21f**, 69637-66-7; **21g**, 78804-68-9; **22e**, 78804-69-0; **22f**, 54109-55-6; **22g**, 78804-70-3; **23e**, 78804-71-4; **23f**, 54109-56-7; **23g**, 78804-72-5; **24e**, 78804-73-6; **24f**, 60916-75-8; **24g**, 78804-74-7; **25e**, 61747-55-5; **25f**, 16822-06-3; **25g**, 3725-04-0; **26**, 4743-96-8; **27**, 78804-75-8; **28**, 61892-54-4; **29**, 62873-16-9; 1-iodobutane, 542-69-8; 1-bromobutane, 109-65-9; iodomethane, 74-88-4; iodoethane, 75-03-6; allyl bromide, 106-95-6; 3-bromocyclopentene, 36291-48-2; 3-bromocyclohexene, 1521-51-3; 3-bromocycloheptene, 36291-49-3.

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Addition Compounds of Alkali-Metal Hydrides. 21. Rapid Reaction of Dialkyl- and Monoalkylboranes with Lithium Aluminum Hydride in the Presence of Triethylenediamine. A Facile and Quantitative Synthesis of Lithium Dialkyl- and Monoalkylborohydrides[1]

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Dialkylboranes react rapidly with lithium aluminum hydride in diethyl ether in the presence of triethylenediamine (TED) at 0 °C to form the corresponding lithium dialkylborohydrides and aluminum hydride: $R_2BH + LiAlH_4 \rightarrow LiR_2BH_2 + AlH_3$. The aluminum hydride precipitates as its triethylenediamine adduct. In a similar manner, monoalkylborane–triethylenediamine adducts ($TED{\cdot}BH_2R$) react with lithium aluminum hydride at 65 °C in tetrahydrofuran (THF) to give the corresponding lithium monoalkylborohydrides with concomitant precipitation of the triethylenediamine–aluminum hydride adduct ($TED{\cdot}AlH_3$). The reaction is quantitative and is applicable to a wide variety of di- and monoalkylboranes. Consequently, the present procedure provides a general, convenient synthesis of lithium di- and monoalkylborohydrides of greatly varying steric requirements.

It has been well established that the trialkylborohydrides are exceptionally powerful selective reducing agents[3] and very versatile synthetic intermediates.[4] From our preliminary exploration of different alkyl-substituted boro-

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