concentrated to yield 0,542 g of a light orange solid. Column chromatography on silica gel (elution with 5% EtOAc-hexane) furnished 0.289 g (78%) of **42** as yellow crystals; mp 112-113 °C; IR (CCl_4) 3060, 2990, 2940, 2880, 2840, 1945, 1910, 1740, 1630, 1480, 1455, 1430, 1380, 1350, 1330, 1300, 1200, 1150, 1130, 1090, 1040, 935, 845, and 655 cm^{-1}; UV max (CH_3CN) 325 (ϵ = 5600), 314 (5200), 293 (17000), 263 (13000), 230 (38200), and 208 (29200) nm; ^1H NMR (250 MHz, $CDCl_3$) δ 8.10 (dd, J = 8.0 and 1.0 Hz, 1 H), 7.91 (dd, J = 8.0 and 1.0 Hz, 1 H), 7.46 (m, 1 H), 7.35 (m, 1 H), 7.40 (s, 1 H), 3.99 (s, 3 H), 2.38 (s, 3 H), and 1,72 (s, 9 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 155.3, 150.2, 139.9, 135.4, 127.5, 125.4, 124.8, 123.2, 121.0, 120.7, 119.4, 116.5, 116.0, 100.2, 84.7, 56.2, 28.0, and 10.8. Anal. Calcd for $C_{20}H_{20}F_3NO_6S$; C, 52.29; H, 4,39; N, 3.05. Found: C, 52.58; H, 4.53; N, 2.73.

Hyellazole (43). A threaded Pyrex tube (2.5 cm o.d., 1.8 cm i.d., 17 cm in length) fitted with a rubber septa was charged with the triflate **42** (0.416 g, 0.91 mmol), LiCl (0.114 g, 2.72 mmol), 4 mL of dioxane, $PhMe_3Sn$ (0.262 g, 1.09 mmol), and $Pd(PPh_3)_4$ (0.052 g, 0.045 mmol). The resulting yellow suspension was degassed by two freeze-pump-thaw cycles (-196 °C, <0.5 mmHg) and then sealed with a threaded Teflon cap. The yellow reaction mixture was heated at 94 °C for 24 h during which time the color changed to black. The reaction mixture was then allowed to cool to room temperature, and an additional portion of $Pd(PPh_3)_4$ (0.052 g, 0.045 mmol) was added, The mixture was degassed by one freeze-pump-thaw cycle (-196 °C, <0.5 mmHg) and was heated at 94 °C for 14 h and then at 150 °C for 6 h. The resulting mixture was allowed to cool to room temperature, diluted with 10 mL of Et_2O, and washed with two 10-mL portions of 10% NH_4OH solution. The combined aqueous layers were extracted with two 4-mL portions of Et_2O, and the combined organic layers were washed with 10 mL of H_2O, 10 mL of 10% HCl solution, and 10 mL of saturated NaCl solution. The organic phase was dried over Na_2SO_4, filtered, and concentrated to yield 1.02 g of a brown solid, Column chromatography on silica gel (elution with 30% benzene-hexane) furnished 0.163 g (63%) of **43** as white crystals (mp 132-133 °C, lit. mp 133-134 °C) with spectroscopic data fully consistent with that previously reported[20] for hyellazole: IR (CCl_4) 3485, 3065, 3040, 3000, 2945, 2840, 1550, 1495, 1460, 1425, 1380, 1350, 1310, 1295, 1210, 1160, 1150, 1080, 1050, 1030, 1005, 985, 805, 720, 660, 640, and 610 cm^{-1}; ^1H NMR (250 MHz, acetone-d_6) δ 9,55 (br s, 1 H), 8.11 (br d, J = 8.0 Hz, 1 H), 7.71 (s, 1 H), 7.40-7.56 (m, 6 H), 7.30 (dt, J = 7.0 and 1.0 Hz, 1 H), 7.13 (dt, J = 7.0 and 1.0 Hz, 1 H), 3.99 (s, 3 H), and 2.16 (s, 3 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 152.7, 139.5, 137.5, 133.3, 129.9, 128.9, 127.6, 125,5, 125.1, 123.8, 123.7, 120.3, 119.9, 118.8, 110.6, 100.3, 56.1, and 13.7; HRMS, m/e calcd for $C_{20}H_{17}NO$ 287.1310, found 287.1311. Anal. Calcd for $C_{20}H_{17}NO$: C, 83.60; H, 5.96; N, 4.87. Found: C, 83.20; H, 5.90; N, 5.04.

Acknowledgment. We thank the National Institutes of Health for generous financial support.

Registry No. 1, 124687-96-3; **2**, 13279-94-2; **3**, 125569-58-6; **4**, 125569-59-7; **5**, 125569-60-0; **6**, 125569-61-1; **7**, 125569-62-2; **8**, 125569-63-3; **9**, 125569-64-4; **10**, 3282-32-4; **11**, 125569-65-5; **12**, 14088-57-4; **13**, 125569-66-6; **14**, 125569-67-7; **15**, 122760-68-3; **16**, 125569-68-8; **17**, 104875-64-1; **18**, 125569-69-9; **19**, 41441-74-1; **20**, 13169-01-2; **21**, 125569-70-2; **22**, 125569-71-3; **23**, 125569-72-4; **24**, 22744-13-4; **25**, 125569-73-5; **26**, 7023-80-5; **27**, 125569-74-6; **28**, 125569-75-7; **29**, 125569-76-8; **30**, 125569-77-9; **31**, 125569-78-0; **32**, 21443-46-9; **33**, 125569-79-1; **34**, 72676-21-2; **35**, 125569-80-4; **36**, 125569-81-5; **37**, 125569-82-6; **38**, 124687-95-2; **39**, 125569-83-7; **40**, 124688-00-2; **41**, 125569-84-8; **42**, 125569-85-9; **43**, 74364-11-7; 2-ethyl-3-methoxy-4-methyl-1-naphthyl acetate, 125569-86-0; 2-ethyl-3-methoxy-8-methyl-1-naphthyl acetate, 125569-87-1; 2-ethyl-3-methoxy-6-methyl-1-naphthyl acetate, 125569-88-2; 3-ethyl-2-methoxy-5,6,7,8-tetrahydro-4-phenanthryl acetate, 125569-89-3; 2-ethyl-3-methoxy-5,6,7,8-tetrahydro-1-anthryl acetate, 125569-90-6; 3-acetylindole, 703-80-0; 6-diazo-2-ethylidenecyclohexanone, 125569-91-7; 6-diazo-2-ethylidenecycloheptanone, 125569-92-8; 6-ethyl-7-methoxy-4-methyl-5-indanol, 125569-93-9; 3-ethyl-4-methoxy-1-methyl-5,6,7,8-tetrahydro-2-naphthol, 125569-94-0; 1-acetylcyclohexene, 932-66-1; acetophenone, 98-86-2; propiophenone, 93-55-0; 2-methylacetophenone, 577-16-2; *p*-(carbomethoxy)benzoyl chloride, 7377-26-6; *m*-toluoyl chloride, 1711-06-4; 2-acetylfuran, 1192-62-7; 3-acetylthiophene, 1468-83-3.

Tandem Cyclization-Cycloaddition Reaction of Rhodium Carbenoids. Scope and Mechanistic Details of the Process

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Received October 2, 1989

Abstract: Treatment of 1-diazo-2,5-pentanediones with rhodium(II) carboxylates affords cyclic six-ring carbonyl ylide dipoles. These species undergo facile 1,3-dipolar cycloaddition with both electron-deficient and electron-rich dipolarophiles. In certain cases 2:1 cycloadducts are formed. The higher order cycloadducts are derived by further dipolar cycloaddition of the carbonyl ylide across the keto group of the initially formed 1:1 cycloadduct. Attempts to obtain a cycloadduct from the reaction of the diazo dione with nonactivated olefins led to 6-substituted 2*H*-pyran-3(4*H*)-ones. The formation of this ring system proceeds via a 1,4-hydrogen shift from the intermediate carbonyl ylide dipole. The observed regioselectivity in these cycloadditions can be nicely accommodated in terms of frontier molecular orbital theory. A type II FMO interaction is suggested since carbonyl ylides possess one of the smallest HOMO-LUMO energy gaps of the common 1,3-dipoles. The HOMO of the dipole is dominant for reactions with electron-deficient dipolarophiles such as methyl propiolate, while the LUMO becomes important for cycloaddition to more electron-rich species such as propargyl ethers. MNDO calculations indicate that the largest coefficient in the HOMO resides on the enolate carbon, whereas the γ-carbon bears the largest coefficient in the LUMO.

The stereoselective preparation of highly substituted oxygen heterocycles, especially structurally complex tetrahydrofurans and tetrahydropyrans, has attracted considerable attention in recent years.[1,2] These medium size cyclic ethers are becoming increasingly recognized as common structural units in naturally occurring compounds such as the ionophores,[3] the brevetoxins,[4]

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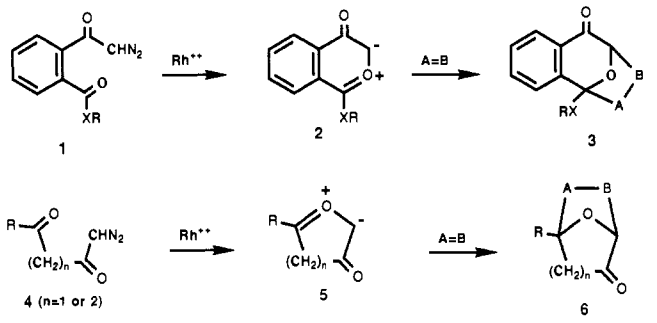
0002-7863/90/1512-3100$02.50/0

Scheme I



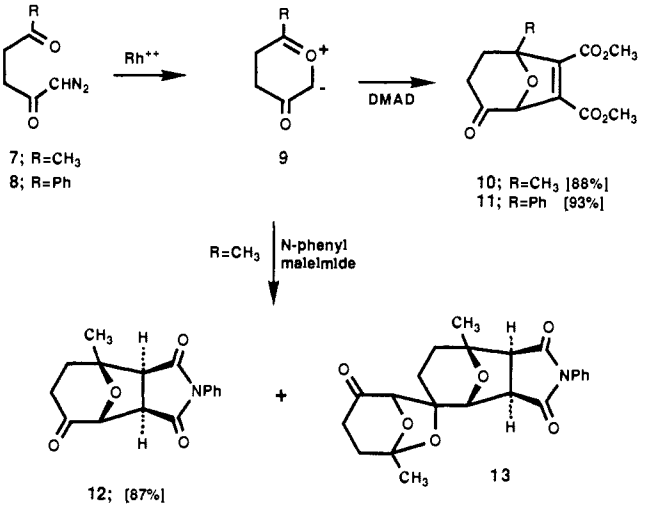
and other marine natural products.[5] Due to the increasing interest in these bioactive molecules and the well-recognized problems in building midsize rings, the synthesis of such systems becomes a challenging synthetic objective, Although a variety of methods exist for dihydro- and tetrahydrofuran synthesis,[1,6] few of these are based on an annulation strategy[7] and, of those that are, single step procedures are uncommon.[8,9] Conceptually, the 1,3-dipolar cycloaddition of carbonyl ylides with π bonds represents an attractive strategy for tetrahydrofuran formation,[10] Several years ago, we developed a [3 + 2] annulation protocol for the synthesis of tetrahydrofurans based on the transition-metal-catalyzed reaction of diazodiones.[11] The reaction involves formation of a cyclic carbonyl ylide which is followed by 1,3-dipolar cycloaddition.[12-16] The general synthetic approach is outlined in Scheme I. Our ongoing interest in the generality and synthetic utility of this method inspired us to take a detailed look at the scope and mechanistic details of the process. The present paper documents the results of these studies.

Results and Discussion

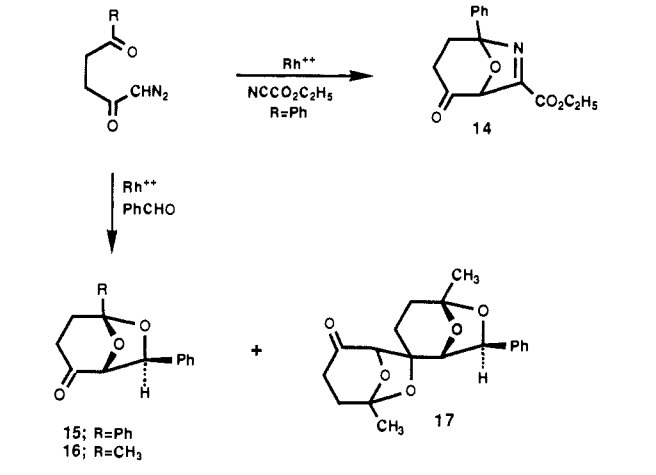
Our initial forays into this tandem cyclization-cycloaddition chemistry involved systems in which the diazo ketone and the remote carbonyl group were attached in a 1,2-fashion on a benzene ring (i.e., **1** → **3**).[11] This arrangement provides interatomic distances and bond angles that are ideal for dipole formation, Our ongoing interest in this procedurally simple methodology brought several questions into focus. What are the geometric and electronic requirements of the remote carbonyl for dipole formation? What sort of stereo- and regioselectivity can be expected in the cycloaddition of these carbonyl ylides? How sensitive are these dipoles to the electronic nature of the dipolarophile? The initial studies used relatively nucleophilic carbonyls (i.e., amides and esters) to trap the metal carbenoid and form the carbonyl ylide.[11] To simultaneously test the geometric and electronic requirements of dipole formation, the 1-diazo-2,5-pentanedione backbone was targeted. Note that in this system (i.e., **7** → **9**) the dipole is being formed by attack of a less nucleophilic ketonic carbonyl and that the tether in this system is a simple dimethylene chain, introducing a conformational "floppiness" not available in the previously studied benzo systems.[17]

Diazo diones **7** and **8** were conveniently prepared from levulinic acid and 3-benzoylpropionic acid, respectively, in the usual manner. The tandem cyclization-cycloaddition reaction was effected by

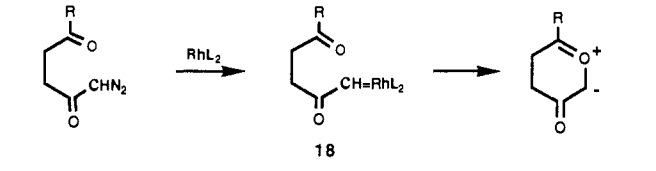
Scheme II



Scheme III



Scheme IV



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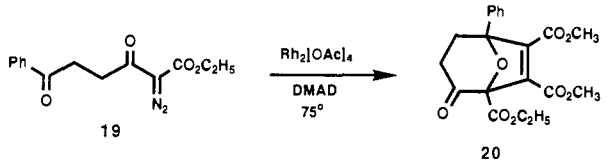
Scheme V



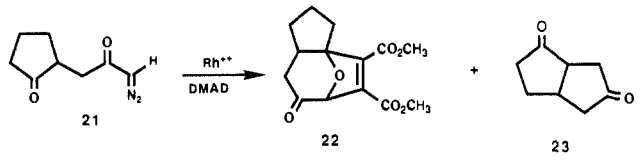
19 20

treating a degassed benzene solution of diazo dione **7** (or **8**) and dimethyl acetylenedicarboxylate (or *N*-phenylmaleimide) with a rhodium carboxylate catalyst at ambient temperature, Subsequent chromatography on silica gel afforded the pure cycloadduct in excellent yield (see Experimental Section).

Several types of dipolarophiles were examined so as to establish the scope and generality of the process. The cycloaddition proceeded readily with both Manders reagent[18] and benzaldehyde giving rise to a single cycloadduct in both cases, Several aspects of this chemistry are notable. First, these tandem cyclization–cycloaddition reactions are very clean. This is a clear testimony to the efficiency of the method and the mildness of the reaction conditions, In addition, the yields are generally quite high (especially with the activated dipolarophiles). In certain cases, however, 2:1 cycloadducts were also formed (i.e., **13**; **17**). Formation of these higher order cycloadducts can be dictated by the stoichiometry employed. An excess of trapping agent leads to predominant formation of the 1:1 adduct, while a dipolarophile deficiency leads to a significant yield of the 2:1 adducts.

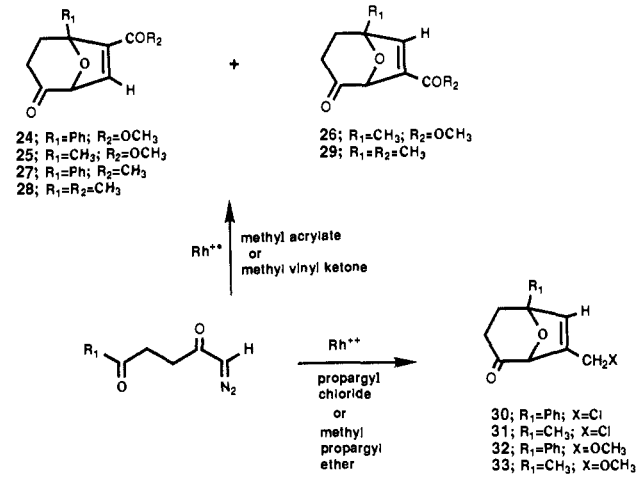
Among all the catalysts which have been developed for carbene addition to multiple π bonds,[20] rhodium(II) carboxylates are the most effective for bimolecular reactions that employ diazo carbonyl compounds.[21,22] We have made similar observations with the above diazo dione systems.[23] Not only are yields significantly higher with rhodium catalysts, but the reaction conditions are frequently gentle enough to allow the reaction to be carried out at 10 °C. Rhodium(II) acetate is a dimer of $Rh(O_2CCH_3)_2$ containing a rhodium–rhodium single bond and four acetate ligands symmetrically attached to the two rhodium atoms.[24] Doyle has suggested that reactions catalyzed by rhodium(II) carboxylates can be viewed as taking place at the carbenic carbon which protrudes from the metal embedded in a wall constructed from its ligands.[21] The rhodium(II)-catalyzed decomposition of diazocarbonyl compounds is believed to involve a metallo-carbenoid intermediate **18** which retains the highly electrophilic properties associated with free carbenes.[21,22] Therefore, in an appropriate acyclic substrate, such an intermediate can be intercepted intramolecularly by the nonbonding electrons on the neighboring carbonyl to effect overall cyclization, Although examples of such cyclizations are known, the reaction has not been widely exploited in synthesis.[16] Several dirhodium(II) compounds with different electronic influences imparted on the rhodium(II) center by its ligands (i,e,, octanoate, mandelate, trifluoroacetate) were prepared so as to determine their catalytic properties, Reactivity evaluations were made from reactions of diazo diones **7** and **8** with several dipolarophiles, The results obtained indicate very little difference in the yield of the cycloadduct. We did find, however, that the more soluble rhodium octanoate was significantly more reactive than the mandelate or acetate catalyst.[25]

Scheme VI



21 22 23

Scheme VII



In order to ascertain what effect an electron-withdrawing substituent would impart on the reactivity of the electrophilic rhodium carbenoid intermediate, we decided to study the chemistry of the diactivated diazo keto ester **19**. This material was synthesized by reacting ethyl 3,6-dioxo-6-phenylhexanoate with methanesulfonyl azide in the usual way.[26] Treatment of **19** with a catalytic quantity of rhodium(II) acetate in benzene at 75 °C in the presence of an excess of DMAD gave the expected cycloadduct **20** in 91% yield. Interestingly, in this case the reaction proceeded very slowly at room temperature and only afforded significant quantities of cycloadduct **20** at the higher temperature. This is presumably a manifestation of the difficulty in losing nitrogen from the destabilized diazo compound and forming the highly reactive rhodium carbenoid derived from **19**.

Since we were interested in the synthetic utility of the cyclization–cycloaddition reaction, we undertook a study of the rhodium(II) acetate catalyzed reaction of the closely related diazocyclopentanone system **21**, Exposure of diazo ketone **21** to the rhodium catalyst in benzene with DMAD afforded a mixture of two products. The major product formed corresponds to cycloadduct **22** derived from a carbonyl ylide intermediate. The minor product **23** (30%) is derived by a competitive C–H insertion which occurs between the metal-stabilized carbene and the methylenic hydrogens on the cyclopentanone ring. There are a variety of examples in the literature of intramolecular C–H insertion by diazo ketones,[27] thereby providing a good precedent for the formation of **23**, Results obtained by Taber and Petty[28] show that there is a kinetic preference for five-membered ring formation, although C–H insertion giving other size rings is also possible, The above results show that C–H insertion of the rhodium carbenoid can be competitive with carbonyl ylide formation and cycloaddition.

Extension of the carbenoid cyclization–cycloaddition sequence to unsymmetrical dipolarophiles was next investigated, so as to

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(23) Representative catalysts which have been examined include Cubronze, $Cu(acac)_2$, $PdCl_2$, $Cu(OTf)_2$, $Mo(CO)_6$, $Fe(CO)_5$, and $Pd(OAc)_2$.
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(25) A typical reaction using 2 mol % of rhodium acetate was complete in 30–45 min at 25 °C in benzene. Using similar amounts of rhodium octanoate as the catalyst, the reaction was generally finished within 5–10 min. Rhodium octanoate dimer can be purchased from Johnson-Matthey, Inc., Chemicals Division, Winslow, NJ 08095. We thank Dr. Thomas J. Blacklock, Merck Sharpe and Dohme Research Labs, Rahway, NJ for a generous sample of this catalyst.
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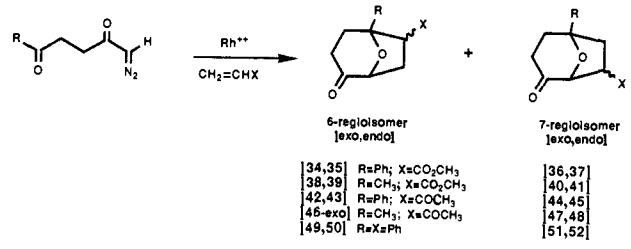
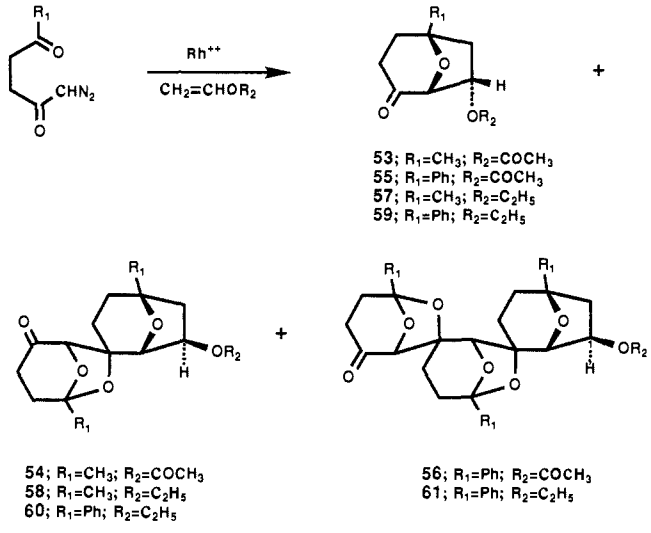
Scheme VIII



Scheme IX



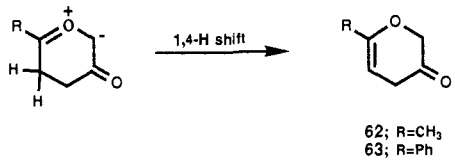
probe the regiochemical aspects of the reaction, To this end, diazo ketone **8** was allowed to react with methyl propiolate. The only product isolated was cycloadduct **24**. The reaction of **7** with methyl propiolate afforded a 4:1 mixture of two regioisomers (**25** and **26**) in 78% overall yield. An analogous set of results was encountered by using 3-butyn-2-one, The dominant regioisomer isolated corresponds to the 6-acetyl-substituted oxabicyclo-[3.2.1]octenone (i.e., **27** or **28**). Most strikingly, when propargyl chloride or methyl propargyl ether was used as the trapping agent, the alternate regioisomeric cycloadduct (i.e., **30–33**) was obtained as the exclusive product.

A variety of other unsymmetrically substituted dipolarophiles were also examined. When methyl acrylate, methyl vinyl ketone, or styrene were used as trapping agents, a mixture of exo/endo isomers of both regioisomeric cycloadducts were obtained.[29] The cycloadducts were separated for full spectral characterization, The assigned regio- and stereochemistry of the products follow from the NMR spectra which show a coupling constant of ca. 8 Hz across the 1,7-positions for both the 6- and the 7-endo isomer. The coupling constant across position 1,7 in the exo isomer is less than 2 Hz, attributable to a dihedral angle approaching 90°. The major isomer isolated with methyl acrylate corresponds to the 6-*exo*-carbomethoxyoxabicyclo[3.2.1]octanone, whereas the 7-exo-substituted regioisomer was the major material formed when methyl vinyl ketone was used (vide infra). Interestingly, the 7-endo isomer is the dominant product produced when styrene was used as the dipolarophile, The effect of the catalyst on the ratio of products was briefly addressed, but the specific catalyst used did not have a pronounced effect on the distribution of products.

We also examined the rhodium-catalyzed reaction of these diazo diones with olefins that do not contain electron-withdrawing substituents on the π bond. The reaction of **7** (or **8**) with vinyl acetate or ethyl vinyl ether afforded a mixture of 1:1, 2:1, and even a 3:1 cycloadduct (see Experimental Section), In these cases, the 1:1 adduct isolated corresponds to the 7-endo substituted regioisomer, while the higher order cycloadducts are derived from

(29) The endo isomer is assigned as that in which the olefinic substituent ends up anti to the oxido bridge.

Scheme X



the 7-*exo*-oxabicyclo[3,2.1]octanone. The cycloaddition does proceed, however, with high regioselectivity producing a single regioisomer in both cases. The formation of the higher order cycloadducts is probably related to the lower reactivity of vinyl acetate and ethyl vinyl ether as compared to the other electron-deficient alkenes (i.e., larger HOMO–LUMO gap).[30] Once the initial 1:1 cycloadduct is formed, it can undergo competitive dipolar cycloaddition across the carbonyl group. All attempts to obtain a cycloadduct from the reaction of the diazo dione with nonactivated olefins (i.e., 1-octene, cyclohexene, etc,) failed. Instead, variable quantities of a 6-substituted 2*H*-pyran-3(4*H*)-one could be detected in the reaction mixture.[31] The formation of **62** (or **63**) involves a 1,4-hydrogen shift from the intermediate carbonyl ylide dipole. It should be noted that Landgrebe and co-workers have encountered a similar transformation in their studies of the transition-metal-catalyzed reaction of aliphatic ketones with ethyl diazo acetate.[32] The isolation of an enol ether was suggested to proceed by an intramolecular 1,4-hydrogen shift from an intermediate carbonyl ylide. In our case the hydrogen-transfer reaction can not take place intramolecularly and presumably involves some other reagent functioning as a base to remove the proton adjacent to the oxonium ion.

The stereochemistry of 1,3-dipolar cycloadditions has been the subject of many studies in the literature.[10] A generally accepted view of these reactions involves an approach of the addends in two parallel planes. Dipolar cycloadditions, like the Diels–Alder reaction, proceed through exo or endo transition states. Examination of the transition states involving cyclic carbonyl ylides (i.e., **9**) with certain substituted 1-alkenes (i.e., acetyl, phenyl, acetoxy) from the perspective of FMO theory suggests that an endo transition state should be favored over its exo counterpart by a favorable secondary orbital interaction.[33] The two plane orientation complex with styrene permits efficient π-overlap of the phenyl and carbonyl groups that are located one above the other. With this system, the attractive van der Waals forces associated with maximal π-overlap are responsible for the preferred cycloaddition stereochemistry giving rise to the endo isomer. The stereochemical outcome of the cycloaddition involving methyl acrylate and methyl vinyl ketone is markedly different. The major products possess the exo stereochemistry. Apparently, with these two systems the transition state leading to the endo isomer suffers repulsive dipole interactions between the two carbonyl groups and consequently the exo orientation is favored. From these results it is clear that the interaction which dominates in a particular case will depend on the individual nature of the substituent groups attached to the alkene and the cyclic carbonyl ylide.

The regioselectivity observed in the above cycloaddition reactions was examined in the light of frontier molecular orbital theory.[33,34] Of the three categories described by Sustmann,[35] type

(30) The 2:1 and 3:1 adducts are formally derived by 1,3-dipolar cycloaddition of the carbonyl ylide across the keto group of the 7-*exo*-oxabicyclo[3.2.1]octanone ring system.

(31) The 6-substituted 2*H*-pyran-3(4*H*)-ones were too labile to be isolated: ^{1}H NMR ($CDCl_3$, 300 MHz) **62** δ 1.85 (s, 3 H), 2.80 (d, 2 H, J = 3.6 Hz), 4.25 (s, 2 H), and 4.73 (t, 1 H, J = 3.6 Hz); ^{1}H NMR **63**: δ 3.04 (d, 2 H, J = 4.0 Hz), 4.40 (s, 2 H), 5.57 (t, 1 H, J = 4.0 Hz), and 7.2–7.9 (m, 5 H).

(32) Landgrebe, J. A.; Iranmanesh, H. *J. Org. Chem.* **1978**, *43*, 1244; Lottes, A. C.; Landgrebe, J. A.; Larsen, K. *Tetrahedron Lett.* **1989**, 4089, 4093.

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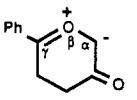
(34) Houk, K. N.; Sims, J.; Duke, R. E.; Strozier, R. W.; George, J. K. *J. Am. Chem. Soc.* **1973**, *95*, 7287.

(35) Sustmann, R. *Tetrahedron Lett.* **1971**, 2717. Sustmann, R.; Trill, H. *Angew Chem., Int. Ed. Engl.* **1972**, *11*, 838. Huisgen, R. *J. Org. Chem.* **1976**, *41*, 403.

Table I. HOMO and LUMO Energies and Coefficients for Cyclic Carbonyl Ylide **9** (R = Ph)



atom no.	α	β	γ
HOMO coeff	−0.51		+0.66
LUMO coeff	+0.49	−0.41	+0.31

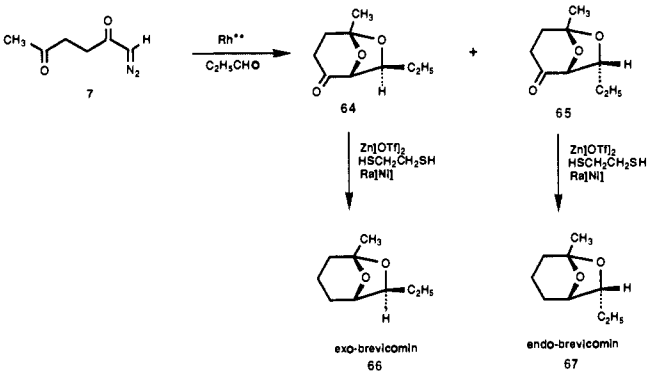
dipolarophile	energy separation (ΔE eV) type I[a]	type III[b]
methyl propiolate	8.03	10.09
methyl propargyl ether	9.63	9.04
methyl acrylate	7.80	9.65
methyl vinyl ketone	7.85	9.41
styrene	7.82	7.56
ethyl vinyl ether	9.21	8.02
vinyl acetate	8.47	8.45

[a] $[HOMO_{(dipole)}-LUMO_{(dipolarophile)}]$. [b] $[HOMO_{(dipolarophile)}-LUMO_{(dipole)}]$.

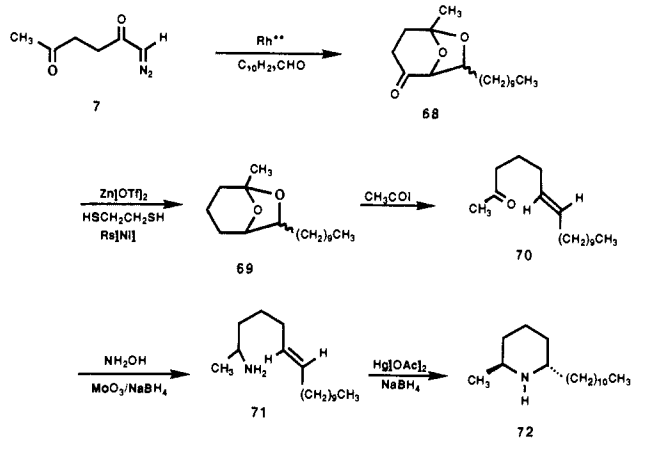
II is particularly common for carbonyl ylides since they possess one of the smallest HOMO–LUMO gaps of the common 1,3-dipoles.[34] According to the FMO treatment of such reactions, the preferred regioisomer will be that in which the atoms bearing larger coefficients of the interacting frontier orbitals overlap,[33] Approximate sizes of the frontier orbital coefficients at the reaction centers of these cyclic carbonyl ylides were calculated by using the QCPE AMPAC program with the AM1 Hamiltonian. The MNDO calculations indicate that the atomic coefficient at the α-position is larger than the γ-position in the HOMO for these cyclic carbonyl ylides (see Table I).[36] The calculations also indicate that the largest coefficient in the LUMO resides on the γ-position (which bears either the methyl or phenyl group),[36] In general, the C_β coefficient of both the HOMO and LUMO is larger than the C_α coefficient for electron-deficient alkenes and alkynes. With methyl propiolate and 3-butyn-2-one, the dominant interaction is between its LUMO and the HOMO of the dipole (type I), which predicts the 6-regioisomer as the major product, exactly as observed, The regiochemical crossover encountered with propargyl chloride or methyl propargyl ether can also be nicely accounted for. With these alkynes, the dominant interaction is the [LUMO-dipole HOMO-dipolarophile] (type III), which correctly predicts formation of the 7-substituted regioisomer. For methyl acrylate the main interaction is between its LUMO and the HOMO of the dipole (type I) which accommodates the predominance of the 6-regioisomer. Interestingly, the addition of methyl vinyl ketone to the dipole affords a 1:2 mixture favoring the 7-substituted isomer. This result can be explained by the involvement of the [HOMO(MVK)–LUMO(dipole)] interaction (type III) which participates here more than with methyl acrylate. This type III interaction favors the 7-regioisomer since the relative coefficient sizes in the LUMO of the dipole differ more significantly than in the HOMO. A similar argument can be made with styrene, since, with this alkene, the energy differences between the type I (ΔE = 7.82) and type III interactions (ΔE = 7.56) are very close. Under these circumstances the 7-substituted regioisomer should dominate, exactly as found. The addition of vinyl acetate or ethyl vinyl ether to the dipole gives exclusively the 7-regioisomer, and this can be attributed to the importance of the type III FMO interaction. Thus, all the regiochemical results encountered can be readily accommodated in terms of perturbation theory.

(36) Calculations were performed with the AMPAC program (QCPE 506). The calculations show that for the methyl carbonyl ylide **9** (R = CH_3) the LUMO is located at −0.93 eV and the HOMO at −7.95 with coefficients of +0.55 (γ) and −0.68 (α) in the HOMO and coefficients of −0.62 (γ), +0.45 (β), and −0.37 (α) in the LUMO. The general trends outlined with **9** (R = Ph) also hold for the methyl-substituted dipole although some slight differences in regiochemistry are noted (see Experimental Section).

Scheme XI



Scheme XII



At this point in our studies we felt that it would be desirable to demonstrate the synthetic utility of this methodology by the total synthesis of some appropriate naturally occurring material, With this thought in mind we turned our attention to the synthesis of brevicomin. The exo and endo isomers of brevicomin are exuded by the female Western pine beetle and the exo isomer is known to be a key component of the aggregation pheremone of this destructive pest.[37] The endo isomer is a potent inhibitor of the aggregation behavior of the likewise destructive Southern pine beetle.[38,39] Our route to *exo*- and *endo*-brevicomin is based on the finding that diazo diones **7** and **8** react with benzaldehyde to give the 6,8-dioxabicyclo[3.2.1]octanone system (**15** or **16**) in 85% yield. In a similar manner, treatment of 1-diazo-2,5-hexanedione (**7**) with a catalytic amount of rhodium(II) acetate in benzene with propionaldehyde afforded the 6,8-dioxabicyclo[3,2,1]octane ring system in 60% yield as a 2:1 mixture of exo (**64**) and endo (**65**) isomers. The regiochemistry observed can be readily rationalized in terms of maximum overlap of the dipole HOMO–dipolarophile LUMO. The mixture of isomers was separated by silica gel chromatography. Each stereoisomer was treated with ethanedithiol in the presence of zinc triflate. The resulting cyclic dithioketals were reduced with Raney nickel giving rise to both *exo*- (**66**) and *endo*-brevicomin (**67**) in 87% yield.

Solenopsin A (**72**) corresponds to one of the constituents of the venom derived from the fire ant, *Solenopsis saevissima*.[40] The

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(39) See: Oehlschlager, A. C.; Johnston, B. D. *J. Org. Chem.* **1987**, *52*, 940 for leading references for some alternate syntheses of brevicomin.

(40) Adrouny, G. A.; Derbes, V. J.; Jung, R. C. *Science* **1958**, *128*, 306. Blum, M. S.; Walker, J. R.; Callahan, P. S.; Novak, A. F. *Science* **1958**, *128*, 306.

(41) Mundy, B. P.; Bjorklund, M. *Tetrahedron Lett.* **1985**, 3899. We thank Professor Brad Mundy for providing spectral data of **69** for comparison purposes.

acetyl iodide induced fragmentation of 6,8-dioxabicyclo[3.2.1]-octane **69** has previously been reported as an approach to solenopsin A.[41] Thus, a new synthesis of **69** would constitute a formal synthesis of the fire ant venom. The preparation of the requisite bicyclic ketal was readily achieved by the rhodium(II) acetate induced cycloaddition of diazo dione **7** with undecylic aldehyde. The reaction afforded a 2:1 mixture of the exo and endo isomers (**68**) in 75% isolated yield, The exo isomer was treated with ethanedithiol and then reduced with Raney nickel to give bicyclic ketal **69** in 90% yield.

In conclusion, the high efficiency of the rhodium carbenoid induced cyclization of these acyclic diazodiones coupled with the simplicity of the procedure promises to provide an efficient route to a variety of cyclic tetrahydrofurans. The tandem cyclization-cycloadditions were successful with both electron-deficient and electron-rich dipolarophiles as well as with a variety of carbonyl compounds. The observed regioselectivity is in complete agreement with FMO theory. Other aspects of this reaction and its application to more complex natural product synthesis will appear in forthcoming papers.

Experimental Section

Melting points were determined on a Thomas-Hoover capillary melting point apparatus and are uncorrected. Infrared spectra were run on a Perkin-Elmer Model 283 infrared spectrometer. Proton NMR spectra were obtained on a Varian EM-390 and a GE QE-300 MHz spectrometer. ^{13}C NMR spectra were recorded on an GE QE-300 75 MHz spectrometer. Microanalyses were performed at Atlantic Microlabs, Atlanta, GA. Mass spectra were determined with a VG MM-7070S mass spectrometer at an ionizing voltage of 70 eV.

Preparation of 1-Diazo-2,5-hexanedione (7). To a solution containing 2.32 g of levulinic acid and 1.6 mL of methyl chloroformate in 60 mL of ether was added 2.8 mL of triethylamine. After stirring for 30 min at room temperature, the solution was filtered from the triethylamine hydrochloride, and the filtrate was added to a solution of diazomethane in ether at 0 °C. After stirring the solution overnight at 10 °C, the solvent was removed under reduced pressure and the crude residue was chromatographed on a silica gel column using a 25% ethyl acetate–hexane mixture as the eluent. The major fraction contained 2.1 g (75% yield) of a pale yellow oil whose structure was assigned as 1-diazo-2,5-hexanedione (**7**): IR (neat) 3100, 2910, 2100, 1720, 1640, 1380, 1325, 1170, 1140, 1110, 1040, 990 and 930 cm^{-1}; ^1H NMR (90 MHz, CCl_4) δ 2.13 (s, 3 H), 2.51 (t, 2 H, J = 6.0 Hz), 2.65 (t, 2 H, J = 6.0 Hz), and 5.30 (s, 1 H).

Preparation of 1-Diazo-5-phenyl-2,5-pentanedione (8). To a solution containing 1.78 g of 3-benzoylpropionic acid and 0.9 mL of methyl chloroformate in 50 mL of ether was added 1.5 mL of triethylamine. The resulting white suspension was stirred at room temperature under nitrogen for 2 h. The precipitated triethylamine hydrochloride was removed by filtration, and the resulting pale yellow solution was immediately treated with 25 mmol of freshly prepared diazomethane at 0 °C. The mixture was allowed to warm to room temperature overnight. The solvent was removed under reduced pressure, and the resulting yellow oil was chromatographed on a silica gel column by using a 3:1 hexane–ethyl acetate mixture as the eluent to give 1.36 g of 1-diazo-5-phenyl-2,5-pentanedione (**8**) (67%) as yellow needles, mp 55–56 °C: IR (KBr) 3100, 2920, 2110, 1690, 1645, 1385, 1360, 755 and 700 cm^{-1}; ^1H NMR (CCl_4, 90 MHz) δ 2.65 (t, 2 H, J = 6.0 Hz), 3.25 (t, 2 H, J = 6.0 Hz), 5.30 (s, 1 H), 7.30–7.50 (m, 3 H), and 7.80–8.00 (m, 2 H). Anal. Calcd for $C_{11}H_{10}N_2O_2$: C, 65.34; H, 4.98; N, 13.85. Found: C, 65.43; H, 5.02; N, 13.81.

Preparation and Rhodium(II) Acetate Catalyzed Reaction of Ethyl 2-Diazo-3,6-dioxo-6-phenylhexanoate (19). A solution containing 5.35 g of benzoylpropionic acid in 100 mL of tetrahydrofuran was treated with 4.86 g of carbonyl diimidazole. The resulting yellow solution was stirred at room temperature overnight. A freshly prepared solution containing 45 mmol of isopropyl magnesium bromide in tetrahydrofuran was cooled to 0 °C and was treated with 45 mmol of ethyl hydrogen malonate. After stirring the off-white slurry at 0 °C for 30 min, the mixture was allowed to warm to room temperature for 30 min and was then heated at reflux for 30 min. A solution of the dianion of ethyl malonate was cooled to 0 °C, and the solution of the previously prepared imidazolide was added all at once. The mixture immediately turned green-brown in color, and a gummy precipitate was observed to form. After standing at room temperature for 4 h, the reaction mixture was poured onto an ice cold 1.0 M phosphoric acid solution. The aqueous phase was extracted with ethyl acetate, and the combined organic layers were washed with a saturated sodium bicarbonate solution and dried over anhydrous sodium sulfate. The solvent was removed under reduced pressure, and the crude mixture was chromatographed on silica gel by using a 1:1 hexane–ethyl acetate mixture as the eluent to give 3.5 g (47%) of ethyl 3,6-dioxo-6-phenylhexanoate as a pale orange oil: ^1H NMR (CCl_4, 90 MHz) δ 1.27 (t, 3 H, J = 7.5 Hz), 2.90 (t, 2 H, J = 6.0 Hz), 3.23 (t, 2 H, J = 6.0 Hz), 3.50 (s, 2 H), 4.18 (q, 2 H, J = 7.5 Hz), 7.24–7.66 (m, 3 H), and 7.94–8.20 (m, 2 H).

A solution containing 3.5 g of the above compound in 50 mL of acetonitrile was treated with 20 g of methanesulfonyl azide and 4.5 mL of triethylamine at ambient temperature for 12 h. The dark red reaction mixture was poured onto 150 mL of a 10% sodium hydroxide solution, and the mixture was extracted with ethyl acetate. The combined organic layer was dried over anhydrous sodium sulfate. The solvent was removed under reduced pressure, and the crude residue was chromatographed on silica gel by using a 3:1 hexane–ethyl acetate mixture as the eluent to give 1.6 g (41% yield) of diazo keto ester **19**: IR (neat) 3010, 2960, 2150, 1720, 1685, 1655, 1605, 1455, 1375, 1320, 1300, 1275, 1230, 1200, 1175, 1150, 1090, 1025, 770, 755 and 700 cm^{-1}; ^1H NMR (CCl_4, 90 MHz) δ 1.34 (t, 3 H, J = 7.5 Hz), 3.21 (br s, 4 H), 4.30 (q, 2 H, J = 7.5 Hz), 7.28–7.60 (m, 3 H), and 7.83–8.13 (m, 2 H).

A solution containing 267 mg of diazo keto ester **19** and 0.15 mL of dimethyl acetylenedicarboxylate in 10 mL of benzene was treated with 2 mg of rhodium(II) acetate, and the mixture was heated to 75 °C for 30 min. Chromatography of the crude residue on silica gel using a 5% methanol–methylene chloride mixture as the eluent gave 369 mg (91% yield) of cycloadduct **20** as a golden oil: IR (neat) 2980, 1730, 1655, 1440, 1380, 1270, 1205, 1140, 1105, 1045, 905, 760, 710, and 690 cm^{-1}; ^1H NMR ($CDCl_3$, 90 MHz) δ 1.28 (t, 3 H, J = 7.5 Hz), 2.17–3.36 (m, 4 H), 3.80 (s, 6 H), 4.31 (q, 2 H, J = 7.5 Hz), and 7.24–7.60 (m, 4 H); HRMS calcd for $C_{20}H_{20}O_8$ 388.1158, found 388.1154.

Preparation and Rhodium(II) Acetate Catalyzed Reaction of 1-Diazo-3-(2-oxocyclopentyl)-2-propanone (21). A solution containing 1.0 g of (2-oxocyclopentyl)acetic acid in 50 mL of ether was treated with 0.9 mL of methyl chloroformate and 1.5 mL of triethylamine. The resulting white suspension was stirred at ambient temperature for 4 h. The reaction mixture was filtered and was then treated with 25 mmol of freshly prepared diazomethane at 0 °C. The yellow solution was slowly allowed to warm to room temperature overnight. The solvent was removed under reduced pressure, and the crude product was chromatographed on silica gel by using a 3:1 hexane–ethyl acetate mixture as the eluent to give 0.61 g (53% yield) of diazo ketone **21** as a yellow oil: IR (neat) 2980, 2900, 2100, 1735, 1640, 1380, 1335, and 1160 cm^{-1}; ^1H NMR (CCl_4, 90 MHz) δ 1.25–3.15 (m, 9 H) and 5.42 (s, 1 H).

A solution containing 610 mg of diazo ketone **21** and 0.6 mL of dimethyl acetylenedicarboxylate in 40 mL of benzene was treated with 5 mg of rhodium(II) acetate. The mixture was allowed to stir at room temperature for 12 h, and then the solvent was removed under reduced pressure. Chromatography of the resulting oil on silica gel using a 3:1 hexane–ethyl acetate mixture as the eluent gave two products. The first fraction contained 582 mg (60%) of 4,5-dicarbomethoxy-2,3,6,7,8,8a-hexahydro-7-oxa-1*H*-3a,b-epoxyazulene (**22**) as a colorless oil; IR (neat) 2975, 2890, 1730, 1640, 1435, 1325, 1265, 1235, 1205, 1125, 1080, 1015, 970, and 800 cm^{-1}; NMR ($CDCl_3$, 300 MHz) δ 1.47–1.75 (m, 2 H), 1.79–2.21 (m, 3 H), 2.33–2.49 (m, 1 H), 2.55 (dd, 1 H, J = 17.7 Hz and 5.1 Hz), 2.85 (dd, 1 H, J = 17.7 Hz and 8.0 Hz), 3.74 (s, 3 H), 3.81 (s, 3 H), and 4.81 (s, 1 H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 24.5, 33.1, 33.6, 41.1, 42.7, 52.5, 52.6, 85.0, 96.6, 135.7, 148.4, 161.2, 163.8, and 200.2; HRMS calcd for $C_{14}H_{16}O_6$ 280.0947, found 280.0946.

The second fraction contained 156 mg (30%) of a pale yellow oil which was identified as *cis*-bicyclo[3.3.0]octane-3,6-dione (**23**) on the basis of its spectral properties: IR (neat) 2960, 2880, 1770, 1730, 1450, 1410, 1280, 1225, 1200, 1125, and 1065 cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz) δ 1.56–1.73 (m, 2 H), 2.03–2.42 (m, 4 H), 2.40–2.65 (m, 1 H), 2.56 (d, 1 H, J = 17.0 Hz), 2.70 (dd, 1 H, J = 17.0 and 6.9 Hz), and 2.82–2.96 (m, 1 H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 17.6, 36.1, 37.2, 44.2, 47.3, 58.9, 210.3 and 215.6; HRMS calcd for $C_8H_{10}O_2$ 138.0680, found 138.0678.

General Procedure for the Rhodium-Catalyzed Cycloaddition Reaction of 1-Diazoalkanediones with Various Dipolarophiles. A 0.05 M benzene solution containing the appropriate diazoalkanedione and 1.2 equiv of the appropriate dipolarophile was degassed under a nitrogen atmosphere. To this solution was added a catalytic amount of rhodium acetate dimer. The yellow solution was allowed to stir under a nitrogen atmosphere at room temperature for 1 h until no more nitrogen was evolved. The solvent was removed under reduced pressure, and the residue was sub-

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(43) Chaquin, P.; Morizur, J. P.; Kossanji, J. *J. Am. Chem. Soc.* **1977**, *99*, 903.
(44) Cohen, T.; Bhupathy, M. *Tetrahedron Lett.* **1983**, 4163.

jected to silica gel chromatography by using an ethyl acetate–hexane mixture as the eluent to give the cycloadducts. The products were identified on the basis of their spectroscopic properties.

Preparation of 6,7-Dicarbomethoxy-5-methyl-8-oxabicyclo[3.2.1]oct-6-en-2-one (10). This compound was obtained in 88% yield from the reaction of 1-diazo-2,5-hexanedione (**7**) with dimethyl acetylenedicarboxylate: mp 60–61 °C; IR (KBr) 3000, 2970, 2940, 1731, 1665, 1443, 1395, 1335, 1275, 1240, 1145, 1075, 1030, 870, 800, and 760 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 1.52 (s, 3 H), 2.18–2.25 (m, 2 H), 2.48 (dt, 1 H, J = 17.8 and 3.8 Hz), 2.75 (dt, 1 H, J = 17.8 and 8.8 Hz), 3.75 (s, 3 H), 3.85 (s, 3 H), and 4.79 (s, 1 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 22.1, 32.7, 32.9, 52.8, 52.6, 85.9, 88.3, 135.8, 147.0, 161.4, 163.9, and 199.3; UV (acetonitrile) 324 nm (ϵ 460); *m/e* 254, 222, 194, 167, 153, 137, 108, and 93; HRMS calcd for $C_{12}H_{14}O_6$ 254.0790, found 254.0787.

Preparation of 6,7-Dicarbomethoxy-5-phenyl-8-oxabicyclo[3.2.1]oct-6-en-2-one (11). This material was obtained in 93% yield from the reaction of 1-diazo-5-phenyl-2,5-pentanedione (**8**) with dimethyl acetylenedicarboxylate as a colorless oil: IR (neat) 3010, 2960, 1730, 1660, 1450, 1280, 1140, 1030, 765, and 710 cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz) δ 2.55–2.75 (m, 2 H), 2.97–3.01 (m, 2 H), 3.64 (s, 3 H), 3.78 (s, 3 H), 5.06 (s, 1 H), and 7.15–7.55 (m, 5 H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 31.1, 33.0, 52.9, 53.0, 86.6, 91.3, 126.6, 129.3, 129.6, 135.0, 138,7, 149.1, 161.9 and 164.9; HRMS calcd for $C_{17}H_{16}O_6$ 316.0947, found 316.0932.

Preparation of 5-Methyl-2-oxo-*N*-phenyl-8-oxabicyclo[3.2.1]octan-6,7-*exo*-dicarboximide (12). This material was obtained in 87% yield as a white solid from the reaction of 1-diazo-2,5-hexanedione (**7**) with 1.1 equiv of *N*-phenylmaleimide: mp 192–193 °C; IR (KBr) 3000, 2960, 1733, 1713, 1603, 1502, 1390, 1201, 1103, 1030, 853, 762 and 700 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 1.56 (s, 3 H), 2.14 (dd, 1 H, J = 13.4 and 9.6 Hz), 2.25 (dd, 1 H, J = 13.4 and 7.5 Hz), 2.44 (dd, 1 H, J = 17.0 and 9.6 Hz), 2.55 (dd, 1 H, J = 17.0 and 7.5 Hz), 3.36 (d, 1 H, J = 7.5 Hz), 3.50 (d, 1 H, J = 7.5 Hz), 4.70 (s, 1 H), and 7.30–7.50 (m, 5 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 23.0, 32.5, 37.9, 50.5, 51.0, 83.2, 83.6, 126.3, 129.0, 129.3, 131.5, 174.4, 174.4 and 202.9; UV (acetonitrile) 300 nm (ϵ 450). Anal. Calcd for $C_{16}H_{15}O_4N$: C, 67.36; H, 5.30; N, 4.91. Found: C, 67.26; H, 5.31; N, 4.88.

Spiro[5-methyl-6,8-dioxabicyclo[3.2.1]octan-2-one-7,2′-5′-methyl-*N*-phenyl-8′-oxabicyclo[3.2.1]octane]-6′,7′-*exo*-dicarboximide (**13**) was isolated as a 2;1 adduct (61%) from the reaction of **7** when only 0.6 equiv of *N*-phenylmaleimide was used as the trapping reagent; mp 226–227 °C; IR (KBr) 3000, 2950, 1715, 1505, 1385, 1205, 1192, 1096, 1060, 855, 765, and 750 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 1.44 (s, 3 H), 1.65 (s, 3 H), 1.50–1.75 (m, 3 H), 1.81–1.92 (m, 1 H), 2.05 (ddd, 1 H, J = 14.0, 8.5, and 3.8 Hz), 2.15 (dt, 1 H, J = 14.0 and 7.3 Hz), 2.40 (dt, 1 H, J = 18.0 and 8.5 Hz), 2.54 (ddd, 1 H, J = 18.0, 9.0, and 3.8 Hz), 4.48 (s, 1 H), 4.62 (s, 1 H), 3.13 (d, 1 H, J = 7.7 Hz), 3.63 (d, 1 H, J = 7.7 Hz), and 7.25–7.51 (m, 5 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 22.5, 23.7, 25.1, 32.9, 33.5, 36.0, 47.6, 51.1, 79.3, 81.3, 83.1, 83.4, 108.3, 126.3, 128.7, 129.1, 131.8, 175.2, 176.6 and 205.5. Anal. Calcd for $C_{22}H_{23}O_6N$: C, 66.49; H, 5.83; N, 3.52. Found: C, 66.48; H, 5.87; N, 3.51.

Preparation of 7-Carbethoxy-5-phenyl-8-oxa-6-azabicyclo[3.2.1]oct-6-en-2-one (14). Treatment of 1-diazo-5-phenylpentane-2,5-dione (**8**) with ethyl cyanoformate according to the general procedure outlined above afforded 7-carbethoxy-5-phenyl-8-oxa-6-azabicyclo[3.2.1]oct-6-en-2-one (**14**) as a white solid in 85% yield; mp 92–93 °C; IR (KBr) 1745, 1635, 1455, 1380, 1350, 1320, 1265, 1230, 1095, 910, 770, and 705 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 1.38 (t, 3 H, J = 7.2 Hz), 2.47–2.68 (m, 4 H), 4.42 (q, 2 H, J = 7.2 Hz), 5.02 (s, 1 H), 7.38–7.46 (m, 3 H), and 7.72 (dd, 2 H, J = 7.8 and 1.3 Hz); ^{13}C NMR (75 MHz, $CDCl_3$) 13.9, 33.1, 33.8, 62.9, 87.9, 109.5, 125.4, 128.4, 128.8, 138.4, 159.8, 163.7, and 195.6. Anal. Calcd for $C_{15}H_{15}NO_4$: C, 65.93; H, 5.53; N, 5.13. Found: C, 65.98; H, 5.58; N, 5.13.

Preparation of 5,7-*exo*-Diphenyl-6,8-dioxabicyclo[3.2.1]octan-2-one (15). This material was obtained in 80% yield as a colorless oil from the reaction of 1-diazo-5-phenyl-2,5-pentanedione (**8**) with benzaldehyde: IR (neat) 3085, 3060, 2990, 2960, 1745, 1505, 1460, 1365, 1320, 1290, 1265, 1215, 1135, 1060, 1035, 920, 770, and 710 cm^{-1}; NMR (300 MHz, $CDCl_3$) δ 2.42–2.57 (m, 2 H), 2.68 (ddd, 1 H, J = 17.5, 8.0, and 2.5 Hz), 2.85 (dt, 1 H, J = 17.5 and 8.7 Hz), 4.52 (s, 1 H), 5.32 (s, 1 H), and 7.20–7.80 (m, 10 H); UV (acetonitrile) 246 (ϵ 850) and 300 nm (ϵ 150); ^{13}C NMR (75 MHz, $CDCl_3$) δ 33.0, 37.1, 80.5, 86.9, 109.6, 125.0, 125.8, 128.0, 128.3, 128.4, 128.6, 139.1, 139.9, and 204.6; *m/e* 280, 223, 174, 158, 132, 105 (base), 104, 91 and 77; HRMS calcd for $C_{18}H_{16}O_3$ 280.1099, found 280.1102.

Preparation of 5-Methyl-7-*exo*-phenyl-6,8-dioxabicyclo[3.2.1]octan-2-one (16). This material was obtained in 85% yield as a colorless oil from the reaction of 1-diazo-2,5-hexanedione (**7**) with benzaldehyde: IR (neat) 3000, 2940, 1725, 1500, 1465, 1390, 1265, 1200, 1170, 1095, 1040, 1020, 910, 850, 745, and 700 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 1.76 (s, 3 H), 2.22 (dd, 2 H, J = 8.7 and 6.0 Hz), 2.62 (dt, 1 H, J = 17.5 and 8.7 Hz), 2.51 (dt, 1 H, J = 17.5 and 6.0 Hz), 4.34 (s, 1 H), 5.07 (s, 1 H), and 7.30–7.40 ppm (m, 5 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 23.9, 32.5, 35.3, 80.2, 86.9, 109.1, 125.9, 128.2, 128.6, 140.4, and 205.3; UV (acetonitrile) 260 (ϵ 300) and 300 nm (ϵ 130); HRMS calcd for $C_{13}H_{14}O_3$ 218.0943, found 218.0942.

The minor product isolated in 7% yield from the reaction of **7** with benzaldehyde was identified as spiro[5-methyl-6,8-dioxabicyclo[3,2.1]-octan-2-one-7,2′-5′-methyl-7′-*exo*-phenyl-6′,8′-dioxabicyclo[3.2.1]octane] (**17**): mp 232–233 °C; IR (KBr) 3000, 2960, 1720, 1390, 1220, 1200, 1180, 1165, 1095, 1045, 1040, 1010, 980, 910, 875, 870, 855, 765, and 710 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 1.59 (s, 3 H), 1.64 (s, 3 H), 1.70–1.90 (m, 2 H), 2.10–2.17 (m, 2 H), 2.26–2.61 (m, 4 H), 4.07 (s, 1 H), 4.60 (s, 1 H), 5.30 (s, 1 H), and 7.25–7.40 (m, 5 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 23.3, 23.5, 25.2, 32.9, 33.7, 34.7, 78.4, 79.9, 84.0, 84.1, 107.9, 108.6, 125.5, 127.5, 128,4, 140.5, and 205.3.

Preparation of 6-Carbomethoxy-5-phenyl-8-oxabicyclo[3.2.1]oct-6-en-2-one (24). This material was obtained in 89% yield from the reaction of 1-diazo-5-phenyl-2,5-pentanedione (**8**) with methyl propiolate: mp 109–110 °C; IR (KBr) 3010, 2960, 1725, 1622, 1506, 1450, 1440, 1330, 1250, 1135, 1105, 1070, 1055, 1030, 900, 810, 760, and 710 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 2.50–2.70 (m, 2 H), 2.70–2.90 (m, 2 H), 3.61 (s, 3 H), 4.89 (d, 1 H, J = 2.2 Hz), 7.10 (d, 1 H, J = 2.2 Hz), and 7.30–7.55 (m, 5 H); UV (acetonitrile) 250 (ϵ 1900) and 310 nm (ϵ 320); ^{13}C NMR (75 MHz, $CDCl_3$) δ 28.9, 32.9, 51.9, 86.1, 86.4, 87.7, 126.7, 128.1, 128.3, 138.7, 139.6, 142.1, 162.9, and 200.8. Anal. Calcd for $C_{15}H_{14}O_4$: C, 69.76; H, 5.46. Found: C, 69.71; H, 5.49.

Preparation of 6-Carbomethoxy-5-methyl-8-oxabicyclo[3.2.1]oct-6-en-2-one (25). The major product (62%) isolated from the reaction of 1-diazo-2,5-hexanedione (**7**) with methyl propiolate was assigned as 6-carbomethoxy-5-methyl-8-oxabicyclo[3.2.1]oct-6-en-2-one (**25**): mp 75–76 °C; IR (neat) 2960, 1725, 1630, 1443, 1390, 1360, 1335, 1250, 1210, 1120, 1080, 1035, 900, 855, 810, 780, and 760 cm^{-1}; NMR (360 MHz, $CDCl_3$) δ 1.58 (s, 3 H), 2.10–2.20 (m, 2 H), 2.43 (dddd, 1 H, J = 18.8, 7.0, 3.3, and 1.2 Hz), 2.58 (dt, 1 H, J = 18.8 and 9.4 Hz), 3.78 (s, 3 H), 4.62 (dd, 1 H, J = 2.6 and 1.2 Hz), and 7.00 (d, 1 H, J = 2.6 Hz); ^{13}C NMR (75 MHz, $CDCl_3$) δ 22.8, 31.6, 33.1, 51.9, 85.7, 139.8, 141.5, 163.0, and 201.1; UV (acetonitrile) 250 nm (ϵ 1200) and 324 nm (ϵ 200); *m/e* 196, 164, 142, 141, 137, 125, 109, 108 and 95; HRMS calcd for $C_{10}H_{12}O_4$ 196.0735, found 196.0741.

The minor product (16% yield) isolated from the same reaction corresponded to 7-carbomethoxy-5-methyl-8-oxabicyclo[3.2.1]oct-6-en-2-one (**26**): mp 70–71 °C; IR (neat) 2960, 1735, 1635, 1443, 1390, 1345, 1280, 1120, 1060, 1040, 860, and 780 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 1.50 (s, 3 H), 1.92 (ddd, 1 H, J = 13.9, 8.8, and 1.1 Hz), 2.22 (dt, 1 H, J = 13.9 and 8.2 Hz), 2.43 (ddd, 1 H, J = 18.0, 8.2, and 1.1 Hz), 2.65 (dt, 1 H, J = 18.0 and 8.8 Hz), 3.73 (s, 3 H), 4.77 (s, 1 H), and 7.01 (s, 1 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 23.2, 32.5, 32.6, 52.2, 85.7, 86.5, 136.3, 147.4, 162.2, and 200.6; UV (acetonitrile) 324 nm (ϵ 420); *m/e* 196, 165, 140, 136, and 109; HRMS calcd for $C_{10}H_{12}O_4$ 196.0735, found 196.0734.

Preparation of 6-Acetyl-5-phenyl-8-oxabicyclo[3.2.1]oct-6-en-2-one (27). Treatment of 1-diazo-5-phenylpentane-2,5-dione (**8**) with 1.2 equiv of 3-butyn-2-one gave 6-acetyl-5-phenyl-8-oxabicyclo[3.2.1]oct-6-en-2-one (**27**) in 95% yield: IR (neat) 1730, 1680, 1605, 1500, 1450, 1370, 1310, 1235, 765, and 705 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 2.20 (s, 3 H), 2.58–2.78 (m, 4 H), 4.89 (d, 1 H, J = 2.1 Hz), 6.97 (d, 1 H, 2.1 Hz), and 7.30–7.55 (m, 5 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 28.1, 29.0, 32.8, 86.2, 88.3, 126.6, 128.0, 128.1, 128.2, 128.5, 138.1, 139.7, 149.5, 194.6 and 201.1; *m/e* 242, 197, 171, 157, 129, 105, 91 and 77; HRMS calcd for $C_{15}H_{14}O_3$ 242.0943, found 242.0938.

Preparation of 6-Acetyl-5-methyl-8-oxabicyclo[3.2.1]oct-6-en-2-one (28). Treatment of 1-diazohexane-2,5-dione (**7**) with 3-butyn-2-one in the presence of a catalytic amount of rhodium acetate produced a mixture of two compounds which could be separated by silica gel chromatography. The major fraction (64%) was assigned as cycloadduct **28**; IR (neat) 1730, 1675, 1610, 1450, 1370, 1325, 1230, 1060, 890, and 850 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 1.61 (s, 3 H), 2.13–2.19 (m, 2 H), 2.41 (s, 3 H), 2.48–2.65 (m, 2 H), 4.70 (d, 1 H, J = 2.0 Hz), and 6.98 (d, 1 H, J = 2.0 Hz); ^{13}C NMR (75 MHz, $CDCl_3$) δ 22.6, 27.7, 31.5, 33.1, 85.5, 86.2, 139.6, 149.0, 194.6 and 201.3; UV (methanol) 228 nm (ϵ 7070) and 325 nm (ϵ 340); HRMS calcd for $C_{10}H_{12}O_3$ 180.0786, found 180.0787.

The minor product (16% yield) was assigned as 7-acetyl-5-methyl-8-oxabicyclo[3.2.1]oct-6-en-2-one (**29**) on the basis of its NMR spectrum: ^1H NMR (300 MHz, $CDCl_3$) δ 1.58 (s, 3 H), 2.02 (dd, 1 H, J = 14.0 and 8.7 Hz), 2.29 (dt, 1 H, J = 14.0 and 8.1 Hz), 2.38 (s, 3 H), 2.48 (dd, 1 H, J = 17.5 and 8.1 Hz), 2.65 (dt, 1 H, J = 17.5 and 8.7 Hz), 4.88 (s, 1 H), and 6.93 (s, 1 H).

Preparation of 7-(Chloromethyl)-5-phenyl-8-oxabicyclo[3.2.1]oct-6-en-2-one (30). Treatment of 1-diazo-5-phenylpentane-2,5-dione (**8**) with 1.2 equiv of propargyl chloride according to the general method outlined above afforded an 85% yield of a 1:1 adduct whose structure was assigned as 7-(chloromethyl)-5-phenyl-8-oxabicyclo[3.2.1]oct-6-en-2-one (**30**) on the basis of its spectral properties: IR (neat) 1735, 1500, 1450, 1345, 1315, 1275, 1055, 1035, 765, and 705 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 2.34 (dd, 1 H, J = 12.2 and 8.7 Hz), 2.48–2.67 (m, 2 H), 2.88 (ddd, 1 H, J = 17.6, 8.8, and 7.3 Hz), 4.20 (s, 2 H), 4.79 (s, 1 H), 6.35 (s, 1 H), and 7.30–7.52 (m, 5 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 32.7, 33,1, 38.0, 87.3, 88.7, 124.8, 127.8, 128.4, 135.1, 140.0, 140.9 and 202.0 ppm; HRMS calcd for $C_{14}H_{13}O_2Cl$ 248.0605, found 248.0603.

Preparation of 7-(Chloromethyl)-5-methyl-8-oxabicyclo[3.2.1]oct-6-en-2-one (31). 1-Diazohexane-2,5-dione (**7**) was treated with 1.2 equiv of propargyl chloride according to the above procedure. Chromatography of the crude mixture using an ethyl acetate–hexane mixture afforded a mixture of the 1:1 and 2:1 cycloadducts. The 1:1 adduct (60%) was assigned as 7-(chloromethyl)-5-methyl-8-oxabicyclo[3.2.1]oct-6-en-2-one (**31**): IR (neat) 1730, 1455, 1385, 1270, 1210, 1180, 1095, 1060, 1040, 865, 810, and 710 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 1.49 (s, 3 H), 1.91 (ddd, 1 H, J = 13.6, 8.8, and 2.2 Hz), 2.21 (dt, 1 H, J = 13.6 and 8.0 Hz), 2.50 (ddt, 1 H, J = 18.0, 8.6, and 1.6 Hz), 2.71 (ddd, 1 H, J = 18.0, 8.5, and 7.6 Hz), 4.16 (s, 2 H), 4.58 (s, 1 H), and 6.15 (s, 1 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 23.6, 32.8, 33.0, 38.2, 85.8, 87.2, 135.5, 140.1 and 202.4; HRMS calcd for $C_9H_{11}ClO_2$ 186.0448, found 186.0443.

The 2:1 cycloadduct (26%) was assigned as spiro[5-methyl-6,8-dioxabicyclo[3.2.1]octan-2-one-7,2′-7′-(chloromethyl)-5′-methyl-8′-oxabicyclo[3.2.1]oct-6′-ene]: mp 131–132 °C; IR 1720, 1445, 1410, 1388, 1380, 1270, 1235, 1205, 1160, 1095, 1035, 860, 720, and 700 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 1.35 (s, 3 H), 1.61 (s, 3 H), 1.35–1.65 (m, 4 H), 1.95–2.11 (m, 2 H), 2.37 (dt, 1 H, J = 18.7 and 8.1 Hz), 2.52 (ddd, 1 H, J = 18.5, 8.6, and 3.1 Hz), 4.37 (s, 2 H), 4.53 (s, 1 H), 4.67 (s, 1 H), and 5.95 (s, 1 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 22.9, 24.0, 25.0, 30.1, 32,9, 33.8, 40.7, 79.1, 81.4, 84.8, 107.6, 132.7, 135.5, 140.9, and 205.7.

Preparation of 7-(Methoxymethyl)-5-phenyl-8-oxabicyclo[3.2.1]oct-6-en-2-one (32). Treatment of 1-diazo-5-phenylpentane-2,5-dione (**8**) with 1.2 equiv of methyl propargyl ether according to the general method afforded 7-(methoxymethyl)-5-phenyl-8-oxabicyclo[3.2.1]oct-6-en-2-one (**32**) in 85% yield: IR (neat) 1730, 1505, 1455, 1200, 1105, 1050, 970, 765, and 705 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 2.27 (dd, 1 H, J = 12.5 and 8.5 Hz), 2.39–2.62 (m, 2 H), 2.83 (dt, 1 H, J = 14.0 and 7.0 Hz), 3.32 (s, 3 H), 3,99 (d, 1 H, J = 14.0 Hz), 4.09 (d, 1 H, J = 14.0 Hz), 4.72 (s, 1 H), 6.18 (s, 1 H), and 7.25–7.48 (m, 5 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 32.6, 33.0, 58.5, 67.1, 87.2, 88.5, 124.8, 127.6, 128.3, 132.4, 141.1, 141.4, and 202.3; HRMS calcd for $C_{15}H_{16}O_3$ 244.1099, found 244.1105.

Preparation of 7-(Methoxymethyl)-5-methyl-8-oxabicyclo[3.2.1]oct-6-en-2-one (33). Treatment of 1-diazohexane-2,5-dione (**7**) with 1.2 equiv of methyl propargyl ether afforded 7-(methoxymethyl)-5-methyl-8-oxabicyclo[3.2.1]oct-6-en-2-one (**33**) in 80% yield: IR (neat) 1730, 1455, 1390, 1205, 1115, 1040, and 870 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 1.50 (s, 3 H), 1.88 (ddd, 1 H, J = 13.5, 8.8, and 1.7 Hz), 2.18 (ddd, 1 H, J = 13.5, 8.7, and 7.2 Hz), 2.50 (ddd, 1 H, J = 18.2, 8.7, and 1.7 Hz), 2.69 (ddd, 1 H, J = 18.2, 8.8, and 7.2 Hz), 3.36 (s, 3 H), 3.97 (d, 1 H, J = 4.0 Hz), 4.08 (d, 1 H, J = 4.0 Hz), 4.55 (s, 1 H), and 6.02 (s, 1 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 23.8, 32.5, 33.0, 58.6, 67.2, 85.5, 87.1, 132.7, 141.2, and 203.0; HRMS calcd for $C_{10}H_{14}O_3$ 182.0943, found 182.0949.

Preparation of 6-*exo*-Carbomethoxy-5-phenyl-8-oxabicyclo[3.2.1]octan-2-one (34). Treatment of 1-diazo-5-phenylpentane-2,5-dione (**8**) with 1.2 equiv of methyl acrylate according to the general procedure afforded 6-*exo*-carbomethoxy-5-phenyl-8-oxabicyclo[3.2.1]octan-2-one (**34**) in 68% yield: IR (neat) 1740 and 1730 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 2.18 (dd, 1 H, J = 14.0 and 9.0 Hz), 2.23–2.28 (m, 1 H), 2.45–2.60 (m, 3 H), 2.77 (ddd, 1 H, J = 14.0, 8.4, and 6.2 Hz), 3.04 (s, 3 H), 3.42 (dd, 1 H, J = 9.0 and 6.2 Hz), 4.57 (d, 1 H, J = 8.4 Hz), and 7.20–7.42 (m, 5 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 32.1, 33.5, 37.9, 51.4, 52.0, 82.1, 86.1, 125.2, 127.5, 127.7, 140.4, 172.9, and 206.1; HRMS calcd for $C_{15}H_{16}O_4$ 260.1048, found 260.1038.

In addition to cycloadduct **34**, three minor products were also obtained. The first of these was assigned as 7-*exo*-carbomethoxy-5-phenyl-8-oxabicyclo[3.2.1]octan-2-one (**36**) (14%): IR (neat) 1740 and 1730 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 2.23–2.30 (m, 2 H), 2.43–2.65 (m, 3 H), 2.62 (dd, 1 H, J = 11.0 and 9.6 Hz), 3.16 (dd, 1 H, J = 9.6 and 5.1 Hz), 3.67 (s, 3 H), 4.72 (s, 1 H), and 7.20–7.42 (m, 5 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 32.8, 37.6, 39.0, 47.0, 52.5, 84.3, 84.7, 124.4, 127.3, 128.3, 144.0, 172.4, and 205.1 ppm.

The third material isolated from the silica gel column was assigned as 6-*endo*-carbomethoxy-5-phenyl-8-oxabicyclo[3.2.1]octan-2-one (**35**) (7%): IR (neat) 1740 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 2.20–2.73 (m, 5 H), 2.87 (dt, 1 H, J = 16.5 and 8.9 Hz), 3.27 (dd, 1 H, J = 12.1 and 5.8 Hz), 3.77 (s, 3 H), 4.52 (d, 1 H, J = 8.6 Hz), and 7.23–7.52 (m, 5 H). The last fraction isolated corresponded to 7-*endo*-carbomethoxy-5-phenyl-8-oxabicyclo[3.2.1]octan-2-one (**37**) (6%): IR (neat) 1740 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 2.22–2.80 (m, 5 H), 2.93 (dd, 1 H, J = 13.1 and 7.0 Hz), 3.59 (ddd, 1 H, J = 12.8, 7.6, and 7.0 Hz), 3.70 (s, 3 H), 4.63 (d, 1 H, J = 7.6 Hz), and 7.23–7.41 (m, 5 H).

Preparation of 6-*exo*-Carbomethoxy-5-methyl-8-oxabicyclo[3.2.1]octan-2-one (38). Treatment of 1-diazohexane-2,5-dione (**7**) with 1.2 equiv of methyl acrylate afforded a mixture of four products. Chromatography of the crude residue on a silica gel plate gave 6-*exo*-carbomethoxy-5-methyl-8-oxabicyclo[3.2.1]octan-2-one (**38**) as the major component in 42% yield: IR (neat) 1740 and 1730 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 1.34 (s, 3 H), 1.95–2.15 (m, 3 H), 2.42 (dd, 2 H, J = 9.0 and 5.8 Hz), 2.73 (ddd, 1 H, J = 13.5, 8.2, and 6.3 Hz), 3.09 (dd, 1 H, J = 9.1 and 6.3 Hz), 3.71 (s, 3 H), and 4.36 (d, 1 H, J = 8.2 Hz); ^{13}C NMR (75 MHz, $CDCl_3$) δ 22.4, 32.0, 33.5, 38.3, 49.7, 51.9, 82.0, 82.5, 173.6 and 206.5; HRMS calcd for $C_{10}H_{14}O_4$ 198.0892, found 198.0894.

The second most prevalent isomer corresponded to 7-*exo*-carbomethoxy-5-methyl-8-oxabicyclo[3.2.1]octan-2-one (**40**) (21%): IR (neat) 1740 and 1730 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 1.47 (s, 3 H), 1.88 (ddd, 1 H, J = 13.3, 7.5, and 3.4 Hz), 2.00–2.20 (m, 1 H), 2.28 (d, 2 H, J = 7.3 Hz), 2.40–2.55 (m, 2 H), 3.08 (t, 1 H, J = 7.3 Hz), 3.70 (s, 3 H), and 4.47 (s, 1 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 25.5, 32.7, 36.4, 37.8, 47.3, 52.3, 81.1, 84.8, 172.7, and 205.3.

The third most prevalent compound was assigned as 6-*endo*-carbomethoxy-5-methyl-8-oxabicyclo[3.2.1]octan-2-one (**39**) (15%): IR (neat) 1740 and 1730 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 1.54 (s, 3 H), 1.86 (ddd, 1 H, J = 14.1, 9.0, and 2.0 Hz), 1.95–2.15 (m, 1 H), 2.27 (ddd, 1 H, J = 18.0, 7.9, and 2.0 Hz), 2.35–2.54 (m, 2 H), 2.63 (dt, 1 H, J = 18.0 and 9.0 Hz), 2.98 (dd, 1 H, J = 11.3 and 6.2 Hz), 3.74 (s, 3 H), and 4.22 (d, 1 H, J = 8.2 Hz); ^{13}C NMR (75 MHz, $CDCl_3$) δ 26,1, 32.0, 33.7, 37.1, 48.2, 52.4, 81.3, 82.2, 172.2, and 206.4.

Finally, the minor component of the mixture was assigned as 7-*endo*-carbomethoxy-5-methyl-8-oxabicyclo[3.2.1]octan-2-one (**41**) (12%): IR (neat) 1740 and 1730 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 1.43 (s, 3 H), 1.92–2.15 (m, 3 H), 2.32–2.50 (m, 3 H), 3.48 (ddd, 1 H, J = 11.8, 7.7, and 7.1 Hz), 3.63 (s, 3 H), and 4.37 (d, 1 H, J = 7.7 Hz); ^{13}C NMR (75 MHz, $CDCl_3$) δ 26.1, 32.1, 33.6, 37.5, 48.2, 52.2, 81.4, 83.9, 171.1, and 205.0.

Preparation of 7-*exo*-Acetyl-5-phenyl-8-oxabicyclo[3.2.1]octan-2-one (44). Treatment of 1-diazo-5-phenylpentane-2,5-dione (**8**) with 1.2 equiv of methyl vinyl ketone in the presence of rhodium acetate dimer gave rise to a mixture of four products. The major isomer was identified as 7-*exo*-acetyl-5-phenyl-8-oxabicyclo[3.2.1]octan-2-one (**44**) in 53% yield: IR (neat) 1720 and 1680 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 2.20 (s, 3 H), 2,20–2.35 (m, 2 H), 2.47–2.61 (m, 4 H), 3.22 (dd, 1 H, J = 8.8 and 5.3 Hz), 4.64 (s, 1 H), and 7.21–7.44 (m, 5 H); ^{13}C NMR (75 MHz, $CDCl_3$) 27.8, 32.7, 37.3, 37.5, 54.7, 83.4, 84.3, 124.3, 127.2, 128.2, 143.8, 204.1, and 205.4 ppm.

The second most prevalent isomer was identified as 6-*exo*-acetyl-5-phenyl-8-oxabicyclo[3.2.1]octan-2-one (**42**) (24%): IR (neat) 1720 and 1680 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 1.55 (s, 3 H), 2.20–2.35 (m, 2 H), 2.47–2.61 (m, 3 H), 2.68 (ddd, 1 H, J = 13.7, 8.1, and 5.9 Hz), 3.58 (dd, 1 H, J = 9.0 and 5.6 Hz), 4.60 (d, 1 H, J = 8.4 Hz), and 7.21–7.44 (m, 5 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 28.4, 32.0, 32.6, 39.0, 59.3, 81.7, 85.5, 125.2, 127.6, 127.9, 140.4, 206.0, and 207.5.

The third most prevalent cycloadduct corresponded to 6-*endo*-acetyl-5-phenyl-8-oxabicyclo[3.2.1]octan-2-one (**43**) (9%): IR (neat) 1730, 1710, 1450, 1365, 1180, 1040, 765, and 705 cm^{-1}; NMR (300 MHz, $CDCl_3$) δ 2.05 (s, 3 H), 2.30–2.48 (m, 3 H), 2.55–2.67 (m, 2 H), 2.85 (dt, 1 H, J = 16.0 and 8.0 Hz), 3.46 (dd, 1 H, J = 11.5 and 6.5 Hz), 4.51 (d, 1 H, J = 8.6 Hz), and 7.25–7.52 (m, 5 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 31.8, 32.1, 32.2, 62.2, 81.4, 84.2, 124.7, 127.9, 128.5, 143.0, 206.2, and 206.3.

Finally, the minor cycloadduct isolated from the silica gel column was assigned as 7-*endo*-acetyl-5-phenyl-8-oxabicyclo[3.2.1]octan-2-one (**45**) (4%): mp 96–97 °C; IR (KBr) 1735, 1715, 1505, 1455, 1360, 1185, 1050, 770, and 710 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 2.22 (s, 3 H), 2.25–2.38 (m, 2 H), 2.26 (dd, 1 H, J = 13.1 and 11.2 Hz), 2.48–2.55 (m, 2 H), 3.02 (dd, 1 H, J = 13.1 and 6.9 Hz), 3.77 (ddd, 1 H, J = 11.2, 7.8, and 6.9 Hz), 4.73 (d, 1 H, J = 7.8 Hz), and 7.23–7.43 (m, 5 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 30.3, 33.8, 35.7, 38.8, 56.6, 83.6, 84.3, 124.1, 127.1, 128.3, 144.5, 203.8, and 204.9; *m/e* 224, 201, 187, 159, 118 (base), 105, and 91; HRMS calcd for $C_{15}H_{16}O_3$ 244.1099, found 244.1094.

Preparation of 7-*exo*-Acetyl-5-methyl-8-oxabicyclo[3.2.1]octan-2-one (47). Treatment of 1-diazohexane-2,5-dione (**7**) and 1.2 equiv of methyl vinyl ketone according the general method gave rise to a mixture of three products. The major cycloadduct obtained was assigned as 7-*exo*-

acetyl-5-methyl-8-oxabicyclo[3.2.1]octan-2-one (**47**) (60%): IR (neat) 1725, 1715, 1465, 1365, 1175, 1105, 1045, and 870 cm^{-1}; NMR (300 MHz, $CDCl_3$) δ 1.50 (s, 3 H), 1.93 (ddd, 1 H, J = 13.4, 7.3, and 3.9 Hz), 2.11 (m, 1 H), 2.12 (dd, 1 H, J = 12.2 and 9.4 Hz), 2.25 (s, 3 H), 2.27 (dd, 1 H, J = 12.2 and 5.0 Hz), 2.43–2.52 (m, 2 H), 3.11 (dd, 1 H, J = 9.4 and 5.0 Hz), and 4.43 (s, 1 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 25.5, 27.8, 32.5, 36.1, 36.3, 55.3, 81.3, 83.7, 204.5 and 206.1; *m/e* 182, 164, 154, 139, 126, 111, 97, 93, 83, and 68 (base); HRMS calcd for $C_{10}H_{14}O_3$ 182.0943, found 182.0938.

The second most prevalent fraction corresponded to 6-*exo*-acetyl-5-methyl-8-oxabicyclo[3.2.1]octan-2-one (**46**) (19%): IR (neat) 1730, 1715, 1450, 1365, 1270, 1175, 1100, 1040, and 845 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 1.38 (s, 3 H), 2.03 (dd, 1 H, J = 14.1 and 8.8 Hz), 2.07–2.23 (m, 2 H), 2.26 (s, 3 H), 2.42–2.53 (m, 2 H), 2.70 (ddd, 1 H, J = 14.1, 8.4, and 6.0 Hz), 3.27 (dd, 1 H, J = 8,8 and 6.0 Hz), and 4.38 (d, 1 H, J = 8.4 Hz); ^{13}C NMR (75 MHz, $CDCl_3$) δ 22.2, 31.1, 31.9, 32.9, 38.8, 56.2, 81.7, 82.2, 206.3, and 208.2.

The minor cycloadduct isolated from the column was assigned as 7-*endo*-acetyl-5-methyl-8-oxabicyclo[3.2,1]octan-2-one (**48**) (11%): IR (neat) 1730, 1715, 1455, 1385, 1365, 1260, 1200, 1180, 1105, 1045, and 865 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 1.46 (s, 3 H), 1.90 (dd, 1 H, J = 13.2 and 11.3 Hz), 1.96–2.15 (m, 2 H), 2.18 (s, 3 H), 2.33–2.42 (m, 2 H), 2.56 (dd, 1 H, J = 13.2 and 6.8 Hz), 3.71 (ddd, 1 H, J = 11.3, 7.7, and 6.8 Hz), and 4.52 (d, 1 H, J = 7.7 Hz); ^{13}C NMR (75 MHz, $CDCl_3$) δ 26.1, 30.2, 33.5, 34.8, 37.2, 57.1, 81.4, 83.7, 204.0, and 205.4 ppm.

Preparation of 5,7-*exo*-Diphenyl-8-oxabicyclo[3.2.1]octan-2-one (51). Treatment of 1-diazo-5-phenylpentane-2,5-dione (**8**) with styrene in the presence of a catalytic amount of rhodium(II) acetate afforded a mixture of four products. Chromatography of the mixture through silica gel using an ethyl acetate–hexane mixture afforded 5,7-*exo*-diphenyl-8-oxabicyclo[3.2.1]octan-2-one (**51**) in 43% yield; IR (neat) 1730, 1495, 1450, 1255, 1045, 1035, 910, 765, and 705 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 2.28–2.42 (m, 3 H), 2.48–2.60 (m, 1 H), 2.72 (dt, 1 H, J = 18.2 and 9.0 Hz), 3,03 (dd, 1 H, J = 13.3 and 9,5 Hz), 3.47 (dd, 1 H, J = 9.5 and 4.3 Hz), 4.42 (s, 1 H), and 7.18–7.54 (m, 10 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 33.0, 38.6, 45.9, 48.5, 84.6, 89.5, 124.3, 126.7, 126.8, 127.1, 128.4, 128.7, 144.6, 144.9, and 205.8; HRMS calcd for $C_{19}H_{18}O_2$ 278.1307, found 278.1302.

The next most prevalent cycloadduct was assigned as 5,6-*exo*-diphenyl-8-oxabicyclo[3.2.1]octan-2-one (**49**) (27%): IR (neat) 1735, 1500, 1455, 1045, 1035, 765, and 705 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 2.38 (dd, 1 H, J = 10.5 and 7.7 Hz), 2.43–2.84 (m, 5 H), 3.76 (dd, 1 H, J = 9.2 and 5.4 Hz), 4.66 (d, 1 H, J = 8.4 Hz), and 6.91–7.22 (m, 10 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 32.5, 39.6, 40.6, 52.3, 81.6, 87.6, 125.3, 125.9, 126.0, 127.3, 127.7, 128.5, 142.4, 143.9, and 207.3.

The third fraction isolated from the column was assigned as 5,7-*endo*-diphenyl-8-oxabicyclo[3.2.1]octan-2-one (**52**) (10%): ^1H NMR (300 MHz, $CDCl_3$) δ 2.25–2.48 (m, 4 H), 2.74 (d, 1 H, J = 11.9 Hz), 2.86 (dd, 1 H, J = 12.6 and 8.2 Hz), 4.10 (dt, 1 H, J = 11.4 and 7.8 Hz), 4.79 (d, 1 H, J = 7.8 Hz), and 7.25–7.60 (m, 10 H). Finally, the last fraction corresponded to 5,6-*endo*-diphenyl-8-oxabicyclo[3.2.1]octan-2-one (**50**) (10%): ^1H NMR (300 MHz, $CDCl_3$) δ 2.15–2.40 (m, 2 H), 2.58–2.72 (m, 3 H), 2.91 (dd, 1 H, J = 13.6 and 9,2 Hz), 3.47 (dd, 1 H, J = 11.7 and 7.5 Hz), 4.66 (dd, 1 H, J = 8.9 and 1.2 Hz), and 7.25–7,60 (m, 10 H).

Preparation of 7-*endo*-Acetoxy-5-methyl-8-oxabicyclo[3.2.1]octan-2-one (53). Treatment of 1-diazohexane-2,5-dione (**7**) with 1.2 equiv of vinyl acetate according to the general method afforded a mixture of 1:1 and 2:1 cycloadducts which could be separated by silica gel chromatography. The 1:1 cycloadduct was assigned as 7-*endo*-acetoxy-5-methyl-8-oxabicyclo[3.2.1]octan-2-one (**53**) (40%): IR (neat) 1750, 1737, 1435, 1385, 1235, 1096, 1050, 900, and 860 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 1,44 (s, 3 H), 1.95–2.05 (m, 2 H), 2.01 (s, 3 H), 2.07–2.23 (m, 2 H), 2.39 (dd, 1 H, J = 13.7 and 10.7 Hz), 2.54 (dd, 1 H, J = 10.1 and 7.4 Hz), 4.39 (d, 1 H, J = 7.2 Hz), and 5.42 (ddd, 1 H, J = 10.7, 7.2, and 3.8 Hz); ^{13}C NmR (75 MHz, $CDCl_3$) δ 20,6, 26.1, 33.8, 36.7, 40.5, 73.4, 80.2, 82.6, 169.8, and 204.1; HRMS calcd for $C_{10}H_{14}O_4$ 198.0892, found 198.0890.

The 2:1 endo cycloadduct was assigned as structure **54** (30%): IR (neat) 1740, 1730, 1385, 1370, 1240, 1095, 1050, 1040, and 860 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 1.30 (s, 3 H), 1.50 (s, 3 H), 1.45–1.70 (m, 3 H), 1,95–2,20 (m, 4 H), 2.03 (s, 3 H), 2.32–2.55 (m, 3 H), 4.20 (dd, 1 H, J = 6.3 and 1.5 Hz), 4.69 (s, 1 H), and 5.42 (ddd, 1 H, J = 11,0, 6.3, and 4.4 Hz).

Preparation of 7-*endo*-Acetoxy-5-phenyl-8-oxabicyclo[3.2.1]octan-2-one (55). Treatment of 1-diazo-5-phenylpentane-2,5-dione (**8**) with 1.2 equiv of vinyl acetate according to the general method afforded a mixture of two products. Chromatography by silica gel afforded 7-*endo*-acetoxy-5-phenyl-8-oxabicyclo[3.2.1]octan-2-one (**55**) in 70% yield: IR (neat) 1750, 1740, 1450, 1375, 1230, 1065, 1030, 910, 770, and 705 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 2.04 (s, 3 H), 2.29–2,38 (m, 2 H), 2.44 (dd, 1 H, J = 14.0 and 4.1 Hz), 2.55–2.66 (m, 1 H), 2.70 (dd, 1 H, J = 11.0 and 8.4 Hz), 2.74 (dd, 1 H, J = 14.0 and 10.8 Hz), 4.60 (d, 1 H, J = 7.2 Hz), 5.48 (ddd, 1 H, J = 10.8, 7.2, and 4.1 Hz), and 7.23–7.40 (m, 5 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 20.6, 34.1, 38.3, 41.1, 72.9, 82.5, 83.1, 124.1, 127.3, 128.3, 144.1, 169.8 and 203.6; *m/e* 260, 218, 200, 172, 161, 144, 130, 105 (base), and 77; HRMS calcd for $C_{15}H_{16}O_4$ 260.1049, found 260.1058.

The minor product isolated from the column corresponds to the 3:1 endo cycloadduct **56** (15% yield): ^1H NMR (300 MHz, $CDCl_3$) δ 1.08 (ddd, 1 H, J = 13.3, 7.7, and 5.5 Hz), 1.53 (dd, 1 H, J = 13.6 and 4.5 Hz), 1.68 (dd, 1 H, J = 13.8 and 4.8 Hz), 1.85–1.96 (m, 1 H), 1.86 (s, 3 H), 2.05–2.40 (m, 4 H), 2.45–2.70 (m, 5 H), 2.78 (ddd, 1 H, J = 13.3, 6.8, and 6.4 Hz), 4.15 (d, 1 H, J = 6.6 Hz), 4.65 (s, 1 H), 5.06 (s, 1 H), 5.31 (ddd, 1 H, J = 11.0, 6.6, and 4.8 Hz), and 6.80–7.60 (m, 15 H).

Preparation of 7-*endo*-Ethoxy-5-methyl-8-oxabicyclo[3.2.1]octan-2-one (57). Treatment of 1-diazohexane-2,5-dione (**7**) with 1.2 equiv ethyl vinyl ether according to the procedure outlined above gave rise to a mixture of 1:1 and 2:1 cycloadducts. Chromatography of the crude reaction mixture through a neutral alumina column using a 3:1 hexane–ether mixture gave rise to both the 1:1 endo (**57**) and the 2:1 adduct (**58**). The 1:1 cycloadduct was identified as 7-*endo*-ethoxy-5-methyl-8-oxabicyclo[3.2.1]octan-2-one (**57**) (24%): IR (neat) 1725, 1455, 1420, 1385, 1350, 1260, 1170, 1120, and 1045 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 1.12 (t, 3 H, J = 7.0 Hz), 1.40 (s, 3 H), 1.98 (ddd, 1 H, J = 13.0, 8.5, and 1.0 Hz), 1.99 (ddd, 1 H, J = 13.5 and 3.9 Hz), 2.08 (ddd, 1 H, J = 13.0, 11.5, and 7.3 Hz), 2.25 (dd, 1 H, J = 13.5 and 9.8 Hz), 2.45 (ddd, 1 H, J = 17.3, 7.3, and 1.0 Hz), 2.68 (ddd, 1 H, J = 17.4, 11.5, and 8.5 Hz), 3.46 (q, 2 H, J = 7.0 Hz), 4.31 (d, 1 H, J = 7.2 Hz), and 4.35 (ddd, 1 H, J = 9.8, 7.2, and 3.9 Hz); ^{13}C NMR (75 MHz, $CDCl_3$) δ 15.0, 26.2, 34.1, 37.3, 41.2, 66.1, 80.0, 80,1, 84.0 and 205.5; *m/e* 184, 169, 139, 127, 110, 99 (base), and 71; HRMS calcd for $C_{10}H_{16}O_3$ 184.1099, found 184.1090. Attempts to isolate the 1:1 exo adduct from the silica gel column failed to give any characterizable material even though the NMR of the crude reaction mixture showed the exo isomer as being present in low yield.

The 2:1 cycloadduct was assigned as spiro[5-methyl-6,8-dioxabicyclo[3.2.1]octan-2-one-7,2′-7′-ethoxy-5′-methyl-8′-oxabicyclo[3.2.1]octane] (**58**) (28%): ^1H NMR (300 MHz, $CDCl_3$) δ 1.23 (t, 3 H, J = 7.0 Hz), 1.37 (s, 3 H), 1.38–1.60 (m, 3 H), 1.60 (s, 3 H), 1.65–1.82 (m, 2 H), 2.00–2.18 (m, 2 H), 2.24 (dd, 1 H, J = 13.5 and 7.7 Hz), 2.38 (ddd, 1 H, J = 11.2, 8.8, and 7.5 Hz), 2.53 (dddd, 1 H, J = 18.2, 8.8, 4.6, and 0.9 Hz), 3.44 (dq, 1 H, J = 9.1 and 7.0 Hz), 3.54 (dq, 1 H, J = 9.1 and 7.0 Hz), 4.00 (s, 1 H), 4.19 (dd, 1 H, J = 6.7 and 3.2 Hz), and 4.68 (s, 1 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 15,2, 24.6, 25.1, 25.2, 32.8, 33.6, 34.6, 44.3, 64.4, 79.8, 80.0, 80.9, 82.3, 83.9, 107.5, and 205.6.

Preparation of 7-*endo*-Ethoxy-5-phenyl-8-oxabicyclo[3.2.1]octan-2-one (59). Treatment of 1-diazo-5-phenylpentane-2,5-dione (**8**) with 1.2 equiv of ethyl vinyl ether according to the general procedure outlined above afforded a mixture of four isomeric cycloadducts. Silica gel chromatography of the mixture using an ethyl acetate–hexane mixture as the eluent gave rise to 7-*endo*-ethoxy-5-phenyl-8-oxabicyclo[3.2.1]octan-2-one (**59**) (28%) as a clear oil: IR (neat) 1740, 1505, 1455, 1420, 1355, 1125, 1055, 770, and 710 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 1.14 (t, 3 H, J = 6.9 Hz), 2.20–2.35 (m, 2 H), 2.42 (dd, 1 H, J = 13.6 and 4.2 Hz), 2.52 (dd, 1 H, J = 17.2 and 6.7 Hz), 2.58 (dd, 1 H, J = 13.6 and 10.1 Hz), 2.84 (ddd, 1 H, J = 17.2, 11.5, and 8.6 Hz), 3.49 (q, 2 H, J = 6.9 Hz), 4.42 (ddd, 1 H, J = 10.1, 6.8, and 4.2 Hz), 4.52 (d, 1 H, J = 6.8 Hz), and 7.23–7.40 (m, 5 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 15.1, 34.4, 38.9, 42.0, 66.3, 79.4, 83.1, 83.8, 124.1, 127.0, 128.2, 144.8, and 205.0; *m/e* 246, 201, 161, 105 (base), 91, and 77; HRMS calcd for $C_{15}H_{18}O_3$ 246.1256, found 246.1262.

A 2:1 cycloadduct **60** was also isolated in 16% yield: ^1H NMR (300 MHz, $CDCl_3$) δ 0.89 (t, 3 H, J = 7.0 Hz), 1.65–1.88 (m, 3 H), 1.95–2.10 (m, 2 H), 2.30–2.45 (m, 2 H), 2.55–2.70 (m, 3 H), 2.91 (m, 2 H), 4.10 (s, 1 H), 4.27 (dd, 1 H, J = 7.6 and 3.2 Hz), 4.94 (s, 1 H), and 7.20–7.63 (m, 10 H).

It was also possible to isolate a 3:1 cycloadduct **61** in 12% yield: ^1H NMR (300 MHz, $CDCl_3$) δ 0.84 (t, 3 H, J = 7.0 Hz), 0.79–0,90 (m, 1 H), 1.31 (dd, 1 H, J = 13.9 and 4.3 Hz), 1.69 (dd, 1 H, J = 13.8 and 5.1 Hz), 1.78 (dd, 1 H, J = 13.5 and 5.6 Hz), 1.86 (d, 1 H, J = 13.7 Hz), 1.97 (dd, 1 H, J = 12.7 and 5.3 Hz), 2.08 (dd, 1 H, J = 13.6 and 5.8 Hz), 2.23–2.35 (m, 1 H), 2.45–2.75 (m, 6 H), 2.85 (m, 2 H), 4.00 (s, 1 H), 4.21 (dd, 1 H, J = 7.3 and 3.3 Hz), 4.59 (s, 1 H), 5.08 (s, 1 H), and 6.90–7.60 (m, 15 H).

Preparation of *exo*- (66) and *endo*-Brevicomin (67). Treatment of 1-diazohexane-2,5-dione (**7**) with 1.2 equiv of propionaldehyde gave rise to a 2:1 mixture of exo/endo cycloadducts, Chromatography of the crude residue through a silica gel column using ethyl acetate–hexane mixture

as the eluent afforded 7-*exo*-ethyl-5-methyl-6,8-dioxabicyclo[3.2.1]octan-2-one (**64**) as the major product in 42% isolated yield: IR (neat) 1740, 1395, 1270, 1210, 1185, 1100, 1040, and 860 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 0.95 (t, 3 H, J = 7.4 Hz), 1.59 (qd, 2 H, J = 7.4 and 6.6 Hz), 1.60 (s, 3 H), 2.10–2.20 (m, 2 H), 2.40–2.60 (m, 2 H), 3.98 (t, 1 H, J = 6.6 Hz), and 4.14 (s, 1 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 9.4, 24.2, 27.6, 32.4, 35.0, 80.1, 83.6, 107.7, and 205.8.

The endo isomer **65** was isolated in 18% yield: IR (neat) 1740, 1395, 1240, 1210, 1185, 1100, 1050, and 860 cm^{-1}; NMR (300 MHz, $CDCl_3$) δ 0.98 (t, 3 H, J = 7.4 Hz), 1.44 (dqd, 1 H, J = 14.4, 7.4, and 7.2 Hz), 1.59 (dqd, 1 H, J = 14.4, 7.4, and 7.2 Hz), 1.60 (s, 3 H), 2.05–2.18 (m, 2 H), 2.37 (ddd, 1 H, J = 18.5, 8.5, and 8.3 Hz), 2.50 (ddd, 1 H, J = 18.5, 8.0, and 5.5 Hz), 4.04 (td, 1 H, J = 7.2 and 4.7 Hz), and 4.31 (d, 1 H, J = 4.7 Hz); ^{13}C NMR (75 MHz, $CDCl_3$) δ 10.3, 22.4, 24.1, 33.2, 34.1, 80.0, 83.2, 107.3, and 205.4 ppm.

To a well-stirred mixture containing 0.3 mL of ethanedithiol and 1.32 g of zinc triflate[42] in 8.0 mL of methylene chloride was added a solution containing 510 mg of either 7-*exo*- (**64**) or 7-*endo*-ethyl-5-methyl-6,8-dioxabicyclo[3.2.1]octan-2-one (**65**) in 2.0 mL of methylene chloride at 25 °C. The reaction mixture was stirred for 3.5 h at room temperature and for 2 h at 80 °C. At the end of this time, 20 mL of water was added, and the resulting mixture was extracted with a 1:1 ether–hexane mixture. The extracts were washed with 20 mL of dilute hydrochloric acid and a saturated aqueous sodium bicarbonate solution, then dried over sodium sulfate, and concentrated under reduced pressure. Chromatography of the residue through silica gel using an ethyl acetate–hexane mixture as the eluent gave 0.60 g (80%) of the *exo*-ethylene thioketal: IR (neat) 2970, 2940, 2890, 1450, 1390, 1280, 1265, 1210, 1200, 1030, 975, and 865 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 0.95 (t, 3 H, J = 7.4 Hz), 1.45 (s, 3 H), 1.55 (qd, 2 H, J = 7.4 and 6.5 Hz), 1.74 (dd, 1 H, J = 13.3 and 5.7 Hz), 1.88 (ddd, 1 H, J = 13.3, 12.5, and 5.2 Hz), 2.07 (dd, 1 H, J = 14.0 and 5.2 Hz), 2.35 (ddd, 1 H, J = 14.0, 12.5, and 5.7 Hz), 3.19–3.38 (m, 4 H), 3.98 (t, 1 H, J = 6.5 Hz), and 4.05 (s, 1 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 9.5, 24.1, 28.4, 35.1, 35.9, 38.5, 38.9, 66.9, 81.1, 86.7, and 107.3.

A mixture containing 5 g of Raney nickel and 200 mg of the above thioketal in 50 mL of ethanol was heated at reflux for 3 h. The solids were removed by filtration, and the solution was concentrated under reduced pressure. Chromatography of the crude oil through a silica gel column using a 5% ether–pentane mixture as the eluent gave 110 mg (87%) of *exo*-brevicomin (**66**) as a colorless oil:[43] ^1H NMR (300 MHz, $CDCl_3$) δ 0.91 (t, 3 H, J = 7.4 Hz), 1.42 (s, 3 H), 1.43–1.95 (m, 8 H), 3.90 (t, 1 H, J = 6.5 Hz), and 4.13 (br s, 1 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 9.6, 17.0, 24.9, 27.8, 28.4, 34.8, 78.1, 81.0, and 107.5.

endo-Brevicomin (**67**) could also be obtained from 7-*endo*-ethyl-5-methyl-6,8-dioxabicyclo[3.2.1]octan-2-one (**65**) in the same manner as described above: 7-*endo*-Ethyl-5-methyl-6,8-dioxabicyclo[3.2.1]octan-2-one ethylene thioketal was prepared in 80% yield: IR (neat) 2970, 2940, 2880, 1455, 1390, 1280, 1265, 1200, 1120, 1030, 975, and 865 cm^{-1}; NMR (300 MHz, $CDCl_3$) δ 1.09 (t, 3 H, J = 7.3 Hz), 1.45 (s, 3 H), 1.70–2.12 (m, 5 H), 2.45 (ddd, 1 H, J = 13.5, 11.6, and 5.8 Hz), 2.99–3.09 (m, 1 H), 3.18–3.45 (m, 3 H), 4.01 (td, 1 H, J = 7.4 and 4.1 Hz), and 4.23 (d, 1 H, J = 4.1 Hz); ^{13}C NMR (75 MHz, $CDCl_3$) δ 11.9, 22.5, 24.1, 35.8, 36.3, 36.4, 40.6, 67.3, 81.9, 84.8, and 106.2; HRMS calcd for $C_{11}H_{18}O_2S_2$ 246.0748, found 246.0760.

This material was converted to *endo*-brevicomin (**67**)[44] in 85% yield: ^1H NMR (300 MHz, $CDCl_3$) δ 0.99 (t, 3 H, J = 7.5 Hz), 1.44 (s, 3 H), 1.50–2.00 (m, 8 H), 3.98 (td, 1 H, J = 7.3 and 4.2 Hz), and 4.2 (br, 1 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 10.8, 17.4, 21.7, 23.5, 24.9, 34.3, 76.4, 81.5, and 106.8.

Preparation of 7-*exo*-Decyl-5-methyl-6,8-dioxabicyclo[3.2.1]octane (69). Treatment of 1-diazohexane-2,5-dione (**7**) with 1.2 equiv of undecyclic aldehyde according to the general procedure outlined above gave rise to a 2:1 mixture of exo and endo cycloadducts in 75% yield. Chromatography of the mixture on a silica gel plate using a 25% ethyl acetate–hexane mixture as the eluent afforded 7-*exo*-decyl-5-methyl-6,8-dioxabicyclo[3.2.1]octan-2-one (**68**) as the major product in 50% yield: IR (neat) 2930, 2860, 1740, 1475, 1390, 1275, 1210, 1180, 1105, 1040, and 865 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 0.88 (t, 3 H, J = 6.9 Hz), 1.26 (br, 18 H), 1.59 (s, 3 H), 2.03–2.20 (m, 2 H), 2.35–2.58 (m, 2 H), 4.04 (t, 1 H, J = 6.6 Hz), and 4.12 (s, 1 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 13.94, 22.51, 24.30, 25.20, 29.16, 29.32, 29.36, 29.42, 31.72, 32.41, 34.62, 35.02, 78.92, 83.94, 107.65, and 205.78.

7-*endo*-Decyl-5-methyl-6,8-dioxabicyclo[3.2.1]octan-2-one was obtained as the minor product in 25% yield: IR (neat) 2930, 2870, 1740, 1475, 1395, 1230, 1205, 1170, 1100, 1045, and 865 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 0.88 (t, 3 H, J = 6.5 Hz), 1.26 (br, 18 H), 1.58 (s, 3 H), 2.05–2.17 (m, 2 H), 2.35–2.55 (m, 2 H), 4.07 (td, 1 H, J = 7.6 and 4.8 Hz), and 4.28 (d, 1 H, J = 4.8 Hz); ^{13}C NMR (75 MHz, $CDCl_3$) δ 13.9, 22.4, 24.1, 26.1, 29.1, 29.1, 29.2, 29.4, 31.7, 33.2, 34.2, 78.6, 83.3, 107.2, and 120.5; HRMS calcd for $C_{17}H_{30}O_3$ 282.2195, found 282.2197.

Reduction of 7-*exo*-decyl-5-methyl-6,8-dioxabicyclo[3.2.1]octan-2-one (**68**) was carried out via the ethylene thioketal intermediate using the same procedure as described above for *exo*-brevicomin (**66**). The structure of thioketal was assigned on the basis of its spectral properties: 7-*exo*-decyl-5-methyl-6,8-dioxabicyclo[3.2.1]octan-2-one ethylene thioketal (90%): IR (neat) 2930, 2860, 1475, 1465, 1455, 1390, 1215, 1200, 1035, and 870 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 0.88 (t, 3 H, J = 6.5 Hz), 1.26 (br, 18 H), 1.45 (s, 3 H), 1.74 (dd, 1 H, J = 13.4 and 5.7 Hz), 1.89 (ddd, 1 H, J = 13.4, 12.1, and 5.3 Hz), 2.07 (dd, 1 H, J = 14.0 and 5.3 Hz), 2.35 (ddd, 1 H, J = 14.0, 12.1, and 5.7 Hz), 3.19–3.38 (m, 4 H), 4.03 (t, 1 H, J = 7.2 Hz), and 4.04 (s, 1 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 14.0, 22.5, 24.1, 25.2, 29.2, 29.35, 29.40, 29.44, 29.46, 31.8, 35.1, 35.6, 35.9, 38.6, 39.0, 67.0, 80.0, 87.1, and 107.3; HRMS calcd for $C_{19}H_{34}O_2S_2$ 358.2000, found 358.2007.

This material was converted to 7-*exo*-decyl-5-methyl-6,8-dioxabicyclo[3.2.1]octane (**69**)[41] in 90% yield using Raney nickel: IR (neat) 2930, 2860, 1470, 1390, 1250, 1200, 1185, 1045, 1015, and 855 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 0.88 (t, 3 H, J = 6.6 Hz), 1.26 (br, 18 H), 1.42 (s, 3 H), 1.42–1.58 (m, 2 H), 1.58–1.67 (m, 2 H), 1.70–1.98 (m, 2 H), 3.99 (t, 1 H, J = 6.3 Hz), and 4.12 (s, 1 H); ^{13}C NMR (75 MHz, $CDCl_3$) 14.0, 17.0, 22.5, 25.0, 25.4, 27.8, 29.2, 29.4, 31.8, 34.8, 35.6, 78.5, 79.8, and 107.5 ppm; HRMS calcd for $C_{17}H_{32}O_2$ 268.2402, found 268.2411.

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