21.06, 14.61, 5.48 ppm; *m/e* (M^+) calcd 316.1311, obsd 316.1291.

Reaction of 10 with *N*-Methyltriazolinedione. To a stirred solution of **10** (100 mg, 0.63 mmol) in ethyl acetate (25 mL) cooled to −78 °C was added a solution of *N*-methyltriazolinedione (72 mg, 0.64 mmol) in the same solvent (5 mL). Decoloration occurred immediately to give a solid residue which was indicated by ^{13}C NMR to be a mixture of **48** and **49** (85:15 ratio): ^1H NMR ($CDCl_3$) δ 5.13 (s, 3 H), 2.91 (br s, 2 H), 2.76 (s, 3 H), 2.24 ($^1/_2$AB, *J* = 8.5 Hz, 1 H), 1.88 ($^1/_2$AB, *J* = 8.5 Hz), 1.50 ($^1/_2A_2B_2$, *J* = 7.6 Hz, 2 H), 1.20–1.13 (m, 1 H), 0.99 ($^1/_2A_2B_2$, *J* = 7.6 Hz, 2 H), 0.80–0.67 (m, 3 H). The ^{13}C NMR data for **48** and **49** are given in Table I; *m/e* (M^+) calcd 271.1321, obsd 271.1303.

Acknowledgment is made to the National Cancer Institute (Grant CA-12115) for the financial support of this research. FT-NMR (300 MHz) spectra were obtained at The Ohio State University Chemical Instrument Center (funded in part by National Science Grant CHE-7910019).

Registry No. 2, 73321-24-1; **10**, 93304-29-1; **11**, 93304-30-4; **13a**, 36439-90-4; **13b**, 36439-89-1; **14a** (isomer 1), 93304-31-5; **14a** (isomer 2), 93381-81-8; **14b** (isomer 1), 93304-32-6; **14b** (isomer 2), 93381-82-9; **15**, 73321-39-8; **16**, 93304-33-7; **17**, 93304-34-8; **18**, 73347-30-5; **19**, 93381-83-0; **20a**, 93304-35-9; **20b**, 93304-36-0; **21a**, 93381-84-1; **21b**, 93381-85-2; **22**, 93304-37-1; **23**, 93381-86-3; **24**, 93304-38-2; **25**, 93381-87-4; **26**, 93304-39-3; **27**, 93304-40-6; **28**, 93381-88-5; **29**, 93304-41-7; **30**, 93304-42-8; **31**, 93381-89-6; **32**, 93304-43-9; **33**, 93381-90-9; **34**, 93349-06-5; **35**, 93304-44-0; **36**, 93304-45-1; **37**, 74987-28-3; **38**, 74998-57-5; **39**, 93304-46-2; **40**, 93381-91-0; **41**, 93381-92-1; **42**, 93304-47-3; **43**, 93381-93-2; **44**, 93304-41-7; **45**, 93304-48-4; **46**, 93381-94-3; **47**, 93381-95-4; **48**, 93304-49-5; **49**, 93381-96-5; phenyl(tribromomethyl)mercury, 3294-60-8; dimethyl acetylenedicarboxylate, 762-42-5; maleic anhydride, 108-31-6; *N*-phenylmaleimide, 941-69-5; phenyl(vinyl)sulfone, 5535-48-8.

Electronic Control of Stereoselectivity. 27. The Effect of Apical Spirocyclopropane Substitution on the Stereochemical Course of Diels–Alder Cycloadditions to Norbornyl-Fused Diene Systems[1a]

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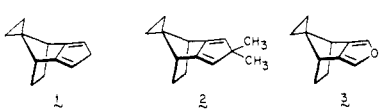
Abstract: The three new 7-spirocyclopropyl-substituted isodicyclopentadiene analogues **1–3** were prepared, and their stereoselective behavior toward various dienophiles was evaluated. Whereas the unadorned diene **1** exhibits no strong predilection for above-plane or below-plane [4 + 2] cycloaddition, the furan analogue **3** enters into Diels–Alder reaction totally by top-face bonding. This contrasting behavior is analyzed from the theoretical vantage point and attributed to the existence of strong σ/π interaction and its effect on the subjacent orbital (π_1). In the case of the parent hydrocarbon (**36**), strong disrotatory tilting of the terminal pπ orbitals of the diene unit toward the methano bridge is encountered and below-plane addition is kinetically favored in most instances. Where **1** is concerned, the spirocyclopropane function at C-7 reduces the size of the p_y coefficient at these centers. The observable effect is greatly reduced π-face stereoselectivity. The heterocyclic ring in furan **3** induces disrotatory motion in a direction opposite to that of **36** and gives rise to opposite stereochemical phenomena. The behavior of sterically congested **2** is believed to be controlled instead by intermolecular steric interactions. The X-ray crystal structure of adduct **32** indicates the molecule to be downwardly pyramidalized at its double bond by an astounding 21.8°.

In the preceding paper, it was shown that incorporation of a cyclopropane ring along one of its edge bonds into a bicyclic fused cyclopentadiene as in tetracyclo[5.3.2.$0^{2,6}$.$0^{8,10}$]dodeca-2,5,11-triene and -2,5-diene does not lead to pronounced stereocontrol of Diels–Alder cycloadditions by the three-membered ring.[1] Presently, attention is turned to the triad of molecules **1–3** which share in common a 7-spirocyclopropylnorbornane part structure. The impetus for this study arose from two directions.



1 **2** **3**

The first originates from photoelectron (PE) spectroscopic measurements which reveal that considerable through-space interaction operates between the e_A Walsh orbital in **4** and the antisymmetric π-linear combination of the two double bonds.[2a] Although this phenomenon is expectedly attenuated in **5**[3] and **6**,[4] the effects continue to persist at a reasonable level. Our theoretical model for π-face differentiation in isodicyclopentadiene and its analogues rests heavily, however, on the existence of long-range electronic interaction through the σ bond network.[5] On this basis, through-space options[6] were expected to have little

4 **5** **6**

† The Ohio State University.

(1) (a) Part 26: Charumilind, P.; Paquette, L. A. *J. Am. Chem. Soc.*, preceding paper in this issue. (b) Universität Heidelberg. (c) Individual to whom queries regarding the X-ray crystal structure analysis should be directed at The Ohio State University.

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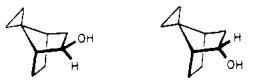
overall impact on the Diels–Alder stereoselectivity exhibited by **1–3**.[1] These dienes should therefore respond to dienophiles in a manner paralleling that observed for the parent hydrocarbon,[7-10] unless perturbation of the σ energy levels by another mechanism(s) is possible.

In actuality, spiro fusion of a three-membered ring not only necessitates the return to a strained norbornyl framework but also ensures a specific geometrical relationship between the cyclopropyl and dienyl moieties in **1–3**. Several recorded observations suggest that these structural features are particularly conducive to added electronic involvement between the 7-spirocyclopropyl moiety and nearby unsaturated center. For example, **7** enters readily into [3 + 2] cycloaddition, whereas the 7,7-dimethyl derivative remains totally unreactive.[11] In a similar vein, ketone **8** is reduced by sodium borohydride only 2 times more slowly than norcamphor, but 60 times more rapidly than **9**.[12] Like norcamphor (endo/exo

7 **8** **9**

= 87:13), **8** is transformed predominantly to its endo alcohol under these conditions (75:25); a reversed product distribution arises from **9** (20:80). Since these reductions involve a single transition state and are both irreversible and kinetically controlled, the product ratios directly reflect the rates of exo and endo hydride delivery.[13] Although these findings have been construed to be diagnostic of a progression from minimal, intermediate, and relatively high degrees of steric hindrance to exo approach, this need not be the sole or even major factor underlying the reactivities of **7** and **8**.

In this connection, the circular dichroism spectrum of (−)-**8** is characterized by notably small rotational strengths due in large part to the nearly orthogonal relationship of the cyclopropane ring to the carbonyl n system.[14] Additionally, equilibration of **10** with **11** in the presence of aluminum isopropoxide gives a mixture in which **10** is substantially favored (exo/endo = 1.46). For the



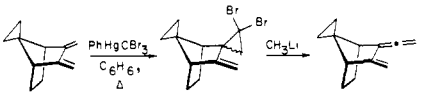
10 **11**

2-norbornanols, a closely comparable value of 3.54 has been determined.[15] Unfortunately, similar data for the 7,7-dimethyl substitution plan appear not to be available.

At issue, therefore, is whether the electronic effects introduced by a 7-spirocyclopropane ring act cooperatively with, or in opposition to, the ground-state character of isodicyclopentadiene in relation to its ability to control the π-face stereoselectivity of [4 + 2] cycloadditions. At a minimum, induction of an upward shift in the energies of the highest occupied σ orbitals can be anticipated, much as in 7-isopropylidenenorbornane.[2b]

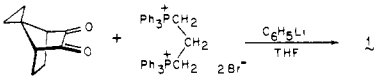
Results

Synthesis. Initially, consideration was given to application of the Skattebøol rearrangement[16] to **12**[17] as a possible route to **1**. Heating **12** with 1 equiv of phenyl(tribromomethyl)mercury in benzene[18] did indeed lead successfully to a 4:3 mixture of the exo and endo isomers of monoadduct **13**. Also, it proved an easy matter to effect reaction of **13** with methyllithium. However, wide variations in substrate concentration, stoichiometry of organometallic reagent, temperature, and reaction time afforded the allene **14** predominantly if not exclusively.



12 **13** **14**

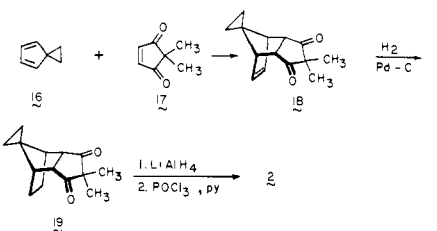
This complication was bypassed by engaging α-diketone **6**[4] in Wittig condensation with bisphosphonium salt **15**. Whereas



6 **15**

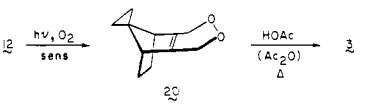
conditions previously applied to camphorquinone[19] proved ineffective in this instance, success was realized when recourse was made to methodology more closely related to Wittig's original work with *o*-phthaldialdehyde.[20] The use of 1.6 molar equiv of **15** and 2.04 molar equiv of phenyllithium delivered the desired diene in 23% isolated yield.

The preparation of **2**, adapted from earlier work in this laboratory,[8] consisted of sequential cycloaddition of 2,2-dimethyl-4-cyclopentene-1,3-dione (**17**)[21] to **16**, saturation of the norbornene double bond, hydride reduction, and twofold dehydration.



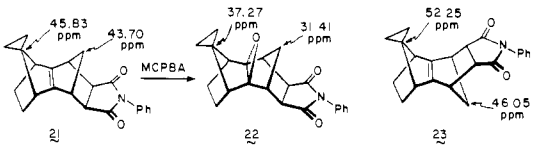
16 **17** **18** **19**

To arrive at **3**, **12** was photooxygenated[22] to form *endo*-peroxide **20**, heating of which in acetic acid containing 1% acetic anhydride[9] furnished the norbornenofuran.



20

Cycloadditions to 1. In principle, four isomeric adducts can be formed in the [4 + 2] cycloaddition of *N*-phenylmaleimide to **1**. When allowed to react in chloroform solution at 0 °C for 5 h, only the non-Alder products **21** and **23** were formed in a 46:54 ratio. Following separation of these adducts by thin-layer



21 **22** **23**

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(10) For exceptions to this general trend, consult: Bartlett, P. D.; Wu. C. *J. Org. Chem.* **1984**, *49*, 1880.
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(12) Turro, N. J.; Farrington, G. L. *J. Am. Chem. Soc.* **1980**, *102*, 6051.
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(16) (a) Skattebøl, L. *Tetrahedron* **1967**, *23*, 1107. (b) Butler, D. N.; Gupta, I. *Can. J. Chem.* **1977**, *56*, 80. (c) Reinarz, R. B.; Fonken, G. J. *Tetrahedron Lett.* **1973**, 4591. (d) Brinker, U.; Fleischhauer, I. *J. Am. Chem. Soc.* **1981**, *103*, 2116; *Tetrahedron* **1981**, *37*, 4495.
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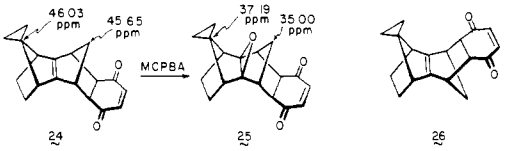
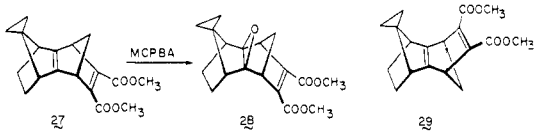
chromatography, their three-dimensional structures were assigned on the basis of spectral and chemical evidence. In neither example was significant coupling observed between the α-carbonyl and neighboring bridgehead protons, thereby indicating the exo configuration of the maleimide moiety in both cases.[23] The *syn*-sesquinorbornene nature of **21** follows from its efficient conversion to **22** with *m*-chloroperbenzoic acid (**23** is unreactive to these conditions)[8,24] and the strong upfield shift of both apical carbons in the epoxide vis-à-vis the olefin.[1,8,24] The consequences of oxirane magnetic anisotropy[25] on the proximal apical hydrogens are also evident in the ^{1}H NMR spectrum of **22**.

With *p*-benzoquinone, a 39:61 mixture of the isomeric exo adducts **24** and **26** (determined by ^{1}H NMR) was produced. In common with all of the cycloadditions described here, reaction progress was monitored by ^{1}H NMR; in no instance was reversibility observed. Both components could be obtained in a pure state and their structure deduced as before by detailed spectral analysis and the susceptibility of **24** to peracid oxidation. The conversion to **25** was accompanied by the usual diagnostic spectral changes.



Where dimethyl acetylenedicarboxylate is concerned, formation of the somewhat sensitive compounds **27** and **29** was observed in the relative ratio of 68:32. In this instance, individual spectral features allowed unequivocal structural assignments to be made. Thus, the two protons positioned endo on the enthano bridge in **27** are substantially shielded (δ 0.60–0.55) relative to those in **29** (δ 1.12) due to the anisotropy contributions of the maleate π cloud which they penetrate to a substantial degree.[26] Conversely, whereas the four cyclopropyl protons in **27** appear as two nicely separated multiplets of equal intensity (δ 0.55–0.47 and 0.29–0.24), they are seen in **29** as a lone narrow multiplet (δ 0.32–0.20). The



^{13}C shifts of the cyclopropyl carbon atoms are similarly affected (see Experimental Section). The geometry of *anti*-sesquinorbornadiene **29** is presumably such[26] that the relationship of the peripheral double bond to the spirocyclopropane functionality places the latter in a deshielding zone. As expected, **27** was readily converted to epoxide **28**.

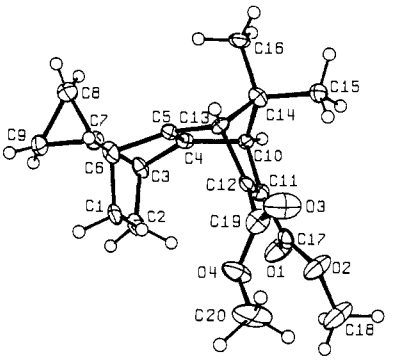
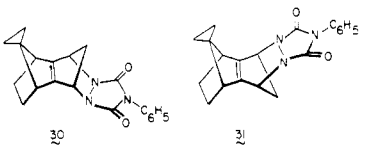


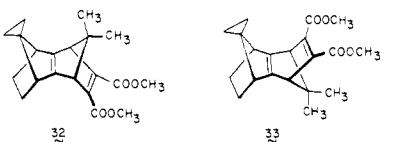
Figure 1. ORTEP drawing of **32** showing the numbering system used. Non-hydrogen atoms are drawn with 50% probability ellipsoids, while hydrogen atoms are drawn with an artificial radius.

Condensation of **1** with *N*-phenyltriazolinedione at −78 °C gave rise to a 50:50 mixture of **30** and **31**. Since these adducts proved unstable to chromatography, individual structural assignments are pending. The noteworthy point here is the absence of a kinetic preference for bonding to one or the other π face.



Cycloadditive Behavior of 2. In line with earlier kinetic studies involving 4,5,6,7-tetrahydro-2,2-dimethyl-4,7-methano-2*H*-indene (**37**),[8] it was anticipated that **2** would prove reasonably sluggish in Diels–Alder reactions. This recalcitrancy was indeed encountered. For example, heating **2** with *N*-phenylmaleimide at 140 °C for 15 h gave no evidence for adduct formation. Consequently, this phase of our study was restricted to the most reactive dienophiles.

Condensation of **2** with dimethyl acetylenedicarboxylate (DMAD, 60 °C, 2.5 h) furnished a 65:35 mixture of **32** and **33**. This product distribution is remarkably similar to that previously observed for **27** and **29**. The syn and anti character of the new sesquinorbornadienes were established in the same manner as before.



Because **32** represents the first available *syn*-sesquinorbornene derivative which is fully substituted at both apical positions, its crystal structure analysis was carried out. A major point of interest was the extent to which the central double bond in this molecule deviates from planarity. A computer-generated ORTEP diagram of the final X-ray structure of **32** is provided in Figure 1. Curiously, the two carboxylate groups are seen to be oriented differently with respect to the C10–C11–C12–C13 plane. The dihedral angle between the C10–C11–C12–C13 plane and the C12–C19–O3–O4 plane is 54.1 (3)° with the carbonyl oxygen O(3) located on the same side of the C10–C11–C12–C13 plane as the bridgehead C14 carbon. The dihedral angle between the C10–C11–C12–C13 plane and the C11–C17–O1–O2 plane is 28.3 (3)° with the carbonyl oxygen O(1) located on the opposite side of the C10–C11–C12–C13 plane as the bridgehead carbon. These two orientations of the carboxylate groups indicate that this molecule can exist as conformational enantiomers; in the crystal structure determined here, only one such enantiomer was observed.

As anticipated, the most notable feature of **32** is the nonplanarity observed about the C4–C5 double bond. The dihedral angle between the plane through the C3–C4–C5–C6 atoms and the plane through the C10–C4–C5–C13 atoms is a remarkable 21.8 (4)°.

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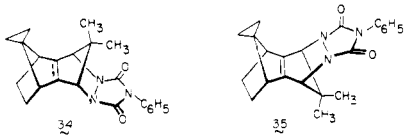
For the plane through the C3–C4–C5–C6 atoms, the C10 and C13 atoms are on one side of this plane and the C14 atom is on the other side. For the plane through the C10–C4–C5–C13 atoms, the C3 and C6 atoms lie on one side of this plane, while atom C7 essentially lies in this plane. *Importantly, the nonplanarity about the C4–C5 bond does not appear to be the result of steric interactions between the substituents on the norbornane bridgehead carbon, as the C8···C16 distance is 4.68* Å.

The large bend of the inner double bond in **32** is comparable in magnitude to the 22.1° deviation from planarity encountered in A.[27] The enhanced distortion in this example has been attributed to a somewhat greater repulsive force exerted by a filled π orbital on the bridge oxygen atom relative to a methylene group.

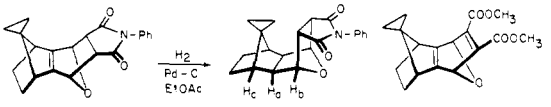
Homoconjugation has been deemed responsible for a similar though less exaggerated efect in B.[26d] In addition to the contributions from the single atom bridges, removal of endo protons from either ethano bridge (by benzo fusion as in **34** or in a manner exemplified by **32** and **35**) allows for greater folding of the entire structural framework, the central π linkage serving as the hinge.

The π-face stereoselectivity exhibited by *N*-phenyltriazolinedione (PTAD) toward **2** (50:50) once again closely paralleled that shown toward **1**. In this instance, it proved possible to achieve chromatographic separation of the two adducts. The usual spectral differences were seen. In particular, the endo protons on the enthano bridge of **34** (δ 1.05) appear unmistakably upfield of those in **35** (δ 1.50).



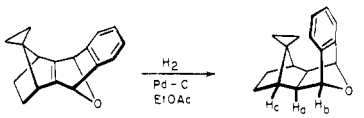
The striking similarity in the response of **1** and **2** to DMAD and PTAD strands in remarkable contrast to the behavior of their non-spirocyclopropanated counterparts **36** and **37** toward these reagents. While below-plane capture of parent hydrocarbon **36** by DMAD is overwhelmingly favored,[7] the C-2 *gem*-dimethyl substitution plane in **37** causes a falloff in stereoselection toward this reagent (70% below plane).[8] Both substrates, on the other hand, exhibit a complete reversal toward triazolinediones (100% above plane).[8,26j] What role does the spirocyclic three-membered ring in **1** and **2** play in the normalization of their cycloaddition stereoselectivity?

Cycloaddition Reactions Involving 3. Furan **3** added 1 equiv of *N*-phenylmaleimide at room temperature in chloroform solution (4 days) to give the single adduct **38** in 53% yield after preparative thin-layer chromatography. That bonding to the dienophile had materialized from the above-plane direction in anti-Alder fashion was suggested by the ^{1}H NMR spectrum. Thus, the α-carbonyl protons are coupled weakly, if at all, to the flanking bridgehead hydrogens, clearly signaling their endo orientation.[23] Further, its cyclopropyl protons are displayed as two well-separated multiplets much as in **23**, and the endo protons of its ethano bridge are somewhat more deshielded than those in **23** (δ 1.29 vs. δ 0.92), the likely result of proximity to the ether bridge. Confirmation of the configurational assignment was derived by means of catalytic hydrogenation. Saturation of the internal double bond from its less sterically hindered surface occurred to give **39**. While the vicinal coupling constant J_{AB} in **39** is 3 Hz, the complementary J_{AC} was too small to measure at 200 MHz.

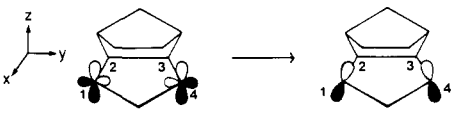


Dimethyl acetylenedicarboxylate adds to **3** at room temperature ($CHCl_3$, 2 days) to deliver a lone adduct whose thermal instability and lability to silica gel permitted isolation of a pure sample only in fair yield. In this instance, the endo protons of the ethano bridge are seen at δ 1.09, a position paralleling that noted earlier for **38** and appropriately downfield of that observed for **27** (δ 0.55). On this basis, the compound is provisionally considered to be **40**.

Where benzyne is concerned, addition occurred to give **41**. Because of anisotropic contributions from the benzene ring, the ^{1}H NMR spectrum of **41** could not be related with confidence to those of the preceding adducts. Accordingly, **41** was catalytically hydrogenated. With **42** in hand, it proved an easy matter to recognize the existence of J_{AB} (3 Hz) and the absence of J_{AC}. Benzyne, therefore, has also added to **3** from that direction syn to the spirocyclopropane functionality.



Theoretical Model. Previously, we have described a simple, theoretically sound principle to explain the stereoselectivity observed during [4 + 2] cycloadditions to **36**.[5,7,8] Fusion of a strained, unsymmetrical bicyclic unit to a cyclopentadiene ring engenders coupling between orbitals of pure π character and high-lying σ orbitals. As a direct result of this interaction, those canonical molecular orbitals having predominant π character experience tilting. Where **36** is concerned, for example, a rotation of the pπ lobes at C(1) and C(4) of the diene unit occurs within the lowest occupied π orbital in such a way that a disrotatory twist toward the apical norbornyl CH_2 occurs (as illustrated).



This rotation can be described roughly as the superposition of the p_y compoonent from the σ frame and the p_z component from the π network. On this basis, an approximate measure of the level of π/σ interaction should be the *size* of the p_y coefficient in the wave function. Information about the sense of rotation can be gained from the *sign* of the p_y coefficient. Thus, if p_y and p_z show the same sign at center 1 (opposite sign at center 4) of the diene system, the p_z lobes at these centers are rotated toward the methano bridge of the norbornane fragment as shown in the drawing. Conversely, if the signs of the p_z and p_y at center 1 are opposite (same at center 4), we find the p lobes at these sites to be tilted away from the methano bridge.

The p_y coefficients at C(1) of the diene units in **1–3**, as well as those in **36** and **37** for comparison, have been compiled in Table V. The results are derived from MNDO calculations[28] and a minus sign has been adopted for the p_z coefficient. This computational method was chosen because it is known to predict correctly the orbital sequencing (π above σ orbitals) previously ascertained experimentally in the PE studies of **36 37**, and related compounds.[5,7]

For **1**, **2**, **36**, and **37**, the predicted sense of rotation conforms to that in the illustrated model, meaning that cycloaddition with a dienophile should be favored from the side syn to the ethano group, if steric effects do not interfere. The reduced size of the

(27) Bartlett, P. D.; Combs, G. L., Jr. *J. Org. Chem.* **1984**, *49*, 625.

(28) Dewar, M. J. S.; Thiel, W. *J. Am. Chem. Soc.* **1977**, *99*, 4899.

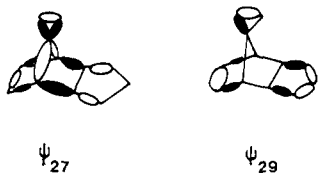


Figure 2. Schematic drawing of the most important precanonical σ orbitals which interact with π_+ of **1**.

p_y coefficients in **1** can be expected to translate into a diminished stereoselectivity related to that observed for the other three substrates. The difference between **1** and **36** can be traced back to interaction of the precanonical[29] σ orbitals with the localized π orbitals. In contrast to **36**,[5,7] the precanonical σ orbitals of **1** show large coefficients in the cyclopropano and norbornyl components (Figure 2). We ascribe the low-level strereoselection in **2** to steric effects which seem to dominate over the electronic influences (see below).

For **3**, our simple criterion predicts cycloaddition from the above-plane direction. This behavior is comparable to that observed for the anion from **36**[24b] where a similar rotation in the lowest occupied π orbital has been noted.

Discussion. Three new 7-spirocyclopropyl-substituted isodicycloentadiene analogues (**1–3**) have been prepared in expedient fashion. The Diels–Alder selectivity exhibited by these systems is mixed. Quite unlike the parent hydrocarbon, **1** enters into [4 + 2] cycloaddition with minimal preference for above- or below-plane dienophile capture. This chemical response appears to be a manifestation of long-range through-bond interaction between the three-membered ring and the cyclopentadiene π network. Various molecular orbital calculations make it clear that the frontier orbital in **1** and its congeners, viz., π_2 of the diene component, exhibits no feature which would make dienophile approach more kinetically advantageous from one or the other face. The prevailing σ/π interactions do, however, impact on π_1 and cause disrotatory tilting of the p_π orbitals at the diene termini.[5,7] For the parent hydrocarbon **36**, the usual end result of these electronic influences is below-plane stereoselectivity for [4 + 2] cycloadditions and above-plane stereoselectivity for [3 + 4] and [6 + 4] cycloadditions.[30] An important aspect of the ground-state properties of **1** is the greatly reduced level of tilting in π_1, the direct end result of the acceptor role played by the cyclopropane ring which decreases the magnitude of the p_y coefficient at C_1 and C_4 (Table V). Stereoselectivity is appropriately diminished as a consequence.

As is customary for most isodicyclopentadienes, endo-Alder dienophile capture operates on neither diene surface. Steric effects usually disfavor such endo-bonding schemes. The relevant competition is therefore between exo attack from the above- and below-plane directions. The exo pathways are believed to be much less influenced by steric differences relative to orbital tilting within π_1 of the cyclopentadiene. In these terms, the 50% decrease in the size of the p_y coefficient for **1** relative to **36** should result in an observable falloff in below-plane Diels–Alder stereoselectivity. This prediction receives strong experimental support from the data reported above (Table V).

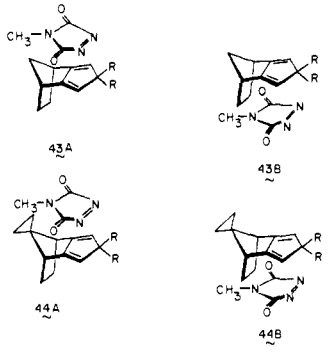
Remarkably, the aromatic character of the furan ring in **3** gives rise to an entirely different effect. Appropriate mixing of the precanonical σ orbitals and localized π orbitals of the heterocyclic moiety results in a return of pronounced disrotatory tilting. In striking contrast to **36** and the unadorned furan counterpart,[26d] however, the disrotation in **3** is *away from* the methano bridge. This opposite behavior should foster preferential above-plane [4 + 2] bonding as is encountered (Table V).

Houk et al. have offered an alternative explanation for the π-facial selectivity exhibited by **36**.[31] With use of MM2 procedures, the below-plane transition state was computed to be favored over that associated with the above-plane approach because of somewhat heightened classical torsional repulsions in the latter. The striking differences in the π-facial stereoselectivities described herein for **1** and **3** are difficult to appreciate in these terms. Perhaps additional forces are at work. In any event, the p_y/p_z dissection protocol advanced above is simple and potentially adaptable to a broad spectrum of 7-substituted isodicyclopentadiene derivatives. We hope to report on significant developments in this arena at a later date.

When the cyclopentadienyl methylene unit in **1** is substituted by methyl groups as in **2**, access to either face of the unsaturated five-membered ring becomes sterically impeded (compare **37**). The nonbonded repulsions which are generated during [4 + 2] cycloaddition from either direction are no longer negligible. As a consequence, these steric repulsions dominate the electronic interactions which are usually in control of the reaction stereoselectivity. Although the small angles of the cyclopropane ring serve to contract its global steric bulk relative to the geminal methyl pair,[32] intermolecular steric interactions with the approaching dienophile are energetically costly. These effects and those offered competitively by the ethano bridge on the endo surface guide the product distribution.

Thus, the experimental facts denote that the adopted model based on the calculated molecular orbital characteristics of ground-state isodicyclopentadienes can account qualitatively for the π-facial stereoselectivities of their Diels–Alder reactions. Two facets of Table V warrant additional brief comment. The behavior of **2** and **37** cannot strictly be integrated because of overwhelming steric inhibition to reaction. In these examples, all avenues of dienophile approach are highly hindered and intramolecular terms dominate. These important distinctions surface in different ways. For example, **2** has been shown to be unreactive to *N*-phenylmaleimide. Although **37** does react with this dienophile, the above-plane adduct that is formed exclusively possesses endo stereochemistry. One of the *gem*-dimethyl substituents must therefore be more bulky than the methano bridge.

The other point to be made concerns the anomalous behavior of *N*-methyltriazolinedione that continues to be apparent. It has been detailed elsewhere[26j] that the exceptionally high reactivity of this dienophile and the ancitipated early timing of its cycloaddition transition states very likely cause endo-Alder addition to be energetically preferred. Should this be the case, an unique sensitivity to steric effects not encountered with other lesser reactive dienophiles would become evident. In these terms, cycloaddition to **36** should result in kinetically favored passage via transition-state **43A** (R = H) relative to **43B** (R = H) for obvious steric reasons.



The presence of the spirocyclopropyl group in **1** engenders an increase in above-plane steric congestion adequate to promote approximately equal levels of reaction through **44A** and **44B** (R = H). An entirely comparable reaction profile is exhibited by **37** and **2**. It was previously shown that **37** prefers to enter into

(29) Heilbronner, E.; Schmelzer, A. *Helv. Chim. Acta* **1975**, *58*, 936.
(30) (a) Paquette, L. A.; Hathaway, S. J.; Kravetz, T. M.; Hsu, L.-Y. *J. Am. Chem. Soc.* **1984**, *106*, 5741. (b) Paquette, L. A.; Hsu, L.-Y.; Gallucci, J. C.; Korp, J. D.; Bernal, I.; Kravetz, T. M.; Hathaway, S. J. *Ibid.* **1984**, *106*, 5743.
(31) (a) Rondan, N. G.; Paddon-Row, M. N.; Caramella, P.; Houk, K. N. *J. Am. Chem. Soc.* **1981**, *103*, 2436. (b) Rondan, N. G.; Paddon-Row, M. N.; Caramella, P.; Mareda, J.; Mueller, P. H.; Houk, K. N. *Ibid.* **1982**, *104*, 4974. (c) Houk, K. N.; Brown, F. K., private communication.
(32) See, for example: (a) Reference 11. (b) Kaufmann, D.; de Meijere, A. *Chem. Ber.* **1983**, *116*, 1897.

[4 + 2] cycloaddition in endo-top fashion. Consequently, the triazolinedione can be expected to add as in **43A** (R = CH_3), although the facile pyramidalization at nitrogen precludes us from proving this point absolutely. Only the above-plane adduct is isolated. The 50:50 distribution of urazoles produced by **2** signals operation of the same steric perturbation as with **36** → **37**. The internal consistency in product distribution is impressive. For these reasons, triazolinedione cycloaddition must be viewed as a sterically controlled process not subject to the same electronic effects that influence the course of less exothermic Diels–Alder reactions.

Finally, we call specific attention to the large exo distortion of the carbon skeleton in **32**. At the present time, this molecule (and A) represents an extreme case of alkene pyramidalization. Its astounding 21.8° bend and the attendant stress on the π bond merit detailed theoretical and experimental scrutiny.[33]

Experimental Section[34]

Dibromocyclopropanation of 12. A mixture of **12** (1.75 g, 12.0 mmol), phenyl(tribromomethyl)mercury (6.4 g, 12.1 mmol) and anhydrous benzene (90 mL) was heated at the reflux temperature for 4 h, cooled to 20 °C, and filtered through Celite. Following solvent evaporation, the residual brown oil was purified by preparative TLC on silica gel (elution with petroleum ether). There was isolated 2.5 g (65%) of **13** as a 4:3 mixture of isomers: ^{1}H NMR ($CDCl_3$) δ 5.03 (s, 0.6 H), 4.87 (s, 0.4 H), 4.60 (s, 0.4 H), 4.57 (s, 0.6 H), 2.24–1.49 (m, 8 H), 0.62–0.44 (m, 6 H); ^{13}C NMR ($CDCl_3$) 154.81, 154.55, 104.97, 103.43, 53.85, 53.46, 51.39, 38.48, 27.94, 35.04, 34.88, 32.31, 31.10, 29.74, 27.82, 26.40, 25.31, 5.74 (3 C), 4.75 ppm (2 quaternary carbons not observed).

Anal. Calcd for $C_{12}H_{14}Br_2$: C, 45.60; H, 4.46. Found: C, 45.32; H, 4.46.

Skattebøl Rearrangement of 13. A cold (−40 °C), magnetically stirred solution of **13** (700 mg, 2.2 mmol) in anhydrous ether (400 mL) was blanketed with nitrogen and treated dropwise with methyllithium (10 mL of 0.33 M in ether) during 1 h. Following an additional hour at this temperature, the reaction mixture was allowed to warm to 20 °C and water (50 mL) was added. The organic phase was washed with brine, dried, and evaporated to leave a yellow oil which was subjected to distillation in a Kugelrohr apparatus (100 °C, 0.3 torr). Allene **14** was obtained as a colorless oil (140 mg, 40%): IR (CH_2Cl_2) 3060, 2960, 1950 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 5.05–4.85 (m, 4 H), 2.45–1.35 (m, 6 H), 0.50–0.40 (m, 4 H); ^{13}C NMR ($CDCdl_3$) 201.08, 155.65, 151.27, 108.85, 80.40, 79.32, 49.31, 28.75, 6.28, 6.07 ppm; *m/e* (M^+) calcd 158.1095, obsd 158.1105.

Wittig Annulation of 6. A magnetically stirred solution of **15** (2.64 g, 3.63 mmol) in dry tetrahydrofuran (80 mL) was warmed to 60 °C and treated with freshly prepared ethereal phenyllithium (60 mL of 1.25 M, 7.4 mmol). The resulting dark solution was stirred for 2 h, cooled to room temperature, and treated dropwise with a solution of **6** (470 mg, 3.13 mmol) in dry tetrahydrofuran (10 mL). After 2 h at room temperature, the reaction mixture was again heated to 60 °C for 8 h. The cooled solution was diluted with ether (150 mL), filtered, and poured into water (200 mL). The aqueous phase was reextracted with ether, and the combined organic layers were washed with water (2 × 100 mL) and brine (100 mL), dried, and evaporated. Preparative TLC on silica gel (pentane elution) afforded 115 mg (23%) of **1** as a colorless oil: ^{1}H NMR ($CDCl_3$) δ 5.68 (s, 2 H), 3.23 ($^1/_2$AB, J = 22.6 Hz, 1 H), 3.06 ($^1/_2$AB, J = 22.6 Hz, 1 H), 2.28 (m, 2 H), 2.04 (m, 2 H), 1.43 (dd, J = 10.4 and 3.4 Hz, 2 H), 0.53–0.40 (m, 4 H); ^{13}C NMR ($CDCl_3$) 155.65, 114.10, 44.83, 44.56, 28.76, 6.40, 6.01 ppm (apical quaternary carbon not observed); *m/e* (M^+) calcd 158.1096, obsd 158.1127.

This diene was not subjected to C, H analysis because of limited stability under oridinary conditions.

Cycloaddition of 2,2-Dimethyl-4-cyclopentene-1,3-dione to 16. A solution of **16** (1.60 g, 17.4 mmol) and **17** (2.16 g, 17.4 mmol) in dry benzene (30 mL) containing a small quantity of hydroquinone was heated at the reflux temperature for 30 h, cooled, and evaporated. The residue was charomatographed on silica gel (elution with 10% ethyl acetate in petroleum ether) to give 2.75 g (73.2%) of **18** as a colorless solid: mp 68 °C (from ligroin); IR (CH_2Cl_2) 1720 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 6.12 (t, J = 1.9 Hz, 2 H), 3.66 (d of d, J = 2.8 and 1.9 Hz, 2 H), 2.81 (m, 2 H), 1.07 (s, 3 H), 0.93 (s, 3 H), 0.58–0.52 (m, 4 H); ^{13}C NMR ($CDCl_3$) 217.19, 135.49, 58.58, 51.30, 52.30, 48.04, 22.81, 15.40, 8.30, 6.84 ppm; *m/e* (M^+) calcd 216.1197, obsd 216.1169.

Catalytic Hydrogenation of 18. A solution of **18** (2.50 g, 11.6 mmol) in ethyl acetate (50 mL) containing 10% palladium on charcoal (20 mg) was subjected to atmospheric hydrogenation until 1 equiv of hydrogen had been adsorbed. Celite was added and the mixture was filtered to provide a filtrate whose evaporation gave **19** as a colorless solid (2.40 g, 94.8%): mp 78.0–79.5 °C (from ligroin); IR (CH_2Cl_2) 1720 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 3.52 (m, 2 H), 2.00 (m, 2 H), 1.75–1.72 (m, 2 H), 1.25–1.22 (m, 2 H), 1.15 (s, 3 H), 1.09 (s, 3 H), 0.60–0.56 (m, 4 H); ^{13}C NMR ($CDCl_3$) 219.11, 58.07, 54.36, 45.74, 38.71, 24.91, 24.21, 15.78, 6.45, 5.94 ppm; *m/e* (M^+) calcd 218.1306, obsd 218.1354.

Anal. Calcd for $C_{14}H_{18}O_2$: C, 77.03; H, 8.31. Found: C, 76.41; H, 8.42.

Reduction–Dehydration of 19. A solution of **19** (100 mg, 0.46 mmol) in dry tetrahydrofuran (15 mL) was added dropwise to a stirred slurry of lithium aluminum hydride (53.2 mg, 1.4 mmol) in the same solvent (20 mL). The reaction mixture was stirred for 10 h, treated slowly with saturated aqueous sodium sulfate solution until hydrogen evolution ceased, and filtered. The filtrate was evaporated to give 90 mg (88%) of diol: mp 94–96 °C; ^{1}H NMR ($CDCl_3$) δ 3.65 (br s, 2 H), 2.65 (br s, 2 H), 2.45–2.40 (m, 4 H), 1.63–1.55 (m, 4 H), 1.09 (s, 3 H), 0.86 (s, 3 H), 0.45–0.35 (m, 4 H); ^{13}C NMR ($CDCl_3$) 82.88, 52.70, 47.95, 45.60, 42.54, 25.31, 24.82, 18.42, 6.45, 6.12 ppm; *m/e* ($M^+ - H_2O$) calcd 204.1514, obsd 204.1496.

To a solution of the diol (1.81 g, 8.23 mmol) in pyridine (50 mL) was added phosphorus oxychloride (2.75 g, 18.1 mmol) dropwise. The reaction mixture was heated at 60 °C for 2 h, cooled, and poured onto a 10% hydrochloric acid–ice slurry. The product was extracted into ether, and the combined ethereal layers were washed with saturated sodium bicarbonate solution and brine prior to drying. Evaporation of the solvent left a light brown oil which was filtered through a column of silica gel (elution with petroleum ether) to give **2** as a clear colorless oil: ^{1}H NMR ($CDCl_3$) δ 5.45 (s, 2 H), 2.13 (m, 2 H), 2.04–2.00 (m, 2 H), 1.46–1.44 (m, 2 H), 1.19 (s, 3 H), 1.17 (s, 3 H), 0.48–0.44 (m, 4 H); ^{13}C NMR ($CDCl_3$) 150.40, 128.04, 57.30, 44.23, 40.89, 28.87, 23.84, 22.96, 6.34, 5.80 ppm; *m/e* (M^+) calcd 186.1409, obsd 186.1369.

Anal. Calcd for $C_{14}H_{18}$: C, 90.26; H, 9.74. Found: C, 90.05; H, 9.84.

Singlet Oxygenation of 12. A solution of **12** (690 mg, 4.73 mmol) and methylene blue (10 mg) in dichloromethane (200 mL) was irradiated at 0 °C with a Sylvania 500-W tungsten halogen lamp for 35 min while oxygen was bubbled continuously through the sample. Following evaporation of the solvent, the residue was subjected to flash chromatography over silica gel (elution with dichloromethane) to give the endoperoxide as a clear oil (630 mg, 75%): ^{1}H NMR ($CDCl_3$) δ 4.76 (dm, J = 14.0 Hz, 2 H), 4.50 (dm, J = 14.0 Hz, 2 H), 2.13 (m, 2 H), 1.89–1.83 (m, 2 H), 1.17 (dd, J = 10.9 and 3.9 Hz, 2 H), 0.56–0.48 (m, 2 H), 0.36–0.28 (m, 2 H); ^{13}C NMR ($CDCl_3$) 137.17, 70.25, 48.06, 29.69, 26.68, 7.33, 6.23 ppm; *m/e* calcd (M^+) 178.0993, obsd 178.1014.

The endoperoxide (570 mg, 3.2 mmol) was heated in acetic acid (70 mL) and acetic anhydride (0.5 mL) for 1.5 h at 80 °C. Pentane and water were added, and the separated aqueous phase was extracted with pentane. The combined organic layers were washed with water, saturated sodium bicarbonate solution, and brine prior to drying and solvent evaporation. Kugelrohr distillation at 80 °C and 0.15 torr gave **3** as a clear colorless oil (120 mg, 23.4%); ^{1}H NMR ($CDCl_3$) δ 7.03 (s, 2 H), 2.53 (m, 2 H), 2.11–2.05 (m, 2 H), 1.40 (dd, J = 10.7 and 3.7 Hz, 2 H), 0.52–0.47 (m, 4 H); ^{13}C NMR ($CDCl_3$) 134.82, 130.01, 46.42, 42.75, 28.98, 7.33, 6.29 ppm.

Anal. Calcd for $C_{11}H_{12}O$: C, 82.45; H, 7.55. Found: C, 82.62, H, 7.57.

Reaction of 1 with *N*-Phenylmaleimide. To a cold (0 °C) solution of **1** (62.6 mg, 0.396 mmol) in chloroform (4 mL) was added *N*-phenylmaleimide (63.0 mg, 0.364 mmol), and the reaction mixture was stirred at this temperature for 5 h. The solvent was evaporated, and the residue was subjected to multiple (3×) elution preparative TLC (silica gel, elution with 10% ethyl acetate in petroleum ether). In this manner, the pure adducts **21** (38.9 mg, 29.7%) and **23** (43.7 mg, 33.3%) were isolated.

For **21**: colorless solid; ^{1}H NMR ($CDCl_3$) δ 7.47–7.24 (m, 5 H), 3.47 (s, 2 H), 3.01 (s, 2 H), 2.24 (br s, 2 H), 2.04–1.97 (m, 2 H), 1.72 ($^{1/2}$AB, J = 8.1 Hz, 1 H), 1.62 ($^{1/2}$AB, J = 8.1 Hz, 1 H), 1.35–1.26 (m, 2 H), 0.33 (s, 4 H); ^{13}C NMR ($CDCl_3$) 176.99, 154.14, 129.21, 128.66, 126.47,

(33) Houk, K. N.; Rondan, N. G.; Brown, F. K.; Jorgensen, W. L.; Madura, J. D.; Spellmeyer, D. C. *J. Am. Chem. Soc.* **1983**, *105*, 5980.

(34) All cycloaddition reactions were conducted simultaneously on a preparative scale and on a microscale in an NMR tube. The progress or each Diels–Alder process was monitored by integrating the disappearance of starting diene and dienophile, as well as the appearance of the adduct(s) vs. time. In no instance was formation of an extraneous product noted, and complete consumption of diene was invariably achieved. The less than quantitative isolated yields are the result of mechanical losses during chromatography (scale depentent) and, in certain cases (DMAD adducts, ethylene extrusion; MA adducts, partial hydrolysis during chromatography), brought on by a chemical side reaction. In no example was reversibility noted. On this basis, the product ratios are tacitly assumed to be the end result of kinetic control.

48.56, 48.45, 47.09, 45.83, 43.70, 25.87, 7.23, 6.57 ppm; *m/e* (M^+) calcd 331.1572, obsd. 331.1530.

For **23**: white needles, mp 196 °C (from ethyl acetate); ^1H NMR ($CDCl_3$) δ 7.5–7.23 (m, 5 H), 3.53 (s, 2 H), 2.79 (s, 2 H), 2.38 (s, 2 H), 1.82 (d, *J* = 7.4 Hz, 2 H), 1.74 (d, *J* = 10.3 Hz, 1 H), 1.55 (d, *J* = 10.3 Hz, 1 H), 0.92 (d, *J* = 7.4 Hz, 2 H), 0.55–0.50 (m, 2 H), 0.33–0.28 (m, 2 H); ^{13}C NMR ($CDCl_3$) 177.15, 156.98, 129.20, 128.60, 126.47, 52.23, 49.88, 47.09, 46.21, 46.05, 26.91, 9.96, 5.86 ppm; *m/e* (M^+) calcd 331.1572, obsd 331.1509.

Anal. Calcd for $C_{22}H_{21}NO_2$: C, 79.73; H, 6.39. Found: C, 79.41; H, 6.38.

Epoxidation of 21. A solution of **21** (42.7 mg, 0.13 mmol) in dichloromethane (10 mL) was treated with buffer-washed *m*-chloroperbenzoic acid (33.54 mg, 0.20 mmol). This solution was heated at the reflux temperature for 10 h, cooled, and treated with saturated sodium thiosulfate solution. The organic layer was separated, washed with water and brine, dried, and evaporated. Preparative TLC of the residual solid (silica gel, elution with 10% ethyl acetate in petroleum ether) afforded 40 mg (92%) of **22** as colorless crystals: mp 286 °C (from ethyl acetate); ^1H NMR ($CDCl_3$) δ 7.49–7.2 (m, 5 H), 3.62 (s, 2 H), 3.31 (s, 2 H), 2.15 (s, 2 H), 2.15–2.0 (m, 2 H), 1.91–1.79 (m, 3 H), 0.92 nd, *J* = 11.0 Hz, 1 H), 0.79–0.73 (m, 2 H), 0.21–0.16 (m, 2 H); ^{13}C NMR ($CDCl_3$) 169.90, 129.24, 128.80, 126.36, 5.25, 47.40, 47.23, 44.75, 37.27, 31.41, 27.14, 12.06, 3.07 ppm.

Anal. Calcd for $C_{22}H_{21}NO_3$: C, 75.84; H, 6.37. Found: C, 75.69; H, 6.27.

Reaction of 1 with *p*-Benzoquinone. A solution of **1** (120 mg, 0.76 mmol) and *p*-benzoquinone (77.8 mg, 0.72 mmol) in chloroform (5 mL) was stirred at room temperature for 3 days and evaporated. The residue was subjected to multiple elution (3×) preparative TLC (silica gel, elution with 5% ethyl acetate in petroleum ether). There was isolated 40.2 mg (20%) of **24** and 18.9 mg (7.1%) of **26**.

For **24**: yellow solid, mp 141–142 °C (from ethyl acetate; ^1H NMR ($CDCl_3$) δ 6.59 (s, 2 H), 3.34 (s, 2 H), 2.63 (s, 2 H), 2.24 (s, 2 H), 2.1–1.9 (m, 2 H), 1.35–1.25 (m, 4 H), 0.26 (s, 4 H); ^{13}C NMR ($CDCl_3$) 199.17, 153.63, 141.93, 50.46, 49.26, 48.55, 46.03, 45.65, 25.97, 7.16, 6.56 ppm; *m/e* (M^+) calcd 266.1307, obsd 266.1293.

For **26**: yellow solid, mp 146 °C (from ethyl acetate); ^1H NMR ($CDCl_3$) δ 6.7 (s, 2 H), 3.4 (s, 2 H), 2.41 (s, 2 H), 2.39 (s, 2 H), 1.79 (d, *J* = 10.3 Hz, 2 H), 1.50 ($^{1/2}$AB, *J* = 12.9 Hz, 1 H), 1.32 ($^{1/2}$AB, *J* = 12.9 Hz, 1 H), 0.5 (m, 2 H), 0.31 (m, 2 H); ^{13}C NMR ($CDCl_3$) 199.72, 156.31, 141.66, 52.62, 50.24, 49.75, 47.29, 46.96, 26.95, 9.84, 5.69 ppm; *m/e* (M^+) calcd 266.1307, obsd 266.1266.

Epoxidation of 24. A solution of **24** (36.3 mg, 0.137 mmol) and *m*-chloroperbenzoic acid (26.12 mg, 0.21 mmol) in dichloromethane (10 mL) was stirred at 0 °C for 9.5 h and worked up in the predescribed manner. There was isolated 35 mg (90.6) of **25** as yellow prisms: mp 248–250 °C (from ethylene acetate); ^1H NMR ($CDCl_3$) δ 6.77 (s, 2 H), 3.47 (d, *J* = 2.4 Hz, 2 H), 3.29 (s, 2 H), 2.15 (s, 2 H), 1.86–1.82 (m, 5 H), 0.75 (t, *J* = 7.7 Hz, 2 H), 0.66 (d, *J* = 10.2 Hz, 1 H), 0.16 (t, *J* = 7.7 Hz, 2 H); ^{13}C NMR ($CDCl_3$) 197.87, 142.00, 58.79, 50.48, 47.41, 46.87, 37.19, 35.00, 27.46, 12.10, 3.08 ppm.

Anal. Calcd for $C_{18}H_{18}O_3$: C, 76.57; H, 6.43. Found: C, 76.30; H, 6.54.

Reaction of 1 with DMAD. A cold (−20 °C) solution of **1** (120 mg, 0.76 mmole and DMAD (102 mg, 0.72 mmol) in chloroform (4 mL) was stirred for 6 h and evaporated. Multiple elution (3×) TLC of the residue (silica gel, elution with 5% ethyl acetate in petroleum ether) afforded pure samples of **27** (30.3 mg, 13.3%) and **29** (5.8 mg, 2.5%). Extensive decomposition was noted during the purification process.

For **27b** yellowish oil; ^1H NMR ($CDCl_3$) δ 3.75 (s, 2 H), 3.73 (s, 6 H), 2.49 (d, *J* = 6.9 Hz, 1 H), 2.34 (br s, 2 H), 2.22 (d, *J* = 6.9 Hz, 1 H), 1.61 (m, 2 H), 0.6–0.47 (m, 4 H), 0.29–0.24 (m, 2 H); ^{13}C NMR ($CDCl_3$) 166.09, 158.60, 150.68, 70.04, 52.43, 51.99, 48.71, 44.07, 23.13, 6.18 ppm; *m/e* (M^+) calcd 300.1362, obsd 300.1362.

For **29**: yellowish oil; ^1H NMR ($CDCl_3$) δ 3.79 (s, 2 H), 3.77 (s, 6 H), 2.60 (d, *J* = 6.7 Hz, 1 H), 2.49 (s, 2 H), 2.12 (d, *J* = 6.7 Hz, 1 H), 1.90 (d, *J* = 7.2 Hz, 2 H), 1.12 (dd, *J* = 12.8 and 3.9 Hz, 2 H), 0.32–0.20 (m, 4 H); ^{13}C NMR ($CDCl_3$) 166.21, 161.39, 153.74, 77.80, 51.10, 51.94, 48.77, 48.11, 26.57, 8.47, 6.18 ppm; *m/e* (M^+) calcd 300.1362, obsd 300.1369.

Epoxidation of 27. A solution of **27** (94 mg, 0.313 mmol) and *m*-chloroperbenzoic acid (54 mg, 0.313 mmol) in dichloromethane (40 mL) was heated at the reflux temperature for 10 h. The usual workup followed to give 45 mg (45.5%) of **28** as a yellowish oil: ^1H NMR ($CDCl_3$) δ 3.79 (s, 6 H), 3.42 (br s, 2 H), 2.22 (d, *J* = 8.2 Hz, 1 H), 1.94 (br s, 2 H), 1.82 (d, *J* = 8.2 Hz, 1 H), 1.67 (m, 2 H), 1.25 (m, 2 H), 0.69 (t, *J* = 7.2 Hz, 2 H), 0.14 (t, *J* = 7.2 Hz, 2 H); ^{13}C NMR ($CDCl_3$) 165.06, 149.58, 66.37, 55.22, 52.27, 48.71, 46.14, 46.14, 37.34, 25.31, 10.99, 2.24 ppm.

Anal. Calcd for $C_{18}H_{20}O_5$: C, 68.34; H, 6.37. Found: C, 68.20; H, 6.56.

Reaction of 1 with PTAD. *N*-Phenyltriazolinedione (66.5 mg, 0.38 mmol) in ethyl acetate (5 mL) was added to a cold (−78 °C) solution of **1** (64.8 mg, 0.41 mmol) in the same solvent 40 mL). The reaction mixture was stirred at this temperature for 5 h, warmed to 20 °C, and evaporated. There was obtained a 1:1 mixture of **30** and **31** as a tan oil which was not stable during attempted separation of any type. For the mixture: ^1H NMR ($CDCl_3$) δ 7.6–7.2 (m, 5 H), 5.27 (br s, 1 H), 5.19 (br s, 1 H), 2.53–2.44 (m, 2.5 H), 2.27–2.26 (m, 1 H), 2.03–1.75 (m, 2.5 H), 1.3–1.16 (m, 1 H), 1.06–0.9 (m, 1 H), 0.6–0.15 (m, 4 H); *m/e* (M^+) calcd 333.1477, obsd 333.1449.

Reaction of 2 with DMAD. A solution of **2** (110 mg, 0.59 mmol) and DMAD (84 mg, 0.71 mmol) in chloroform (6 mL) was heated at 60 °C for 2.5 h and evaporated. TLC purification of the residue (9-fold elution with 2% ethyl acetate in petroleum ether on silica gel) furnished 82.1 mg (42.4%) of **32** and 42.1 mg (21.8%) of **33**.

For **32**: colorless prisms, mp 76 °C (from hexanes); ^1H NMR ($CDCl_3$) δ 3.72 (s, 6 H), 3.30 (s, 2 H), 2.28 (br s, 2 H), 1.60 (m, 2 H), 1.29 (s, 3 H), 1.26 (s, 3 H), 0.61 (dd, *J* = 11.0 and 3.4 Hz, 2 H), 0.56–0.49 (m, 2 H), 0.27–0.19 (m, 2 H); ^{13}C NMR ($CDCl_3$) 166.64, 157.46, 149.91, 83.05, 62.27, 51.94, 48.77, 44.18, 23.95, 23.67, 22.52, 5.90 ppm; *m/e* (M^+) calcd 328.1675, obsd 328.1620.

For **33**: yellowish oil; ^1H NMR ($CDCl_3$) δ 3.75 (s, 6 H), 3.41 (s, 2 H), 2.30 (br s, 2 H), 2.0 (m, 2 H), 1.35 (m, 2 H), 1.22 (s, 3 H), 0.94 (s, 3 H), 0.23 (s, 4 H); ^{13}C NMR ($CDCl_3$) 166.44, 160.31, 153.37, 86.01, 62.94, 51.84, 51.62, 48.40, 25.76, 23.74, 22.92, 9.85, 5.75 ppm; *m/e* (M^+) calcd 328.1675, obsd 328.1696.

Reaction of 2 with PTAD. *N*-Phenyltriazolinedione (91 mg, 0.52 mmol) in ethyl acetate (5 mL) was added to a cold (−78 °C) solution of **2** (100 mg, 0.54 mmol) in the same solvent (20 mL). The reaction mixture was allowed to slowly warm to room temperature during 5 h. The solvent was evaporated, and the isomeric adducts were separated by preparative TLC (4-fold elution with 3.5% ethyl acetate in petroleum ether on silica gel).

For **34**: 27 mg (13.9%); yellow oil; ^1H NMR ($CDCl_3$) δ 7.53–7.49 (m, 5 H), 4.69 (s, 2 H), 2.45 (br s, 2 H), 1.93 (m, 2 H), 1.41 (s, 3 H), 1.24 (s, 3 H), 1.05 (dd, *J* =11.5 and 5.1 Hz, 2 H), 0.60 (m, 2 H), 0.35 (m, 2 H); ^{13}C NMR ($CDCl_3$) 152.93, 129.14, 128.08, 125.65, 125.03, 71.82, 64.90, 49.04, 47.59, 25.88, 22.02, 21.42, 7.43, 6.36 ppm; *m/e* (M^+) calcd 361.1790, obsd 361.1752.

For **35**: 3.1 mg (1.6%); yellowish solid; ^1H NMR ($CDCl_3$) δ 7.4–7.2 (m, 5 H), 4.6 (s, 2 H), 2.3 (br s, 2 H), 2.0 (m, 2 H), 1.5 (br s, 2 H), 1.3 (s, 3 H), 0.90 (s, 3 H), 0.20 (m, 4 H)f *m/e* (M^+) calcd 361.1790, obsd 361.1778.

Reaction of 3 with *N*-Phenylmaleimide. A solution of **3** (108 mg, 0.68 mmol) and *N*-phenylmaleimide (117.3 mg, 0.68 mmol) in chloroform (5 mL) was stirred at room temperature for 4 days. The solvent was evaporated and the residue subjected to preparative thin-layer chromatography on silica gel (elution with 10% ethyl acetate in petroleum ether). There was isolated 120 mg (53%) of **38** as a colorless crystalline solid: mp 173.5–174.5 °C (from ethyl acetate) as the sole product; ^1H NMR ($CDCl_3$) δ 7.87–7.60 (m, 5 H), 5.81 (s, 2 H), 3.23 (s, 2 H), 2.91 (s, 2 H), 2.34–2.28 (m, 2 H), 1.29 (dd, *J* = 10.1 and 2.5 Hz, 2 H), 1.06–0.99 (m, 2 H), 0.79–0.74 (m, 2 H); ^{13}C NMR ($CDCl_3$) 175.32, 154.82, 129.24, 129.15, 128.74, 126.63, 81.68, 48.82, 47.24, 46.85, 25.36, 7.06, 6.63 ppm; *m/e* calcd (M^+) 333.1365, obsd 333.1343.

Hydrogenation of 38. A solution of **38** (7 mg, 0.021 mmol) in ethyl acetate (10 mL) containing 10% palladium on carbon (10 mg) was hydrogenated at atmospheric pressure until 1 equiv of hydrogen had been consumed. Celite was added, and the reaction mixture was filtered through a pad of Celite. Evaporation of the filtrate and recrystallization from ethyl acetate afforded **39** as a colorless solid: mp 229–230 °C; ^1H NMR ($CDCl_3$) δ 7.5–7.23 (m, 5 H), 4.85 (t, *J* = 2.5 Hz, 2 H), 3.78 (s, 2 H), 2.93–2.88 (m, 2 H), 1.87 (br s, 4 H), 1.57 (br s, 2 H), 0.62–0.58 (m, 2 H), 0.49–0.45 (m, 2 H); ^{13}C NMR ($CDCl_3$) 177.53, 129.15, 128.99, 128.71, 126.53, 83.12, 49.38, 47.58, 44.35, 43.5., 24.84, 6.36, 5.92 ppm.

Anal. Calcd for $C_{21}H_{21}NO_3$: C, 75.19; H, 6.32. Found: C, 74.99; H, 6.49.

Reaction of 3 with DMAD. A solution of **3** (140 mg, 0.88 mmol) and DMAD (125 mg, 0.88 mmol) in chloroform (5 mL) was stirred at room temperature for 2 days. Evaporation of the solvent left a residue which was purified by preparative TLC on silica gel (elution with 20% ethyl acetate in petroleum ether) to afford the labile adduct **40** (40 mg, 15%) as an off-white solid: ^1H NMR ($CDCl_3$) δ 5.10 (d, *J* = 0.9 Hz, 2 H), 3.86 (s, 6 H), 2.04 (br s, 2 H), 1.79 (m, 2 H), 1.09 (dd, *J* = 13.6 and 3.9 Hz, 2 H), 0.82–0.74 (m, 2 H), 0.24–0.16 (m, 2 H); ^{13}C NMR ($CDCl_3$) 161.30, 148.72, 136.53, 81.37, 53.10, 44.68, 38.28, 25.55, 11.06, 8.98 ppm.

Table I. Crystallographic Data for **32** ($C_{20}H_{24}O_4$)

formula wt, amu	328.41
space group	$P2_12_12_1$—D_2^4
a, Å	9.608 (2)
b, Å	9.437 (3)
c, Å	19.157 (4)
volume, Å^3	1737
Z	4
density (calcd), g/cm^3	1.255
crystal size, mm^3	0.10 × 0.32 × 0.47
radiation	Mo Kα with graphite monochromator
linear abs coeff, cm^{-1}	0.81
T, °C	−127 (1)
2θ limits, deg	4.0 to 50.0
scan speed, deg/min in ω	2.0 to 24.0
background time/scan time	0.5
scan range, deg in ω	1.8
data collected	$+h,+k,+l$
unique data	1773
unique data with $F_o^2 > 0.5\sigma(F_o^2)$	1554
final no. of variables	217
$R(F)$	0.087
$R_w(F)$	0.061
error in observation of unit wt, e	1.56
R (on F for $F_o^2 > 3\sigma(F_o^2)$)	0.057

Table II. Final Bond Lengths for **32**

bond	length, Å	bond	length, Å
C1–C2	1.560 (8)	C10–C14	1.558 (8)
C1–C6	1.524 (8)	C14–C15	1.526 (8)
C2–C3	1.568 (8)	C14–C16	1.542 (8)
C3–C4	1.526 (8)	C10–C11	1.533 (7)
C4–C5	1.327 (7)	C11–C12	1.327 (7)
C5–C6	1.529 (8)	C12–C13	1.557 (7)
C6–C7	1.510 (8)	C11–C17	1.470 (8)
C3–C7	1.523 (8)	C12–C19	1.480 (8)
C7–C8	1.490 (8)	C17–O1	1.190 (7)
C8–C9	1.518 (8)	C19–O3	1.188 (7)
C7–C9	1.497 (8)	C17–O2	1.320 (7)
C4–C10	1.526 (7)	C19–O4	1.321 (7)
C5–C13	1.514 (8)	O2–C18	1.434 (7)
C13–C14	1.584 (8)	O4–C20	1.456 (7)

Reaction with 3 with Benzyne. To a refluxing solution of **3** (130 mg, 0.81 mmol) in anhydrous dimethoxyethane (1.5 mL) was added simultaneously solutions of anthranilic acid (113 mg, 0.82 mmol) and isoamyl nitrite (114.6 mg, 0.98 mmol) in the same solvent (0.5 and 0.2 mL, respectively) dropwise during 15 min. When gas evolution ceased (5 min), the reaction mixture was evaporated and the residual brown solid was recrystallized from ethyl acetate to give **41** as colorless crystals (50.7 mg, 26%), mp 165 °C, as the only observable adduct: ^{1}H NMR ($CDCl_3$) δ 7.14–6.9 (m, 4 H), 5.59 (s, 2 H), 2.43 (br s, 2 H), 1.44–1.38 (m, 2 H), 0.60–0.53 (m, 2 H), 0.26–0.19 (m, 2 H), 0.0 to −0.70 (7, 2 H); ^{13}C NMR ($CDCl_3$) 159.55, 147.96, 125.05, 120.02, 82.1o, 48.34, 44.35, 24.62, 6.25, 6.03 ppm; m/e calcd (M^+) 236.1201, obsd 236.1231.

Hydrogenation of 41. Catalytic reduction of **41** (20.4 mg) in the predescribed manner furnished 16.5 mg (80%) of **42** as a colorless solid: mp 104–105 °C; ^{1}H NMR ($CDCl_3$) δ 7.31–7.14 (m, 4 H), 5.15 (t, J = 2.4 Hz, 2 H), 3.14 (br, s, 2 H), 1.40 (br s, 2 H), 1.02 (d, J = 8.3 Hz, 2 H), 0.64–0.58 (m, 4 H), 0.33–0.28 (m, 2 H); ^{13}C NMR ($CDCl_3$) 146.84, 126.03, 121.44, 81.56, 48.07, 43.42 (3C), 24.56, 5.89, 5.29 ppm; m/e calcd (M^+) 238.1382, obsd 238.1357.

X-ray Analysis of 32. The crystal used for data collection was a clear, colorless rectangular plate which had been cut from a larger crystal. Since crystals of **32** appear to sublime at room temperature, it was necessary to collect data at low temperature. The systematic absences $h00$, $h = 2n + 1$, $0k0$, $k = 2n + 18$ and $00l$, $l = 2n + 1$, uniquely determine the space group as $P2_12_12_1$. At −127 °C, the unit cell constants a = 9.608 (2) Å, b = 9.437 (3) Å, and c 19.157 (4) Å were determined by the least-squares fit of the diffractometer setting angles for 20 reflections in the 2θ ranges 17.5 to 23.4° with Mo Kα radiation.

The intensities were generally broad and weak. Data were collected in the ω scan mode on a Syntex P$\bar{1}$ diffractometer equipped with graphite monochromated Mo Kα radiation and an LT-1 low-temperature device. A total of 1773 unique intensities was measured and 1024 of these satisfy the condition $F_o^2 > 3\sigma(R_o^2)$. The data were corrected fopr Lorentz and polarization effects and put on an absolute scale by means of a Wilson plot.[35] Because of the small linear adsorption coefficient, no correction for absorption was made.

The structure proved to be difficult to solve, probably because of the weak nature of the data set. The Patterson search option of the DIRDIF

Table III. Final Bond Angles for **32**

angle	deg	angle	deg
C1–C2–C3	102.2 (5)	C11–C10–C14	99.7 (4)
C2–C3–C4	104.9 (5)	C10–C11–C12	107.6 (5)
C2–C3–C7	99.8 (5)	C10–C11–C17	122.6 (5)
C4–C3–C7	97.4 (5)	C12–C11–C17	129.8 (5)
C3–C4–C5	108.4 (5)	C11–C12–C13	107.7 (5)
C3–C4–C10	138.5 (5)	C11–C12–C19	129.2 (6)
C5–C4–C10	106.9 (5)	C13–C12–C19	123.0 (5)
C4–C5–C6	107.9 (5)	C12–C13–C5	103.6 (5)
C4–C5–C13	109.0 (5)	C12–C13–C14	97.8 (4)
C6–C5–C13	137.6 (5)	C5–C13–C14	98.3 (4)
C1–C6–C5	105.4 (5)	C13–C14–C10	92.2 (4)
C1–C6–C7	100.1 (4)	C13–C14–C15	114.7 (5)
C5–C6–C7	98.1 (5)	C13–C14–C16	113.7 (5)
C6–C1–C2	104.7 (5)	C10–C14–C(15)	113.5 (5)
C3–C7–C6	97.4 (5)	C10–C14–C16	115.6 (5)
C3–C7–C8	126.6 (5)	C15–C14–C16	107.1 (5)
C3–C7–C9	122.8 (5)	C11–C17–O1	124.3 (6)
C6–C7–C8	125.6 (5)	C11–C17–O2	112.2 (6)
C6–C7–C9	123.3 (5)	O1–C17–O2	123.5 (6)
C8–C7–C9	61.1 (4)	C17–O2–C18	115.6 (5)
C7–C8–C9	59.7 (4)	C12–C19–O3	122.8 (7)
C8–C9–C7	59.2 (4)	C12–C19–O4	111.8 (6)
C4–C10–C11	103.6 (5)	O3–C19–O4	125.4 (6)
C4–C10–C14	99.4 (4)	C19–O4–C20	114.6 (6)

Table IV. Least-Squares Planes for **32**

Coefficients of the Plane Equation $Ax + By + Cz = D$[a]

plane	A	B	C	D
1	0.109	0.833	0.542	8.515
2	0.469	0.759	0.451	8.562
3	0.988	−0.044	−0.151	2.965
4	−0.456	0.059	0.888	8.186
5	0.867	0.414	−0.277	1.196

Deviations (Å) from Planes

	plane 1	plane 2	plane 3	plane 4	plane 5
C3	−0.002	−0.545[b]			
C4	0.004	0.0002			
C5	−0.004	−0.0002			
C6	0.002	−0.533[b]			
C7		−0.006[b]			
C10	−0.536[b]	−0.0001	0.005		
C11			−0.008		
C12			0.008	0.000	0.001
C13	−0.538[b]	0.0001	−0.005		
C14	0.063[b]		0.903[b]		
C19			0.108[b]	0.000	
O3			0.956[b]	0.000	
O4			−0.848[b]	0.000	
C17			−0.035[b]		−0.004
O1			−0.506[b]		0.002
O2			0.542[b]		0.001

Dihedral Angle between Planes

planes	angle, deg
1–2	21.8 (4)
3–4	54.1 (3)
3–5	28.3 (3)

[a] The plane is described in an orthogonal coordinate system according to the method in Schomaker et al.: Schomaker, V.; Waser, J.; Marsh, R.; Bergman, G. *Acta Crystallogr.* **1959**, **12**, 600. [b] Atoms not included in the calculation of the plane.

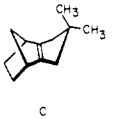
(35) The programs used for data reduction are from the CRYM crystallographic computing package (modified by G. G. Christoph at The Ohio State University, Columbus, Ohio): Duchamp, D. J. "Program and Abstracts"; American Crystallographic Association Meeting, Bozeman, MT, 1964.

Table V. p_y Coefficients at C(1) of the Diene Subunits (Lowest Occupied π Orbital) in Various Isodicyclopentadiene Congeners and Experimental Diels-Alder Cycloaddition Ratios

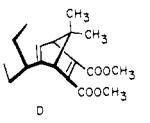
		product ratios (above-plane:below-plane)[a]				
compd	p_y coeff	PM	BQ	benzyne	DMAD	MTAD
2	−0.016				35:65	50:50
36	−0.014	0:100[b]	0:100	0:100	0:100	100:0
37	−0.014	[100:0][c]			30:70	100:0
1	−0.007	54:46	61:39		32:68	50:50
3	+0.018	100:0		100:0	100:0	

[a] PM = *N*-phenylmaleimide; BQ = *p*-benzoquinone; DMAD = dimethyl acetylenedicarboxylate; MTAD = *N*-methyltriazolinedione. [b] Green, K. E., unpublished results. [c] The adduct obtained in this example possesses Alder stereochemistry and cannot strictly be compared with the anti-Alder products formed in the other examples (see text).

package[36] was used to obtain the best possible orientation for fragment C of the molecule. The coordinates for this structural subunit were derived from an earlier study.[30b] The best orientation was then used as



C



D

input to MULTAN 80[37] as a correctly oriented fragment. The C map with the highest combined figure of merit (3.00) also had a fairly high residual 23.7, but it clearly revealed the presence of fragment D. The two mixing carbon atoms were then located on an electron density map.

All full-matrix least-squares refinements were done in the SHELX-76 system.[38] After isotropic refinement of the non-hydrogen atoms converged (R = 0.123), one cycle of anisotropic refinement and a difference electron density mpa revealed the positions of the majority of the hydrogen atoms. The hydrogen atoms were then included in the model as fixed contributions with C-H = 1.00 Å and $B_H = B_{C(iso)} + 1.0$ Å^2. The final refinement cycle with anisotropic non-hydrogen atoms resulted in agreement indices of R = 0.087 and R_w = 0.061 (based on F) for the 1544 intensities with $F_o^2 > 0.5\sigma(R_o^2)$ and 217 variables. A final structure factor calculation on the intensities with $F_o^2 > 3\sigma(R_o^2)$ yielded an R index of 0.057. The final difference electron density map contained maximum and minimum peak heights of 0.41 and −0.45 e Å^{-3}. Scattering factors for the carbon and oxygen atoms[39a] and for the hydrogen atom[39b] were taken from the usual sources.

The crystallographic details for **32** are compiled in Table I and relevant bond lengths and bond angles in Tables II and III, respectively. Selected least-squares planes are included in Table IV.

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Registry No. 1, 93255-09-5; **2**, 93255-10-8; **3**, 93255-11-9; **6**, 70705-73-6; **12**, 36439-88-0; *exo*-**13**, 93255-12-0; *endo*-**13**, 93379-66-9; **14**, 93255-30-2; **15**, 7333-67-7; **16**, 765-46-8; **17**, 26154-22-3; **18**, 93255-13-1; **19**, 93255-14-2; **19** (diol), 93255-31-3; **20**, 93255-15-3; **21**, 93255-16-4; **22**, 93255-17-5; **23**, 93379-60-3; **24**, 93255-18-6; **25**, 93255-19-7; **26**, 93379-61-4; **27**, 93255-20-0; **28**, 93255-21-1; **29**, 93379-62-5; **30**, 93255-22-2; **31**, 93379-63-6; **32**, 93255-23-3; **33**, 93379-64-7; **34**, 93255-24-4; **35**, 93379-65-8; **38**, 93255-25-5; **39**, 93255-26-6; **40**, 93255-27-7; **41**, 93255-28-8; **42**, 93255-29-9; DMAD, 762-42-5; PTAD, 4233-33-4; phenyl(tribromomethyl)mercury, 3294-60-8; *p*-benzoquinone, 106-51-4; benzyne, 462-80-6; anthranilic acid, 118-92-3; isoamyl nitrite, 110-46-3; *N*-phenylmaleimide, 941-69-5.

Supplementary Material Available: Stereodrawing of the unit cell, final positional and thermal parameters, and observed and calculated structure factors for **32** (12 pages). Ordering information is given on any current masthead page.

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Syntheses of Calcium-Selective, Substituted Diaza-Crown Ethers: A Novel, One-Step Formation of Bibracchial Lariat Ethers (BiBLEs)

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Abstract: Ten N,N-disubstituted derivatives of 4,13-diaza-18-crown-6 (**7**) have been prepared, three of which exhibit Ca^{2+}, over either Na^+ or K^+, selectivity. This selectivity has been achieved by utilizing polar, yet uncharged, donor groups such as carbethoxymethyl. Several of these compounds have been prepared by a novel, one-step reaction of aliphatic primary amines with triethylene glycol diiodide. The compounds prepared by this method include examples having the following substituents on nitrogen: benzyl, 2-methoxybenzyl, 2-hydroxyethyl, allyl, 2-furylmethyl, and 2-pyridylmethyl. Isolated yields of pure product for the one-step reaction were in the range 26 ± 4%. The corresponding derivatives of **7** having 2-methoxyethyl, carbethoxymethyl, carboxymethyl, and 2-hydroxybenzyl sidearms were also prepared so that cation selectivity as a function of structure could be assessed. Homogeneous stability constants (K_s) for the association between the various ligands and Na^+, K^+, and Ca^{2+} were determined and are reported. Significant Ca^{2+} selectivity is achieved for the first time in these systems which should retain a high degree of binding dynamics since the donor groups of primary interest in this study are non-ionizable.

During the past decade, there has been enormous synthetic activity in the macrocyclic polyether area. Several thousand novel and interesting structures have been prepared as part of this effort.[1] Although it is quite difficult to characterize all classes of these

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