Intramolecular Diels-Alder Reactions of Sorbyl Citraconate and Mesaconate Esters[1]

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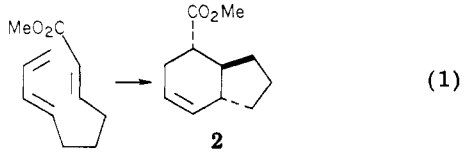
The intramolecular Diels-Alder reaction of **21**, prepared from citraconic anhydride and sorbyl alcohol, gave **23**, whereas the esters **29** and **32** produced trans-fused adducts **30** and **33**, respectively. These were isomerized in base to **31** and **34**. The (*E*)-citraconate **39** furnished **40** and **31** in the ratio 4.3:1, respectively. The major isomer of this pair was converted by base to the ester **24**, prepared from **23**. The mesaconate diester **45** upon cycloaddition afforded **46** and **47** in the ratio 4.7:1, and sorbyl tetrolate **51** underwent a Diels-Alder reaction to **52**. A possible explanation for the prevalence for exo cycloaddition of **29**, **39**, and **45** is advanced in terms of a nonsynchronous (but concerted) pathway.

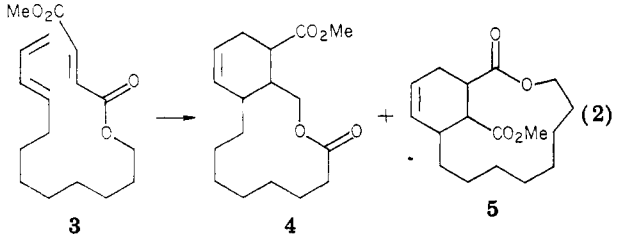
The intramolecular Diels-Alder reaction is acknowledged to be a valuable extension of its intermolecular counterpart for the synthesis of cyclic structures. Much of the impetus for the current activity in this area can be traced to two particularly interesting publications in 1963. One of these, by Klemm, described an elegant synthesis of γ-apopicropodophyllin using the intramolecular Diels-Alder addition of a tetrolic ester.[2] The other, by Brieger, reported an approach to longifolene which, although unsuccessful, revealed the potential of this cycloaddition for assembling complex, polycyclic systems.[3] Within the last 5 years, a plethora of examples has appeared in the literature which affirm the importance of the intramolecular Diels-Alder reaction as a general stratagem in organic synthesis.[4]

An intrinsic feature of the Diels-Alder reaction is the firm regio- and stereocontrol exercised during the addition, with the consequence that the placement and orientation of substituents emerge in a highly predictable fashion. The first systematic study of these properties, as they relate to the intramolecular addition, was carried out by House and Cronin, who found that cycloaddition of the 2,7,9-decatrienoate **1** gave a single bicyclic product, **2**.[5] It has now become clear that, with a short chain (six atoms or less) interposed between the diene and dienophile, syn regiochemistry of addition is to be expected. In fact, even with a linkage of ten atoms (e.g., **3**), the fused adduct **4** is favored over the bridged lactone **5** by a ratio of 2:1.[6]



(1)

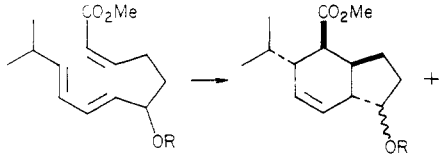
1 **2**



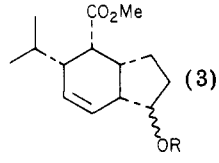
(2)

3 **4** **5**

A further aspect of the cycloaddition of **1** is the apparent preference for exo geometry of the linking chain (or, perhaps in this case, a preferred endo orientation of the terminal ester). However, attempts to decide whether the Alder endo rule applies to intramolecular (4 + 2) cycloadditions have resulted in frustrating ambiguities. Related to this, of course, is the broader question of whether the mechanism of the intramolecular Diels-Alder process truly parallels the concerted pathway generally pictured for the intermolecular reaction. Roush, in an extension of the earlier work of House, observed that **6** afforded a mixture of cycloadducts **7** and **8** in which the trans-fused hydroindane **7** (eq 3) predominated over the cis isomer by a ratio



6 **7**



(3)

8

varying from 2:1 to 5:1, dependent on the R substituent.[7] Reversal of the dienophile geometry to trans had only a small effect on this ratio.

In contrast to these results, Gschwend found that the amine **9** underwent cycloaddition to give a mixture of *cis*-hydroisoindole **10** and trans fused isomer **11** (eq 4) in the ratio 5:1, indicating that endo addition prevails in this instance.[8] However, in a series of related amides **12** (R = H, Ph, CO_2Me), the proportion of cycloadducts **13** and

(1) A preliminary account of this work was presented at the Sino-American Symposium on Natural Products Chemistry, Shanghai, China, Oct 27-31, 1980.

(2) L. H. Klemm and K. W. Gopinath, *Tetrahedron Lett.*, 1243 (1963); L. H. Klemm, K. W. Gopinath, D. H. Lee, F. W. Kelly, E. Trod, and T. M. McGuire, *Tetrahedron*, **22**, 1797 (1966).

(3) G. Brieger, *J. Am. Chem. Soc.*, **85**, 3787 (1963).

(4) For a review, see W. Oppolzer, *Angew. Chem., Int. Ed. Engl.*, **16**, 10 (1977). For some striking recent examples, see: D. J. Morgans and G. Stork, *Tetrahedron Lett.*, 1959 (1979); F. Naf, R. Decorzant, and W. Thommen, *Helv. Chim. Acta*, **62**, 114 (1979); G. Buchi, A. Hauser, and J. Limacher, *J. Org. Chem.*, **42**, 3323 (1977); H. Greuter, H. Schmid, and G. Frater, *Helv. Chim. Acta*, **60**, 1701 (1977).

(5) H. O. House and T. H. Cronin, *J. Org. Chem.*, **30**, 1061 (1965).

(6) E. J. Corey and M. Petrzilka, *Tetrahedron Lett.*, 2537 (1975).

(7) W. R. Roush, *J. Org. Chem.*, **44**, 4008 (1979). Very recently, Roush has generalized this observation with a study of the intramolecular Diels-Alder reaction of systems related to **6** in which the OR substituent is absent. Thermal cyclization [W. R. Roush, A. I. Ko, and H. R. Gillis, *J. Org. Chem.*, **45**, 4264 (1980)] afforded trans- and cis-fused hydrindanes in ratios from 60:40 to 72:28, whereas Lewis acid catalyzed cycloaddition [W. R. Roush and H. R. Gillis, *J. Org. Chem.*, **45**, 4267 (1980)] in many cases gave exclusively the trans-fused product.

(8) H. W. Gschwend, A. L. Lee, and H. D. Meier, *J. Org. Chem.*, **38**, 2169 (1973).

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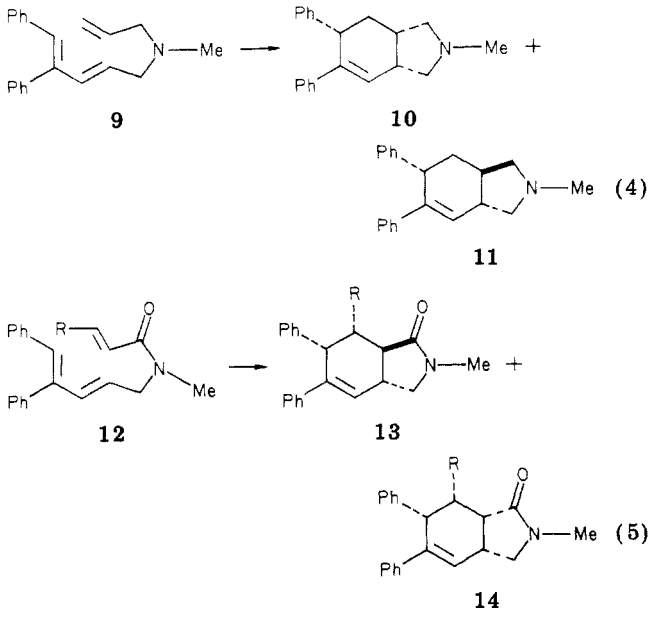
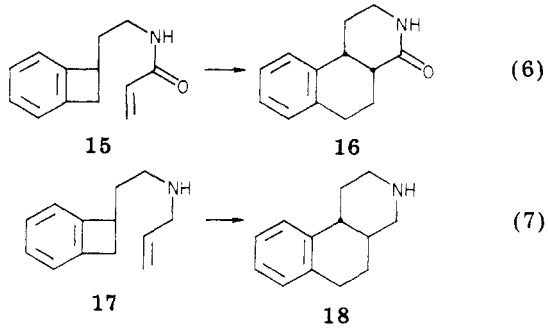


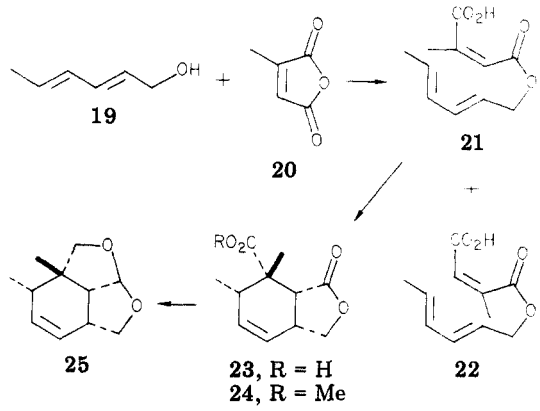
14 (eq 5) increased in favor of the trans-fused lactam from 1:1 (R = H) to 8:1 (R = Ph), whereas from **12** (R = CO_2Me) only the corresponding trans lactam **13** was obtained. The stereochemical sensitivity of the intramolecular Diels–Alder reaction to substituent factors is also apparent in a study by Oppolzer of internal cycloadditions of substituted benzocyclobutenes.[9] Thus, cycloaddition of the *o*-xylylene intermediate from **15** gave mainly the cis-fused δ-lactam **16** (eq 6), whereas the amine **17** afforded **18** in a seven-fold excess over the corresponding cis-fused product (eq 7).



Results

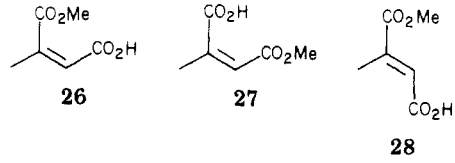
The inviting prospect of employing the intramolecular Diels–Alder reaction for assembling functionalized cyclohexane rings common to certain terpenoids (including nonisoprenoid systems such as the irones) led us to examine the thermal reaction of citraconic esters bearing an appropriate diene moiety. Treatment of sorbyl alcohol (**19**) with citraconic anhydride (**20**) afforded an inseparable mixture of half esters **21** and **22** with no apparent selectivity (Scheme I). When this mixture was heated at reflux in xylene for 24 h, a single crystalline product, along with a substantial quantity of polymer, was formed. The IR spectrum of this product showed the carbonyl frequency (1765 cm^{-1}) expected for a γ-lactone, and its NMR spectrum exhibited features, in the form of methyl signals at δ 1.2 and 1.5 and signals for two olefinic protons (δ 5.6 and 5.8), clearly indicative of a cycloadduct **23**. The stereochemistry of the ring fusion could not be deduced from

Scheme I



the data at hand, but exposure of **23** to diazomethane afforded methyl ester **24**, in which H_a was now clearly visible as a doublet at δ 3.05 with a coupling constant of 9 Hz. From an inspection of a Dreiding model of **24**, this coupling is consistent only with a cis ring fusion. Confirmation of this assignment was obtained when **24** was allowed to react with diisobutylaluminum hydride at −70 °C. The product, tricyclic acetal **25**, can only arise if the substituent ester, the lactone carbonyl, and the oxygen-bearing methylene group are all cis. Final proof of the stereostructure was obtained by an X-ray crystallographic analysis on the cycloadduct **23**.[10] No evidence for a second cycloadduct could be found in the product mixture from **21** and **22**, and it therefore appears that **21** undergoes intramolecular Diels–Alder reaction exclusively via the endo mode. Isomer **22** does not yield a cycloadduct under these conditions but is apparently destroyed through an autocatalytic polymerization.

Our inability to separate **21** from **22** (the corresponding methyl esters also proved to be inseparable) led us to examine a route which would afford a derivative of **21** selectively. It has been reported that citraconic anhydride, upon treatment with sodium methoxide in cold methanol, affords a single ester, **26**.[11] However, we found that **26**



is accompanied by about 10% each of the alternate ester **27** and geometrical isomer **28**. In practice, the mixture of **26**–**28** was reacted with oxalyl chloride and then with sorbyl alcohol in pyridine to afford **29** in good yield after chromatographic purification.

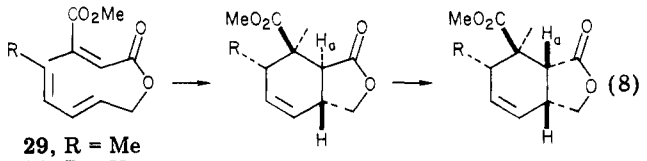
To our surprise, exposure of **29** to refluxing xylene for 24 h did not give **24**, but instead a new cycloadduct was produced. Its IR spectrum showed that the material was again a γ-lactone (1775 cm^{-1}), and its NMR spectrum showed features similar in most respects to those found in **24**. A significant difference, however, was that the angular proton (H_a) adjacent to the lactone carbonyl now exhibited a 14-Hz coupling to its neighbor. This is clearly consonant with a trans-fused adduct **30**, arising via an exo cyclization of **29**[12] (eq 8). An examination of a Dreiding

(9) W. Oppolzer, *J. Am. Chem. Soc.*, **93**, 3834 (1971), and references cited.

(10) J. D. White, B. G. Sheldon, B. A. Solheim, and J. Clardy, *Tetrahedron Lett.*, 5189 (1978).

(11) S. Veibel and C. Pedersen, *Acta Chem. Scand.*, **9**, 1674 (1955).

(12) L. M. Jackson and S. Sternhell, "Applications of Nuclear Magnetic Resonance Spectroscopy in Organic Chemistry", 2nd ed., Pergamon Press, Oxford, England, 1969, pp 295–296.



(8)

29, R = Me
32, R = H

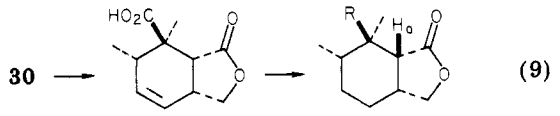
30, R = Me
33, R = H

31, R = Me
34, R = H

model of **30** suggested that the trans ring fusion was more strained than the cis arrangement, and, in accord with this, it was observed that treatment of **30** with 0.1 equiv of sodium methoxide furnished the new lactone quantitatively. The most striking characteristic associated with this transformation was the downfield shift by 1.2 ppm of the angular proton which had undergone replacement, indicating that H_a was now deshielded by the cis, vicinal ester function. Unfortunately, the coupling of H_a was obscured by other resonances.

An exactly parallel sequence was executed with the pentadienyl ester **32**, prepared from 2,4-pentadienol[13] and **20**. Trans lactone **33** was the sole Diels–Alder product, although in this case the pentadienyl ester **32** underwent substantial polymerization, and the yield of addition was lower than for **29**. As before, facile isomerization to cis lactone **34** could be induced with base.

An important question which arises in connection with the chemistry of these Diels–Alder adducts is whether the oxidation level of substituents, particularly that of the methyl ester, can be adjusted in a selective fashion. Adduct **30** was chosen as a convenient substrate for an investigation of this point and was first saponified to carboxylic acid **35** (eq 9), which was shown from spectral data



(9)

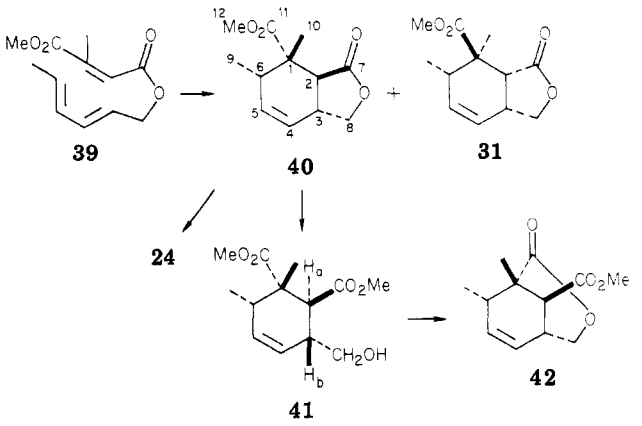
35

36, R = CO_2H
37, R = CH_2OH
38, R = CH_2I

to be a stereoisomer of **23**. Although the NMR spectrum of **35** failed to disclose unambiguous evidence for epimerization at the ring fusion accompanying saponification, the hydrogenation product **36** of **35** showed the angular proton H_a as a doublet with a coupling constant of 5.5 Hz. This is consistent only with a cis ring fusion.[12] The carboxyl group of **36** was reduced selectively with diborane to give primary alcohol **37**, accompanied by a small quantity of the corresponding aldehyde; that the γ-lactone remained intact in this process was evident from retention of the IR band at 1760 cm^{-1}. However, although **37** could be converted to iodide **38** with methyltriphenoxyphosphonium iodide,[14] no method could be found for reductive removal of the halogen substituent. The highly hindered environment of this functionality evidently interferes with the last stage of the reductive sequence from **36**, so that access to geminal dimethyl substitution by this route is blocked.

Since the citraconate esters **29** and **32** gave exclusively the thermodynamically disfavored, trans-fused lactones upon cycloaddition, it was decided to investigate the intramolecular Diels–Alder reaction of the corresponding mesaconate esters to determine whether the same selectivity for exo addition prevailed in this case. Conversion of **28** to its chloride with oxalyl chloride, followed by treatment with sorbyl alcohol (**19**) in pyridine, afforded **39** in good yield. It was found that cycloaddition of **39** was appreciably slower than that of **29** and **32**, and, after 5 days in refluxing xylene, only 60% conversion to product had taken place. A mixture of two γ-lactones, **40** and **31** (Scheme II), in the ratio 4.3:1 was isolated in 84% yield on the basis of the amount of **39** consumed. The minor isomer was shown to be identical with cis lactone **31**, obtained from epimerization of **30**, and it was assumed that the major isomer **40** posessed the corresponding trans ring fusion, although the coupling constant of the angular proton adjacent to the lactone carbonyl could not be measured to confirm this. It was expected, on the basis of observations made with **30** (vide supra), that epimerization of **40** would yield the cis-fused lactone **24** prepared earlier. However, treatment of **40** with sodium methoxide in methanol gave a diester, which was shown to be **41**. The coupling of H_a (13 Hz) in this structure confirmed its trans relationship to H_b. It was not possible to regenerate γ-lactone **40** from **41**, but a δ-lactone, assigned structure **42**, was formed in moderate yield upon treatment of **41** with *p*-toluenesulfonic acid in benzene. Recognizing that the assignment of stereochemistry to **40** from these results is presumptive, an unambiguous correlation with a substance of known configuration was sought. Thus, exposure of **40** to sodium hydride in tetrahydrofuran led in quantitative yield to **24**, whose configuration is defined through its relationship to carboxylic acid **23** deduced from X-ray analysis. The formation of trans lactone **40** as the major product from **39** indicates that cycloaddition again proceeds mainly via a transition state with exo geometry of the linkage joining diene and dienophile.

Scheme II

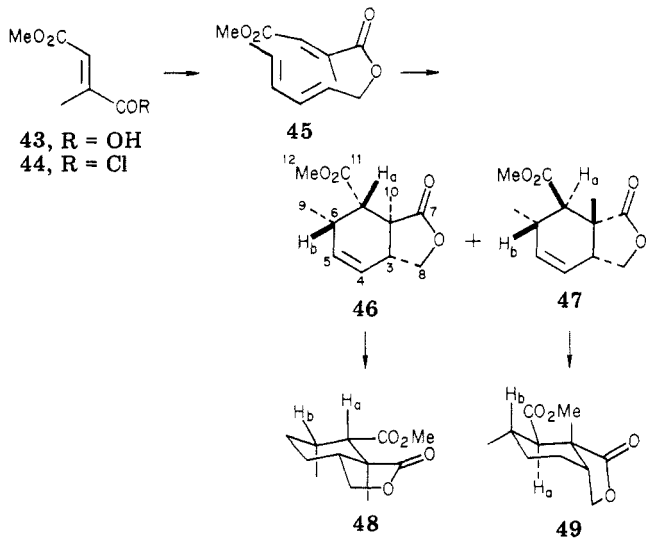


For comparison with these results, it was of interest to determine whether the isomer of **39**, in which methyl and sorbyl ester groups were interchanged, would undergo analogous intramolecular Diels–Alder addition. Accordingly, the half-ester (**43**) of mesaconic acid, prepared by selective saponification of dimethyl mesaconate with methanolic potassium hydroxide,[15] was converted to its acid chloride, **44**, with oxalyl chloride. Treatment of **44** with sorbyl alcohol furnished the desired ester **45**.

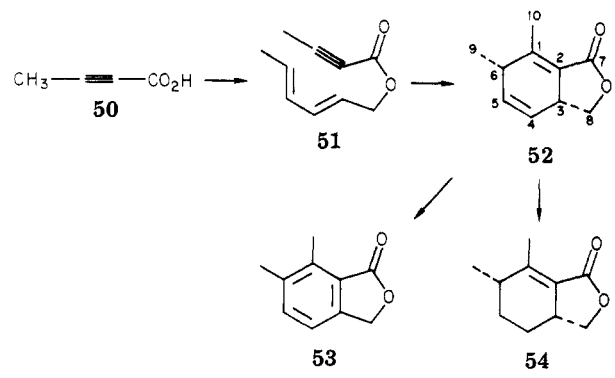
The cycloaddition of **45** in refluxing xylene was substantially slower than for **39** and was only 50% complete after 11 days. Workup at this stage furnished an 85% yield (based on **45** consumed) of two γ-lactones in the proportion 4.7:1. The NMR spectra of these lactones were in good agreement with the expected structures **46** and **47** (Scheme

(13) W. Cocker, T. B. H. McMurry, and D. M. Sainsbury, *J. Chem. Soc. C*, 1152 (1966).
(14) J. P. H. Verheyden and J. G. Moffatt, *J. Org. Chem.*, **35**, 2319 (1970).
(15) J. E. H. Hancock and R. P. Linstead, *J. Chem. Soc.*, 3490 (1953).

Scheme III



Scheme IV



III) derived from an intramolecular Diels–Alder reaction, and, in the minor isomer (**47**), H_a was a clearly visible doublet with a coupling constant of 12 Hz. This suggests a trans orientation of the methyl ester and the adjacent, secondary methyl group which implies the cis ring fusion shown. Unfortunately, the coupling associated with the corresponding proton in major isomer **46** could not be reliably determined due to overlap with allylic protons, and hence a definitive stereochemical assignment could not be made. It was reasoned that saturation of the cyclohexene double bond in **46** and **47** would remove this ambiguity, and dihydro derivatives **48** and **49** were prepared by hydrogenation of **46** and **47**, respectively, over Adams' catalyst in ethyl acetate. The proton H_a in **48** now appeared as a doublet with a coupling constant (5 Hz) indicative of an axial–equatorial relationship with its neighbor H_b, whereas **49** retained the 12-Hz coupling constant characteristic of a diaxial relationship of these two hydrogens.[16] Since the relative configurations of the ester and lactone carbonyl (trans) and of the methylene and secondary methyl (cis) groups on the cyclohexane are determined by the geometry of the starting ester **45**, the ring fusion in the major cycloaddition product **46** must therefore be trans.

In contrast to the very slow cyclization observed with **45**, the sorbyl ester **51** of tetrolic acid (**50**) underwent virtually complete intramolecular Diels–Alder reaction during 24 h in refluxing xylene. The product showed a carbonyl stretching frequency in its IR spectrum at 1745 cm^{-1}, indicative of an α,β-unsaturated γ-lactone, and the NMR spectrum was fully consistent with the 1,4-cyclohexadiene structure of **52** (Scheme IV). The latter was treated with lithium dimethylcuprate in an attempt to generate a geminal dimethyl substituent by conjugate addition. However, the sole product isolated was the aromatic lactone **53**. In the hope that this facile aromatization could be forestalled by removal of the disubstituted double bond, **52** was hydrogenated over Adams' catalyst to give **54** in excellent yield. Unfortunately, **54** proved to be completely inert to conjugate addition.

Discussion

A growing body of evidence, some of which is cited in the introductory section of this paper, supports the contention that the Alder endo rule, which governs most (though not all) intermolecular Diels–Alder additions, is not generally valid for the intramolecular case. Our results show that esters **29**, **32**, **39**, and **45** undergo intramolecular Diels–Alder reaction predominantly or exclusively via a geometry in which the linkage connecting the diene and dienophile is exo. The configuration (*E* or *Z*) of the dienophile has little influence on the preference for exo addition, as was observed by Roush, although it does affect the rate of addition ($k_Z > k_E$). A comparison of results obtained from **45** with those from **29** and **39** indicates that the position of an alkyl substituent on the dienophile does not significantly perturb the predilection for exo cyclization, but it does exert a profound effect on the rate of reaction (e.g., $k_{39} \gg k_{45}$).

The carboxylic acid **21** is the exception in this series to the observed bias toward exo addition. It is tempting to draw mechanistic inferences from the fact that **23** is the sole cycloadduct in this case, but neither steric nor electronic factors provide a completely satisfactory explanation of this result. It is conceivable that the intramolecular Diels–Alder reaction of **21**, in contrast to the reactions of esters **29**, **39**, and **45**, is reversible (with the retroreaction perhaps catalyzed by internal protonation of the lactone carbonyl), so that the thermodynamically favored, cis-fused lactone is produced. An accurate, experimental test of this proposal is complicated by the fact that the sorbyl moiety of **21** is susceptible to polymerization in the presence of a carboxylic acid, but the available evidence does suggest that **23** may revert to **21**.[17] It should also be noted that the yield of **23** from **21** is significantly lower than that observed in the intramolecular Diels–Alder reaction of the corresponding ester.

In his analysis of the Diels–Alder reaction of **6**, Roush states that the preference for exo addition is a "consequence of the conformations adopted by the chain linking diene and dienophile". While it is true that the OR substituent in this case could exert a steric effect resulting in a conformational bias toward the exo mode of addition, no such effect is evident in systems such as **1**, **12**, **29**, **32**, **39**, or **45**. In fact, the torsional displacements of the linking chain which must occur along the reaction profile from acyclic to bicyclic structures are virtually the same for both the exo and endo addition pathways. However, a close scrutiny with molecular models of the reaction continuum for these intramolecular processes reveals that a truly synchronous addition of diene and dienophile, in which both new σ bonds progress at the same rate, is virtually impossible with a linking chain of only three atoms. Although the existence of nonsynchronous Diels–Alder reactions has been suggested and rationalized

(16) L. M. Jackman and S. Sternhell, "Applications of Nuclear Magnetic Resonance Spectroscopy in Organic Chemistry", 2nd ed., Pergamon Press, Oxford, England 1969, p 288.

(17) J. D. White and P. R. Raghavan, unpublished results.

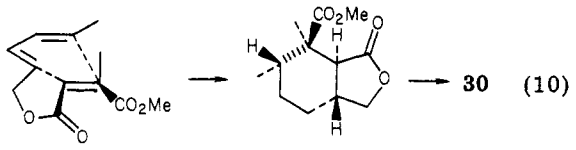
Table I. ^{13}C NMR Chemical Shifts of Diels-Alder Adducts and Related Compounds

compd	carbon[a] 1	2	3,6	4,5	7,11	8	9,10	12
24	45.5	44.4	37.6, 35.0	123.6, 133.8	176.7, 174.7	70.9	17.3, 25.4	51.6
30	46.0	44.8	38.0, 38.7	122.1, 136.2	174.1, 175.8	69.5	16.8, 19.7	52.1
31	46.3	44.2	35.0, 35.8	122.9, 133.7	176.2, 177.0	70.8	14.7, 15.7	52.5
33	43.0	48.9	38.0, 38.7	123.6, 129.1	173.9, 175.0	69.9	24.0	52.3
34	43.0	43.9	37.1, 30.8	125.9, 129.6	176.1, 176.3	71.0	22.4	52.4
40	43.9	44.0	37.4, 41.2	121.0, 134.6	173.5, 173.7	69.7	17.9, 18.2	51.3
41	48.7	41.6	40.2, 40.4	125.7, 132.3	not obsd, not obsd	64.6	17.7, 18.9	51.6, 51.8
42	45.2	47.4	33.4, 36.8	122.7, 135.6	not obsd, not obsd	72.2	15.6, 21.6	51.9
46	32.8	42.1	45.9, 47.8	120.2, 135.7	171.5, 177.7	68.0	11.1, 18.6	51.3
47	29.9	42.6	44.0, 48.8	121.4, 134.0	172.6, not obsd	70.2	17.4, 19.6	51.7
52	120.2	150.3	36.6, 38.8	122.3, 133.7	169.4	69.5	14.6, 18.3	
54	119.9	135.4	39.8, 35.0	29.4, 21.3	153.0	71.5	16.5, 19.8	

[a] Refer to structures 40, 46, and 52 for carbon numbers.

on previous occasions,[18] the idea has particular relevance to the intramolecular cases studied here.

Given an asymmetric pathway,[19] in which the formation of one σ bond advances more rapidly than the other, it would be expected on steric grounds that a system such as **29** would adopt a conformation for cycloaddition (A, eq 10) which permits closure of the five-membered lactone



A **30** (10)

ahead of the nine-membered ring. In the absence of overriding, torsional stresses, the stereochemical preference for trans-oriented side chains on the γ-lactone should probably prevail at this point, so that the result of the cycloaddition would be a trans ring fusion and an apparent exo addition. It is noteworthy that no evidence could be found in the intramolecular Diels–Alder reactions of **29**, **39**, and **45** for cycloaddition products in which the configurational fidelity of the dienophile had been lost. Hence, a discrete, two-step (diradical) pathway appears to be excluded.[20] The suggestion of a nonsynchronous pathway for these cycloadditions (but concerted in the sense that both bonds are *initiated* simultaneously) is tentative at this stage, and, clearly, a broader set of intramolecular Diels–Alder reactions must be examined before firm conclusions can be drawn.

Experimental Section

Infrared spectra (IR) were recorded on a Perkin-Elmer 727B spectrophotometer. ^1H nuclear magnetic resonance spectra (NMR) were recorded on a Varian EM-360A or HA-100 spectrometer and ^{13}C spectra were measured on a Varian FT-80A spectrometer (see Table I). Chemical shifts are reported in parts per million (δ) with tetramethylsilane as the internal standard. Coupling constants (J) are given in hertz; the abbreviations s, d, t, q, and m refer to singlet, doublet, triplet, quartet, and multiplet, respectively. Mass spectra were obtained on a Varian MAT CH-7 spectrometer, and exact masses were measured by using a CEC-103B spectrometer at an ionization potential of 70 eV. Combustion analyses were performed by Micro-Tech Laboratories. Analytical thin-layer chromatography (TLC) was done on Merck TLC sheets precoated with silica gel 60 F-254 (0.2 mm thick). Preparative layer chromatography was done on Analtech precoated silica gel GF-259 plates (1 mm thick). Merck silica gel 60 (0.06–0.02 mm, activity 2–3) was used for column chromatography. All boiling points (bp) and melting points (mp) are uncorrected. Dry tetrahydrofuran (THF) was obtained by distillation, under nitrogen, from sodium–benzophenone ketyl. Hexamethylphosphoramide (HMPA) and dimethylformamide (DMF) were dried by distillation from calcium hydride at reduced pressure. Other solvents were purified by using standard procedures.

***trans,trans*-2,4-Hexadienyl Citraconates (21 and 22).** To a solution under nitrogen of sorbyl alcohol (9.80 g, 0.10 mol), pyridine (8.0 mL, 0.1 mol), and 2,6-di-*tert*-butyl-*p*-cresol (50 mg) in 20 mL of dry benzene was added 9.0 mL (11.2 g, 0.10 mol) of citraconic anhydride. The solution darkened and became warm; the temperature was maintained at 50 °C for 8 h. After the mixture was cooled, the solvent was removed by evaporation in vacuo to yield 12.1 g (60%) of a 1:1 mixture of **21** and **22** as a pale brown oil: IR (film) 3000, 1725, 1705, 1450 cm^{-1}; ^1H NMR ($CDCl_3$) δ 10.00 (1 H, s), 6.5–5.5 (5 H, m), 4.75 (2 H, m), 2.08 (3 H, s), 1.8 (3 H, d, J = 6 Hz). Attempts to purify this material by distillation resulted in decomposition.

3α-(Hydroxymethyl)-1β,6α-dimethylcyclohex-4-ene-1α,2α-dicarboxylic Acid γ-Lactone (23). The mixture of **21** and **22** was dissolved in 500 mL of xylene (distilled from sodium) and refluxed under a nitrogen atmosphere for 15 h. The solvent was removed by distillation in vacuo to yield 11.7 g of a thick, brown oil which partially crystallized on standing. Trituration with chloroform–cyclohexane and filtration, followed by crystallization from ethyl acetate–hexane, yielded 2.00 g (32% from **21**) of **23**: mp 168–170 °C; IR (Nujol) 3000, 1760, 1350, 1200, 1050, 975 cm^{-1}; ^1H NMR ($CDCl_3$) 7.7 (1 H, br s), 5.8 (1 H, dd, J = 2, 9 Hz), 5.6 (1 H, br d, J = 10 Hz), 4.4 (1 H, dd, J = 8, 9 Hz), 4.2 (1 H, dd, J = 3, 8 Hz), 3.2 (1 H, m), 3.05 (1 H, d, J = 9 Hz), 2.4 (1 H, m), 1.5 (3 H, s), 1.2 (3 H, d, J = 7 Hz); mass spectrum, m/e 210.089 (M^+, calcd for $C_{11}H_{14}O_{11}$ 210.089).

3α-(Hydroxymethyl)-1β,6α-dimethyl-1α-(methoxycarbonyl)cyclohex-4-ene-2α-carboxylic Acid γ-Lactone (24). A sample of **23** (0.210 g, 1.00 mmol) was treated with excess, freshly prepared, ethereal diazomethane. Evaporation of the ether in vacuo yielded 0.220 g (98%) of **24** as a pale brown oil: IR (film) 2990, 1770, 1700, 1460, 1380, 1280, 1230, 1140, 1080, 990, 800 cm^{-1}; ^1H NMR ($CDCl_3$) δ 5.8 (1 H, dq, J = 2, 9 Hz), 5.5 (1 H, dt, J = 2, 9 Hz), 4.45 (1 H, dd, J = 8, 9 Hz), 4.15 (1 H, dd, J = 4, 9 Hz), 3.75 (3 H, s), 3.18 (1 H, m), 3.05 (1 H, d, J = 9 Hz), 2.4 (1 H, m),

(18) M. J. S. Dewar and R. S. Pyron, *J. Am. Chem. Soc.*, **92**, 3098 (1970); M. T. H. Lin and C. Schmidt, *Tetrahedron*, **27**, 5289 (1971); J. W. McIver, *Acc. Chem. Res.*, **7**, 72 (1974).

(19) MINDO/3 calculations [M. J. S. Dewar, S. Olivella, and H. S. Rzepa, *J. Am. Chem. Soc.*, **100**, 5650 (1978)] permit highly skewed transition states for conventionally concerted intermolecular Diels–Alder reactions. It should be noted, however, that SCF theory does not concur with this view [R. E. Townsend, G. Ramunni, G. A. Segal, W. J. Hehre, and L. Salem, *J. Am. Chem. Soc.*, **98**, 2190 (1976); K. N. Houk, *Acc. Chem. Res.*, **8**, 361 (1975)].

(20) R. A. Firestone, *Tetrahedron*, **33**, 3009 (1977).

1.50 (3 H, s), 1.20 (3 H, d, J = 7 Hz); mass spectrum, m/e 224.106 (M^+, calcd for $C_{12}H_{16}O_4$ 224.106).

1,10-Dimethyl-3,5-dioxatricyclo[5.3.1.0^{4,11}]undec-8-ene (25). To a solution of **24** (530 mg, 2.38 mmol) in 25 mL of dry toluene cooled to −70 °C was added 4.8 mL (2 equiv) of 1.6 M diisobutylaluminum hyride in hexane. After 1.5 h another equivalent (2.4 mL) of diisobutylaluminum hydride was added. After a total reaction time of 4 h, 40 mL of 10% H_2SO_4 was added to the cold solution, which was then allowed to warm to room temperature. The layers were separated, and the aqueous phase was extracted with portions of ether (3 × 20 mL). The combined organic layers were washed with portions of water (2 × 20 mL) and once with saturated NaCl and dried over $MgSO_4$. Filtration and evaporation of the solvent in vacuo gave 350 mg of a pale yellow oil. Preparative TLC (25% acetone–cyclohexane) yielded 300 mg (60%) of **25** as a colorless oil: IR (film) 2980, 2890, 1100, 1020, 960 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 5.82 (1 H, d, J = 5 Hz), 5.70 (1 H, ddd, J = 3, 3, 10 Hz), 5.50 (1 H, ddd, J = 6, 12 Hz), 3.42 (1 H, dd, J = 8, 10 Hz), 2.90–2.58 (1 H, m), 2.40 (1 H, dd, J = 5, 10 Hz), 2.9–2.2 (1 H, m), 1.18 (3 H, s), 0.98 (3 H, d, J = 8 Hz); mass spectrum, m/e 180.115 (M^+, calcd for $C_{11}H_{16}O_2$ 180.115).

A solution of **25** (300 mg, 1.5 mmol) in 25 mL of ethanol was hydrogenated over 33 mg of 10% palladium on charcoal. The reduction was stopped when 1.25 equiv of hydrogen was taken up, the catalyst was filtered, and the filtrate was evaporated in vacuo. Preparative TLC (25% acetone-hexane) of the residual oil afforded 180 mg (60%) of 1,10-dimethyl-3,5-dioxatricyclo-[5.3.1.0^{4,11}]undecane: IR (film) 2975, 2945, 2880 cm^{-1}; ^{1}H NMR (CCl_4) δ 5.65 (1 H, d, J = 3 Hz), 3.7 (3 H, dd, J = 2, 4 Hz), 3.45 (1 H, dd, J = 2, 6 Hz), 3.35 (1 H, d, J = 4 Hz), 2.2 (2 H, m), 1.7 (2 H, m), 1.4 (2 H, m), 1.1 (3 H, t), 0.90 (3 H, d, J = 3 Hz); mass spectrum, m/e 182.131 (M^+, calcd for $C_{11}H_{18}O_2$ 182.131).

***trans,trans*-2,4-Hexadienyl Methyl Citraconate (29).** A suspension of 1.50 g (10.4 mmol) of **26**[11] in 10 mL of dry benzene was treated with 6 mL of oxalyl chloride. When the effervescence had decreased, the solution was warmed to 50 °C for 1 h. The excess oxalyl chloride and benzene were removed by evaporation in vacuo, a further quantity of benzene was added, and the solvent was again evaporated in vacuo to yield an oil. This was added to a solution of 0.93 g (9.5 mmol) of *trans,trans*-2,4-hexadienol (**19**) and 0.79 g (10 mmol) of pyridine in 10 mL of dry benzene at 0 °C under a nitrogen atmosphere. After being allowed to stand at room temperature overnight, the reaction mixture was diluted with ether and washed sequentially with saturated $CuSO_4$ solution, dilute H_2SO_4, water, saturated $NaHCO_3$ solution, water, and saturated NaCl solution. After the mixture was dried over $MgSO_4$, the solvent was evaporated in vacuo to give 1.8 g of a brown oil. Column chromatography (10% ethyl acetate–hexane) of this oil afforded 1.62 g (70%) of **29**: IR (film) 2990, 1745, 1665, 1450 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 6.5–5.5 (5 H, m), 5.8 (1 H, d, J = 2 Hz), 4.60 (2 H, m), 3.73 (3 H, s), 2.02 (3 H, d, J = 2 Hz), 1.78 (3 H, d, J = 7 Hz); mass spectrum, m/e 224.102 (M^+, calcd for $C_{12}H_{16}O_4$ 224.105).

Anal. Calcd for $C_{12}H_{16}O_4$: C, 64.26; H, 7.20. Found: C, 63.98; H, 7.03.

In addition, there was obtained from chromatography 180 mg (10%) of **39**: IR (film) 3000, 2950, 1745, 1450, 1170 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 6.80 (1 H, m), 6.5–5.5 (4 H, m), 4.70 (2 H, d, J = 6 Hz), 3.80 (3 H, s), 1.29 (3 H, d, J = 2 Hz), 1.78 (3 H, d, J = 6 Hz); mass spectrum, m/e 224.102 (M^+, calcd for $C_{12}H_{16}O_4$ 224.105).

1α-(Methoxycarbonyl)-3α-(hydroxymethyl)-1α,6β-dimethylcyclohex-4-ene-2β-carboxylic Acid γ-Lactone (30). The ester **29** (1.80 g, 9.00 mmol) and 50 mg of 2,6-di-*tert*-butyl-*p*-cresol were dissolved in 150 mL of xylene, and the solution was refluxed for 24 h under a nitrogen atmosphere. The solvent was removed by distillation in vacuo to leave a thick, brown oil which was purified by column chromatography on 100 g of silica gel. Elution with 300 mL of chloroform and then 300 mL of 2% methanol in chloroform, followed by evaporation of the solvent and crystallization of the residue from chloroform–cyclohexane, yielded 0.75 g (40%) of **30**: mp 94–96 °C; IR (film) 2980, 1775, 1460, 980 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 5.72 (2 H, s), 4.45 (1 H, dd, J = 7, 8 Hz), 3.8 (1 H, dd, J = 8, 11 Hz), 3.72 (3 H, s), 3.05 (2 H, m), 2.15 (1 H, d, J = 13 Hz), 1.54 (3 H, s), 1.05 (3 H, d, J = 7 Hz); mass spectrum, m/e 224.104 (M^+ for $C_{12}H_{16}O_4$ 224.105).

3α-(Hydroxymethyl)-1α,6α-dimethyl-1β-(methoxycarbonyl)cyclohex-4-ene-2α-carboxylic Acid γ-Lactone (31). To a solution of **30** (370 mg, 1.65 mmol) in 5 mL of methanol was added 0.6 mL of 5 M (3.3 mmol) sodium methoxide in methanol. After being stirred at room temperature overnight, the reaction mixture was diluted with 10% H_2SO_4 and extracted with ether. The ether extract was washed with saturated $NaHCO_3$ solution and saturated NaCl solution and dried over $MgSO_4$. Filtration and evaporation of the solvent, followed by crystallization of the residue from CH_2Cl_2–cyclohexane, afforded 247 mg (68%) of **31**: mp 89–91 °C; IR (film) 1775, 1735, 1240 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 5.8 (2 H, m), 4.45 (1 H, m), 3.9 (1 H, m), 3.76 (3 H, s), 3.3 (2 H, m), 2.9–2.6 (1 H, m), 1.27 (3 H, s), 0.97 (3 H, d, J = 7 Hz); mass spectrum, m/e 224.102 (M^+, calcd for $C_{12}H_{16}O_4$ 224.105).

***trans*-2,4-Pentadienyl Methyl Citraconate (32).** A solution of 1.50 g (10.4 mmol) of **26** in 10 mL of dry benzene was treated with 13 mL (32 mmol) of oxalyl chloride, and, after the effervescence had decreased, the mixture was warmed to 50 °C for 1 h. The excess oxalyl chloride and benzene were removed by evaporation, a further quantity of benzene was added, and the solvent was again removed by evaporation to provide a clear yellow oil. This was added to a solution of 0.80 g (9.5 mmol) of *trans*-2,4-pentadienol and 0.79 g (10 mmol) of pyridine in 10 mL of dry benzene which had been cooled to 0 °C under nitrogen. After the mixture warmed to room temperature and was allowed to stand overnight, the mixture was diluted with ether and washed with saturated $CuSO_4$ solution, dilute H_2SO_4, water, saturated $NaHCO_3$ solution, and saturated NaCl solution. After the mixture was dried over $MgSO_4$, the solvent was removed by evaporation to yield 1.90 g (90%) of **32**: IR (film) 2990, 1745, 1665, 1601, 1020, 960 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 6.9–6.2 (2 H, m), 5.9 (1 H, m), 5.4–5.1 (2 H, m), 4.65 (2 H, d, J = 6 Hz), 3.8 (3 H, s), 2.1 (3 H, d, J = 1 Hz); mass spectrum, m/e 210 (M^+).

Anal. Calcd for $C_{11}H_{14}O_4$: C, 62.83; H, 6.72. Found: C, 63.01; H, 6.60.

3α-(Hydroxymethyl)-1α-methyl-1β-(methoxycarbonyl)-cyclohex-4-ene-2β-carboxylic Acid γ-Lactone (33). A mixture of **32** (3.95 g, 20 mmol) and 100 mg of 2,6-di-*tert*-butyl-*p*-cresol was refluxed in 250 mL of xylene for 32 h under a nitrogen atmosphere. The solvent was evaporated in vacuo to yield 3.98 g of semicrystalline material. Chromatography on silica gel (5% ethyl acetate–hexane) afforded 0.40 g (10%) of **32** and 2.00 g (55%) of **33** which was crystallized from chloroform–cyclohexane: mp 96–98 °C; IR (film) 2980, 2920, 1775, 1735 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 5.78 (2 H, s), 4.48 (1 H, dd, J = 7, 8 Hz), 3.80 (1 H, dd, J = 7, 13 Hz), 3.73 (3 H, s), 3.1 (1 H, m), 2.95 (1 H, dt, J = 2, 19 Hz), 3.19 (1 H, d, J = 14 Hz), 2.1 (1 H, ddd, J = 2, 4, 19 Hz), 1.53 (3 H, s); mass spectrum, m/e 210.088 (M^+, calcd for $C_{11}H_{14}O_4$ 210.089).

3α-(Hydroxymethyl)-1α-methyl-1β-(methoxycarbonyl)-cyclohex-4-ene-2α-carboxylic Acid γ-Lactone (34). To a solution of **33** (210 mg, 1.0 mmol) in 5 mL of methanol was added 0.9 mL of 5 M (5 mmol) sodium methoxide. After being stirred for 40 h, the mixture was acidified with 10% H_2SO_4 and extracted with ether. The organic extract was washed with saturated $NaHCO_3$ solution and saturated NaCl solution and dried over $MgSO_4$. The solvent was evaporated to yield 120 mg (59%) of **34**: IR (film) 2950, 2900, 1775, 1735 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 6.0–5.8 (1 H, ddt, J = 2, 5, 10 Hz), 5.56 (1 H, br d, J = 10 Hz), 4.36 (1 H, dd, J = 5, 9 Hz), 4.05 (1 H, d, J = 9 Hz), 3.72 (3 H, s), 3.2 (2 H, m), 2.8–2.5 (1 H, m), 2.1 (1 H, dq, J = 2, 18 Hz), 1.6 (3 H, s); mass spectrum, m/e 210.088 (M^+, calcd for $C_{11}H_{14}O_4$ 210.089).

3α-(Hydroxymethyl)-1α,6α-dimethylcyclohex-4-ene-1β,2α-dicarboxylic Acid γ-Lactone (35). A solution of 2.4 g (10.7 mmol) of **30** in 50 mL of 2 N NaOH was refluxed for 3 h and then heated at 80 °C overnight. The mixture was acidified with 10% H_2SO_4 and heated for 0.5 h at 80 °C. After it had cooled, the mixture was extracted with ether, and the extract was dried over $MgSO_4$. Removal of the solvent and crystallization of the residue from ethyl acetate–hexane gave 2.20 g (97%) of **35** as a colorless solid: mp 144–147 °C; IR (Nujol) 1765, 1700 cm^{-1}; ^{1}H NMR (acetone-d_6) δ 5.7 (2 H, s), 4.5 (1 H, m), 3.9 (1 H, m), 3.4 (2 H, m), 2.8 (1 H, br q, J = 7 Hz), 1.25 (3 H, s), 1.0 (3 H, d, J = 7 Hz); mass spectrum, m/e 210.089 (M^+, calcd for $C_{11}H_{14}O_4$ 210.089).

3α-(Hydroxymethyl)-1α,6α-dimethylcyclohexane-1β,2α-dicarboxylic Acid γ-Lactone (36). Adams' catalyst (200 mg) was suspended in 100 mL of ethyl acetate and stirred under an atmosphere of hydrogen for 30 min, at which time it had taken up 50 mL of hydrogen. A solution of **35** (2.0 g, 9.5 mmol) in 15 mL of ethyl acetate was added with a syringe. Stirring was begun and, 1 equiv of hydrogen (230 mL) was taken up in 30 min. The mixture was filtered through Celite, and the solvent was evaporated to yield 2.02 g (100%) of **36** as a colorless solid which was recrysatllized from ethyl acetate–hexane: mp 196–198 °C; IR (Nujol) 1760, 1695 cm^{-1}; ^1H NMR ($CDCl_3$) δ 4.25 (1 H, dd, J = 5.5, 9 Hz), 3.95 (1 H, dd, J = 3, 9 Hz), 3.1 (1 H, d, J = 5.5 Hz), 2.8–2.6 (1 H, m) 2.4–2.2 (1 H, m), 1.8–1.4 (4 H, m), 1.55 (3 H, s), 0.97 (3 H, d, J = 7 Hz); mass spectrum, m/e 212.104 (M^+, calcd for $C_{11}H_{16}O_4$ 212.105).

1β,3α-(Dihydroxymethyl)-1α,6α-dimethylcyclohexane-2α-carboxylic Acid 2,3-γ-Lactone (37). To a solution of **36** (0.212 g, 1.0 mmol) in 5 mL of tetrahydrofuran at 0 °C was added 1.1 mL (1.1 mmol) of 1 M borane–tetrahydrofuran complex. The mixture was stirred at 0 °C for 8 h, diluted with an equal amount of ethyl acetate, washed with $NaHCO_3$ solution and saturated NaCl solution, and dried over $MgSO_4$. Evaporation of the filtrate afforded 146 mg of an oil, which was chromatographed on silica (ethyl acetate–hexane) to give 115 mg (60%) of colorless, oily **37**: IR (film) 3400, 2900, 1755 cm^{-1}; ^1H NMR ($CDCl_3$) δ 4.25 (1 H, m), 4.0 (1 H, m), 3.55 (2 H, dd, J = 11, 18 Hz), 3.4 (1 H, m, exchanged with D_2O), 2.8 (2 H, m), 1.8–1.4 (4 H, m), 0.95 (3 H, d, J = 6 Hz), 0.90 (3 H, s); mass spectrum, m/e 180.116 (M^+ – 18, calcd for $C_{11}H_{18}O_2$ 180.115).

Also isolated by chromatography was 20 mg (6%) of 1β-formyl-3α-(hydroxymethyl)-1α,6α-dimethylcyclohexane-2α-carboxylic acid γ-lactone: IR (film) 1760, 1772 cm^{-1}; ^1H NMR ($CDCl_3$) δ 9.3 (1 H, s), 4.3 (1 H, dd, J = 5, 9 Hz), 3.95 (1 H, dd, J = 2, 9 Hz), 2.90 (1 H, d, J = 7 Hz), 2.8–2.5 (1 H, m), 2.2–1.95 (1 H, m), 1.7–1.4 (4 H, m), 1.38 (3 H, s), 1.05 (3 H, d, J = 7 Hz); mass spectrum, m/e 196.110 (M^+, calcd for $C_{11}H_{16}O_3$ 196.110).

1α,6α-Dimethyl-3α-(hydroxymethyl)-1α-(iodomethyl)-cyclohexane-2α-carboxylic Acid γ-Lactone (38). A solution of **37** (198 mg, 1.0 mmol) and triphenylphosphite methiodide (675 mg, 1.5 mmol) was stirred in dimethylformamide under a nitrogen atmosphere for 1.5 h. The reaction was quenched with 1 mL of methanol and diluted with ether. The mixture was washed with three portions of water, 2 N NaOH, water, and saturated NaCl solution. After the mixture was dried over $MgSO_4$, the ethereal extract was filtered, and the solvent was evaporated to leave a colorless oil, which was mainly **38** and diphenyl methylphosphonate by TLC. Column chromatography of this mixture (10% ethyl acetate–hexane followed by 33% ethyl acetate–hexane) gave 80 mg (25%) of **38**: IR (film) 3400 (phenol contaminant), 2900, 1755 cm^{-1}; ^1H NMR ($CDCl_3$) δ 7.3, 6.9, 6.5 (phenol), 4.4–4.0 (2 H, m), 3.8 (1 H, d, J = 10 Hz), 3.3 (1 H, d, J = 10 Hz), 2.3 (1 H, m), 1.8–1.4 (4 H, m), 1.1 (3 H, s), 0.90 (3 H, d, J = 6 Hz); mass spectrum, m/e 308.020 (M^+, calcd for $C_{11}H_{17}O_2I$ 308.027).

3α-(Hydroxymethyl)-1β,6α-dimethyl-1α-(methoxycarbonyl)cyclohex-4-ene-2β-carboxylic Acid γ-Lactone (40). A solution of **39** (1.45 g, 6.5 mmol) and 100 mg of 2,6-di-*tert*-butyl-*p*-cresol in 250 mL of xylene was refluxed under nitrogen for 5 days. Evaporation of the solvent in vacuo afforded a brown solid. Recrystallization from ether–hexane afforded 401 mg (28%) of **40**: mp 126–128 °C; IR (Nujol) 1775, 1735, 1460, 1260 cm^{-1}; ^1H NMR ($CDCl_3$) δ 5.72 (2 H, br s), 4.48 (1 H, m), 3.95 (H, m), 3.76 (3 H, s), 2.8 (2 H, m), 2.3 (1 H, m), 1.28 (3 H, s), 0.95 (3 H, d, J = 6 Hz); mass spectrum, m/e 224.108 (M^+, calcd for $C_{12}H_{16}O_4$ 224.105).

Column chromatography of the mother liquor (30% ethyl acetate in hexane) afforded 576 mg (40%) of **39** and 328 mg (23%) of a thick oil which was shown by NMR analysis to be a 60:40 mixture of **40** and **31**, respectively.

Epimerization of 40 with Sodium Hydride. A solution of **40** (30 mg, 0.14 mmol) and 4 mg of a 50% suspension of NaH in mineral oil (0.08 mmol) was stirred for 17 h. The mixture was diluted with 0.1 N HCl and extracted with ether. The ethereal extract was washed with water and saturated NaCl solution and dried over $MgSO_4$. Evaporation of the solvent in vacuo afforded 32 mg (100%) of **24**, identical in all respects with the material prepared from **23**.

3α-(Hydroxymethyl)-1β,6α-dimethyl-1α,2β-bis(methoxycarbonyl)cyclohex-4-ene (41). A solution of **40** (40 mg, 0.18 mmol) in 2 mL of methanol containing 0.05 mmol of sodium methoxide was stirred for 24 h at room temperature. The mixture was acidified with acetic acid and concentrated in vacuo. The residue was triturated with ether, and the ethereal solution was filtered and evaporated. Preparative TLC (ethyl acetate–hexane, 1:1) of the residue gave 30 mg (66%) of **41**: IR (film) 3450 (br), 2950, 1740, 1735 cm^{-1}; ^1H NMR ($CDCl_3$) δ 5.8 (1 H, ddd, J = 3, 5, 10 Hz), 5.6 (1 H, d, J = 10 Hz), 3.76 (3 H, s), 3.70 (3 H, s), 2.95 (1 H, d, J = 12 Hz), 2.6–2.1 (3 H, 1 H was exchanged with D_2O), 1.52 (3 H, s), 0.92 (3 H, d, J = 7 Hz); mass spectrum, m/e 238.121 (M^+ – 18, calcd for $C_{13}H_{18}O_4$ 238.121).

3α-(Hydroxymethyl)-1β,6α-dimethyl-2β-(methoxycarbonyl)cyclohex-4-ene-1α-carbocyclic Acid δ-Lactone (42). A solution of **41** (30 mg, 0.12 mmol) in 20 mL of benzene containing 2 mg (0.01 mmol) of *p*-toluenesulfonic acid was refluxed for 7 h with a Dean–Stark trap. After cooling, the reaction mixture was diluted with ether and was washed with $NaHCO_3$ solution and saturated NaCl solution. After being dried over $MgSO_4$, the solution was filtered, and the solvent was evaporated. Preparative TLC (ethyl acetate–hexane, 30:70) of the residue afforded 14 mg (53%) of **42**: IR (Nujol) 1740, 1733 cm^{-1}; ^1H NMR ($CDCl_3$) δ 5.74 (2 H, s), 4.21 (1 H, dd, J = 3, 11 Hz), 4.15 (1 H, dd, J = 1, 11 Hz), 3.70 (3 H, s), 2.90 (2 H, br s), 2.76 (1 H, br q, J = 9 Hz), 1.50 (3 H, s), 1.04 (3 H, d, J = 7 Hz); mass spectrum, m/e 224.103 (M^+, calcd for $C_{12}H_{16}O_4$ 224.105).

***trans,trans*-2,4-Hexadienyl Methyl Mesaconate (45).** A solution of **43**[15] (3.00 g, 20.8 mmol) and 5 mL of oxalyl chloride in 20 mL of benzene was heated at 50 °C for 3 h. The mixture was concentrated by evaporation in vacuo, and benzene was added and again removed by evaporation to afford acid chloride **44** as a light brown oil. This was added to a solution of *trans,trans*-2,4-hexadienol (2.00 g, 20 mmol) and 2 mL (25 mmol) of pyridine in 20 mL of benzene at 0 °C. After being warmed to room temperature and stirred for 3 h, the reaction mixture was diluted with ether, and the ethereal layer was washed sequentially with saturated $NaHCO_3$ solution, water, and saturated NaCl solution. After being dried over $MgSO_4$, the ethereal extract was filtered, and the solvent was evaporated to afford a brown oil. Column chromatography (10% ethyl acetate–hexane) of this oil provided 3.30 g (71%) of **45**: IR (film) 1725, 1645 cm^{-1}; ^1H NMR ($CDCl_3$) δ 6.7 (1 H, m), 6.5–5.5 (4 H, m), 4.70 (2 H, d, J = 6 Hz), 3.77 (3 H, s), 2.20 (3 H, d, J = 2 Hz), 1.77 (3 H, d, J = 6 Hz); mass spectrum, m/e 224.103 (M^+, calcd for $C_{12}H_{16}O_4$ 224.105).

3α-(Hydroxymethyl)-2α,6α-dimethyl-1α-(methoxycarbonyl)cyclohex-4-ene-2β-carboxylic Acid γ-Lactone (46) and 3α-(Hydroxymethyl)-2β,6α-dimethyl-1β-(methoxycarbonyl)cyclohex-4-ene-2α-carboxylic Acid γ-Lactone (47). A solution of **45** (1.00 g, 4.48 mmol) and 2,6-di-*tert*-butyl-*p*-cresol (100 mg) in 200 mL of xylene was refluxed under a nitrogen atmosphere for 11 days. The solvent was removed in vacuo, and the brown oily residue was subjected to column chromatography (35% ethyl acetate–hexane). Along with 495 mg (50%) of starting material there was isolated 350 mg (35%, 70% based on **45** consumed) of **46**, which was crystallized from ethyl acetate–hexane: mp 122–125 °C; IR (film) 2950, 1780, 1740 cm^{-1}; ^1H NMR ($CDCl_3$) δ 5.73 (2 H, s), 4.40 (1 H, dd, J = 7, 8 Hz), 4.27 (1 H, dd, J = 8, 12 Hz); mass spectrum, m/e 224.104 (M^+, calcd for $C_{12}H_{16}O_4$ 224.105). Further elution gave 75 mg (7.5%, 15% based on **45** consumed) of **47** as an oil: ^1H NMR ($CDCl_3$) δ 5.70 (2 H, m), 4.48 (1 H, dd, J = 8, 8 Hz), 3.90 (1 H, dd, J = 8, 9 Hz), 3.70 (3 H, s), 2.95–2.50 (2 H, m), 2.40 (1 H, d, J = 10 Hz), 1.26 (3 H, s), 1.04 (3 H, d, J = 6 Hz); mass spectrum, m/e 224 (M^+).

3α-(Hydroxymethyl)-2α,6α-dimethyl-1α-(methoxycarbonyl)cyclohexane-2β-carboxylic Acid γ-Lactone (48). A solution of **46** (55 mg, 0.24 mmol) in 1 mL of methanol was added to a stirred suspension of 6 mg of Adams' catalyst in 3 mL of methanol under a hydrogen atmosphere. After cessation of hydrogen uptake, the mixture was filtered, and the solvent was evaporated to afford 58 mg (100%) of **48**: IR (film) 2950, 1780, 1740 cm^{-1}; ^1H NMR ($CDCl_3$) δ 4.48 (1 H, dd, J = 7, 9 Hz), 4.10 (1 H, dd, J = 9, 11 Hz), 3.37 (3 H, s), 2.69 (1 H, d, J = 6 Hz), 2.55–2.3 (1 H, m), 2.2–1.90 (1 H, m), 1.8–1.5 (4 H, m), 1.48 (3 H, s), 1.05 (3 H, d, J = 7 Hz); mass spectrum, m/e 226.119 (M^+, calcd for $C_{12}H_{18}O_4$ 226.121).

3α-(Hydroxymethyl)-2β,6α-dimethyl-1β-(methoxycarbonyl)cyclohexane-2α-carboxylic Acid γ-Lactone (49). A mixture of **47** (40 mg, 0.18 mmol) and 5 mg of Adams' catalyst in 3 mL of methanol was stirred under a hydrogen atmosphere until gas uptake had ceased. Filtration and evaporation of the solvent afforded 40 mg (98%) of **49**: IR (film) 2950, 1775, 1735 cm^{-1}; ^1H NMR ($CDCl_3$) δ 4.30 (1 H, d, J = 2 Hz), 4.20 (1 H, d, J = 4 Hz), 3.75 (3 H, s), 2.6–2.2 (2 H, m), 2.35 (1 H, d, J = 11 Hz), 2.1–1.6 (4 H, m), 1.33 (3 H, s), 0.98 (3 H, d, J = 6 Hz); mass spectrum, m/e 226.121 (M^+, calcd for $C_{12}H_{18}O_4$ 226.121).

***trans,trans*-2,4-Hexadienyl Tetrolate (51).** A solution of tetrolic acid (1.64 g, 20 mmol) and 4 mL of oxalyl chloride in 20 mL of dry benzene was heated to 50 °C for 1 h. Careful concentration in vacuo (20 °C bath) afforded a brown oil. This oil was added slowly to a solution of sorbyl alcohol (**19**; 1.96 g, 20 mmol) and pyridine (2 mL, 25 mmol) in 20 mL of benzene at 0 °C. After being stirred at room temperature for 4 h, the mixture was diluted with ether, and the ethereal layer was washed with saturated $CuSO_4$ solution, water, and saturated NaCl solution. The ethereal extracts were dried over $MgSO_4$, filtered, and evaporated to give an oil. Column chromatography (30% ethyl acetate–hexane) of this material afforded 1.0 g (50%) of sorbyl alcohol and 1.20 g (42%) of **51**: IR (film) 2950, 2250, 1710, 1250 cm^{-1}; ^1H NMR ($CDCl_3$) δ 6.4–5.4 (4 H, m), 4.65 (2 H, d, J = 6 Hz), 1.96 (3 H, s), 1.76 (3 H, d, J = 6 Hz); mass spectrum, m/e 164 (M^+).

3α-(Hydroxymethyl)-1,6α-dimethylcyclohexa-1,4-diene-carboxylic Acid γ-Lactone (52). A solution of 1.20 g (7.3 mmol) of **51** and 100 mg of 2,6-di-*tert*-butyl-*p*-cresol was refluxed for 24 h under a nitrogen atmosphere. After cooling, the solvent was removed in vacuo to yield 1.25 g (96%) of a light brown oil which was shown by TLC to be virtually pure **52**. Column chromatography (30% ethyl acetate–hexane) provided an analytically pure sample of **52**: IR (Nujol) 1745 cm^{-1}; ^1H NMR ($CDCl_3$) δ 6.72 (2 H, s), 4.55 (1 H, dd, J = 7, 7 Hz), 3.75 (1 H, dd, J = 7, 10 Hz), 3.7–3.3 (1 H, m), 3.15–2.75 (1 H, m), 2.21 (3 H, t, J = 1.5 Hz), 1.25 (3 H, d, J = 7 Hz); mass spectrum, m/e 162.069 ($M^+ - H_2$, calcd for $C_{10}H_{10}O_2$ 162.068).

3α-(Hydroxymethyl)-1,6α-dimethylcyclohex-1-ene-carboxylic Acid γ-Lactone (54). A suspension of 50 mg of platinum oxide in 25 mL of ethyl acetate was stirred under a hydrogen atmosphere until hydrogen uptake had stopped, and a solution of **52** (710 mg, 4.3 mmol) in 5 mL of ethyl acetate was added by syringe. Stirring was initiated, and the mixture took up 4.3 mmol of hydrogen over a period of 35 min. At this point, gas uptake slowed, and the reaction mixture was removed from the hydrogen atmosphere and filtered. Evaporation of the solvent in vacuo afforded 685 mg (95%) of **54**: IR (film) 2950, 2870, 1775, 1679 cm^{-1}; ^1H NMR ($CDCl_3$) δ 4.46 (1 H, dd, J = 8, 8 Hz), 3.77 (1 H, dd, J = 8, 10 Hz), 3.1–2.7 (1 H, m), 2.5–2.2 (1 H, m), 2.13 (3 H, d, J = 2 Hz), 2.0–1.6 (4 H, m), 1.12 (3 H, d, J = 7 Hz); mass spectrum, m/e 166.100 (M^+, calcd for $C_{10}H_{14}O_2$ 166.099).

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Facile Synthesis of Ethynylated Benzoic Acid Derivatives and Aromatic Compounds via Ethynyltrimethylsilane†

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The coupling reaction between an aromatic halide and ethynyltrimethylsilane under the catalysis of palladium(0) generated in situ, followed by treatment of the (trimethylsilyl)ethynyl product with potassium carbonate in methanol at ambient temperatures, provides a simple approach to various ethynylated benzoic acid derivatives and other aromatic compounds. The conditions for the removal of the trimethylsilyl group were very mild, so that base-sensitive functionalities on the aromatic moiety could be tolerated.

Classical methods[1] for the synthesis of terminal arylacetylenes in general involve manipulation of preformed, two-carbon side chains and include methods such as the Vilsmeier method,[2-4] the halogenation–dehydrohalogenation sequence of vinyl aromatics[5] and ketones,[6,7] and the dehydrohalogenation of β,β-dihalo olefins.[8,9] Other methods that deviate from the classical approach have utilized the decomposition of preconstructed heterocyles.[10,11] A recent innovation in the synthesis of arylacetylenic compounds has been the use of protecting groups.[12] Acetylene, protected at one end, can be introduced onto an aromatic nucleus via coupling at the free end. Subsequent removal of the protecting group generates a terminal arylacetylene.

The widely accepted procedure for the introduction of an acetylenic substituent onto an aromatic nucleus is the Stephens–Castro coupling reaction[13-15] between an aryl

† During the preparation of this manuscript, a report on a similar method appeared.[52]

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