facility at Stanford University was made possible by NSF Grant CHE81-09064. We thank Prof. R. D. Simoni for the use of his liquid scintillation counter and Max Hoberg for electron microscopy. The University of Hawaii authors acknowledge financial support from the National Science Foundation and thank Dr. Rolf Herb for his assistance with the underwater experiments.

Registry No. **1D**, 119147-12-5; **2D**, 22643-62-5; **3D**, 57760-53-9; **4D**, 57-87-4; **5D**, 434-16-2; **6D**, 19432-13-4; **2N**, 34347-28-9; **4N**, 474-67-9; **5N**, 57-88-5; **7N**, 52936-69-3; **8N**, 71486-08-3; **9N**, 474-63-5; **10N**, 102607-76-1; **11N**, 313-04-2; **12N**, 26033-10-3; **13N**, 4651-51-8.

An Anionic 3 + 2 Cyclization–Elimination Route to Cyclopentenes

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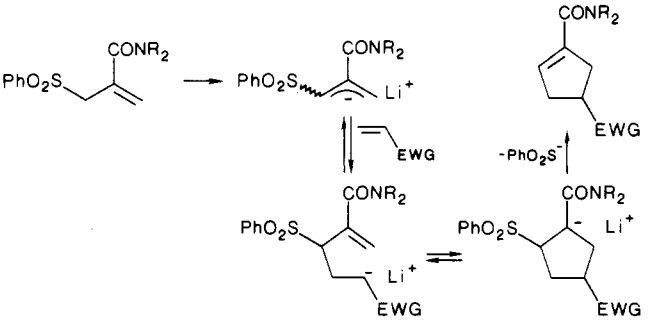
The formation and reactions of [1-(phenylsulfonyl)-2-(diisopropylcarbamoyl)allyl]lithium (**10**) are reported. When **10** is allowed to react with olefins bearing an electron-withdrawing group the 4-substituted cyclopent-1-enecarboxamides **11–19** are produced in 22–89% yields. Methyl-substituted analogues of **10**, the allyllithium reagents **23** and **25**, react in a similar manner to produce cyclopentenes that have methyl groups in the 2 or 5 positions. The corresponding [2-(dimethylcarbamoyl)allyl]lithium and [2-(phenylcarbamoyl)allyl]lithium reagents also react with electron-deficient olefins to produce the substituted cyclopentenes **28** and **30**, which can be hydrolyzed readily to the carboxylic acid **42**. The formation of the cyclopentenes occurs in a stepwise fashion by an initial highly regioselective addition to the electron-deficient olefin by the allyllithium reagent followed by a *5-Endo-Trig* cyclization and elimination of benzenesulfinate. The allyllithium **10** undergoes polydeuteration on reaction with methanol-*O*-*d* and acetone-d_6, alkylation with methyl iodide, and addition–dehydration on reaction with benzaldehyde.

Introduction

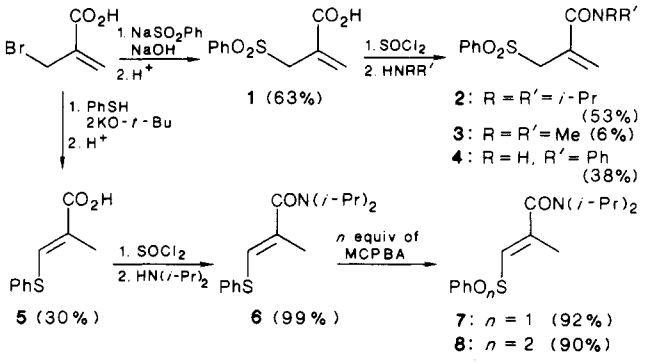
The development of methodology for the synthesis of five-membered carbocycles has been an active area of investigation in recent years and many ingenious approaches have emerged.[1] One of the most efficient methods of cyclopentane formation would be a regio- and stereospecific $4\pi s + 2\pi s$ cycloaddition between an allyl anion and an olefin. This reaction, termed the anionic 3 + 2 cycloaddition, was pioneered by Kauffman with early contributions from Böche and Ford.[2] We have reported cyclopentene ring formation by reaction between a [1-(phenylthio)-2-carbamoylallyl]lithium reagent and an acrylamide in a sequence that involves a formal anionic 3 + 2 cycloaddition as the key step.[3,4] We subsequently communicated the fact that the use of a phenylsulfonyl group at the β' position of the α,β-unsaturated amide overcomes the drawbacks of the phenylthio system in this synthetic

Scheme I[a]



[a] EWG = electron-withdrawing group.

Scheme II



(1) For summaries and examples of a variety of approaches, see: Paquette, L. A. *Top. Curr. Chem.* **1984**, *119*, 1. Ramaiah, M. *Synthesis* **1984**, 529. Trost, B. M. *Chem. Soc. Rev.* **1982**, *11*, 141. Paquette, L. A. *Top Curr. Chem.* **1979**, *79*, 41. Schmidt, R. R.; Talbiersky, J. *Angew. Chem., Int. Ed. Engl.* **1978**, *17*, 204. Iosbe, K.; Fuse, M.; Kosugi, H.; Hagiwara, H.; Uda, H. *Chem. Lett.* **1979**, 785. Marino, J. P.; Katterman, L. C. *J. Chem. Soc., Chem. Commun.* **1979**, 946. Miyata, O.; Schmidt, R. R. *Tetrahedron Lett.* **1982**, *23*, 1793. Boger, D. L.; Brotherton, C. E. *J. Am. Chem. Soc.* **1986**, *108*, 6695. Little, R. D.; Muller, G. W.; Venegas, M. G.; Carroll, G. L.; Bukhari, A.; Patton, L.; Stone, K. *Tetrahedron* **1981**, *37*, 4371. Trost, B. M. *Angew. Chem., Int. Ed. Engl.* **1986**, *25*, 1. Trost, B. M.; Mignani, S. M. *Tetrahedron Lett.* **1986**, *27*, 4137. Trost, B. M.; Chan, D. M. T. *J. Am. Chem. Soc.* **1983**, *105*, 2315. Bucheisster, A.; Klemarczyk, P.; Rosenblum, M. *Organometallics* **1982**, *1*, 1679. Noyori, R. *Acc. Chem. Res.* **1979**, *12*, 61. Noyori, R.; Yokoyama, K.; Makino, S.; Hayakawa, Y. *J. Am. Chem. Soc.* **1978**, *100*, 1799. Danheiser, R. L.; Carini, D. J.; Fink, D. M.; Basak, A. *Tetrahedron* **1983**, *39*, 935. Molander, G. A.; Shubert, D. C. *J. Am. Chem. Soc.* **1986**, *108*, 4683. Denmark, S. E.; Jones, T. K. *J. Am. Chem. Soc.* **1982**, *104*, 2542. Santelli-Rouvier, C.; Santelli, M. *Synthesis* **1983**, 429. Hudlicky, T.; Koszyk, F. J.; Kutchan, T. M.; Sheth, J. P. *J. Org. Chem.* **1980**, *45*, 5020. Hudlicky, R.; Kutchan, T. M.; Naqvi, S. M. *Org. React.* **1983**, *33*, 247. Hudlicky, T.; Radesca, L.; Luna, H.; Anderson, F. E., III *J. Org. Chem.* **1986**, *51*, 4746. Oppolzer, W.; Snieckus, V. *Angew. Chem., Int. Ed. Eng.* **1978**, *17*, 476. Oppolzer, W.; Cunningham, A. F. *Tetrahedron Lett.* **1986**, *27*, 5467. Danishefsky, S. *Acc. Chem. Res.* **1979**, *12*, 66. Bal, S. A.; Marfat, A.; Helquist, P. *J. Org. Chem.* **1982**, *47*, 5045. Brunce, R. A.; Wamsley, E. J.; Pierce, J. D.; Shellhammer, A. J., Jr.; Drumright, R. E. *J. Org. Chem.* **1987**, *52*, 464. Curran, D. P.; Chen, M. H. *J. Am. Chem. Soc.* **1987**, *109*, 6558.

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sequence.[5] In effect, the β′-(phenylsulfonyl) group activates the β′-hydrogen for metalation, provides a stable (2-carbamoylallyl)lithium reagent, directs a highly regioselective addition to the electron-deficient olefin and, following the cyclization step, acts as a leaving group to drive the reaction thermodynamically to the cyclopentene product. The sequence is shown in Scheme I.

The phenylsulfonyl group has displayed similar chemistry in related systems. Tanaka and co-workers have reported the formation and electrophilic substitution of the formal dianion [1-(phenylsulfonyl)-2-(lithiophenylcarbamoyl)allyl]lithium.[6] They found that this reagent reacted with electrophiles to give β′-substituted products, whereas the corresponding sulfide gave a mixture of β- and β′-substituted products. This result is consistent with other observations that allyl anions containing a 1-(phenylsulfonyl) substituent undergo highly regioselective electrophilic additions at the carbon bearing the phenylsulfonyl group.[7] More recently, Padwa and Yeske have reported that (phenylsulfonyl)allene reacts with electron-deficient olefins to give cyclopentenes in a sequence that has steps similar to that of Scheme I.[8]

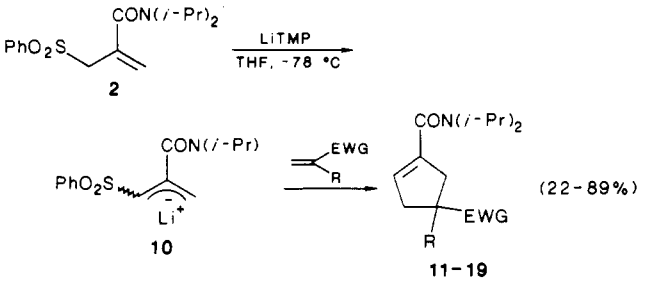
In this work we report the results of our study on the use of [(1-phenylsulfonyl)-2-carbomoylallyl]lithium reagents in a synthetically useful anionic 3 + 2 cyclization–elimination sequence to give cyclopentenes. Evidence that the reaction proceeds in a stepwise manner is provided.

Results and Discussion

Synthesis of 3-(Phenylsulfonyl)-2-methylenepropanamides 2, 3, and 4 and (*E*)-3-(Phenylsulfonyl)-*N*,*N*-diisopropyl-2-methylpropenamide (8). The readily available 2-(bromomethyl)acrylic acid was converted to 3-(phenylsulfonyl)-2-methylenepropanoic acid (1) and then to the 3-(phenylsulfonyl)-2-methylenepropanamides **2**, **3**, and **4** by standard procedures as shown in Scheme II. The (*E*)-3-(phenylsulfonyl)-*N*,*N*-diisopropyl-2-methylpropenamide (8) was prepared via the sulfides **5** and **6** also as shown in the scheme. The sulfone–amides were characterized by proton nuclear magnetic resonance (^{1}H NMR), infrared (IR), and mass spectral (MS) data and by elemental analysis.

The stereochemistry of the double bond of **8** was determined by the method described by Uda and co-workers in which the ^{1}H NMR chemical shift of a methyl group cis to a sulfoxide is observed to exhibit a downfield shift of 0.2 ppm compared to the corresponding sulfide while the chemical shift of a methyl group trans to the sulfoxide exhibits very little change when compared to the corresponding sulfide.[9] The chemical shift of the methyl substituent is, in the sulfide **6**, 1.96 ppm, and, in the sulfoxide **7**, 2.33 ppm, thus showing a 0.37 ppm shift downfield consistent with the *E* configuration. We have also compared the chemical shift of the methyl group in the *E* sulfone–amide **8** of 2.33 ppm with that of the methyl group in the *Z* sulfone–amide **9** of 2.03 ppm, which is consistent with these assignments. The *Z* isomer **9** is obtained as a minor product in protic quenches of **10** (vide infra).

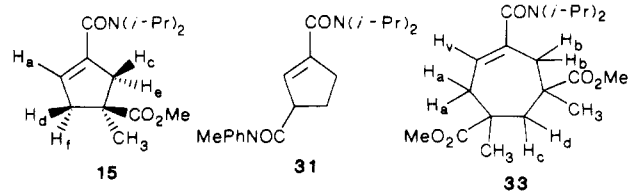
Scheme III[a]



[a] EWG = CO_2-c-C_6H_{11}, COPh, CONPhMe, CO_2-*n*-Bu, CO_2Me, SO_2Ph, CN. R = CH_3, H, $SiMe_3$.

Reaction of [1-(Phenylsulfonyl)-2-(diisopropylcarbamoyl)allyl]lithium (10) with Electron-Deficient Olefins. Cyclopentene Formation. When the sulfone–amide **2** was treated with lithium tetramethylpiperidide (LiTMP) in tetrahydrofuran (THF) at −78 °C to give **10**, and then 1.1 equiv of an electron-deficient olefin was added, followed by warming to 25 °C and protic quench, the cyclopentenes **11–19** were isolated in 89 to 22% yield as shown in Scheme III and detailed in Table I, entries 1–9.

All cyclopentene products were fully characterized by ^{1}H NMR, IR, MS, and elemental analysis. The 360-MHz ^{1}H NMR spectrum for **15** exhibits a singlet at 1.37 ppm that is assigned to the methyl group substituted on the ring. The vinyl ring proton appears as a multiplet at 5.59 ppm with fine coupling to the four other ring protons. The four resonances for the ring protons appear as doublets of multiplets at 3.14 ppm, J = 16 Hz, 3.01 ppm, J = 17 Hz, 2.50 ppm, J = 16 Hz, and 2.36 ppm, J = 17 Hz. The large and equal coupling constants of 16 Hz for the proton resonances at 3.14 and 2.50 ppm suggest that these are geminal methylene hydrogens and they are assigned as H_c and H_e, respectively. Similarly the protons at 3.01 and 2.36 ppm with J = 17 Hz are assigned to H_d and H_f. Irradiation of either resonance at 3.14 or 2.50 ppm causes the other resonance to become a singlet with additional fine coupling. Likewise, irradiation of either resonance at 3.01 or 2.36 ppm causes the other resonance to become a singlet with fine coupling. Irradiation of any of the ring proton resonances appears to somewhat simplify all the multiplets in the spectrum, suggesting that all of the ring protons are coupled. The structure of cyclopentene **18** was confirmed by comparison with an authentic sample.[4] Comparison by gas chromatography (GC) of a 3:1 mixture of **18**:**31** previously obtained[4] showed the reaction product to be the two isomeric cyclopentenes, **18** and **31**, in a ratio of 99.7:0.3. In no other case did we isolate or observe the isomeric cyclopentene corresponding to the alternative possible cyclization product. The structures of the remaining cyclopentenes were assigned by their MS, IR, and elemental analysis and by comparison of their ^{1}H NMR spectrum with that of **15**. The formation of these cyclopentenes demonstrates that **10** can react with electron-deficient olefins to form cyclopentenes via the formal 3 + 2 anionic cyclization–elimination sequence of Scheme I.



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(6) Tanaka, K.; Yoda, H.; Kaji, A. *Tetrahedron Lett.* **1985**, *26*, 4747, 4751. **Note Added in Proof.** See also: Tanaka, K.; Horiuchi, H.; Yoda, H. *J. Org. Chem.* **1989**, *54*, 63.
(7) Seebach, D.; Giess, K. H. In *New Applications of Organometallic Reagents in Organic Synthesis*; Seyferth, D., Ed.; Elsevier: Amsterdam, 1976; p 1. Bielmann, J. F.; Ducep, J. B. *Org. React.* **1982**, *27*, 1. Magnus, P. D. *Tetrahedron* **1977**, *33*, 2019. Trost, B. M.; Schmuff, N. R. *J. Am. Chem. Soc.* **1985**, *107*, 396. Trost, B. M.; Schmuff, N. R.; Miller, M. J. *J. Am. Chem. Soc.* **1980**, *102*, 5979. Schlosser, M. *Angew. Chem., Int. Ed. Engl.* **1974**, *13*, 701.
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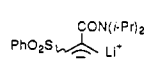
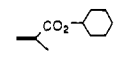
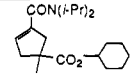
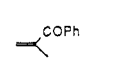
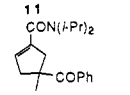
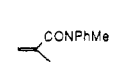
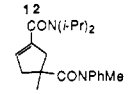
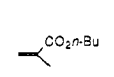
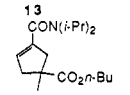
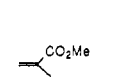
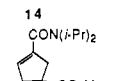
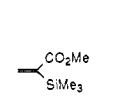
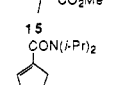
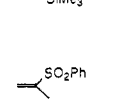
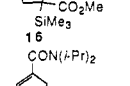
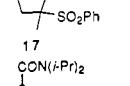
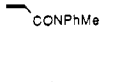
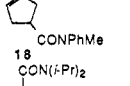
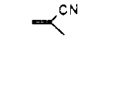
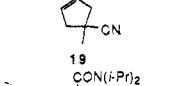
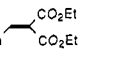
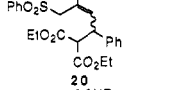
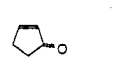
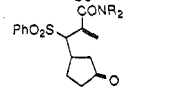
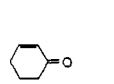
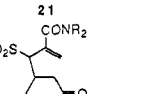
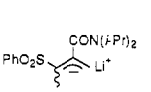
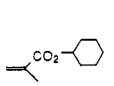
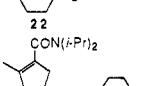
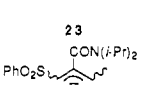
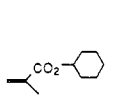
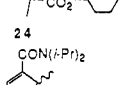
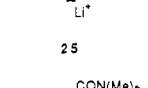
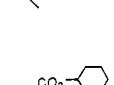
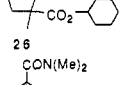
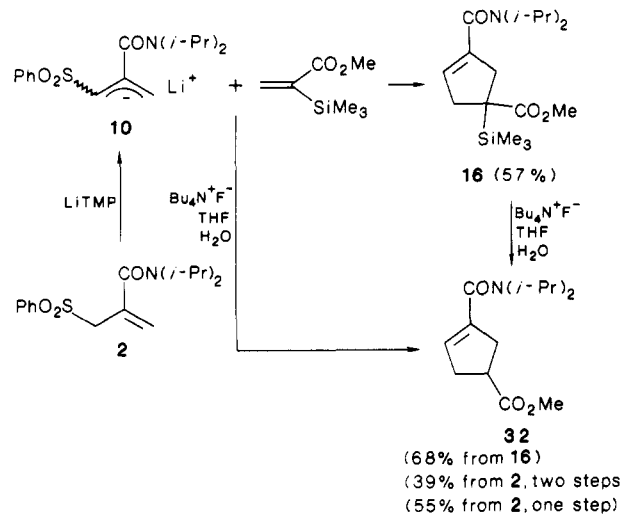
Table I. Reaction of [1-(Phenylsulfonyl)-2-carbamoylallyl]lithium Reagents with Electron-Deficient Olefins[a]

entry	allyllithium reagent	olefin	product	yield[b]
1	 10		 11	89% 89%[c] 75%[d]
2	10		 12	74%
3	10		 13	65%
4	10		 14	61%[d,e]
5	10		 15	59%[f]
6	10		 16	57%
7	10		 17	49%
8	10		 18	33%[g] 36%[g,h]
9	10		 19	22%
10	10		 20	95%
11	10		 21	76%[i]
12	10		 22	43%[i]
13	23		 24	56%
14	 25		 26	29%
15	 27		 28	49%
16	 29		 30	19%[j]

[a] Conditions: (1) **2**, LiTMP, THF, −78 °C; (2) 1.1 equiv olefin, THF, −78 °C; (3) 1 h, −78 °C; (4) 24 h, 25 °C; (5) 10% HCl/saturated NH_4Cl. [b] Yields are for analytically pure material. [c] Conditions: (1) **8**, LiTMP, THF, −78 °C; (2) 1.1 equiv of olefin, THF, 78 °C; (3) $CuBr{\cdot}Me_2S$; (4) 1 h, −78 °C; (5) 95 h, 25 °C; (6) 10% HCl/saturated NH_4Cl. [d] From **8**, using LDA as base. [e] Using *n*-BuLi/TMEDA as base. [f] Accompanied by 4% of cycloheptene **33**. [g] Trace of isomer **31** also present. [h] From **8**. [i] Using *n*-BuLi/DMPU as base. [j] Using 2 equiv of LiTMP to form **29**.

Scheme IV



As Table I shows, we have used a variety of functional groups as the electron-withdrawing substituent on the electron-deficient olefins for reactions with **10**. Cyclohexyl methacrylate gave the highest yield, 89%, and methacrylonitrile provided the lowest yield, 22%, of cyclopentene products, as shown in entries 1 and 9. Methyl methacrylate gave a somewhat lower yield, 59%, than cyclohexyl methacrylate possibly due to the ester being less hindered and more susceptible to unwanted nucleophilic attack on the carbonyl carbon. Use of the phenyl ketone, *N*-phenyl-*N*-methylamide, *n*-butyl ester, and phenylsulfonyl groups as the electron-withdrawing substituent also provide acceptable yields of cyclopentene products.

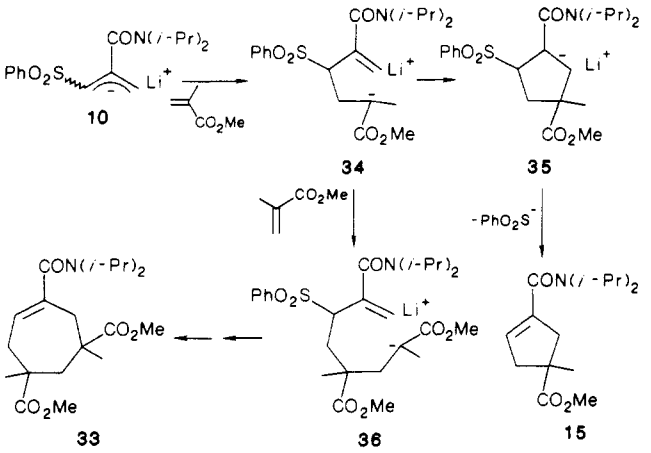
The absence of a substituent on the α position of the Michael acceptor appears to decrease the yield of cyclopentene product. This is most evident in the comparison of *N*-phenyl-*N*-methylacrylamide and *N*-phenyl-*N*-methylmethacrylamide as the electron-deficient olefins. The methacrylamide provided the cyclopentene **13** in 65% yield while the acrylamide provided the cyclopentene **18** in 33% yield. The α substituent may also protect the carbonyl carbon from unwanted 1,2-addition and/or inhibit polymerization of the 2π component.

Since α-unsubstituted Michael acceptors did not give good yields of cyclopentene products, we developed a two-step sequence to provide this product. When methyl α-(trimethylsilyl)acrylate was allowed to react with the allyllithium reagent **10**, the (trimethylsilyl)-substituted cyclopentene **16** was isolated in 57% yield. Treatment of **16** with tetrabutylammonium fluoride in wet THF produced the desired cyclopentene **32** in 68% yield as shown in Scheme IV. The cyclopentene **32** was characterized by IR, MS, and elemental analysis and also by comparison of its ^1H NMR spectrum to that of **15**. The yield for **32** from the starting sulfone–amide **2** in this two-step procedure was 39%. Since we had observed some desilylation of product **16** under the cyclization–elimination reaction conditions, we carried out the reaction in a one-flask procedure without isolation of **16**. The yield of **32** increased to 55%, as shown in Scheme IV, with this approach.

When methyl methacrylate was used as the Michael acceptor, we obtained the cyclopentene **15** along with 4% of a product whose structure is assigned as the cycloheptene **33** on the basis of ^{13}C NMR, ^1H NMR, MS, and elemental analysis.

The 360-MHz ^1H NMR spectrum for **33** exhibits two resonances at 3.624 and 3.618 ppm, which are assigned to

Scheme V

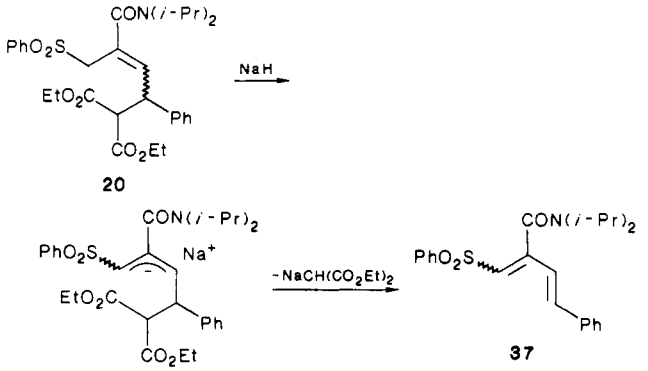


the methyl ester protons, and the two methyl groups substituted on the ring appear at 1.22 and 1.26 ppm. The vinyl ring proton (H_v) appears as a triplet at 5.84 ppm, J = 6 Hz, with additional fine coupling. The resonances assigned to the two H_a allyl ring protons appear as doublets of doublets at 2.61 ppm, J = 15 and 8 Hz, and 2.13 ppm, J = 15 and 6 Hz. When the signal at 5.84 ppm is irradiated, the resonances at 2.61 and 2.13 ppm become doublets with J = 15 Hz. Irradiation of either resonance at 2.61 or 2.13 ppm causes the other resonance to become a doublet with J = 7 Hz and causes the triplet at 5.84 ppm to become a doublet with J = 7 Hz. The two other allyl ring protons, H_b, appear as doublets at 2.90 ppm, J = 15 Hz, and 2.25 ppm, J = 15 Hz. When either of these two resonances are irradiated the other becomes a singlet. The final two ring protons, H_c and H_d, appear as doublets at 2.68 and 1.53 ppm with J = 15 Hz. When either of these resonances are irradiated the other becomes a singlet.

Pathways for the formation of the cycloheptene **33** and cyclopentene **15** are shown in Scheme V. The allyllithium reagent **10** can undergo a highly regioselective electrophilic addition to the methyl methacrylate to produce the proposed intermediate **34**. This acyclic intermediate can then undergo intramolecular cyclization to give **35** and then eliminate benzenesulfinate to produce the cyclopentene. Alternatively **34** could undergo Michael addition to another equivalent of methyl methacrylate to produce **36**. The seven-carbon acyclic chain can then undergo intramolecular cyclization followed by elimination to produce the observed cycloheptene **33**.

Reaction of [1-(Phenylsulfonyl)-2-(diisopropylcarbamoyl)allyl]lithium (10) with β-Substituted Electron-Deficient Olefins. Addition of the allyllithium reagent **10** to β-substituted electron-deficient olefins would allow the synthesis of 3-substituted cyclopentenes and, with cyclic enones, provide an annulation sequence. However, under the typical reaction conditions, lithiation of **2** by LiTMP in THF at −78 °C followed by the addition of the electrophile and warming to 25 °C for 24 h, the allyllithium reagent **10** did not undergo addition to β-substituted electron-deficient olefins. Reactants were recovered or if the reaction was heated to reflux decomposition occurred.

In order to force the allyllithium reagent to add to β-substituted electron-deficient olefins, we employed an olefin bearing two geminal electron-withdrawing substituents. When diethyl benzylidenemalonate was allowed to react with the allyllithium reagent **10**, we isolated the acyclic product **20** in 95% yield as shown in Table I, entry 10. The product **20** was characterized by MS, IR, and elemental analysis and the structure was assigned by its ^{13}C and ^1H NMR spectra along with ^1H NMR decoupling experiments. When **20** was treated with NaH in THF and heated to reflux for 19 h a diene, **37**, was produced in 17% yield. The product is the same as that derived from the benzaldehyde trap of the allyllithium reagent **10** (vide infra). The diene could arise from formation of an allyl anion, which can eliminate the sodium salt of diethyl malonate.



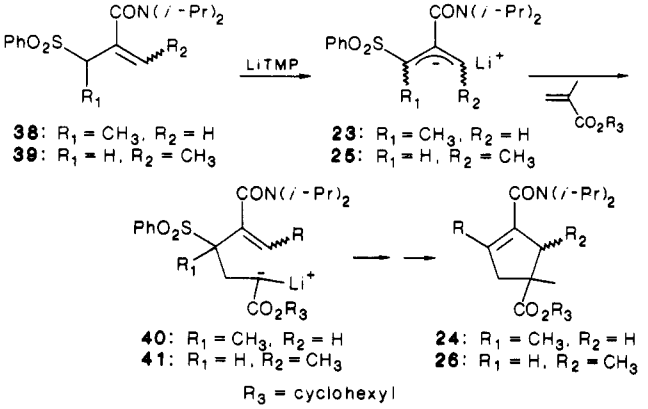
This reaction provides one of the few examples where electrophilic addition to the allyllithium reagent **10** occurs at the unsubstituted terminus. Consistency with prior regiochemistry could be rationalized if the olefin adds to the carbon bearing the phenylsulfonyl substituent, but this is reversible and eventually leads to addition at the less substituted carbon which then leads to **20**.

Hirama has reported conditions, lithiation by *n*-BuLi/hexamethylphosphoramide (HMPA), under which 1-(phenylsulfonyl)allyl carbanions will undergo 1,4-addition to various β-substituted enones.[10] We have employed these conditions, but used *N,N'*-dimethylpropyleneurea (DMPU) in place of HMPA, in order to achieve addition of the allyllithium reagent **10** to cyclic enones. When a mixture of sulfone–amide **2** and DMPU was treated with *n*-BuLi followed by either cyclopentenone or cyclohexenone, the two addition products **21** and **22** were obtained in 76% and 43% yield, respectively, as shown in Table I, entries 11 and 12. Attempts to induce cyclization by treating **21** with potassium *tert*-butoxide resulted in isolation of some starting material along with 14% of **2**, suggesting that the addition is reversible under these conditions. Cyclohexyl methacrylate was used as the trap for **10** using *n*-BuLi/DMPU and **11** was isolated in 50% yield along with 24% of the sulfone–amide **2** to show that the cyclization–elimination steps can occur under these different metalation conditions.

Alkyl-Substituted Allyllithium Reagents. The effects of alkyl substitution on these reactions were investigated by studies with **38** and **39**. When the methyl-substituted sulfone–amide **38** was treated with LiTMP and then allowed to react with cyclohexyl methacrylate, the cyclopentene **24** was isolated in 56% yield as shown in Table I, entry 13. When the methyl-substituted sulfone–amide **39** was treated with LiTMP and then allowed to react with cyclohexyl methacrylate, the cyclopentene **26** was isolated in 29% yield as shown in Table I, entry 14. These results are consistent with the formation of a stable allylithium reagent, **23** and **25** respectively, and a regioselective electrophilic addition of the methacrylate to the carbon bearing the phenylsulfonyl substituent. The acyclic intermediates **40** and **41** thus formed could undergo cyclization and elimination to produce the observed products. Even with the added steric hindrance of the methyl sub-

(10) Hirama, M. *Tetrahedron Lett.* **1981**, *22*, 1905.

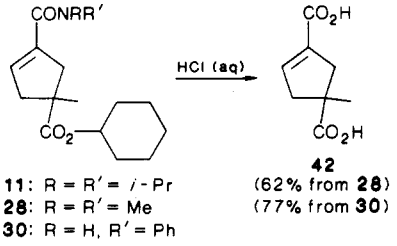
stituents the reactions still proceed as in the unsubstituted cases, albeit in lower yield. No products arising from addition of the methacrylate at the unsubstituted end of allyllithium reagent **23** were obtained.



Allyllithium Reagents from Less Sterically Hindered and Secondary Amides. Since the diisopropyl amide can be difficult to functionalize, it would be advantageous to use other groups in the 2 position of the allyllithium reagent. Padwa and co-workers have used a similar allyl anion where the phenylsulfonyl group is in the 1 and 2 positions of the allyl anion reagent.[8]

When the sulfone–amides **3** and **4** were treated with LiTMP and allowed to react with cyclohexyl methacrylate, the cyclopentenes **28** and **30** were obtained in 49% and 19% yields, respectively, as shown in Table I entries 15 and 16. These products are consistent with the formation of stable allyllithium reagents, which undergo regioselective additions to cyclohexyl methacrylate followed by cyclizations and eliminations to produce the observed products. The low yield for cyclopentene **30** is consistent with a dianion intermediate, which would have low activation for cyclization.

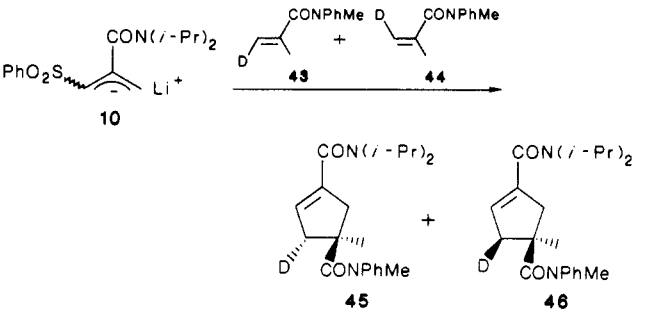
The cyclopentenes **28** and **30** were hydrolyzed to the diacid-substituted cyclopentene **42** in 62% and 77% yield, respectively. Under the same hydrolysis conditions, the diisopropylamide-substituted cyclopentene **11** was not converted to the diacid.



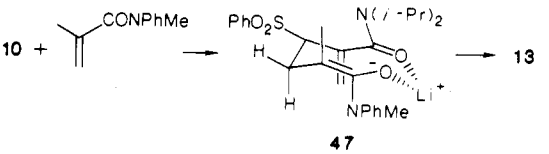
Pathway of the Cyclization–Elimination Sequence. Although Scheme I is written in terms of a stepwise reaction, the mechanism for formation of the five-membered ring could be either concerted or stepwise. The presence of noncyclized addition products can be used to suggest stepwise mechanisms for similar anionic 3 + 2 cyclization reactions, albeit, the cyclization is a *5-Endo-Trig* process.[2-4,11] We have not isolated or observed the formation of products from possible acyclic intermediates in reactions that produce cyclopentene products. Even by carrying out the reaction at −100 °C and quenching within 5 min after the addition of cyclohexyl methacrylate only the cyclic product **11** and the starting sulfone–amide **2** were obtained in 37% and 42% yields, respectively. The same products, **11** and **2**, were isolated in 74% and 15% if the reaction temperature was raised to −78 °C. When the reaction was quenched after 1 h at −78 °C the cyclopentene **11** was obtained in 88% yield.

Three results can be taken to suggest that the cyclization is stepwise in the present cases. The formation of the cycloheptene **33** can be rationalized by the stepwise mechanism as shown in Scheme V. Formation of the addition products **21** and **22** also can be taken to suggest that the mechanism is stepwise, even though in these cases no cyclized products were observed.

We have also employed (*E*)- and (*Z*)-β-deuteriomethacrylamides as the electron-deficient olefins to determine the stereochemistry of the reaction with respect to the double bond. A concerted mechanism would be predicted to give retention while a stepwise mechanism would be expected to give loss of configuration. When the allyllithium reagent **10** was allowed to react with a (3.2 ± 0.6):1 mixture of (*E*)- and (*Z*)-β-deuteriomethacrylamides **43** and **44**, a (1.7 ± 0.3):1 mixture of trans to cis deuterio-substituted cyclopentenes **45** and **46** was produced. Similarly when a 1:(3.8 ± 0.8) mixture of **43** and **44** was allowed to react with the allyllithium reagent **10**, a 1:(2.3 ± 0.5) mixture of **45** and **46** was isolated. The errors for the



ratios of products and starting materials were determined by assuming a maximum error of 10% in the integration of the ^1H NMR spectra. While these results show some loss of olefin configuration in the cyclopentene products, there is some net retention. These results can be explained by a stepwise mechanism where bond rotation is competitive with the cyclization of the unobserved acyclic intermediate. It is possible that the acyclic intermediate is chelated in such a way that bond rotation would be somewhat hindered, as shown for **47**.



Reaction of 10 with Other Electrophiles. The reaction of **10** with a few other electrophiles was investigated. The results are shown in Scheme VI and summarized in the supplementary section.

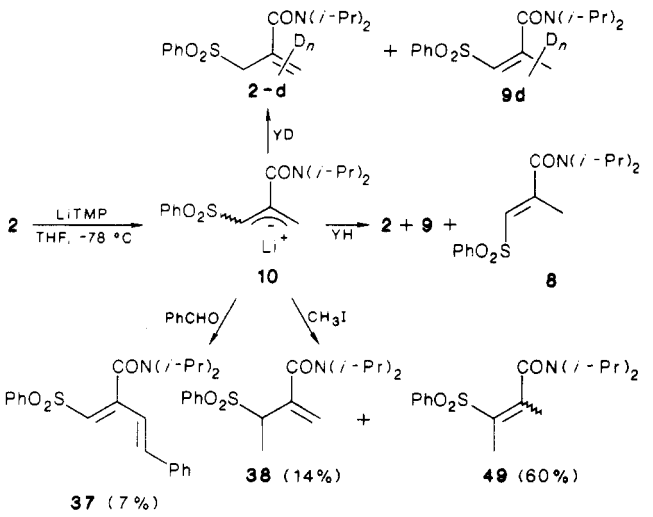
Summary. In this report we have demonstrated that a number of [1-(phenylsulfonyl)-2-carbamoylallyl]lithium reagents react with electron-deficient olefins to produce substituted cyclopentenes in an anionic 3 + 2 cyclization–elimination sequence. This appears to be a versatile anionic 3 + 2 route to five-membered rings.

Experimental Section

General. Proton nuclear magnetic resonance (NMR) spectra were obtained on Nicolet NT-360 (360 MHz), GE QE-300 (300 MHz), Varian XL-200 (200 MHz), or Varian EM-390 (90 MHz) spectrometers. Carbon-13 NMR spectra were obtained on Nicolet NT-360 (90.546 MHz) or Varian XL-200 (50.31 MHz) spectrom-

(11) Baldwin, J. E., Lusch, M. J. *Tetrahedron* **1982**, *38*, 2939 and references cited therein.

Scheme VI



eters. Chemical shifts are reported in parts per million (ppm) downfield from an internal tetramethylsilane standard for ^1H NMR spectra and are referenced from the $CDCl_3$ solvent peak (77.0 ppm) for ^{13}C NMR spectra. When peak multiplicites are given, the following abbreviations are used: s, singlet; d, doublet; t, triplet; q, quartet; m, multiplet; b, broadened. All NMR spectra were obtained on solutions in deuteriochloroform, unless otherwise noted. All decoupling experiments were performed on Nicolet NT-360 or Varian XL-200 spectrometers. Infrared (IR) spectra were obtained on Perkin-Elmer 137, Perkin-Elmer 1320, or IBM IR/32 spectrometers. Peaks are reported in units of cm^{-1}. Mass spectra (MS) were obtained on a Varian MAT CH-5 mass spectrometer with an ionization voltage of 70 eV. Data are reported in the form *m/e* (intensity relative to base = 100). Flame ionization (FI) MS were obtained on a Finnigan MAT 731 spectrometer. Elemental analyses were performed at the University of Illinois Microanalytical Service Laboratory by J. Nemeth and associates. Medium pressure liquid chromatography (MPLC) separations were performed on columns packed with Ventron 43–64-mesh or Silica Wielm 32–63-mesh silica gel. High pressure liquid chromatography (HPLC) separations were performed on a RAININ Rabbit HPX HPLC on a DYNAMAX 21.4 mm × 25 cm silica column. Chromatotron chromatographic separations were performed on a Harrison Research 7924 chromatotron using chromatotron plates poured with 60 PF254 silica gel. Analytical gas chromatography (GC) was performed on a Hewlett-Packard 5790A gas chromatograph equipped with a programmable temperature control and a flame ionization detector. The column used was a 25-m SC-52 capillary column; injector temperature was 270 °C, detector temperature was 300 °C, and programs were as indicated. Retention times and peak integrals were obtained from a Hewlett-Packard 3390A recorder. Melting points were obtained on a Thomas-Hoover capillary melting point apparatus and are uncorrected. Bulb-to-bulb distillations were performed on an Aldrich Kugelrohr apparatus; approximate boiling points refer to air-bath temperatures and are uncorrected.

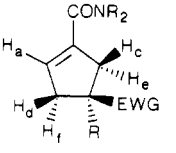
Materials. All compounds obtained from commercial sources were used without further purification, unless otherwise noted. Tetrahydrofuran (THF) was freshly distilled from sodium/benzophenone under an atmosphere of dry nitrogen. Tetramethylenediamine (TMEDA) and 2,2,6,6-tetramethylpiperidine (HTMP) were distilled from CaH_2 under dry nitrogen. Commercial solutions of *n*-butyllithium (*n*-BuLi) in hexanes and *sec*-butyllithium (*sec*-BuLi) in cyclohexane were titrated by using a modification of Tischler and Tischler's procedure.[12] All glassware was oven or flame dried prior to use, and all reactions were performed under a dry nitrogen atmosphere. Brine refers to a saturated solution of sodium chloride.

3-(Phenylsulfonyl)-2-methylenepropanoic Acid (1). A solution of 2-(bromomethyl)acrylic acid (16 g, 97 mmol) and NaOH (3.9 g, 97 mmol) in 500 mL of methanol was heated until the solids dissolved. The sodium salt of benzenesulfinic acid (16 g, 97 mmol) was added and the solution was heated to reflux for 2 h. The mixture was then cooled and the solvent removed in vacuo. To the concentrate was added 200 mL of 2.5% NaOH, and the aqueous layer was washed with Et_2O. The aqueous layer was then acidified and cooled. The crystals were collected and dried in a drying pistol at 0.1 Torr and 117 °C for 5 h to give 13.2 g (62%) of crude acid product **1**, which was used without further purification: ^1H NMR (200 MHz, DMSO-d_6) δ 7.85–7.6 (m, 5 H, Ph), 6.31 (s, 1 H, =CH), 5.71 (s, 1 H, =CH), 4.31 (s, 2 H, CH_2SO_2Ph).

***N,N*-Diisopropyl-3-(phenylsulfonyl)-2-methylenepropanamide (2).** A solution of **1** (1.0 g, 4.4 mmol) in excess thionyl chloride (10 mL, 140 mmol) was heated to reflux for 4 h. The excess thionyl chloride was removed in vacuo and the acid chloride was dissolved in 100 mL of methylene chloride. The solution was cooled in an ice bath and diisopropylamine (4.0 mL, 28 mmol) was added. The solution was warmed to room temperature and stirred for 16 h. The solvent was removed in vacuo and the organic products were taken up in Et_2O. The organic layer was washed with 5% HCl, saturated $NaHCO_3$, and then brine, dried over $MgSO_4$, filtered, and concentrated in vacuo to give a yellow oil. Recrystallization from EtOAc/hexanes gave 0.73 g (53%) of **2**, mp 98–100 °C: ^1H NMR (360 MHz, $CDCl_3$) δ 7.98–7.52 (m, 5 H, SO_2Ph), 5.49 (s, 2 H, $=CH_2$), 4.5 (b, 1 H, CONCH), 4.15 (s, 2 H, CH_2SO_2Ph), 3.45 (b, 1 H, CONCH), 1.33 (bd, 12 H, CON(*i*-Pr)$_2$); IR (neat) 300, 1650, 1505, 1480, 1400, 1370, 1340, 1275, 1235, 1175, 1130, 1105, 1060, 765, 737, 717, 695 cm^{-1}; MS *m/e* (rel int) 309 (M^+, 0.4), 294 (12), 209 (100), 168 (83), 125 (74), 105 (20), 86 (11), 77 (38), 43 (33), 41 (21), 40 (13). Anal. Calcd for $C_{16}H_{23}NO_3S$: C, 62.11; H, 7.49; N, 4.53; S, 10.36. Found: C, 62.07; H, 7.65; N, 4.48; S, 10.15.

General Procedure for Cyclization–Elimination Reactions. The alkyllithium was added dropwise to a solution of 35 mL of dry THF containing 1–2 mg of *N*-benzylbenzamide at −78 °C until a pale blue color formed and persisted. A measured amount of the alkyllithium was then added. This was then followed by the addition of HTMP to form lithium 2,2,6,6-tetramethylpiperidide (LiMP) or by the addition of diisopropylamine in order to form lithium diisopropylamide (LDA), depending on the base desired for lithiation. The solution was stirred for 10 min and then the sulfone–amide to be lithiated, usually *N,N*-diisopropyl-3-(phenylsulfonyl)-2-methylenepropanamide (**2**), was added in 15 mL of THF. The solution was allowed to stir for 10 min followed by the dropwise addition of the olefin in 10 mL of THF via a syringe and syringe pump or via an addition funnel over 10 min. After the addition was complete the solution was stirred for 1 h, warmed to room temperature, and allowed to stir at that temperature for 24 h. The reaction was quenched by the addition of 6 mL of a 10% HCl solution saturated with NH_4Cl, and the solvent was removed in vacuo. The organic products were extracted with Et_2O, and the ether layer was washed with 5% HCl, saturated $NaHCO_3$, and then brine, dried over $MgSO_4$, filtered, and concentrated in vacuo to give the crude product.

The ring protons for the cyclopentene products are assigned in the ^1H NMR spectra as shown below.



***N,N*-Diisopropyl-4-[(cyclohexyloxy)carbonyl]-4-methylcyclopent-1-enecarboxamide (11). Procedure A.** According to the general procedure for the cyclization–elimination reaction, **2** (0.20 g, 0.65 mmol) was added to a solution of LiTMP (0.65 mmol) followed by cyclohexyl methacrylate (0.12 mL, 0.71 mmol). Purification by MPLC on a 9 $^1/_2$ in. × $^3/_4$ in. column of silica gel using 15% EtOAc/hexanes as eluent followed by Kugelrohr distillation at 150–170 °C and 1.0 Torr gave 193 mg (89%) of **11**: ^1H NMR (200 MHz, $CDCl_3$) δ 5.60 (m, J = 2 Hz, 1 H, H_a), 4.79 (m, 1 H, CO_2CH), 4.1 (b, 1 H, CONCH), 3.6 (b, 1 H, CONCH), 3.14 (dm, J = 16 Hz, 1 H, H_c), 3.02 (dm, J = 18 Hz, 1 H, H_d), 2.50 (dm, J = 18 Hz, 1 H, H_e), 2.34 (dm, J = 18 Hz, 1 H, H_f), 1.9–1.6 (m, 4 H, cyclohexyl), 1.6–1.1 (bm, 18 H, CON(*i*-Pr)$_2$ +

(12) Tischler, A. N.; Tischler, M. H. *Aldrichemica Acta* **1978**, *11*, 20.

cyclohexyl); decoupling, irradiation at 3.14 ppm decoupled the resonance at 2.50 ppm, leaving a singlet; irradiation at 3.02 ppm decoupled the resonance at 2.34 ppm, leaving a singlet; irradiation at 2.50 ppm decoupled the resonance at 3.14 ppm, leaving a singlet; irradiation at 2.34 ppm decoupled the resonance at 3.02 ppm, leaving a singlet; IR (KBr) 2950, 2865, 1720, 1650, 1625, 1445, 1383, 1373, 1340, 1290, 1215, 1163, 1090, 1033, 1018 cm^{-1}; MS *m/e* (rel int) 335 (M^+, 11), 208 (45), 167 (60), 125 (100), 83 (45), 81 (37), 58 (30), 55 (29), 43 (28), 41 (27). Anal. Calcd for $C_{20}H_{33}NO_3$: C, 71.60; H, 9.91; N, 4.18. Found: C, 71.30; H, 9.76; N, 4.34.

***N,N*-Diisopropyl-4-benzoyl-4-methylcyclopent-1-enecarboxamide (12).** According to the general procedure for the cyclization–elimination reaction, **2** (0.40 g, 1.3 mmol) was added to a solution of LiTMP (1.3 mmol) followed by 2-methyl-1-phenylprop-2-en-1-one[13] (0.21 g, 1.4 mmol). The reaction provided 440 mg of crude material. Purification by MPLC on a 9 1/2 in. × 1/2 in. column of silica gel using 15% EtOAc/hexanes as eluent followed by Kugelrohr distillation at 100–190 °C and 0.5 Torr gave 299 mg (74%) of **12**: ^1H NMR (200 MHz, $CDCl_3$) δ 8.0–7.3 (m, 5 H, Ph), 5.68 (m, 1 H, H_a), 4.3–3.3 (b, 2 H, CONCH), 3.51 (dm, *J* = 17 Hz, 1 H, H_c), 3.32 (dm, *J* = 18 Hz, 1 H, H_d), 2.68 (dm, *J* = 17 Hz, 1 H, H_e), 2.51 (dm, *J* = 17 Hz, 1 H, H_f), 1.51 (s, 3 H, Me), 1.33 (bm, 12 H, CON(*i*-Pr)$_2$); IR (Nujol) 2960, 2920, 1675, 1620, 1440, 1370, 1342, 1290, 1210, 710 cm^{-1}; MS *m/e* (rel int) 314 (0.50), 313 (M^+, 0.28), 209 (5), 208 (34), 128 (9), 105 (20), 86 (8). Anal. Calcd for $C_{20}H_{27}NO_2$: C, 76.64; H, 8.68; N, 4.47. Found: C, 76.77; H, 8.86; N, 4.62.

***N,N*-Diisopropyl-4-(methoxycarbonyl)-4-methylcyclopent-1-enecarboxamide (15) and *N,N*-Diisopropyl-4,6-bis(methoxycarbonyl)-4,6-dimethylcyclohept-1-enecarboxamide (33).** According to the general procedure for the cyclization–elimination reaction, **2** (0.40 g, 1.3 mmol) was added to a solution of LiTMP (1.3 mmol) followed by methyl methacrylate (0.15 g, 1.4 mmol). Separation by MPLC on a 9 1/2 in. × 3/4 in. column of silica gel using 15% EtOAc/hexanes as eluent gave 17 mg (4%) of **33** and after Kugelrohr distillation at 130–140 °C and 1.0 Torr gave 204 mg (59%) of **15**.

15: ^{13}C NMR (90.546 MHz, $CDCl_3$) δ 178.0 (CO_2Me), 168.1 ($CONR_2$), 138.3 (=CR_2), 126 (=CHR), 52.1 (CO_2CH_3), 49.5 (b, $CONCHMe_2$), 48.0 (R_2CMeCO_2Me), 45.8 (CH_2), 44.5 (CH_2), 25.8 (CH_3), 21.0 ($CONCH(CH_3)_2$); ^1H NMR (360 MHz, $CDCl_3$) δ 5.59 (m, *J* = 2 Hz, 1 H, H_a), 4.1 (b, 1 H, CONCH), 3.70 (s, 3 H, CO_2CH_3), 3.4 (b, 1 H, CONCH), 3.14 (dm, *J* = 16 Hz, 1 H, H_c), 3.01 (dm, *J* = 17 Hz, 1 H, H_d), 2.50 (dm, *J* = 16 Hz, 1, H, H_e), 2.36 (dm, *J* = 17 Hz, 1 H, H_f), 1.37 (s, 3 H, CH_3), 1.3 (b, 12 H, CON(*i*-Pr)$_2$); decoupling, irradiation at 3.14 ppm decoupled the resonance at 2.50 ppm, leaving a singlet; irradiation at 3.01 ppm decoupled the resonance at 2.36 ppm, leaving a singlet; irradiation at 2.50 ppm decoupled the resonance at 3.14 ppm, leaving a singlet; irradiation at 2.36 ppm decoupled the resonance at 3.01 ppm, leaving a singlet; IR (Nujol) 1730, 1618, 1340, 1287, 1210, 1160, 1115, 1030 cm^{-1}; MS *m/e* (rel int) 267 (M^+, 8), 252 (10), 208 (11), 167 (54), 139 (100), 107 (61), 86 (21), 81 (14), 79 (50), 77 (12), 58 (14). Anal. Calcd for $C_{15}H_{25}NO_3$: C, 67.38; H, 9.43; N, 5.24. Found: C, 67.68; H, 9.25; N, 5.16.

33: ^{13}C NMR (90.546 MHz, $CDCl_3$) δ 176.9 (CO_2Me), 176.8 (CO_2Me), 172.7 ($CONR_2$), 138.0 (=CR_2), 126.9 (=CHR), 51.7 (CO_2CH_3), 48.7 (CO_2CH_3), 44.3 (R_2CMeCO_2Me), 43.5 (R_2CMeCO_2Me), 43–51 (b, $CONCHMe_2$), 37.6 (=CCH_2), 35.3 (=CCH_2), 29.9 (CH_3), 29.8 (CH_3), 21.0 ($CONCH(CH_3)_2$), 20.7 (CH_2); ^1H NMR (360 MHz, $CDCl_3$) δ 5.84 (t, *J* = 6 Hz, 1 H, H_v), 4.1–4.3 (b, 1 H, CONCH), 3.624 (s, 3 H, CO_2CH_3), 3.618 (s, 3 H, CO_2CH_3), 3.6–3.9 (b, 1 H, CONCH), 2.90 (d, *J* = 15 Hz, 1 H, H_b), 2.68 (d, *J* = 15 Hz, 1 H, H_c), 2.61 (dd, *J* = 15 and 8 Hz, 1 H, H_a), 2.25 (d, *J* = 15 Hz, 1 H, H_b), 2.13 (dd, *J* = 15 and 6 Hz, 1 H, H_a), 1.53 (d, *J* = 15 Hz, 1 H, H_d), 1.26 (s, 3 H, CH_3), 1.22 (s, 3 H, CH_3), 1.7–1.1 (b, 12 H, CON(*i*-Pr)$_2$); decoupling, irradiation at 5.84 ppm decoupled the resonances at 2.61 ppm and 2.13 ppm, leaving two doublets, *J* = 15 Hz; irradiation at 2.90 ppm decoupled the resonance at 2.25 ppm, leaving a singlet; irradiation at 2.68 ppm decoupled the resonance at 1.53 ppm, leaving a singlet; irradiation at 2.61 ppm decoupled the resonances at 2.13 ppm and 5.84 ppm, leaving two doublets, *J* = 7 Hz; irradiation at 2.25 ppm decoupled the resonance at 2.90 ppm, leaving a singlet; irradiation at 2.13 ppm decoupled the resonances at 2.61 ppm and 5.84 ppm, leaving two doublets, *J* = 7 Hz; irradiation at 1.53 ppm decoupled the resonance at 2.68 ppm, leaving a singlet; MS *m/e* (rel int) 367 (M^+, 25), 352 (9), 308 (19), 267 (28), 239 (11), 207 (100), 180 (15), 179 (69), 167 (47), 161 (12), 147 (19), 146 (10), 121 (13), 119 (33), 107 (12), 105 (12), 91 (13), 86 (11), 79 (13), 59 (12), 43 (40), 41 (23). Anal. Calcd for $C_{20}H_{33}NO_5$: C, 65.37; H, 9.05; N, 3.81. Found: C, 65.15; H, 9.12; N, 3.75.

***N,N*-Diisopropyl-4-(methoxycarbonyl)-4-(trimethylsilyl)cyclopent-1-enecarboxamide (16).** According to the general procedure for the cyclization–elimination reaction, **2** (0.40 g, 1.3 mmol) was added to a solution of LiTMP (1.3 mmol) followed by methyl 2-(trimethylsilyl)propenate[14] (0.23 g, 1.4 mmol). The reaction provided 450 mg of crude material. Purification by MPLC on a 9 1/2 in. × 3/4 in. column of silica gel using 25% EtOAc/hexanes as eluent followed by Kugelrohr distillation at 100–160 °C and 0.3 Torr gave 240 mg (57%) of **16**: ^{13}C NMR (50.31 MHz, $CDCl_3$) δ 176.9 (CO_2Me), 167.8 ($CONR_2$), 138.8 (=CR_2), 126.2 (=CHR), 51.0 (CO_2CH_3), 47.0 (b, $CONCHMe_2$), 41.9 (R_2CMeCO_2Me), 39.5 (CH_2), 38.4 (CH_2), 20.3 ($CONCH(CH_3)_2$), −4.4 ($Si(CH_3)_3$); ^1H NMR (200 MHz, $CDCl_3$) δ 5.54 (m, *J* = 2 Hz, 1 H, H_a), 3.61 (s, 3 H, CO_2CH_3), 3.8 (b, 1 H, CONCH), 3.5 (b, 1 H, CONCH), 3.18 (dm, *J* = 17 Hz, 1 H, H_c), 3.09 (dm, *J* = 17 Hz, 1 H, H_d), 2.75 (dm, *J* = 17 Hz, 1 H, H_e), 2.53 (dm, *J* = 17 Hz, 1 H, H_f), 1.22 (b, 12 H, CON(*i*-Pr)$_2$), 0.00 (s, 9 H, $Si(CH_3)_3$); IR (KBr) 2950, 1705, 1645, 1613, 1435, 1365, 1342, 1280, 1245, 1232, 1208, 1175, 843 cm^{-1}; MS *m/e* (rel int) 325 (M^+, 9), 310 (14), 252 (25), 197 (13), 167 (26), 111 (16), 93 (100), 89 (13), 86 (15), 73 (52), 65 (12), 43 (18). Anal. Calcd for $C_{17}H_{31}NO_3Si$: C, 62.72; H, 9.60; N, 4.30. Found: C, 62.87; H, 9.74; N, 4.26.

***N,N*-Diisopropyl-4-(phenylsulfonyl)-4-methylcyclopent-1-enecarboxamide (17).** According to the general procedure for the cyclization–elimination reaction, **2** (0.40 g, 1.3 mmol) was added to a solution of LiTMP (1.3 mmol) followed by 2-(phenylsulfonyl)propene[15] (0.26 g, 1.4 mmol). The reaction provided 497 mg of crude material. Recrystallization from EtOAc/hexanes gave 223 mg (49%) of **17**, mp 137–140 °C: ^1H NMR (300 MHz, $CDCl_3$) δ 8.0–7.5 (m, 5 H, Ph), 5.59 (m, 1 H, H_a), 4.1 (b, 1 H, CONCH), 3.5 (b, 1 H, CONCH), 3.41 (bdm, 2 H, H_cH_d), 2.52 (dm, *J* = 17 Hz, 1 H, H_e), 2.39 (dm, *J* = 18 Hz, 1 H, H_f), 1.47 (s, 3 H, Me), 1.35 (b, 12 H, CON(*i*-Pr)$_2$); IR (KBr) 2970, 1642, 1616, 1445, 1370, 1350, 1287, 1142, 1083, 618, 552 cm^{-1}; MS *m/e* (rel int) 349 (M^+, 2), 334 (8), 306 (6), 230 (5), 208 (29), 108 (9), 107 (100), 86 (11), 58 (9). Anal. Calcd for $C_{19}H_{27}NO_3S$: C, 65.29; H, 7.79; N, 4.01; S, 9.17. Found: C, 65.51; H, 7.58; N, 3.92; S, 9.01.

***N,N*-Diisopropyl-3-(phenylsulfonyl)-3-(3-oxocyclopentyl)-2-methylenepropanamide (21).** According to the procedure described by Hirama,[10] **2** (0.30 g, 0.97 mmol) in 4 mL of dry THF was treated with *N,N'*-dimethylpropyleneurea (DMPU, 0.24 mL, 1.9 mmol) and cooled to −78 °C. *n*-BuLi (1.1 mL, 1.4 mmol) was added and the solution was stirred at −78 °C for 10 min. Cyclopentenone (0.10 mL, 1.2 mmol) was then added and the solution was stirred for 30 min. Acetic acid (0.1 mL) was then added followed by 2 mL of saturated aqueous NH_4Cl and the solution was warmed to room temperature. The solvent was removed in vacuo and the organic products were taken up in Et_2O. The organic layer was washed with 5% HCl and then brine, dried over $MgSO_4$, filtered, and concentrated in vacuo to give 0.40 g of crude product. Purification by chromatotron on a 2-mm plate of silica gel using 60% EtOAc/hexanes as eluent gave 0.29 g (76%) of **21**, mp 143–145 °C: ^1H NMR (200 MHz, $CDCl_3$) δ 8.0–7.5 (m, 5 H, Ph), 5.61 (s, 1 H, =CH), 5.55 (s, 1 H, =CH), 4.44 (d, *J* = 9 Hz, 1 H, $PhSO_2CH$), 4.4 (b, 1 H, CONCH), 3.5 (b, 1 H, CONCH), 3.0–2.0 (m, 7 H, cyclopentanone), 1.5–1.0 (bm, 12 H, CON(*i*-Pr)$_2$); IR (KBr) 2960, 1735, 1730, 1615, 1445, 1305, 1250, 1155, 1140 cm^{-1};

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MS m/e (rel int) 391 (M^+, 0.21), 376 (4), 291 (16), 251 (17), 250 (100), 208 (6), 168 (7), 149 (5), 125 (32). Anal. Calcd for $C_{21}H_{29}NO_4S$: C, 64.42; H, 7.46; N, 3.58; S, 8.19. Found: C, 64.42; H, 7.48; N, 3.48; S, 8.11.

Registry No. 1, 36526-15-5; 2, 110426-80-7; 2-d_n, 119039-24-6; 3, 119039-00-8; 4, 87504-85-6; 5, 77199-25-8; 6, 105970-70-5; 7, 119039-01-9; 8, 119039-02-0; 9, 119039-03-1; 9-d_n, 119039-25-7; 10, 119073-05-1; 11, 110426-81-8; 12, 119039-04-2; 13, 110426-82-9; 14, 119039-05-3; 15, 110426-83-0; 16, 110426-84-1; 17, 119039-06-4; 18, 105970-96-5; 19, 110426-85-2; 20, 119039-07-5; 21, 119039-08-6; 22, 119039-09-7; 23, 119073-06-2; 24, 119039-10-0; 25, 119073-07-3; *trans*-26, 119039-11-1; *cis*-26, 119039-15-5; 27, 119073-08-4; 28, 119039-12-2; 29, 99699-08-8; 30, 119039-13-3; 31, 105970-95-4; 32, 110426-86-3; 33, 119039-14-4; 37, 119039-16-6; 38, 119039-17-7; 39, 119070-24-5; 39 (sulfide), 119039-26-8; 42, 119039-18-8; 43, 119039-19-9; 43 (acid), 66241-77-8; 44, 119039-20-2; 44 (acid), 74903-61-0; 45, 119039-21-3; 46, 119039-22-4; 49, 119039-23-5; $H_2C{=}C(CH_3)CO_2C_6H_{11}$, 101-43-9; $H_2C{=}C(CH_3)COPh$, 2177-70-0; $H_2C{=}C(CH_3)CONPhMe$, 15796-89-1; $H_2C{=}C(CH_3)CO_2n$-Bu, 97-88-1; $H_2C{=}C(CH_3)CO_2Me$, 80-62-6; $H_2C{=}C(SiMe_3)CO_2Me$, 18269-31-3; $H_2C{=}C(CH_3)SO_2Ph$, 76380-14-8; $H_2C{=}CHCONPhMe$, 6273-94-5; $H_2C{=}C(CH_3)CN$, 126-98-7; $PhCH{=}C(CO_2Et)_2$, 5292-53-5; 2-(bromomethyl)acrylic acid, 72707-66-5; thiophenol, 108-98-5; sodium benzenesulfinate, 873-55-2; 2-cyclopenten-1-one, 930-30-3; 2-cyclohexen-1-one, 930-68-7; *N*-methylaniline, 100-61-8.

Supplementary Material Available: Experimental details for the syntheses of 3-9, 13, 14, 18-20, 22, 24, 26, 28, 30, 32, 37-39, 42-46, and 49 (21 pages). Ordering information is given on any current masthead page.

Crotofolane Diterpenoids from the African Shrub *Croton dichogamus* Pax.

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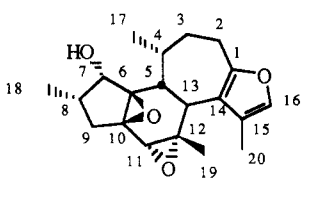
Two new crotofolane diterpenoids, crotoxides A (1) and B (2), have been isolated from the African shrub *Croton dichogamus*. The structure of crotoxide A (1) was determined by a combination of spectroscopic and single-crystal X-ray diffraction analyses. The proposed structure of crotoxide B (2) was based on spectroscopic comparison to crotoxide A (1).

Elephants in the Serengeti-Mara region of northern Tanzania and southern Kenya feed on a wide variety of trees and shrubs, but they show distinct preferences.[1] In particular, they prefer *Acacia* species such as *A. gerradii* Benth. while eating the *Croton dichogamus* Pax. to a lesser extent and another shrub *Euclea divenorum* Hiern. to an even lesser extent.[2] We have examined the chemical constituents of *C. dichogamus* leaves as part of an ongoing program aimed at identifying plant metabolites that might influence the elephants' browsing behavior. Our investigations have resulted in the isolation of two interesting new crotofolane diterpenoids, crotoxide A (1) and crotoxide B (2), whose structures we now report.



1 2

The dichloromethane-soluble portion of the methanol extract of air-dried *C. dichogamus* leaves was fractionated by silica gel flash and silica gel preparative TLC chromatographies to give crude samples of crotoxides A (1) and B (2). Final purification of each of the metabolites proved to be extremely difficult due to the presence of numerous minor but persistent contaminants. Mild hydrogenation of each of the crude samples substantially changed the polarity of the contaminants without altering the metabolites of interest, as shown by ^1H NMR and TLC analysis of the crude samples before and after hydrogenation. HPLC fractionation of each of the hydrogenated crude fractions gave pure samples of diterpenoids 1 and 2.

Crotoxide A (1), obtained as colorless needles (mp 149-152 °C) from hexane, gave a parent ion in the HREIMS at m/z 330.1837 Da (daltons), appropriate for a molecular formula of $C_{20}H_{26}O_4$ (ΔM + 0.6 mmu), requiring eight sites of unsaturation. The ^{13}C NMR spectrum of crotoxide A (Table II) showed well-resolved resonances for all 20 carbons, and an APT[3] experiment demonstrated that 25 of the protons were attached to carbon atoms. An IR band at 3477 cm^{-1} revealed that the remaining proton was part of an alcohol functionality.

Four deshielded carbon resonances (δ (C_6D_6) 118.9 (C), 121.6 (C), 137.2 (CH), and 150.5 (C); Table II) and a deshielded proton resonance (δ (C_6D_6) 6.92 br s; Table I) were assigned to an α,β,β'-trisubstituted furan fragment. A COSY experiment (C_6D_6) showed coupling between the furan proton (δ 6.92) and a set of methyl protons at δ 1.96 (d, J = 1 Hz), and irradiation of the methyl protons induced a NOE in the furan proton. The methyl residue, therefore, had to be attached to the β-carbon adjacent to

(1) For prior studies on this general topic, see: Sinclair, A. R. E.; Jogia, M. K.; Andersen, R. J. *J. Chem. Ecol.* **1988**, *14*, 1505.

(2) Dublin, H. T. Ph.D. Thesis. Decline of the Mara Woodlands: The Role of Fire and Elephants. Dept. of Zoology, University of British Columbia, 1986.

(3) Patt, S. L.; Shoolery, J. N. *J. Magn. Reson.* **1982**, *46*, 535.

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