280.0 (33.1%), 139.1 (42.9%), 83.2 (92.5%).

l-Menthyl 6-(2,6-dideoxy-β-arabinohexapyranosyl)-9,10-dihydro-1,5-dihydroxy-β-methyl-9,10-dioxo-2-anthracenebutanonate 42 and 43. Reaction of *l*-menthyl ester bromomagnesium salt **41** with ketone **37** under the above reaction conditions afforded *epi*-vineomycinone B_2 *l*-menthyl ester **43** in fraction 1, vineomycinone B_2 *l*-menthyl ester **42** in fraction 3, and two other isomers in fraction 2. The IR, ^1H NMR, and mass spectra of *l*-menthyl ester **42** were identical with those of *d*-menthyl ester **47**, and the corresponding spectrum of *l*-menthyl ester **43** was identical with that of *d*-menthyl ester **48**.

Vineomycinone B_2 Methyl Ester 2b. A mixture of *l*-menthyl ester **42** (8.0 mg, 0.013 mmol), anhydrous K_2CO_3 (100 mg), and MeOH (0.5 mL) in a stoppered flask was heated in a 70 °C bath for 22 h. Ice–water (5 mL) was added to the mixture, and the solution was carefully acidified with 1 N H_2SO_4 until the pH of the solution was 3. The acidified solution was extracted with CH_2Cl_2 (40 mL × 2). The combined organic layers were dried over Na_2SO_4 and then CH_2N_2/Et_2O (1.4 mg, 0.5 mmol) solution was added at 0 °C. After stirring for 1 h the solution was concentrated in vacuo. The residue (6.0 mg) was purified by HPLC (μ-Bondapak–CN/ethyl acetate–hexane 1:3/2 mL/min) to afford vineomycinone B_2 methyl ester **2b** (0.8 mg, 0.0016 mmol) and recovered *l*-menthyl ester **42** (1.0 mg, 0.0016 mmol): IR ($CDCl_3$) 1715, 1620, 1600, 1255 cm^{-1}; ^1H NMR ($CDCl_3$, 500 MHz) δ 13.23 (s, 1 H), 13.11 (s, 1 H), 7.93 (d, J = 7.9 Hz, 1 H), 7.87 (d, J = 8.1 Hz, 1 H), 7.82 (d, J = 7.9 Hz, 1 H), 7.71 (d, J = 8.1 Hz, 1 H), 4.96 (dd, J = 10.5, 1.2 Hz, 1 H), 3.88 (ddd, J = 11.8, 9.0, 4.2 Hz, 1 H), 3.72 (s, 3 H), 3.55 (dq, J = 8.9, 6.1 Hz, 1 H), 3.23 (dd, J = 9.0, 8.9 Hz, 1 H), 3.12 (d, J = 13.5 Hz, 1 H), 3.04 (d, J = 13.5 Hz, 1 H), 2.58 (d, J = 14 Hz, 1 H), 2.57 (d, J = 14 Hz, 1 H), 2.55 (ddd, J = 12.0, 4.2, 1.2 Hz, 1 H), 1.50 (ddd, J = 12.0, 11.8, 10.5 Hz, 1 H), 1.43 (d, J = 6.1 Hz, 3 H), 1.32 (s, 3 H); MS (20 eV), m/e 485.1 ($M^+ - 15$), 384.1 (35%), 281.1 (18.9%), 280.0 (50.9%), 117.1 (100%); $[\alpha]_D$ +109.1° (c 0.00066, $CDCl_3$), mp 183–184 °C.

***epi*-Vineomycinone B_2 Methyl Ester 51.** Treatment of *d*-menthyl ester **48** with potassium carbonate in methanol under the above reaction conditions afforded *epi*-vineomycinone B_2 methyl ester **51**: IR ($CDCl_3$) 1713, 1640, 1450, 1250 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 13.23 (s, 1 H), 13.11 (s, 1 H), 7.93 (d, J = 7.9 Hz, 1 H), 7.87 (d, J = 8.1 Hz, 1 H), 7.82 (d, J = 7.9 Hz, 1 H), 7.71 (d, J = 8.1 Hz, 1 H), 4.96 (dd, J = 10.5, 1.2 Hz, 1 H), 3.88 (ddd, J = 11.8, 9.0, 4.2 Hz, 1 H), 3.72 (s, 3 H), 3.55 (dq, J = 8.0, 6.1 Hz, 1 H), 3.23 (dd, J = 9.0, 8.9 Hz, 1 H), 3.10 (d, J = 13.5 Hz, 1 H), 3.06 (d, J = 13.5 Hz, 1 H), 2.58 (d, J = 14 Hz, 1 H), 2.57 (d, J = 14 Hz, 1 H), 2.55 (ddd, J = 12.0, 4.2, 1.2 Hz, 1 H), 1.50 (ddd, J = 12.0, 11.8, 10.5 Hz, 1 H), 1.43 (d, J = 6.1 Hz, 3 H), 1.32 (s, 3 H).

Acknowledgment. This work was supported by PHS Grant CA28824. NMR spectra were obtained through the auspices of the Northeast Regional NSF/NMR Facility at Yale University, which was supported by NSF Chemistry Division Grant CHE 7916210. We also thank Prof. N. Ikekawa and Prof. M. Ohno for providing us with samples of vineomycin B_2 and aquayamycin for purposes of preparing aglycon **3**.

Registry No. 2b, 89495-27-2; **9**, 89414-68-6; **10**, 88083-96-9; **11**, 94110-19-7; **12**, 94110-20-0; **13**, 94110-21-1; **14**, 94110-22-2; **15**, 94110-23-3; **18**, 94110-24-4; **19**, 922-00-9; **19a**, 94110-25-5; **20** (isomer 1), 94110-26-6; **20** (isomer 2), 94110-27-7; **21**, 94110-28-8; **22** (isomer 1), 94110-29-9; **22** (isomer 2), 94110-30-2; **23**, 615-93-0; **25**, 94110-31-3; **26**, 89414-71-1; **27**, 94110-32-4; **29**, 94110-33-5; **30**, 94110-34-6; **31**, 94110-35-7; **32**, 94110-36-8; **33**, 94110-37-9; **34**, 94110-38-0; **35**, 94110-39-1; **36**, 94160-45-9; **37**, 94160-46-0; **38** (diastereomer 1), 94160-47-1; **38** (diastereomer 2), 94160-48-2; **39** (diastereomer 1), 94160-49-3; **39** (diastereomer 2), 94160-50-6; **41**, 55284-67-8; **42**, 89414-79-9; **43**, 89495-29-4; **44**, 94160-51-7; **45**, 94160-52-8; **47**, 94160-53-9; **48**, 94160-54-0; **49**, 89495-31-8; **50**, 89495-30-7; **51**, 94233-39-3; 3-penten-2-one, 625-33-2; triethylsilyl chloride, 994-30-9; *o*-methoxybenzaldehyde, 135-02-4; benzaldehyde, 100-52-7; methyl crotonate, 18707-60-3; 2-methyl-3-iodopropene, 3756-30-7; methyl acetate, 79-20-9; *d*-menthyl acetate, 5157-89-1; juglone, 481-39-0.

Supplementary Material Available: Full experimental procedures for the alternate route to compound **18** via juglone (3 pages). Ordering information given on any current masthead page.

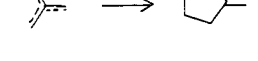
Palladium-Mediated Cycloaddition Approach to Loganin Aglucon

Barry M. Trost* and Thomas N. Nanninga

Contribution from the McElvain Laboratories of Organic Chemistry, Department of Chemistry, University of Wisconsin, Madison, Wisconsin 53706. *Received May 7, 1984*

Abstract: The concept of a cycloaddition approach to the most illustrious member of the iridoid family, loganin aglucon, is outlined. Palladium-catalyzed cycloaddition of a substituted 2-[(trimethylsilyl)methyl]allyl carboxylate to cyclopentenone creates the proper substitution pattern of loganin. Conversion of the [(2,4,6-triisopropylphenyl)sulfonyl]hydrazone of the adduct to its corresponding vinyllithium and carboxylation are followed by deconjugation of the enoate. The crucial resultant bicyclo[3.3.0]octene suffers double cleavage in a single step to create the keto form of loganin alucon in five steps from cyclopentenone. The efficiency of this approach demonstrates the utility of a cycloaddition strategy. The questions associated with the use of substituted TMM units in complex synthesis are probed.

The explosive growth in the number of natural products containing five-membered rings provided great stimulation to develop cyclopentannulation methods.[1] In considering the types of strategy that would be particularly useful, a cycloaddition approach seemed most appealing. Among the types of cycloadditions that could be considered, the addition of trimethylenemethane offers the opportunity of forming a five-membered ring and simultaneously introducing the exocyclic methylene group as a useful functionality for further structural elaboration (see eq 1).[1c,2-10] Metal-catalyzed



(1)

(1) (a) For an excellent review, see: Paquette, L. A. *Top. Curr. Chem.* **1984**, *119*, 1. (b) Also, see: Trost, B. M. *Chem. Soc. Rev.* **1982**, *11*, 141. (c) For some leading references, see: Trost, B. M.; Chan, D. M. T. *J. Am. Chem. Soc.* **1983**, *105*, 2315.

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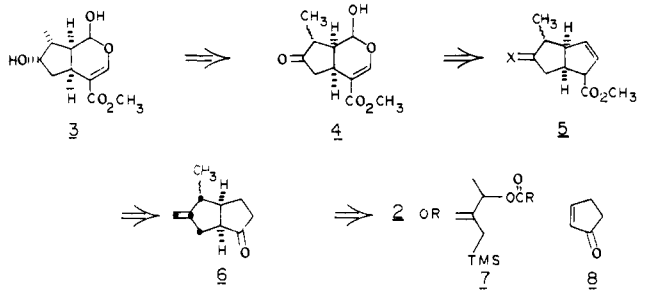
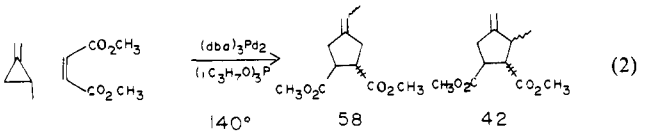
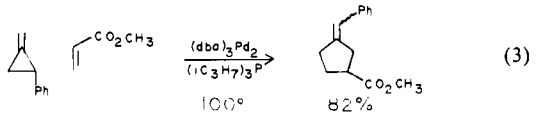
Scheme I. Retrosynthetic Analysis of Loganin Aglycon vis Cycloaddition Strategy



cooligomerizations of methylenecyclopropanes offer one approach for the structural transformation represented in eq 1.[9,10] However, the effect of substitution on the regioselectivity in these reactions either showed little selectivity (eq 2)[11] or preferentially placed the



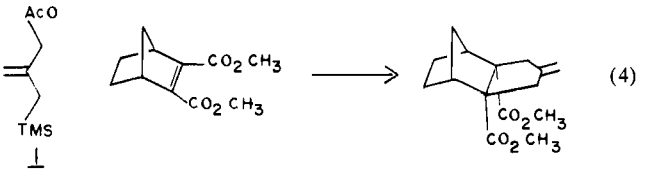
(2)



(3)

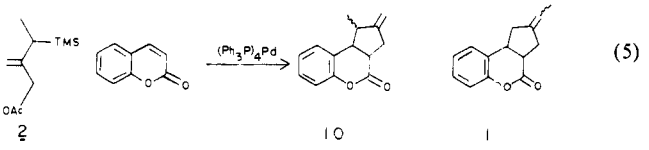
substituent on the carbon of the exocyclic double bond (see eq 3).[12] The low selectivity of the former reaction and eventual loss of the substituent in the latter case when the exocyclic double bond is used as a synthon for a carbonyl group makes such substituted systems of less synthetic interest.[13] It should also be noted that these "codimerizations" do not necessarily pass through a (trimethylenemethane)palladium complex as an intermediate.

We have developed the bifunctional conjunctive reagent **1** as a source of trimethylenemethane in cycloadditions (eq 4).[1c,2,14]



(4)

A key question is the effect of substituents on the reaction. In contrast to the methylenecyclopropane reaction, good regioselectivity was observed with a methyl-substituted derivative (eq 5).[14a]



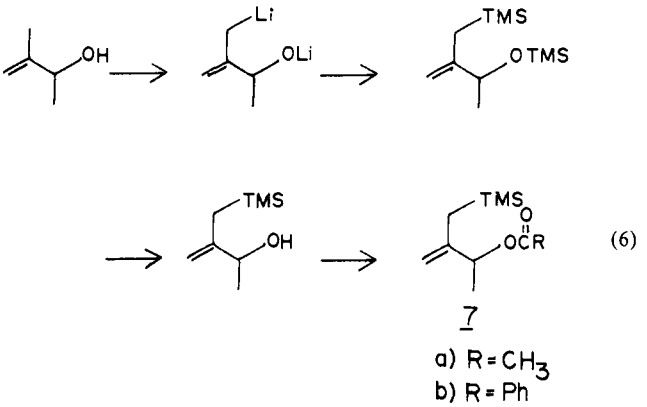
(5)

Among the most important simple cyclopentanoid terpenes are the iridoids. One member of this class, loganin, is a particularly pivotal compound due to its role as a biosynthetic intermediate in natural products chemistry[15] and its use in folk medicine.[16] As an illustrious member of the iridoid family, the utility of a cycloaddition strategy toward iridoids, in particular, and more complex natural products, in general, would be established if an efficient approach to the aglucon of loganin (**3**) could be found (Scheme I).

In almost all of the syntheses of loganin extant,[17] the 6-keto derivative as in **4** was the precursor. As such, the stereochemistry of the methyl group at C(7) becomes unimportant since base-catalyzed equilibration permits creation of the correct stereoisomer. The well-established recognition of a cyclopentene as a precursor to the hydroxydihydropyranyl ring[17] simplifies the problem to **5** (X = 0). Simultaneously, we can replace the carbonyl group by an exocyclic methylene as in **5** (X = CH_2) since (1) the exocyclic methylene group can serve as a protected form of the more reactive carbonyl group and (2) the unmasking of the carbonyl group can occur simultaneously with the cleavage of the cyclopentene.

The presence of a β,γ-unsaturated ester in **5** translates into a saturated ketone as in **6** since (1) the β,γ-isomer can arise from deconjugation of an α,β-isomer and (2) the conversion of a ketone to an α,β-unsaturated ester is well precedented.[18] The important deduction is that **6** constitutes an excellent precursor of loganin. A substituted trimethylenemethane unit stands out in **6** (the carbons are identified by a dot). Therefore, such a molecule should arise by exactly the type of cycloaddition we have developed from cyclopentenone (**8**) and either **2** or **7**. Furthermore, the regioselectivity should correspond to that required. In this paper, we record the first use of this cycloaddition approach with a substituted TMM conjunctive reagent in a more complex natural products synthesis.

Preparation of TMM Precursor. The requisite TMM precursors were prepared by the dianion route according to eq 6.[14a,19]



(6)

A substantial improvement in the metalation and silylation from 43% to 67% arose when the concentration of the starting alcohol was increased to nearly 1 M and no THF was added.

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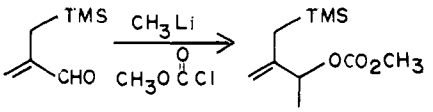
Table I. Variation in Cycloaddition of **7** to **8**[a]

entry	substrate	ratio 8:7	catalyst generation method	temp, °C	time, h	yield, %
1	acetate	1.5	1	66	18	45[c]
2	acetate	9	2[d]	66	16	16
3	acetate	2.2	2[e]	66	16	47
4	acetate	2.0	2[d]	66	32	44
5	acetate	1.5	2[d]	65	16	47
6	acetate	1.4	2[d,m]	85	2.5	48
7	acetate	2.4	4[f]	66	16	41[c]
8	benzoate	2.0	4	66	1.0	43[g]
9	benzoate	2.0	4	50	18	47[h]
10	benzoate	1.7	2[d]	75	6[i]	30
11	benzoate	1.7	2[d,k]	66	5	22
12	carbonate	2.8	2[e]	66	3	32
13	acetate	1.6	1[l]	66	2	50[c]

[a] All reactions were performed in THF using 2–5 mol % $Pd(OAc)_2$ and 14–21 mol % of triisopropyl phosphite as ligand unless otherwise noted. [b] See text. [c] Yield determined by VPC comparison to an isolated run. [d] n-C_4H_9Li used as reductant. [e] DIBAL-H used as reductant. [f] Ligands used relative to Pd were 2 dppp and 3 Ph_3P. [g] In addition, 2% of an uncyclized cyclopentane and 25% of protodesilylated starting material was detected. [h] In addition, 8% of an uncyclized cyclopentane and 13% of protodesilylated starting material was detected. [i] Initially 14% of the starting benzoate was combined with **8** and the remainder added slowly over the stated time. [j] In addition, 40% of protodesilylated starting material was detected. [k] Ligand used was dppb. [l] (+)DIOP was used as ligand. [m] Dioxane used as a solvent.

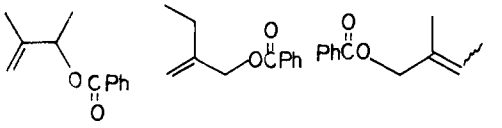
The carbonate was synthesized from our 2-[(trimethylsilyl)-methyl]acrolein,[20] a conjunctive reagent we developed for the facile preparation of substituted TMM precursors. In this case, the alkoxide intermediate generated from methyllithium addition was directly carbomethoxylated to give **7c** in 55% yield.



7c

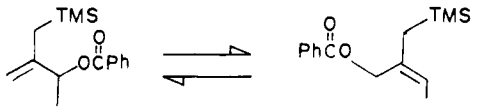
Cycloaddition. A detailed study of the cycloaddition of **7** to cyclopentenone was undertaken. For the cycloadditions, the quality of the catalyst can be quite important. While our standard catalyst $(PPh_3)_4Pd$ works well as long as it is pure, it is difficult to assess its purity quantitatively. Catalyst that has been stored for months that shows little, if any, visible decay can lead to lower yields in the cycloaddition. To enhance the convenience of the cycloaddition methodology, we turned to in situ preparations of the Pd(0) catalysts using one of four techniques: (1) refluxing a THF or toluene solution of $Pd(OAc)_2$ and 1-hexene in the presence of ~6 equiv of ligand, (2) addition of 2 equiv of DIBAL-H or n-butyllithium to a homogeneous THF or toluene solution of $Pd(OAc)_2$ and ~6 equiv of ligand, (3) addition of 1 equiv of DIBAL-H or 1 equiv of n-butyllithium in the same fashion as (2), and (4) initial reduction of $Pd(OAc)_2$ in the presence of ligand with 1-hexene followed by the addition of 1 equiv of n-butyllithium (see Table I). In general for cycloadditions, triisopropyl phosphite appears to be the preferred ligand, although in this particular case, the yields did not differ much from the case of triphenylphosphine. Other ligands which include tri-o-tolylphosphine, triisopropylphosphine, tris(dimethylamino)phosphine, triphenyl phosphite, and tri-o-tolyl phosphite led to substantially inferior yields or no reaction at all. Bidentate ligands like dppp, dppb, and (+)DIOP showed no advantage over triphenylphosphine.

A more interesting dependence on the nature of the leaving group was observed. Initially, attention focused on the nature of the major side reaction. If protodesilylation was the culprit, we would more easily isolate the byproduct from **7** if a larger ester was employed. Indeed, the benzoate of **7** led to identification of the three allyl benzoates **9–11** in a 2:1:1.3 ratio, respectively.



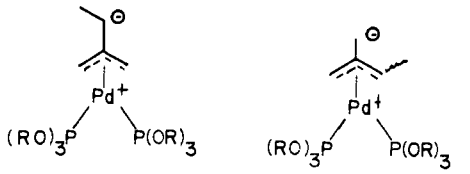
9 **10** **11**

While **9** can arise by a direct protodesilylation, neither **10** nor **11** can. The source of the benzoate migration can be equilibration between **7** (R = Ph) and **12** catalyzed by palladium and prior to



7 **12**

protodesilylation, but such a process would only account for **11**. It would appear that only protonation of our TMM–Pd intermediate **13** or **14** followed by capture of the resultant (π-allyl)-

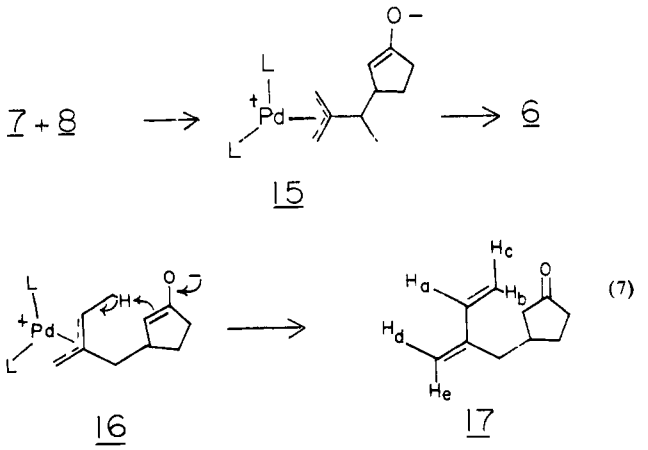


13 **14**

palladium cationic complex fully rationalizes all the products. Nevertheless, the ratio of **9**:**10**:**11** does not agree with this pathway as the exclusive one since **10** not **9** would have been predicted to be the major product.

The amount of protodesilylation did show some dependence on the temperature which could be partially pursued by use of the more reactive benzoate. Dropping the temperature from 66 to 50 °C led to a reduction of protodesilylation from 25% to 13%. Nevertheless, there was an increase in the formation of an additional side product (vide infra). Protodesilylation became a major problem when **7** was added slowly to the trap. The reason for this observation is not clear at present. A trace impurity in the cyclopentenone, however, cannot be ruled out. Although labeling studies were not performed, our earlier work[2] and related studies[21] suggest cyclopentenone as the source of protodesilylation.

A very small amount of an additional byproduct was detected in the NMR spectrum of the reaction mixture. Most diagnostic were the absorptions in the olefinic region which appeared at δ 6.31 (dd, J = 18.3, 10.3 Hz, 1 H, H_a), 5.23 (d, J = 18.3 Hz, 1 H, H_b), 5.09 (d, J = 10.3 Hz, 1 H, H_c), 5.06 (bs, 1 H, H_d), 5.00 (bs, 1 H, H_e)—a pattern in perfect accord with a 2-substituted butadiene as in **17**. This product increases as the temperature



15 **16** **17**

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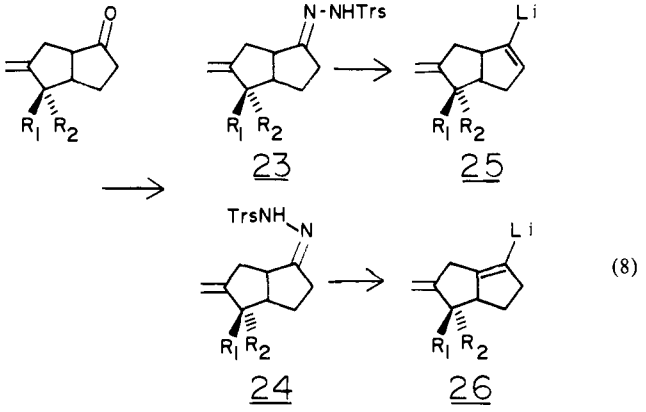


(8)

Table II. Stereoisomers of [(2,4,6-Triisopropylphenyl)sulfonyl]hydrazones

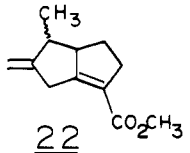
R_1	R_2	% **23**	% **24**
H	CH_3	60	40
CH_3	H	80	20

Table III. Regioselectivity of [(2,4,6-Triisopropylphenyl)sulfonyl]hydrazone Decomposition

base	solvent	total yield, %	% yield **22**	% yield **19**
n-C_4H_9Li	TMEDA/hexane	66	20	53
s-C_4H_9Li	TMEDA/hexane	63	20	50
t-C_4H_9Li	TMEDA/hexane	20	20	16
n-C_4H_9Li	DME	70	25	52
s-C_4H_9Li	DME	46	5	44
t-C_4H_9Li	DME	30	0	30

of the reaction decreases. For this reason, higher temperatures which limit its formation to ≤2% are preferred. Such a product can nicely be rationalized as arising from a competition between the highly favored addition via **15** and a small amount proceeding through **16**. In this case, besides cyclization to give an isomeric bicyclo[3.3.0]octanone, an intramolecular proton transfer can compete to give **17**. By using higher temperatures, we assure equilibration to the thermodynamically most stable TMM intermediate and thus the highest regioselectivity.

Final Steps. Scheme II outlines the conversion of the cycloadduct **6** to loganin aglucon. The first problem involves the conversion of the ketone to the unsaturated ester **19**. The Shapiro modification of the Bamford–Stevens reaction was envisioned to be the most direct way.[18b,22] The [(2,4,6-triisopropylphenyl)-sulfonyl]hydrazone **18** was prepared in acetonitrile by using a catalytic amount of 45% fluoroboric acid at room temperature. Subjecting the crude hydrazone to *n*-butyllithium in TMEDA/hexane formed a deep red solution which when quenched with carbon dioxide, acidified, and esterified with diazomethane gave the desired enoate **19**, but an isomeric byproduct tentatively identified as **22** was also isolated. The anticipation that the anti



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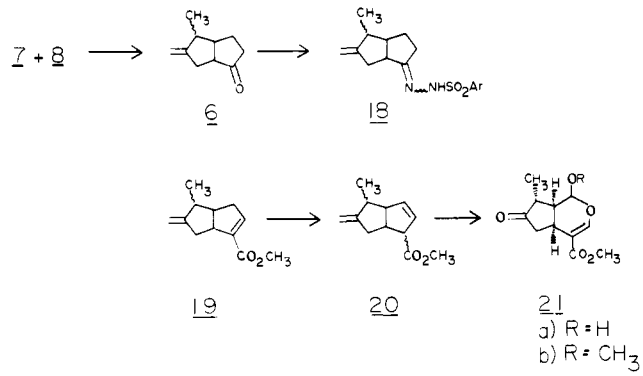
isomer of the trisylhydrazone should dominate, that a methylene proton should be much more acidic than a methine proton and that a $\Delta^{1,2}$ double bond in a bicyclo[3.3.0]octyl system should be much less stable than a $\Delta^{2,3}$ olefin made this result surprising. In order to determine the source of this isomeric product, we examined the structure of the trisylhydrazone since the NMR spectrum of the crude material suggested it may be an isomeric mixture. This analysis was complicated by the fact that the starting material was a mixture isomeric at the carbon bearing the methyl group. Thus, the isomeric ketones were separated and converted to their trisylhydrazone as shown in eq 8 and Table II. If we assume that the geometry of the trisylhydrazone determines the regioselectivity of the deprotonation,[22] the presence of **24** would correlate with the generation of **26** and consequently **22**. Such a result is quite surprising considering the known difficulty in deprotonating at a tertiary position in such reactions[22,23] and the claim that the directional influence of the geometry of the hydrazone is overwhelmed under these conditions.[18b]

Scheme II. Synthesis of Loganin Aglycon



Ascribing the regioselectivity to the formation of the geometric trisylhydrazones, we attempted to improve the ratio in their formation and to equilibrate, but to no avail. Since it is claimed that this geometric dependence on generation of the regioisomers can be overwhelmed by variation of experimental conditions, we examined changing the steric demands of the base and changing solvent (see Table III). As can be seen, use of the sterically more hindered *sec*- or *tert*-butyllithium in DME does minimize or eliminate this problem but the lower total yield still leads to a diminished yield of the desired enoate **19**.

Deconjugation of **19** proceeded uneventfully to give **20** with LDA. It is interesting to note that treating the mixture of **19** and **22** with lithium hexamethyldisilazane followed by acid deconjugates only **22**! The enhanced kinetic acidity of **22** due to the presence of the δ,ε double bond accounts for this observation.

The unmasking of **20** to the keto precursor of loganin was envisioned to occur in one step. Using the typical ozonolysis conditions[17,24] followed by dimethyl sulfide gave only traces of the desired product. Changing solvents and temperature did not change this result. On the contrary, ozonolysis in methylene chloride followed by *reduction with zinc dust* in acetic acid gave the crude hydroxyacetal **21a** whose NMR spectrum indicated it to be quite pure in approximately 50% yield. In this case, a stronger reducing agent than dimethyl sulfide appears to be required. Acetal formation in methanol gave the *O*-methyl ether of loganin aglycon. Epimerization accompanied either of the steps since only a single epimer at the methyl-bearing carbon was obtained. The methyl ether **21b** was identical with an authentic sample prepared from degradation of natural loganin. Since this ketone has been converted to loganin by reduction and hydroxyl inversion,[17] this five-step synthesis of **21a** completes our synthesis of loganin.

Conclusions

Cycloadditions represent a critical approach to six-membered ring compounds, but the lack of such methodology for five-membered ring carbocycles precluded strategy of this type for such

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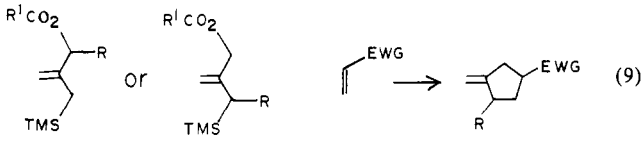
natural products. Of the iridoids, loganin aglucon represents a "classical" challenge. The success of the approach in which the keto form of loganin aglucon is available in only five steps from cyclopent-2-enone speaks to the utility of cycloaddition methodology. Of the cycloaddition type reactions, use of a TMM system has particular virtue due to the presence of the exocyclic methylene group. As this example demonstrates, it serves as a convenient synthon for a carbonyl group. Thus, elaboration of the carbonyl group derived from the cycloaddition acceptor can be easily accomplished prior to the unmasking of this hidden carbonyl group.

The high regioselectivity (>95%) associated with the cycloaddition of substituted TMM units in which the substituent ends up at a structurally useful position is also an important component of this approach. At present, this cycloaddition can be generalized as in eq 9. On the other hand, it is interesting to note that, at



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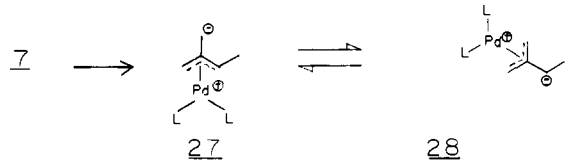
lower cycloaddition temperatures, increasing amounts of a product derived from a different regioselectivity of attack occurred. The kinetic formation of **27** from **7** requires an isomerization to **28**



prior to cycloaddition to account for our major product.[2] The independence of the regiochemistry of the products at elevated temperatures from the structure of the starting material and the predicted greater stability of **28**[25] support this conclusion. Perhaps, at the lower temperatures, cycloaddition with **27** begins to compete more effectively with isomerization. While we have been able to clearly detect such kinetic effects with other types of reactions of our TMM complexes,[2] this example represents the first indication that this equilibration may also be detected by our cycloaddition reactions. Clearly, we are only at the beginning of understanding and utilizing this new approach in synthesis.

The studies also led to the development of tetrakis(triisopropyl phosphite)palladium, generated in situ from palladium acetate by reduction with 1-hexene, DIBAL-H, or, preferably, *n*-butyllithium, as the preferred catalyst for all our cycloadditions. We attribute its better reactivity to the presence of the more electronegative phosphite ligands. In these reactions, initial coordination of the Pd(0) to the electron-rich olefins of the TMM precursor is required. Increasing the acceptor properties of the palladium should facilitate this coordination. Concurrently, the (π-allyl)palladium complex formed should also become more electrophilic—a fact which should facilitate the desilylation to generate the TMM–palladium intermediate. The enhanced electron deficiency associated with (π-allyl)palladium cationic complexes bearing more electronegative ligands should also be effective in improving (π-allyl)palladium reactions involving nucleophilic attack on the allyl unit in general—a prediction which appears to have merit from some of our preliminary studies in this direction.

Experimental Section

Preparation of 3-[(Trimethylsilyl)methyl]-3-buten-2-ol. A 2-L 3-necked flask fitted with a mechanical stirrer, a graduated addition funnel and a condensor was charged with *n*-butyllithium (1.75 M, 363 mL, 634 mmol) and evacuated until all of the hexane was removed. To the resultant oil was added 270 mL of ether, and 109 mL of TMEDA (729 mmol) at 0 °C. 3-Methyl-3-buten-2-ol (21.0 g, 244 mmol) was then added dropwise over 20 min at 0 °C and the reaction was stirred for 2 h at 0 °C during which time much gum formed. The reaction vessel was then cooled to −70 °C and chlorotrimethylsilane (200 mL, 1592 mmol) was added as fast as the very vigorous reaction would allow (ca. 10 min), and the resultant mixture stirred for 30 min until all the gum dissolved. The mixture was then partitioned between 1 L of ether and 1 L of saturated sodium bicarbonate. The organic phase was washed with 1 L water, saturated copper sulfate (2 × 1 L), and water (1 L) and dried over potassium carbonate. After concentration via atmospheric distillation the residue was distilled to give 37 g (67%) of 2-(trimethylsiloxy)-3-[(trimethylsilyl)methyl]-3-butene [bp 67–69 °C (4 mmHg)] along with 4.7 g (6%) of 2-(trimethylsiloxy)-3-[(trimethylsilyl)methyl]-4-(trimethylsilyl)-3-butene [bp 85 °C (1 mmHg)]. The bis(silyl) compound was hydrolyzed as before[19] to give the title compound.[14a]

Preparation of 3-[(Trimethylsilyl)methyl]-3-buten-2-yl Methyl Carbonate (7c). 2-([Trimethylsilyl)methyl]propenal (2.54 g, 17.9 mmol) in 3 mL of ether was added dropwise to a −78 °C solution of 20 mL of ether and 17.9 mL of methyllithium (low halide, 1.5 M, 26.8 mmol) over 10 min. The reaction was allowed to come to 0 °C over 1 h, stirred at 0 °C for 30 min, and then recooled to −78 °C at which point 5 mL (64 mmol) of methyl chloroformate was added. After allowing the reaction to come to room temperature and stirring for 30 min, the flask was placed in a −6 °C freezer for 3 days. The reaction was then partitioned between saturated sodium bicarbonate and ether (100 mL each), and the organic layer was dried ($MgSO_4$), concentrated in vacuo, chromatographed (flash chromatography, 5% ether/pentane), and distilled [bp 50 °C (1 mmHg, Kugelrohr)] to yield 2.14 g (55%) of pure compound: ^{1}H NMR (270 MHz) 5.00 (q, J = 7.0 Hz, 1 H), 4.90 (s, 1 H), 4.65 (s, 1 H), 3.73 (s, 3 H), 1.49 (AB, J = 14 Hz, $\Delta\mu$ = 0.15, 2 H), 1.33 (d, J = 7.0 Hz, 3 H); ^{13}C NMR (15.4 MHz) 154.8, 145.7, 108.4, 77.2, 54.4, 22.5, 19.5, 1.2; IR ($CDCl_3$) 1750, 1642, 1445 cm^{-1}; MS 216 (0.0), 95 (20), 89 (51), 79 (26), 73 (100), 59 (39). Anal. Calcd for $C_{10}H_{20}O_3Si$: 216.1182. Found: 216.1181.

General Procedure for Cycloaddition Reaction. A 10-mL round-bottom flask is charged with palladium acetate (2–4%) and ligand (5–7 equiv with respect to Pd) (if solid) in a glovebag and fitted with a septum. Solvent (and the ligand if liquid) is then added. After a homogeneous solution is obtained (heating may be necessary if solid ligands are used), the reductant is added at room temperature. After stirring at room temperature for 10 min, the acceptor and the substrate are added and the flask is heated until completion as monitored by TLC. The reaction is then concentrated by distillation and chromatographed (flash chromatography, 10:1, pentane/ether). The product was distilled using a bulb-to-bulb apparatus at 65 °C (2 mmHg). Table IV summarizes the experimental details.

For a preparative run, 2.5 mL of THF and 0.25 mL (1.01 mmol) of triisopropyl phosphite was added to 38.1 mg (0.17 mmol) of palladium acetate. After complete solution has occurred, *n*-butyllithium (1.7 M, 0.20 mL, 0.34 mmol) was added via syringe, and the solution allowed to stir for 5 min. The pale yellow solution was then charged with 2-cyclopentenone (0.38 g, 4.63 mmol) and 2-acetoxy-3-[(trimethylsilyl)methyl]-3-butene (0.63 g, 3.15 mmol) and heated at 65 °C for 16 h at which time TLC (10:1, hexane/ether) indicated complete consumption of starting material. The reaction was then concentrated by short-path distillation and purified by flash chromatography (5% ether in pentane). Concentration of the desired fractions followed by distillation (bulb-to-bulb, 2 mmHg, 60–80 °C) yielded 224.0 mg (47%, 1.5 mmol) of pure product as a 1:1 mixture of diastereomers. Analytical sample of each isomer can be obtained by preparative VPC (0.95 × 244 cm 10% pc 710 in Chromosorb W column).[20]

6 (exo isomer): R_t = 20.7 min; NMR (270 MHz) δ 4.82 (m, 1 H), 4.76 (m, 1 H), 2.69–2.59 (m, 3 H), 2.30 (m, 1 H), 2.17–1.98 (m, 2 H), 1.85 (m, 1 H), 1.12 (d, J = 6.8 Hz, 3 H); ^{13}C NMR (15 MHz) δ 222.0, 155.5, 105.2, 50.52, 49.15, 43.44, 35.89, 33.95, 23.95, 16.97; IR (neat) 3080, 2978, 1742, 1662, 1462, 1412, 1263, 1130, 883 cm^{-1}; mass spectrum m/e (%) M$^+$ 150 (3), 59 (7), 58 (72), 57 (7), 44 (68), 43 (100), 42 (52), 41 (17), 40 (11), 39 (37), 38 (17), 37 (13). Anal. Calcd for $C_{10}H_{14}O$: 150.1041. Found: 150.1041.

6 (endo isomer): R_t = 25.5 min; NMR (270 MHz) δ 4.86 (m, 1 H), 4.76 (m, 1 H), 2.80–2.58 (m, 4 H), 2.34–2.18 (m, 3 H), 1.86 (m, 1 H), 1.33 (m, 1 H), 1.06 (d, J = 6.4 Hz, 3 H); ^{13}C NMR (15 MHz) δ 221.4 (s), 153.3 (s), 105.6 (t), 48.75 (m), 45.78 (m), 41.55 (d), 38.92 (t), 34.58 (t), 21.89 (t), 12.06 (q). IR (neat): 3080, 2976, 1745, 1662, 1465, 1417, 1130, 886 cm^{-1}; mass spectrum m/e (%): M$^+$ 150 (2), 581 (1), 93 (1), 91 (1), 79 (2), 59 (10), 58 (61), 57 (1), 53 (1), 44 (6), 43 (100), 42 (12), 41 (12), 41 (4), 40 (8), 39 (8), 38 (3), 37 (2). Anal. Calcd for $C_{10}H_{14}O$: 150.1041. Found: 150.1046.

The following four compounds were isolated from the palladium-catalyzed cycloaddition reactions when the benzoate substrate was used. They were isolated from flash chromatography (TLC R_f 0.6 in 10:1 pentane/ether) and collected as three fractions in a ratio of 2:1.3:1 from VPC (0.32 × 335.3 cm 20% SE 30 in Chromosorb W column).

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Table IV.

entry	substrate, wt (g), mmol	cyclopentenone wt (g), mmol, equiv	$Pd(OAc)_2$ wt (mg) mol%	ligand wt (mg), equiv	reductant, wt (mg), equiv	THF, mL	temp, °C	time, h	yield, mg (%)
1	acetate, 1.89, 9.5	1.17, 14.3, 1.5	42, 1.7	$(i\text{-}C_3H_7O)_3P$ 265, 7	hexene, 76, 5	7	66	18[a]	(45)[b]
2	acetate, 0.79, 3.9	2.9, 36, 9	33, 3.6	$(i\text{-}C_3H_7O)_3P$ 212, 7	$n\text{-}C_4H_9Li$, (1.7 M) 0.16 mL, 2	4	66	16	96 (16)
3	acetate, 5.4, 27	4.9, 60, 2.2	120, 1.9	$(i\text{-}C_3H_7O)_3P$ 824, 7	DIBAL-H, (1 M) 1.1 mL, 2	50	66	16	1910 (47)
4	acetate, 1.8, 8.8	1.5, 18, 2.0	45, 2.2	$(i\text{-}C_3H_7O)_3P$ 292, 7	$n\text{-}C_4H_9Li$, (1.6 M) 0.26 mL, 2	10	66	32	578 (44)
5	benozate, 1.45, 5.5	0.9, 11, 2.0	22, 1.8	$(i\text{-}C_3H_7O)_3P$ 127, 6	hexene, 27,3 $n\text{-}C_4H_9Li$ (1.8 M) 0.10 mL, 1.8	2.2	66	1	372 (43)[c]
6	benozate, 1.52, 5.8	1.0, 12, 2.0	34, 2.6	$(i\text{-}C_3H_7O)_3P$ 177, 6	hexene, 27, 2 $n\text{-}C_4H_9Li$ (1.8 M) 0.1 mL, 1.2	2	50	18	486 (47)[d]
7	carbonate, 0.9, 4.3[e]	1.0, 12, 2.8	37, 3.8	$(i\text{-}C_3H_7O)_3P$ 254, 7.3	DIBAL-H, (1 M) 0.33 mL, 2	9	66	3	207 (32)
8	acetate, 1.0, 5.0	0.6, 7.3, 1.5	44, 3.4	$(i\text{-}C_3H_7O)_3P$ 310, 7	$n\text{-}C_4H_9Li$, (1.8 M) 0.34, 2	1	80	5	375 (50)[f]
9	acetate, 0.63, 3.15	0.4, 4.6, 1.5	38, 5.4	$(i\text{-}C_3H_7O)_3P$ 210, 6	$n\text{-}C_4H_9Li$, (1.8 M) 0.20, 2	2.5	65	16	224 (47)
10	acetate, 0.87, 4.35	0.5, 6.2, 1.4	42, 4.3	$(i\text{-}C_3H_7O)_3P$ 210, 5.5	$n\text{-}C_4H_9Li$, (1.8 M) 0.25, 2	3.0[f]	85	2.5	310 (48)
11	acetate, 0.89, 4.45	0.9, 11, 2.4	26, 2.6	DPPP 106, 2.1 PPh_3 95, 3.1	hexene, 65, 6.5 $n\text{-}C_4H_9Li$, (1.8 M) 0.1, 1.5	10	66	16	(41)[b]
12	acetate, 0.9, 4.45	0.6, 7.1, 1.6	16, 1.6	(+)DIOP 93, 2.6	hexene, 68, 11	3.0	66	2	(50)[b]
13	benzoate, 1.46, 5.5	0.8, 9.6, 1.7	15, 1.2	DPPB 71, 2.5	$n\text{-}C_4H_9Li$, 0.07, 2	7.0	66	5	185 (22)
14	benzoate, 0.87, 3.31	0.5, 5.6, 1.7	36, 5.0	$(i\text{-}C_3H_7O)_3P$ 170, 5.0	$n\text{-}C_4H_9Li$, (1.8 M) 0.18, 2	0.3	75	6[g]	(30)[h]

[a] Initially 0.5 g of acetate added and remainder over 10 h. [b] Yield determined by VPC. [c] % yield of **6**; in addition 25% of protodesilylated starting material and 2% of **17** isolated. [d] % yield of **6**; in addition 13% of protodesilylated starting material and 8% of **17** isolated. [e] Starting material was 90% pure. [f] Dioxane used as solvent. [g] Initially 0.44 mmol of benzoate and 2.2 mmol of cyclopentenone were combined with the catalyst in 1.0 mL of THF. The remainder was added over 5 h. [h] The yield was determined by NMR spectroscopy. In addition 40% of protodesilylated starting material formed. [i] In addition 5% of **17** isolated.

3-Methyl-3-buten-2-yl benzoate (9): ^1H NMR (200 MHz) 8.04 (d, J = 6 Hz, 2 H), 7.52 (m, 1 H), 7.42 (t, J = 6 Hz, 2 H), 5.63 (q, J = 5 Hz, 1 H), 4.69 (s, 2 H), 1.72 (s, 3 H), 1.65 (d, J = 5 Hz, 3 H).

2-Ethallyl benzoate and (*Z)-2-methyl-2-buten-1-yl benzoate as a 3:1 ratio (10 and 11): ^1H NMR (270 MHz) 8.04 (d, J = 6 Hz, 2 H), 7.52 (m, 1 H), 7.42 (t, J = 6 Hz, 2 H), *5.51 (q, J = 5 Hz, 0.25 H), 5.12 (s, 0.75 H), 4.95 (s, 0.75 H), *4.85 (s, 0.5 H), 4.78 (s, 1.5 H), 2.14 (q, J = 5.5 Hz, 1.5 H), *1.82 (s, 0.75 H), *1.70 (d, J = 5 Hz, 0.75 H), 1.11 (t, J = 5.5 Hz, 2.25 H); MS 190 (2.0), 123 (8.7), 105 (100), 85 (2.1), 77 (29), 68 (20). Anal. Calcd for $C_{12}H_{14}O_2$: 190.0994. Found: 190.0994.

(*E*)-2-Methyl-2-buten-1-yl benzoate (11): ^1H NMR (200 MHz) 8.04 (d, J = 6 Hz, 2 H), 7.52 (m, 1 H), 7.42 (t, J = 6 Hz, 2 H), 5.63 (q, J = 5 Hz, 1 H), 4.69 (s, 2 H), 1.72 (s, 3 H), 1.65 (d, J = 5 Hz, 3 H). The assignment of the E and Z isomers is based on the expectation of an upfield shift of the vinyl methyl groups for the Z isomer. This ratio is in agreement with the greater stability of the corresponding anti (π-allyl)palladium species.

Preparation of [(2,4,6-Trilsopropylphenyl)sulfonyl]hydrazone of 2-Methyl-3-methylenebicyclo[3.3.0]octan-6-one (18). The ketone **6** (204.2 mg, 1.36 mmol) was added dropwise to a solution of [(2,4,6-triisopropylphenyl)sulfonyl]hydrazine (405.3 mg, 1.36 mmol) in 2 mL of acetonitrile over 5 min. The solution was allowed to stir at room temperature for 15 min and then 1 drop of 45% aqueous fluoroboric acid was added. Stirring was continued until IR spectroscopy and TLC indicated complete reaction (about 15 min). The solution was then concentrated in vacuo at room temmperature and the sample subjected to pumping in vacuo at 0.05 mmHg with a phosphorus pentoxide trap in line for 12–16 h to yield a white gummy mass which was used directly in the next reaction: R_f 0.66 (6:4 hexane/ethyl acetate); ^1H NMR (270 MHz) 7.17 (s, 2 H), 4.74 (m, 2 H), 4.65 (m, 2 H), 2.91 (m, 1 H), 2.81–1.4 (m, 9 H), 1.27 (m, 18 H), 1.02 and 0.98 (2 ds, J = 9 Hz, 3 H); IR ($CDCl_3$) 3540, 3200, 2940, 1650, 1600, 1360, 1330, 1170, 1050, 900, 660. Endo- and exo-**6** were separated via flash chromatography using 5% ether in pentane and converted to their respective hydrazones as before. ^1H NMR (200 MHz) exo: 7.58 (bs, 1 H), 7.18 (s, 2 H), 4.73 (bs, 0.4 H), 4.63 (bs, 1.6 H), 4.23 (m, 2 H), 2.89 (m, 1 H), 2.6–1.7 (m, 9 H), 1.27 (m, 9 H), 1.06 (d, J = 5.5 Hz, 0.7 H), 1.01 (d, J = 5.5 Hz, 2.3 H). Endo: 7.68 (bs, 1 H), 7.18 (s, 2 H), 4.78 (s, 0.39 H), 4.71 (s, 1.0 H), 4.68 (s, 0.61 H), 4.27 (m, 2 H), 3.0–1.6 (m, 10 H), 1.28 (m, 9 H), 1.02 (d, J = 5.5 Hz, 1.17 H), 0.99 (d, J = 5.5 Hz, 1.83 H). The olefin and methyl regions of the NMR spectra indicate 20% and 40%, respectively, of a minor isomer which is assumed to be the syn isomer. Purification was not desirable since the product was quite pure and attempts at chromatography led to extensive decomposition.

Preparation of 2-Carbomethoxy-6-methyl-7-methylenebicyclo[3.3.0]-oct-6-ene (19). To freshly prepared hydrazone **18** (645 mg, 1.5 mmol) was added 7.5 mL each of TMEDA and hexane via syringe. The flask was cooled to −78 °C and *n*-butyllithium (1.55 M in hexane, 3 mL, 4.65 mmol) was added dropwise. The solution was stirred for 1 h at −78 °C, then allowed to warm to −30 °C for 10 min, and finally held at 0 °C for 5 min whereupon gas evolution occurred and the solution changed from dark red to a lighter orange. The flask was then recooled to −78 °C and cannulated onto excess freshly sublimed dry ice. After the excess carbon

dioxide had evaporated, 25 mL of saturated aqueous sodium bisulfate and 25 mL of ether were added followed by 3 mL of concentrated hydrochloric acid or enough to reach pH 2. The layers were separated, the aqueous layer reextracted with 15 mL of ether and the combined organic layers dried (Na_2SO_4). The organic layer was then cooled to 0 °C and stirred while an ethereal solution of diazomethane was added portionwise until TLC showed complete reaction. Removal of solvent by atmospheric distillation followed by flash chromatography (5% ether in pentane), reconcentration, and distillation (bulb-to-bulb, 80 °C, 0.02 mmHg) yielded 110 mg (0.99 mmol 66%) of ester from the ketone. R_f 0.22 (4:1 hexane/ethyl acetate) for the acid, 0.55 for the ester. The following data were obtained on a sample containing 20% of the bridgehead olefin and a 2:1 ratio of methyl epimers: ^{1}H NMR (270 MHz) 6.68 (m, 1 H), 4.98 (m, 0.13 H), 4.93 (q, J = 2, 0.07 H), 4.88 (m, 0.13 H), 4.86 (q, J = 2, 0.07 H), 4.79 (m, 0.36 H), 4.76 (m, 0.44 H), 4.69 (m, 0.8 H), 3.73 (s, 1.6 H), 3.72 (s, 1.4 H), 3.35 (m, 2 H), 2.9-2.6 (m, 2 H), 2.3-2.1 (m, 3 H), 1.14 (d, J = 7, 0.21 H), 1.09 (d, J = 7, 1.32 H), 0.96 (d, J = 7, 1.08 H), 0.86 (d, J = 8, 0.39 H); IR ($CHCl_3$) 2962, 1705, 1636, 1438, 1275, 1100, 900, 632; MS 192 (54), 161 (13), 160 (19), 133 (62), 132 (50), 117 (22), 105 (17), 91 (26). Anal. Calcd for $C_{12}H_{16}O_2$: C, 74.96; H, 8.39; MW, 192.1150. Found: C, 74.79; H, 8.39; MW, 192.1151.

Preparation of 2-Carbomethoxy-6-methyl-7-methylenebicyclo[3.3.0]-oct-7-ene (20). *n*-Butyllithium (0.56 mL, 0.97 mmol of 1.74 M hexane solution) and HMPA (174 mg, 0.97 mmol) were added to a −78 °C solution of 0.85 mL of THF and 98 mg of diisopropylamine (0.97 mmol). After allowing the solution to warm to −30 °C until the solution became homogeneous, the flask was recooled to −78 °C and the ester (125 mg, 0.65 mmol) in 0.94 mL of THF was added dropwise over 10 min. The light yellow solution was allowed to stir for an additional 10 min, then cannulated onto a biphasic ether/saturated aqueous sodium bisulfate solution (5 mL each), to which was added 15 mL of pentane. After separation, the organic layer was washed with aqueous sodium bicarbonate (1 × 2 mL), saturated aqueous cupric sulfate (2 × 3 mL), water (1 × 2 mL), and dried (Na_2SO_4). Solvent removal via atmospheric distillation followed by bulb-to-bulb distillation [80 °C (0.01 mmHg)] yielded 101 mg (0.45 mmol, 69%) of product. ^{1}H NMR (270 MHz) 6.42 (bs, 0.04 H), 6.35 (bs, 0.08 H), 5.90-5.78 (m, 0.88 H), 5.70-5.60 (m, 0.88 H), 4.80-4.60 (m, 2.0 H); four singlets, 3.73, 3.71, 3.70, 3.69 (3 H), 3.01-1.81 (m, 6 H), 1.14 (d, J = 6.8 Hz, 0.88 H), 1.13 (d, J = 6.8 Hz, 1.76 H), 0.95 (d, J = 6.8 Hz, 0.12 H), 0.93 (d, J = 6.8 Hz, 0.24 H). IR ($CHCl_3$): 1729, 1460, 1440 cm^{-1}. These spectral data represent a sample with 12% of the olefin isomer and a 2:1 ratio of methyl epimers.

Preparation of 1-*O*-Methyldehydrologanin Aglucon (21b). A dry stream of O_3/O_2 was bubbled into a −78 °C solution of 39.5 mg (0.18 mmol, 0.21 mmol of combined olefin isomers) of **20** in 4 mL of methylene chloride until a blue color appeared. After removing the excess ozone with a stream of nitrogen, the solvent was removed in vacuo followed by 2 min on a vacuum pump. Reduction was then accomplished by dissolving the bis(ozonide) in 3 mL of acetic acid and adding zinc dust (80 mg, 1.23 mm) in one portion followed by stirring at room temperature for 2 h. The solution was then added to a separatory funnel containing 25 mL each of ether and saturated aqueous sodium bicarbonate. Solid sodium bicarbonate was added until the acetic acid was decomposed. The aqueous layer was extracted further with ether (3 × 25 mL). The combined organic layers were dried ($MgSO_4$) and concentrated to yield crude hydroxyacetal. The oil was dissolved in 3 mL of methanol containing TsOH (17 mg, 0.1 mmol) for 2 days at room temperature. Sodium methoxide (20 mg, 0.37 mm) was then added to the flask in a glovebag and the flask was kept at 2 °C for 18 h. The reaction was neutralized with acetic acid, concentrated in vacuo, extracted with ether, washed with aqueous sodium bicarbonate, dried ($MgSO_4$), and plated (6:4 hexane/ethyl acetate) to yield 12.1 mg (0.05 mm, 28%) of quite pure material which was identical with material obtained from degradation of natural loganin: R_f 0.30 (6:4 hexane/ethyl acetate) for hydroxyacetal, 0.50 for methoxyacetal. Evidently the deconjugated olefin isomer forms a keto acid upon ozonolysis which is lost in the basic workup.

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Registry No. *exo*-**6**, 79348-44-0; *endo*-**6**, 79390-46-8; **7a**, 79348-40-6; **7b**, 94235-18-4; **7c**, 94235-19-5; **9**, 91495-68-0; **10**, 94235-20-8; (*Z*)-**11**, 94235-21-9; (*E*)-**11**, 94235-22-0; *exo*-**18**, 94235-23-1; *endo*-**18**, 94235-24-2; **19** (isomer 1), 94235-25-3; **19** (isomer 2), 94235-26-4; **20**, 94235-27-5; **20** (bis(ozonide)), 94235-31-1; **21a**, 86342-78-1; **21b**, 50427-62-8; **22**, 94235-28-6; **23** (isomer 1), 94292-76-9; **23** (isomer 2), 94292-77-0; **24** (isomer 1), 94292-78-1; **24** (isomer 2), 94292-79-2; 3-methyl-3-buten-2-ol, 10473-14-0; 2-(trimethylsiloxy)-3-[(trimethylsilyl)methyl]-3-butene, 94235-29-7; 2-(trimethylsiloxy)-3-[(trimethylsilyl)methyl]-4-(trimethylsilyl)-3-butene, 94235-30-0; 3-[(trimethylsilyl)methyl]-3-buten-2-ol, 79348-42-8; 2-[(trimethylsilyl)methyl]propenal, 56407-82-0; 2-cyclopentenone, 930-30-3; [(2,4,6-triisopropylphenyl)sulfonyl]-hydrazine, 39085-59-1.

Supplementary Material Available: General experimental procedures (2 pages). Ordering information is given on any current masthead page.

Exciton Approach to the Optical Activity of C_3-Cyclotriveratrylene Derivatives

Josette Canceill,[†] Andrê Collet,*[†] Jacqueline Gabard,[†] Giovanni Gottarelli,*[‡] and Gian Piero Spada[‡]

Contribution from the Collège de France, Chimie des Interactions Molēculaires,[§] 11, place Marcelin Berthelot, 75005 Paris, France, and the Universitā di Bologna, Istituto di Scienze Chimiche, via S. Donato 15, 40127 Bologna, Italy. *Received July 2, 1984*

Abstract: The circular dichroism of chiral C_3-cyclotriveratrylenes **2-12** in which the substitution patterns correspond to various combinations of R_1 and R_2 = H, OH, O$^-$, and OAc, and *O*-alkyl groups has been analyzed in light of the exciton theory, using the concept of spectroscopic moments. From the observed signs and intensities of the B_{2u} couplets, a self-consistent set of polarization angles for this transition in the OH/*O*-alkyl ortho-disubstituted derivatives has been established. The spectroscopic moments of these substituents have been shown to increase on going from the bulkiest (O-*i*-C_3H_7) to the smallest (OH) group, very likely as a consequence of different equilibria between planar and nonplanar conformers. Finally, the experimental B_{2u} and B_{1u} couplets have been satisfactorily reproduced in most of the cases studied by calculations based on the exciton approximation, with limited p-α configuration interaction.

Cyclotriveratrylene (**1**) and its analogues devoid of bulky substituents ortho to the nine-membered ring are rigid, cone-shaped molecules that exhibit stable optical activity at ambient temperature when the achiral C_{3v} symmetry of the parent compound is destroyed by appropriate substitution (e.g., when $R_1 \neq R_2$).[1] With the exception of a C_1-monobenzyl ether which was partially resolved in 1966 by Lüttringhaus,[2] all the optically active

[†] Collège de France.
[‡] Universitā di Bologna.
[§] Groupe de recherche du C.N.R.S. No. 20.

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