found 434.1542. Anal. Calcd for $C_{21}H_{26}N_2O_6S$: C, 58.04; H, 6.04; N, 6.45. Found: C, 58.16; H, 6.00; N, 6.37.

***rac*-Methyl (2*R**,3a*S**,6a*S**,10a*S**)-3-Methyl-5,10-dioxo-9-(*p*-toluenesulfonyl)-1,2,3,3a,4,5,6,6a,7,8,9,10-dodecahydropyrrolo[2,3-*i*]isoquinoline-2-carboxylate 5-Ethylene Ketal (22).** A mixture of the ketone **21b** (653 mg, 1.5 mmol), ethylene glycol (620 mg, 10 mmol), and $TsOH·H_2O$ (65 mg) in dry benzene (25 mL) was heated under reflux for 13 h with continuous removal of water. The mixture was quenched by the addition of saturated $NaHCO_3$(aq) (10 mL) and extracted with AcOEt. The organic layer was washed with brine and dried over Na_2SO_4, followed by evaporation of the solvent to give a crude residue (720 mg). Crystallization of this material from AcOEt/*n*-hexane (1.5/1) afforded almost pure ketal **22** (418 mg). The mother liquor was concentrated and purified by SiO_2 column (5.0 g, AcOEt/*n*-hexane = 1/5) to afford a further amount of the desired ketal **22** (150 mg, total yield 568 mg, 79%). **22**: mp 171.5–172.5 °C (CH_2Cl_2–AcOEt); IR 2950, 1730, 1680, 1600, 1350, 1160 cm^{-1}; ^1H NMR (500 MHz) δ 1.35 (1 H, t, J = 13.4 Hz, 6a-H), 1.42 (1 H, dd, J = 15.4, 4.6 Hz, 4-H), 1.61 (1 H, dt, J = 13.4, 3.3 Hz, 6-H), 1.75 (1 H, m, 7-H), 1.85 (1 H, dt, J = 15.4, 3.3 Hz, 4-H), 2.02 (1 H, dd, J = 13.4, 4.3 Hz, 1-H), 2.24–2.34 (3 H, m, 1, 6, 7-H), 2.38 (3 H, s, NMe), 2.44 (3 H, s, Me) ,3.64 (3 H, s, OMe), 3.75 (1 H, td, J = 12.2, 5.1 Hz, 8-H), 3.84–3.98 (6 H, m, OCH_2CH_2O, 3a, 2-H), 4.12 (1 H, m, 8-H), 7.30 (2 H, d, J = (8.3 Hz, aromatic), 7.87 (2 H, d, J = 8.3 Hz, aromatic); LRFABMS m/z 479 (MH^+, 100); HRFABMS m/z calcd for $C_{23}H_{31}O_7N_2S$ (MH^+) 479.1852, found 479.1857. Anal. Calcd for $C_{23}H_{30}O_7N_2S$: C, 57.53; H, 6.32; N, 5.85; Found: C, 57.62; H, 6.26; N, 5.69.

***rac*-Methyl (2*R**,3a*S**,6a*S**,10a*S**)-3-Methyl-5,10-dioxo-1,2,3,3a,4,5,6,6a,7,8,9,10-dodecahydropyrrolo[2,3-*i*]isoquinoline-2-carboxylate 5-Ethylene Ketal (23).** Sodium naphthalenide was prepared by stirring a mixture of sodium metal (209 mg, 9 mmol) and naphthalene (1.53 g, 12 mmol) in dry DME (20 mL) under Ar at rt for 2 h. To a cooled (−78 °C) and stirred solution of the *N*-Ts ketal (**22**, 400 mg, 0.83 mmol) in DME (20 mL) was added dropwise the above-prepared sodium naphthalenide solution by cannula until a blue color persisted (6 mL). After TLC analysis, the mixture was quenched by the addition of saturated NH_4Cl(aq) to obtain a neutral aqueous layer, which was extracted with AcOEt. The organic layer was washed with brine and dried over Na_2SO_4. Evaporation of the solvents gave a residue (540 mg), which was purified by SiO_2 column (5.4 g, AcOEt) to afford the pure NH compound **23** (140 mg, 52%) as a white solid. **23**: mp 196.5–197 °C (CH_2Cl_2–AcOEt); IR 3300, 2950, 1730, 1650 cm^{-1}; ^1H NMR (500 MHz) δ 1.58–1.97 (4 H, m, 1, 6, 6a-H), 2.03 (1 H, d, J = 12.0 Hz, 1-H), 2.15 (2 H, m, 4, 7-H), 2.29 (2 H, m, 4, 6-H), 2.45 (3 H, s, NMe), 3.28 (1 H, m, 8-H), 3.41 (1 H, m, 8-H), 3.67 (3 H, s, OMe), 3.72–4.00 (6 H, m, OCH_2CH_2O, 2, 3a-H), 5.76 (1 H, brs, NH); LREIMS m/z 324 (M^+), 265 (100). Anal. Calcd for $C_{16}H_{24}N_2O_5$: C, 59.24; H, 7.46; N, 8.64. Found: C, 59.49; H, 7.49; N, 8.56.

Acknowledgment. Special thanks are due to H. Ohmori and A. Matsumoto in the Instrumentation and Characterization Center, RIKEN for their technical assistance with the high-pressure Diels–Alder reaction. Financial support by a Grant-in-Aid for Scientific Research from the Ministry of Education, Science and Culture and Uehara Memorial Foundation is gratefully acknowledged. We also thank Mrs. H. Seki, Miss R. Hara, and Mr. T. Kuramochi in the Analytical Center of Chiba University for spectral data.

Registry No. **1**, 104196-68-1; **4**, 132143-27-2; **4** (R = H), 6052-73-9; **5**, 54125-02-9; (±)-**6**, 132143-30-7; **10**, 130291-45-1; (±)-**11**, 143076-11-3; (±)-**12a**, 143076-12-4; (±)-**12c**, 143076-20-4; **13** (R = Me), 130291-56-4; **13** (R = Bu-*t*), 56776-34-2; (±)-**14** (isomer 1), 143076-13-5; (±)-**14** (isomer 2), 143076-22-6; (±)-**15** (isomer 1), 143076-14-6; (±)-**15** (isomer 2), 143076-24-8; (±)-**16**, 143076-15-7; (±)-**17**, 143076-16-8; (±)-**18** (isomer 1), 143104-23-8; (±)-**18** (isomer 2), 143076-23-7; **19**, 130291-53-1; (±)-**20** (isomer 1), 143076-17-9; (±)-**20** (isomer 2), 143076-25-9; (±)-**21a**, 143167-08-2; (±)-**21b**, 143167-09-3; (±)-**22**, 143076-18-0; (±)-**23**, 143076-19-1; CH_2=C(COOMe)NHCOOMe, 76637-56-4; CH_2=C(COOMe)NHCOOBu-*t*, 55477-80-0; Ph_2S_2, 882-33-7; *N*-(methoxycarbonyl)-DL-serine methyl ester, 143076-21-5; *N*-tosyl-2-piperidone, 23438-61-1.

Supplementary Material Available: High-resolution ^1H NMR spectra of compounds **10**, **11**, **13**, and **16–21** and ^{13}C NMR spectra of **11**, **13**, **19**, and **21** (17 pages). This material is contained in many libraries on microfiche, immediately follows this article in the microfilm version of the journal, and can be ordered from the ACS; see any current masthead page for ordering information.

Tandem Cyclization–Cycloaddition Reaction of Rhodium Carbenoids. Studies Dealing with Intramolecular Cycloadditions

Albert Padwa,* Susan F. Hornbuckle, Glen E. Fryxell, and Zhijia J. Zhang

Department of Chemistry, Emory University, Atlanta, Georgia 30322

Received May 15, 1992

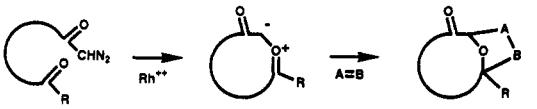
A series of 5-alkenyl-1-diazo-2,5-pentanediones, when treated with a catalytic quantity of rhodium(II) acetate, were found to give cycloadducts derived from the intramolecular trapping of a carbonyl ylide intermediate. Tethers of three or four methylenes readily enter into intramolecular cycloaddition, while longer and shorter tethers were reluctant to do so. Alkenes attached to the formally cationic terminus of the carbonyl ylide readily undergo internal cycloaddition if the tether allows for a relatively strain-free transition state. The internal cycloaddition reaction does not occur when the olefinic side chain is attached by means of an ester functionality. Bimolecular trapping experiments established that carbonyl ylide formation occurred, but the dipole does not undergo intramolecular cycloaddition. The inability of these α-diazo keto esters to undergo internal cycloaddition is related to conformational factors. The equilibrium between the two possible conformations of the dipole lies predominantly on the side of the *Z*-isomer. In this orientation, intramolecular dipolar cycloaddition cannot occur, and instead the dipole collapses by means of a proton transfer to give an enol ether.

A major challenge in organic synthesis today is to devise reactions that can form several carbon–carbon bonds in one operation leading to the construction of polycyclic structures with proper regio- and stereochemical control. The predictability and selectivity with which intramolecular 4 + 2-cycloaddition reactions occur has led to their widespread use in organic synthesis. Intramolecular Diels–Alder cycloadditions have been particularly useful in natural product synthesis since this reaction results in the formation of an extra ring and exhibits increased re-

0022-3263/92/1957-5747$03.00/0

activity due to entropic factors.[1-3] Additional regiochemical constraints frequently result in a marked increase in diastereoselectivity. Much interest has also been focused on reactions that effect formation of 5-membered rings through intramolecular 3 + 2-cycloadditions.[4-16] Among these, cycloaddition reactions of 1,3-dipoles occupy a uniquely important position due to their synthetic as well as theoretical significance.[17-22] Carbonyl ylides represent a well-investigated and synthetically useful class of 1,3-dipoles.[23-27] Except for a few isolated examples,[28-34] however, the intramolecular dipolar cycloaddition reaction of carbonyl ylides with alkenes has not yet attained a synthetically useful level of development.

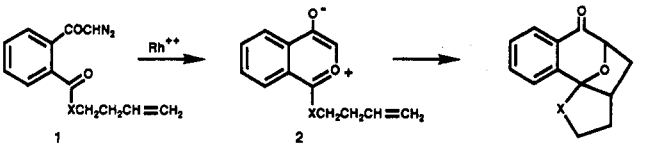
Several years ago, we developed a 3 + 2-annulation method for the synthesis of tetrahydrofurans based on the rhodium(II)-catalyzed reaction of diazo diones.[35] The reaction sequence involves formation of a cyclic carbonyl ylide, followed by a 1,3-dipolar cycloaddition with a suitable dipolarophile.[36] These reactions are performed under



extremely mild conditions, typically at room temperature in a neutral organic solvent. Since these cycloadditions involve cyclic carbonyl ylides, the resulting products are oxabicycles of varying ring size. If the dipolarophile is also intramolecularly tethered to the dipole, the subsequent cycloaddition affords complex oxapolycyclic ring systems with three (or more) component rings.[37] Our preliminary results have shown this to be a highly efficient and stereospecific approach to these heterocycles.[38] In light of our earlier successes and the increasing application of this type of strategy,[39] we felt that a more detailed study of this reaction was warranted. This paper summarizes the results of these studies.

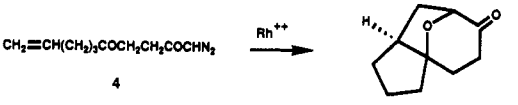
Results and Discussion

The systems that we initially studied were ultimately derived from phthalic anhydride, such that the tethered dipolarophile was attached to the benzene ring backbone via an ester or amide linkage.[35] This arrangement results in a cyclic carbonyl ylide, the π-system of which contributes to an aromatic ring.[40] The carbonyl ylide is also stabilized by the adjacent heteroatom of the dipolarophile tether.



1 2 3

Since we were interested in learning what role these two factors played in the overall reaction pathway, we chose to study the stripped down, bare methylene system (i.e., 4). Both our original phthalate-based dipole precursor 1 as well as α-diazo ketone 4 have the tethered olefin attached to the carbonyl group that cyclizes onto the rhodium carbenoid to form the carbonyl ylide. We refer to this method of connection as "ω attachment", using the carbenoid carbon as the point of reference. Treatment of 4 with Rh_2OAc_4 proceeded quite smoothly, producing cycloadduct 5 in 75% yield. It is worth noting that this



4 5

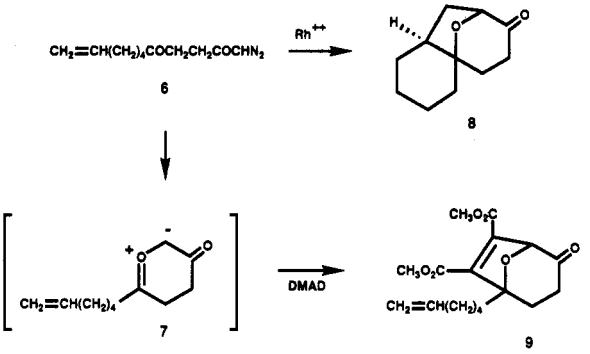
process begins from an acyclic precursor with no stereocenters and in one step, under extremely mild conditions, assembles a tricyclic backbone containing three new stereocenters with complete stereospecificity and in high yield. No bimolecular trapping product was observed when the reaction of 4 was carried out with rhodium(II) acetate in the presence of dimethyl acetylenedicarboxylate

(1) Brieger, G.; Bennett, J. N. *Chem. Rev.* **1980**, *80*, 63.
(2) Ciganek, E. *Org. React.* **1984**, *32*, 1.
(3) Fallis, A. G. *Can. J. Chem.* **1984**, *62*, 183.
(4) Hudlicky, T. *Chem. Rev.* **1989**, *89*, 1467.
(5) Kauffmann, T. *Top. Curr. Chem.* **1980**, *92*, 109.
(6) Beak, P.; Burg, D. A. *J. Org. Chem.* **1989**, *54*, 1647.
(7) Padwa, A.; Yeske, P. E. *J. Am. Chem. Soc.* **1988**, *110*, 1617.
(8) Mann, J. *Tetrahedron* **1986**, *42*, 4611.
(9) Remaiah, M. *Synthesis* **1984**, 529.
(10) Noyori, R.; Hayakawa, Y. *Org. React.* **1983**, *29*, 163.
(11) Noyori, R. *Acc. Chem. Res.* **1979**, *12*, 61.
(12) Hoffmann, H. M. R. *Angew. Chem., Int. Ed. Engl.* **1984**, *23*, 1.
(13) Molander, G. A.; Shubert, D. C. *J. Am. Chem. Soc.* **1986**, *108*, 4683.
(14) Curran, D. P.; Chen, N. H.; Spletzer, E.; Seong, C. M.; Chang, C. T. *J. Am. Chem. Soc.* **1989**, *111*, 8872.
(15) Little, R. D. *Chem. Rev.* **1986**, *86*, 875.
(16) Trost, B. M.; Grese, T. A.; Chan, D. M. T. *J. Am. Chem. Soc.* **1991**, *113*, 7350.
(17) Padwa, A., Ed. *1,3-Dipolar Cycloaddition Chemistry*; Wiley-Interscience: New York, 1984; Vols. I and II.
(18) Padwa, A. *Angew. Chem., Int. Ed. Engl.* **1976**, *15*, 123.
(19) Oppolzer, W. *Angew. Chem., Int. Ed. Engl.* **1977**, *16*, 10.
(20) Confalone, P. N.; Huie, E. M. *Org. React.* **1988**, *36*, 1.
(21) Terao, Y.; Aono, M.; Achiwa, K. *Heterocycles* **1988**, *27*, 981.
(22) Padwa, A.; Schoffstall, A. M. *Advances in Cycloaddition*; JAI Press, Inc.: Greenwich, CT, 1990; Vol. 2, p 1.
(23) Hendrickson, J. B.; Farina, J. S. *J. Org. Chem.* **1980**, *45*, 3359.
(24) Griffin, G. W.; Padwa, A. In *Photochemistry of Heterocyclic Compounds*; Buchardt, O., Ed.; Wiley: New York, 1976; Chapter 2.
(25) Bekhazi, M.; Smith, P. J.; Warkentin, J. *Can. J. Chem.* **1984**, *62*, 1646. Warkentin, J. *J. Org. Chem.* **1984**, *49*, 343.
(26) Shimizu, N.; Bartlett, P. D. *J. Am. Chem. Soc.* **1978**, *100*, 4260.
(27) Hoffman, R. W.; Luthardt, H. *Chem. Ber.* **1968**, *101*, 3861.
(28) Sammes, P. G.; Street, L. J. *J. Chem. Soc., Chem. Commun.* **1983**, 666.
(29) Sammes, P. G.; Street, L. J.; Whitby, R. J. *J. Chem. Soc., Perkin Trans. 1* **1986**, 281.
(30) Wender, P. A.; McDonald, F. E. *J. Am. Chem. Soc.* **1990**, *112*, 4956. Wender, P. A.; Mascarenas, J. L. *J. Org. Chem.* **1991**, *56*, 6267.
(31) Feldman, K. S. *Tetrahedron Lett.* **1983**, 5855.
(32) Brokatzky-Geiger, J.; Eberbach, W. *Chem. Ber.* **1983**, *116*, 2383; **1984**, *117*, 2157; *Tetrahedron Lett.* **1984**, 1137; *Heterocycles* **1983**, *20*, 1519.
(33) Maier, M. E.; Evertz, K. *Tetrahedron Lett.* **1988**, 1677. Maier, M. E.; Schoffing, B. *Chem. Ber.* **1989**, *122*, 1081.
(34) Hertzog, D. L.; Austin, D. J.; Nadler, W. R.; Padwa, A. *Tetrahedron Lett.* **1992**, 4731.
(35) Padwa, A.; Carter, S. P.; Nimmesgern, H. *J. Org. Chem.* **1986**, *51*, 1157. Padwa, A.; Carter, S. P.; Nimmesgern, H.; Stull, P. D. *J. Am. Chem. Soc.* **1988**, *110*, 2894. Padwa, A.; Fryxell, G. E.; Zhi, L. *J. Org. Chem.* **1988**, *53*, 2875.
(36) Padwa, A. *Acc. Chem. Res.* **1991**, *24*, 22.
(37) For another example of the tandem dipole generation–intramolecular dipolar cycloaddition sequence, see: Denmark, S. E.; Schnute, M. E. *J. Org. Chem.* **1991**, *56*, 6738. Denmark, S. E.; Senanayake, C. B. W.; Ho, G. D. *Tetrahedron* **1990**, *46*, 4857. Denmark, S. E.; Moon, Y. C.; Cramer, C. J.; Dappen, M. S.; Senanayake, C. B. *Tetrahedron* **1990**, *46*, 7373. Denmark, S. E.; Moon, Y. C.; Senanayake, C. B. *J. Am. Chem. Soc.* **1990**, *112*, 311.
(38) Padwa, A.; Hornbuckle, S. F.; Fryxell, G. E.; Stull, P. D. *J. Org. Chem.* **1989**, *54*, 817.
(39) Padwa, A.; Hornbuckle, S. F. *Chem. Rev.* **1991**, *91*, 263.
(40) For a review of oxidopyrylium cycloadditions, see: Sammes, P. G. *Gazz. Chim. Ital.* **1986**, *119*, 109. Katritzky, A. R.; Dennis, N. *Chem. Rev.* **1989**, *89*, 827–861. See also footnote 12 in ref 30a.

(DMAD). With this system, intramolecular cycloaddition to the internal π-bond is too rapid to allow bimolecular trapping of the intermediate carbonyl ylide.

Of the many unexplored questions concerning the factors that govern the outcome of intramolecular carbonyl ylide trapping reactions, one that is very easy to formulate focuses upon the course of the reaction as a function of the length of the tether connecting the reacting groups. Our earlier studies have shown that the ring size of the resulting dipole played a significant role in the efficiency of the tandem cyclization–cycloaddition process.[41] The primary spatial requirement for intramolecular cycloaddition is that the distance between the dipole and alkene should be sufficiently close so that effective overlap of the π-orbitals can occur. In this paper the geometric requirements of the intramolecular cycloaddition reaction were evaluated by varying the chain length of the tether and determining what effect that had on the overall process.

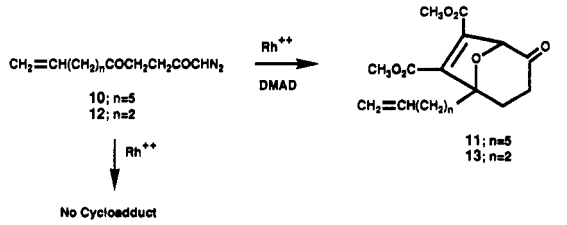
Treatment of α-diazo dione **6** with rhodium(II) acetate in benzene resulted in the formation of tricyclic species ketone **8** in 60% isolated yield. In the presence of DMAD, the intramolecular process was completely shut down, and the only product isolated was the bimolecular cycloadduct **9** derived from the trapping of carbonyl ylide **7**. This



observation indicates that the intramolecular cycloaddition involving a four-carbon tether (to form a six-membered ring) is slower than both bimolecular cycloaddition with DMAD and intramolecular cycloaddition involving a three carbon tether (i.e., **4** → **5**).

Expansion of the tether with a fifth methylene group was accomplished by synthesizing α-diazo ketone **10** (see the Experimental Section). However, treatment of **10** with the rhodium(II) catalyst gave no detectable quantities of an intramolecular cycloadduct. In order to confirm that the dipole was indeed being formed from **10**, the reaction was repeated in the presence of excess DMAD. This reaction afforded the bimolecular cycloadduct **11** in 57% yield. Thus, a five-carbon tether (leading conceptually to a seven-membered ring) is ineffective at directing intramolecular cycloaddition. Going in the opposite direction, we also reduced the tether length to two methylene units, as shown in structure **12**. Not surprisingly, treatment of **12** with $Rh_2(OAc)_4$ afforded no intramolecular cycloadduct. Apparently, the ring strain of the resulting tricyclic cyclobutane is sufficiently reflected in the transition state of cycloaddition so that a substantial kinetic barrier to this process exists. However, the carbonyl ylide is indeed formed, as an identical reaction carried out in the presence of DMAD provided bicyclic ketone **13** in good yield.

The rate of the intramolecular dipolar cycloaddition reaction of these systems is dependent on the energy level



of the open-chain initial state, compared to the transition state resembling the cyclic product. The activation energy of the process also reflects the strain energy of the ring to be formed, which is markedly dependent on ring size, as shown by strain energy data for the cycloalkanes.[42] The magnitude of such strain has been evaluated by Allinger on the basis of force-field calculations.[43] The probability of the alkenyl group coming close enough to the dipole for the reaction to occur decreases as the chain gets longer. In terms of entropy, this implies negative $\Delta S^{\ddagger}$ contributions owing to reduction of freedom of internal rotation about the single bonds of the molecular backbone when the disordered open-chain precursor is converted into the cycloadduct. The ease of internal cycloaddition as a function of ring size was found to significantly diminish on going from five- to seven-membered rings in the cycloadduct. The success of the internal cycloaddition reaction is critically dependent on the relative rates of cycloaddition as compared to unproductive decomposition pathways. In the case of the seven-membered ring, the entropy of activation is significantly more negative than with the systems bearing the shorter tethers, and this can account for why no internal cycloadduct is observed with α-diazo ketone **10**.

In recent years, molecular mechanics has developed into an important technique for the calculation of molecular properties.[44] We have used the Still–Steliou Model 2.94 program to model energy differences in the transition states for the intramolecular carbonyl ylide cycloaddition reaction. Global minima were found by making use of multiconformer generation in Model (TTY, Conf, Statistical, Coordinate) followed by Batch minimization using Bakmdl. The particular parameters used were those of the NOH (no hydrogen) field developed by Still and implemented by Steliou in the program Model. Structures within 3 kcal/mol of the lowest (global) energy conformer were retained for study. The transition-state geometry was approximated by fixing the distance between the reacting centers of the carbonyl ylide and alkene to be 3.0 ± 1.0 Å. A Boltzmann distribution of the various conformers of the carbonyl ylide was obtained from the Bakmdl output. We assume that the relative energy difference between the lowest energy conformation of the starting dipole and "*approximated*" cycloadduct will parallel the activation energy of the reaction. The calculations show an increase from 0.28 kcal/mol ($E_{TS} - E_{GS}$) for the dipole derived from α-diazo ketone **4** to 1.66 kcal/mol for **6** and 3.86 kcal/mol for **10** (see Table I). These values are in perfect accord with the experimental findings. We also note that the "*conformer population*" of the starting carbonyl ylide in the correct orientation to produce cycloadduct (i.e., distance between reacting centers =3.0 ± 1.0 Å) corresponds to 2.34% with **4** and diminishes significantly with the dipoles derived from **6** (0.6%) and **10** (<0.01%). We find that the above values closely approximate the entropic

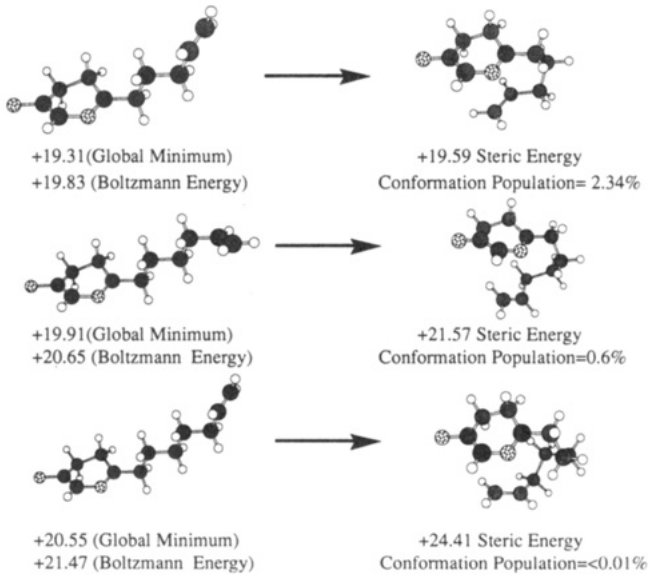
(41) Padwa, A.; Chinn, R. L.; Hornbuckle, S. F.; Zhang, Z. J. *J. Org. Chem.* **1991**, *56*, 3271.

(42) Liebman, J. F.; Greenberg, A. *Chem. Rev.* **1976**, *76*, 311.

(43) Allinger, N. L.; Tribble, M. T.; Miller, M. A.; Wertz, D. H. *J. Am. Chem. Soc.* **1971**, *93*, 1637.

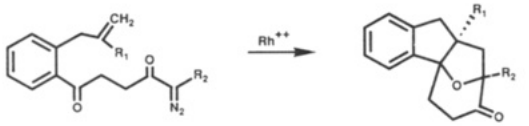
(44) Burkert, Ur; Allinger, N. L. *Molecular Mechanics*; American Chemical Society: Washington, DC, 1982.

Table I



factors associated with these internal cycloadditions. We suspect that this method of estimating entropy will prove to be quite general with other related intramolecular reactions.

Our original phthalate-based systems utilized a benzene ring as the backbone tether. Since we were interested in expanding the scope of the reaction, we prepared α-diazo ketones **14** and **15** in order to study their chemistry. Exposure of these compounds to the standard reaction conditions afforded the tetracyclic adducts **16** and **17** in high yield. Even in the presence of DMAD, the same intra-



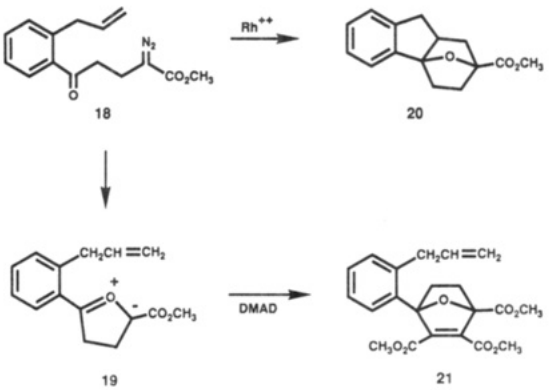
14; R_1=R_2=H
15; R_1=CH_3; R_2=H

16; R_1=R_2=H
17; R_1=CH_3; R_2=H

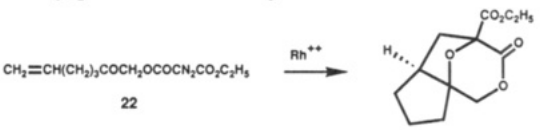
molecular cycloadducts were obtained as the only products. Once again the rapidity of intramolecular cycloaddition with a three-carbon tether significantly overshadows any bimolecular processes. In the case of **15**, this methodology successfully assembled a tetracyclic ring system, containing three new stereocenters and two adjacent quaternary centers stereospecifically in one step and in high yield.

A similar tandem cyclization–cycloaddition sequence also occurred with α-diazo keto ester **18**. In this case, cyclization of the rhodium carbenoid onto the neighboring carbonyl group generates the five-ring carbonyl ylide **19**, which undergoes subsequent dipolar cycloaddition across the tethered alkene giving cycloadduct **20** in 80% yield. Interestingly, when DMAD was added to the reaction mixture (2 equiv) it was possible to isolate the biomolecular cycloadduct **21** in 85% yield.[45]

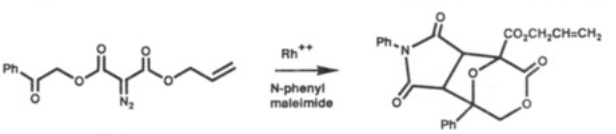
Our earlier studies had revealed some unexpected results when we incorporated heteroatoms at certain positions in the alkene tether. Therefore, we felt that it would prove enlightening to extend these intramolecular studies to include related systems containing heteroatom linkages at various positions in order to more clearly define the scope and generality of the tandem cyclization–cycloaddition methodology. In this spirit we prepared "ω-attached" diazo diester **22** and subjected it to routine rhodium-catalyzed



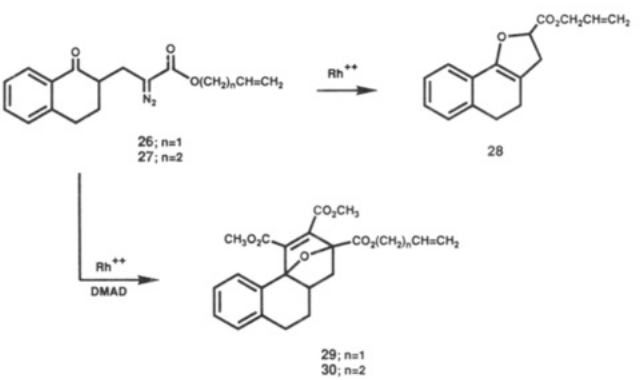
decomposition. Intramolecular cycloadduct **23** was isolated as the only product in 67% yield.



Bolstered by this positive result, we examined the chemistry of several "α-attached" diazo esters. When diazo keto ester **24** was treated with rhodium(II) acetate in benzene a complex mixture of products was obtained that could not be separated, even after extensive chromatography. Examination of the crude NMR spectrum confirmed that the olefinic hydrogens were still present, suggesting that intramolecular dipolar cycloaddition had not taken place. When the decomposition of **24** was repeated in the presence of *N*-phenylmaleimide, carbonyl ylide cycloadduct **25** was isolated in 58% yield. Clearly,



the carbonyl ylide was formed but did not undergo intramolecular cycloaddition. A related set of results was encountered with diazo keto esters **26** and **27**. When the reaction of these compounds with Rh_2OAc_4 was carried out in the presence of DMAD, cycloadducts **29** and **30** were isolated in 89% and 90% yield, respectively. However,

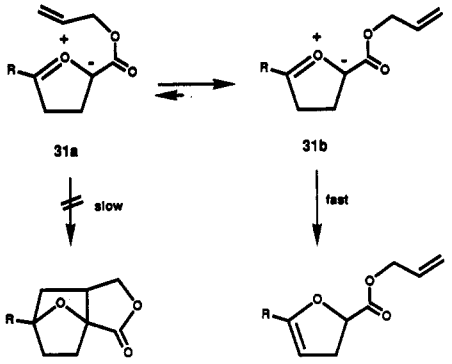


in the absence of any trapping reagent, no internal cycloadducts were found. The only identifiable material obtained from the reaction of **26** corresponded to **28** which is derived by a hydrogen shift from the initially produced dipole.[46–49] We believe that the inability of the above

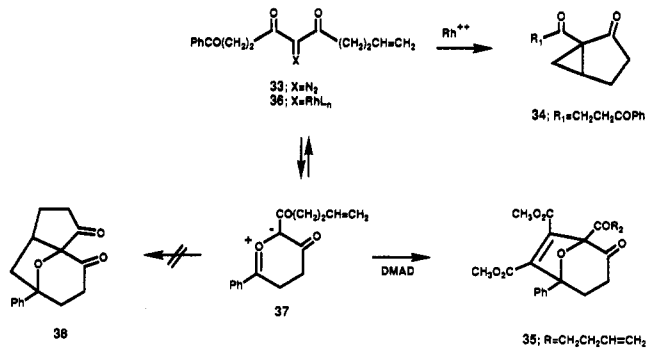
(45) Control experiments indicated that cycloadduct **20** is not converted into **21** upon treatment with DMAD and rhodium(II) acetate.

(46) Kharasch, M. S.; Rudy, T.; Nudenberg, W.; Büchi, G. *J. Org. Chem.* **1953**, *18*, 1030.

α-diazo keto esters to undergo internal cycloaddition is related to conformational factors. It is known that the *Z*-conformers of esters are generally more stable than the *E*-conformers.[50] The difference in energy has been measured for methyl formate (4.8 kcal/mol) and for methyl acetate (8.5 kcal/mol).[51] This strikingly large difference in energy would suggest that the equilibrium between the two conformations of the dipole lies predominantly on the side of the *Z*-isomer (i.e., **31b**). In this orientation, intramolecular dipolar cycloaddition cannot occur and instead the dipole collapses by means of a proton transfer to give enol ether **32**.

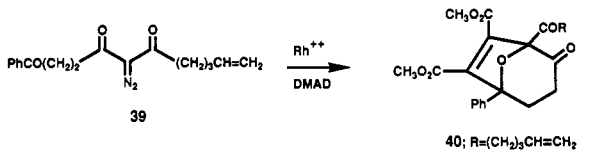


One of the more traditional methods for preparing α-diazo carbonyl compounds involves the diazotization of 1,3-dicarbonyl compounds.[52] We felt that using α-diazo dicarbonyl substrates such as **33** would increase the generalization of the tandem cyclization–cycloaddition methodology, as well as provide a convenient means for introducing functionality at what would ultimately be the bridgehead position in the final cycloadduct. In addition, we were also extremely interested in evaluating the competition between carbonyl ylide formation versus intramolecular cyclopropanation. Since the pioneering observation by Stork and Ficini in 1961,[53] intramolecular cyclopropanations of unsaturated α-diazo ketones have attracted considerable interest.[54] In this spirit, we prepared α-diazo trione **33** and subjected it to typical rhodium(II)-catalyzed decomposition conditions. The only product that could be isolated corresponded to bicyclo[3.1.0]hexanone **34** in 81% yield. The isolation of **34** suggested that perhaps carbonyl ylide formation was somehow disfavored in this instance, thereby allowing intramolecular cyclopropanation to become competitive. To test this hypothesis we repeated the reaction in the presence of DMAD. Most interestingly, this reaction afforded the bimolecular cycloadduct **35** in 68% yield as well as a 15% yield of the bicyclohexanone **34**. Clearly, carbonyl ylide formation is occurring, but intramolecular dipolar cycloaddition to the remote alkene is not competitive with the irreversible cyclopropanation. One possible explanation to account for the failure of carbonyl ylide **37** to undergo intramolecular cycloaddition to give **38** is that the tethered olefin is not able to adopt a conformation is which it is geometrically able to partake in the cycloaddition. The fact that bicyclohexanone **34** is the major product in the absence of DMAD suggests that carbonyl ylide **37** reverts



back to the rhodium carbenoid **36** which then undergoes internal cyclopropanation to produce **34**.[55]

One final system we chose to study corresponds to α-diazo ketone **39** which contains an additional methylene group in the side chain. This system was selected since we hoped that the greater flexibility would allow the internal cycloaddition to take place. However, treatment of **39** with the rhodium(II) catalyst gave rise to a complex mixture of products. No evidence for either the expected cycloadduct or cyclopropane was apparent in the NMR spectrum of the crude reaction mixture. Apparently, the olefinic side chain is too far away from the rhodium carbenoid center to allow for cyclopropanation. Since the olefinic protons were still present in the crude reaction mixture, it is clear that internal cycloaddition did not occur. In the presence of DMAD, the bimolecular cycloadduct **40** was isolated in 46% yield. It remains unclear



at this point in time why the carbonyl ylide derived from **39** is unable to undergo cycloaddition to the remote alkene. Perhaps the two-plane orientation approach required for dipolar cycloaddition cannot be easily achieved.

In conclusion, several trends have surfaced from our investigations in this area. First and foremost, these studies have demonstrated that intramolecular dipolar cycloaddition of carbonyl ylides is a viable method of quickly assembling complex tetrahydrofurans from easily prepared precursors. Three and four carbon atom tethers leading ultimately to five- and six-membered rings fused to the oxabicyclic backbone readily enter into intramolecular cycloaddition processes. Longer tethers appear to be entropically disfavored in this chemistry, whereas shorter tethers lead to high transition-state energies and are therefore not observed. Alkenes attached to the formal cationic terminus of the carbonyl ylide readily undergo internal cycloaddition if the tether allows for a relatively strain-free transition state. We are continuing to explore the scope, generality and synthetic applications of the rhodium(II)-catalyzed tandem cyclization–cycloaddition reaction of α-diazo ketones and will report additional finding at a later date.

Experimental Section

Melting points are uncorrected. Mass spectra were determined at an ionizing voltage of 70 eV. Unless otherwise noted, all reactions were performed in oven-dried glassware under an atmosphere of extra dry nitrogen. Solutions were evaporated under

(47) Gutsche, C. D.; Hillman, M. *J. Am. Chem. Soc.* **1954**, *76*, 2236.
(48) Landgrebe, J. A.; Iranmanesh, H. *J. Org. Chem.* **1978**, *43*, 1244.
(49) Bien, S.; Gillon, A. *Tetrahedron Lett.* **1974**, 3073.
(50) Wiberg, K. B.; Laidig, K. E. *J. Am. Chem. Soc.* **1988**, *110*, 1872.
(51) Blom, C. E.; Gunthard, H. H. *Chem. Phys. Lett.* **1981**, *84*, 267.
(52) Regitz, M. *Angew. Chem., Int. Ed. Engl.* **1967**, *6*, 733.
(53) Stork, G.; Ficini, J. *J. Am. Chem. Soc.* **1961**, *83*, 4678.
(54) Burke, S. D.; Grieco, P. A. *Org. React.* **1979**, *26*, 361.

(55) Varying the catalyst ligand (i.e. Rh_2OAc_4, Rh(II) perfluorobutyrate, and Rh(II) caprolactam) had no effect on the product ratio produced from diazo ketone **33**.

reduced pressure with a rotary evaporator, and the residue was chromatographed on a silica gel column using an ethyl acetate–hexane mixture as the eluent unless specified otherwise.

Preparation and Rhodium(II) Acetate Catalyzed Reaction of 1-Diazo-10-undecene-2,5-dione (6). To a suspension containing 0.75 g (31 mmol) of magnesium turnings in 15 mL of ether was slowly added 3.8 mL (28.4 mmol) of 6-bromo-1-hexene in 6.0 mL of anhydrous ether at 25 °C. The mixture was heated at reflux for 30 min and was then cooled to 0 °C. After the addition of 3.41 g (18.6 mmol) of anhydrous $CdCl_2$, the reaction mixture was heated at reflux for 1 h. The solvent was removed under reduced pressure, and 15 mL of dry benzene was added. A solution containing 4.28 g (28.4 mmol) of methyl 3-(chloroformyl)-propionate in 10 mL of benzene was gradually added to the mixture which had been cooled to 0 °C. After heating to 60 °C for 1 h, the solution was treated with ice and extracted with ether. The combined ethereal extracts were washed with a 5% $NaHCO_3$ and dried over Na_2SO_4. The solvent was removed under reduced pressure, and the residue was distilled at 110 °C (0.6 mm) to give methyl 4-oxo-9-decenoate as a colorless oil in 66% yield: IR (neat) 1745, 1720, 1445, 1180, and 920 cm^{-1}; NMR ($CDCl_3$, 300 MHz), 2.06 (q, 2 H, J = 7.2 Hz), 2.45 (t, 2 H, J = 7.2 Hz), 2.56 (t, 2 H, J = 6.4 Hz), 2.75 (t, 2 H, J = 6.4 Hz), 3.67 (s, 3 H), 4.96 (m, 2 H), and 5.78 (m, 1 H).

A solution containing 2.5 g (12.6 mmol) of the above keto ester in 100 mL of THF was treated with 1.62 g (12.6 mmol) of potassium trimethylsilanoate. After the mixture was stirred for 2 h at 25 °C, 0.97 mL (12.6 mmol) of methyl chloroformate was added. The mixture was stirred for an additional 4 h at rt and was then treated with excess diazomethane in ether at 0 °C. The solution was allowed to warm to 25 °C over a 12-h interval, the solvent was removed under reduced pressure, and the resulting oil was purified via silica gel flash chromatography to give 1.33 g (51%) of 1-diazo-10-undecene-2,5-dione (6) as a yellow oil: IR (neat) 2110, 1715, 1645, 1380, and 920 cm^{-1}; NMR ($CDCl_3$, 300 MHz) δ 1.33 (qu, 2 H, J = 7.3 Hz), 1.54 (qu, 2 H, J = 7.3 Hz), 2.00 (q, 2 H, J = 7.3 Hz), 2.41 (t, 2 H, J = 7.3 Hz), 2.55 (br t, 2 H, J = 6.3 Hz), 2.71 (t, 2 H, J = 6.3 Hz), 4.87–4.97 (m, 2 H), 5.28 (br s, 1 H), and 5.66–5.80 (m, 2 H).

A solution containing 370 mg (1.78 mmol) of 6 in 10 mL of benzene was treated with a catalytic amount of rhodium(II) acetate for 6 h at 25 °C. At the end of this time the solution was filtered and concentrated under reduced pressure. The crude oil was subjected to silica gel flash chromatography to give 193 mg (60%) of decahydro-7*H*-4a,8-oxybenzocyclohepten-7-one (8): IR (neat) 1730, 1450, 1420, 1025, and 890 cm^{-1}; NMR ($CDCl_3$, 300 MHz) δ 1.06–1.17 (m, 2 H), 1.39–1.66 (m, 5 H), 1.77–2.02 (m, 6 H), 2.25–2.41 (m, 2 H), and 4.22 (d 1 H, J = 8.86 Hz); ^{13}C NM<R ($CDCl_3$, 75 MHz) δ 21.1, 23.8, 31.8, 32.2, 33.8, 35.5, 36.4, 41.4, 79.9, 79.9, and 209.9; HRMS calcd for $C_{11}H_{16}O_2$ 180.1150, found 180.1154.

A solution containing 310 mg (1.49 mmol) of 6 and 0.20 mL (1.64 mmol) of DMAD in 8 mL of benzene was treated with a catalytic amount of rhodium(II) acetate for 6 h at 25 °C. At the end of this time the solution was filtered and concentrated under reduced pressure. The crude oil obtained was subjected to silica gel flash chromatography to give 206 mg (43%) of dimethyl 4-oxo-1-(5-hexenyl)-8-oxabicyclo[3.2.1]oct-6-ene-6,7-dicarboxylate (9): IR (neat) 1740, 1650, 1440, 1330, 1020, and 920 cm^{-1}; NMR ($CDCl_3$, 300 MHz) δ 1.27–1.80 (m, 6 H), 1.98 (q, 2 H, J = 6.8 Hz), 2.14–2.19 (m, 2 H), 2.38–2.50 (m, 1 H), 2.70 (dt, 1 H, J = 17.6 and 8.8 Hz), 3.71 (s, 3 H), 3.81 (s, 3 H), 4.77 (s, 1 H), 4.85–4.96 (m, 2 H), and 5.67–5.76 (m, 1 H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 22.9, 28.9, 31.5, 32.9, 33.4, 35.1, 52.6, 52.7, 85.9, 91.3, 114.5, 136.3, 138.5, 146.7, 161.1, 164.1, and 199.7; HRMS calcd for $C_{17}H_{22}O_6$ 322.1416, found 322.1407.

Preparation and Rhodium(II) Acetate Catalyzed Reaction of 1-Diazo-11-dodecene-2,5-dione (10). To a flame-dried, 250-mL round-bottomed flask equipped with a magnetic stir bar and under N_2 were added 780 mg (19.6 mmol) of 60% NaH and 100 mL of THF. After the flask was cooled to 0 °C, 2.48 mL (19.8 mmol) of ethyl acetoacetate was added dropwise over 5 min. The mixture was allowed to stir at 25 °C until the solution became clear and was then cooled to 0 °C, and 12.2 mL of *n*-butyllithium (1.6 M in hexane) (19.6 mmol) was added in one portion. After the mixture was stirred for 30 min, 3.19 g (19.6 mmol) of 6-bromo-1-hexene was added, and the resulting mixture was allowed to warm to rt over a 30-min interval. The solution was diluted with aqueous HCl and extracted with ether. The ether extracts were washed with brine, dried over Na_2SO_4, and concentrated under reduced pressure. The crude residue was purified via silica gel chromatography to give 2.60 g (62%) of ethyl 3-oxo-9-decenoate as a colorless oil: IR (neat) 1750, 1720, 1645, 1415, 1240, 1035, and 915 cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz) δ 1.26 (t, 3 H, J = 7.1 Hz), 1.25–1.41 (m, 4 H), 1.59 (quint, 2 H, J = 7.4 Hz), 2.02 (q, 2 H, J = 7.0 Hz), 2.52 (t, 2 H, J = 7.4 Hz), 3.41 (s, 2 H), 4.18 (q, 2 H, J = 7.1 Hz), 4.90–5.00 (m, 2 H), and 5.70–5.88 (m, 1 H).

To a flame-dried, 250-mL, round-bottomed flask equipped with a magnetic stir bar and under N_2 were added 460 mg (11.5 mmol) of 60% NaH and 75 mL of THF. After the flask was cooled to 0 °C, 2.44 g (11.5 mmol) of the above keto ester was added dropwise over 5 min. The mixture was allowed to stir at 25 °C until the solution became clear and was then cooled to 0 °C, and 1.28 mL (11.5 mmol) of ethyl bromoacetate was added. The mixture was stirred for 30 min at rt, diluted with aqueous HCl, and extracted with ether. The ether extracts were washed with brine, dried over Na_2SO_4, and concentrated under reduced pressure. The crude residue was purified via silica gel chromatography to give 2.20 g (64% yield) of diethyl 2-(1-oxo-7-octenyl)succinate as a colorless oil: IR (neat) 1740, 1720, 1415, 1375, 1030, and 920 cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz) δ 1.23 (t, 3 H, J = 7.1 Hz), 1.25 (t, 3 H, J = 7.1 Hz), 1.29–1.41 (m, 4 H), 1.60 (quint, 2 H, J = 7.4 Hz), 2.03 (q, 2 H, J = 7.0 Hz), 2.54–2.74 (m, 2 H), 2.80 (dd, 1 H, J = 17.5 and 6.2 Hz), 2.95 (dd, 1 H, J = 17.5 and 8.2 Hz), 3.95 (dd, 1 H, J = 8.2 and 6.2 Hz), 4.10 (q, 2 H, J = 7.1 Hz), 4.17 (q, 2 H, J = 7.1 Hz), 4.90–5.00 (m, 2 H), and 5.71–5.84 (m, 1 H).

The above acyl succinate was decarboxylated using a modified procedure of Wehrli and Chu.[56] A 10-mL round-bottom flask equipped with a magnetic stir bar and a Claisen condenser connected to a bubbler was charged with 1.55 g (5.19 mmol) of the above compound and 320 mg of boric acid. This heterogeneous mixture was heated at 150 °C for 1 h followed by heating at 175 °C until the gas evolution had ceased. After cooling to 25 °C, ice was added to the solution and the mixture was extracted with benzene. The benzene extracts were dried over Na_2SO_4 and concentrated under reduced pressure. The crude residue was purified via silica gel chromatography to give 1.02 g (87%) of ethyl 4-oxo-10-undecenoate as a colorless oil: IR (neat) 1740, 1720, 1640, 1185, 1035, and 915 cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz) δ 1.24 (t, 3 H, J = 7.1 Hz), 1.21–1.40 (m, 4 H), 1.61 (quint, 2 H, J = 7.4 Hz), 2.02 (q, 2 H, J = 7.0 Hz), 2.43 (t, 2 H, J = 7.4 Hz), 2.56 (t, 2 H, J = 6.4 Hz), 2.70 (t, 2 H, J = 6.4 Hz), 4.11 (q, 2 H, J = 7.1 Hz), 4.90–5.00 (m, 2 H), and 5.70–5.88 (m, 1 H).

A solution containing 1.28 g (5.65 mmol) of this compound in 60 mL of THF was treated with 720 mg (5.65 mmol) of potassium trimethylsilanolate. After the mixture was stirred at 25 °C for 2 h, 1.31 mL (16.9 mmol) of methyl chloroformate was added. The reaction mixture was stirred for 4 h at rt and was then treated with 50 mmol of diazomethane in ether at 0 °C. The solution was allowed to warm to 25 °C over a 12-h interval. The solvent was removed under reduced pressure, and the resulting oil was purified via silica gel flash chromatography to give 820 mg (66% yield) of 1-diazo-11-dodecene-2,5-dione (10) as a yellow solid: mp 34–35 °C; IR (KBr) 2140, 1710, 1645, 1630, 1140, 1070, and 920 cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz) δ 1.17–1.37 (m, 4 H), 1.52 (quint, 2 H, J = 7.4 Hz), 1.97 (q, 2 H, J = 7.0 Hz), 2.38 (t, 2 H, J = 7.4 Hz), 2.53 (br t, 2 H, J = 6.3 Hz), 2.69 (t, 2 H, J = 6.3 Hz), 4.84–4.94 (m, 2 H), 5.25 (br s, 1 H), and 5.65–5.79 (m, 2 H).

A solution containing 264 mg (1.19 mmol) of 10 and 161 μL (1.31 mmol) of DMAD in 5.0 mL of benzene was treated with 5 mg of rhodium(II) acetate for 2 h at 25 °C. The solution was filtered and concentrated under reduced pressure. The crude oil was subjected to silica gel flash chromatography to give 228 mg (57% yield) of dimethyl 4-oxo-1-(6-heptenyl)-8-oxabicyclo-[3.2.1]oct-6-ene-6,7-dicarboxylate (11): IR (neat) 1740, 1730, 1655, 1445, 1020, and 925 cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz) δ 1.18–1.35 (m, 4 H), 1.40–1.55 (m, 2 H), 1.61–1.85 (m, 2 H), 1.96 (q, 2 H, J = 7.0 Hz), 2.13–2.19 (m, 2 H), 2.38–2.49 (m, 1 H), 2.70 (quint. 1

(56) Wehrli, P.; Chu, V. *Organic Syntheses*; Wiley: New York, 1979; Collect. Vol. VI, p 615.

H, J = 8.7 Hz), 3.72 (s, 3 H), 3.81 (s, 3 H), 4.78 (s, 1 H), 4.84–4.95 (m, 2 H), and 5.68–5.79 (m, 1 H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 23.2, 28.5, 29.1, 31.4, 32.8, 33.5, 35.1, 52.6, 52.7, 85.9, 91.3, 114.3, 136.3, 138.8, 146.7, 161.0, 164.1, and 199.6; HRMS calcd for $C_{18}H_{24}O_6$ 336.1572, found 336.1566.

Preparation and Rhodium(II) Acetate Catalyzed Reaction of 1-Diazo-8-nonene-2,5-dione (12). To a suspension containing 1.5 g (61.7 mmol) of magnesium turnings in 30 mL of anhydrous ether was slowly added 9.0 g (66.7 mmol) of 4-bromo-1-butene in 15 mL of anhydrous ether at 25 °C. The reaction mixture was heated at reflux for 30 min and then cooled to 0 °C. After the addition of 8.0 g (43.6 mmol) of anhydrous $CdCl_2$, the reaction mixture was heated at reflux for 1 h. The solvent was removed under reduced pressure, and then 30 mL of benzene was added. A solution containing 10.0 g (66.4 mmol) of methyl 3-(chloroformyl)propionate in 15 mL of benzene was gradually added to the reaction mixture which had been cooled to 0 °C. After being heated to 60 °C for 1 h, the mixture was treated with ice and extracted with ether. The combined ethereal extracts were washed with 5% $NaHCO_3$ and dried over anhydrous Na_2SO_4. Removal of the solvent under reduced pressure followed by distillation of the residue (bp 58–60 °C (0.5 mm)) afforded methyl 4-oxo-7-octenoate as a colorless oil in 75% yield: IR (neat) 1750, 1645, 1445, and 920 cm^{-1}; NMR ($CDCl_3$ 90 MHz) δ 2.25–2.80 (m, 8 H), 3.70 (s, 3 H), 4.90–5.16 (m, 2 H), and 5.60–6.05 (m, 1 H).

A solution containing 4.0 g (23.5 mmol) of the above keto ester in 150 mL of THF was treated with 3.02 g (23.5 mmol) of potassium trimethylsilanolate. After the mixture was stirred for 2 h, 2.0 mL (25.8 mmol) of methyl chloroformate was added. The reaction mixture was stirred at 25 °C for 4 h and was then treated with excess diazomethane in ether at 0 °C. The solution was allowed to warm to 25 °C over a 12-h interval, the solvent was removed under reduced pressure, and the resulting oil was purified via silica gel flash chromatography to give 2.11 g (50%) of 1-diazo-8-nonene-2,5-dione (12) as a yellow oil: IR (neat) 2120, 1715, 1645, 1325, 1150, and 920 cm^{-1}; NMR ($CDCl_3$, 90 MHz) δ 2.10–2.86 (m, 8 H), 4.93–5.16 (m, 2 H), 5.36 (s, 1 H), and 5.56–6.03 (m, 1 H).

A solution containing 758 mg (4.20 mmol) of 12 and 0.57 mL (4.62 mmol) of DMAD in 40 mL of benzene was treated with a catalytic amount of rhodium(II) acetate for 6 h at 25 °C. The solution was filtered and concentrated under reduced pressure. The crude oil was subjected to silica gel flash chromatography to give 703 mg (56%) of dimethyl 4-oxo-1-(3-butenyl)-8-oxabicyclo[3.2.1]oct-6-ene-6,7-dicarboxylate (13): IR (neat) 1725, 1640, 1435, 1135, 1015, 925, and 740 cm^{-1}; NMR ($CDCl_3$, 300 MHz) δ 1.73–1.92 (m, 2 H), 1.97–2.10 (m, 1 H, 2.14–2.19 (m, 3 H), 2.35–2.46 (m, 1 H), 2.69 (dt, 1 H, J = 18.6 and 8.9 Hz), 3.71 (s, 3 H), 3.80 (s, 3 H), 4.77 (s, 1 H), 4.87–4.97 (m, 2 H), and 5.66–5.80 (m 1 H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 27.7, 31.4, 32.7, 34.3, 52.5, 52.7, 85.8, 90.8, 114.8, 136.5, 137.44, 146.1, 160.9, 163.8, and 199.3; HRMS calcd for $C_{15}H_{18}O_6$ 294.1103, found 294.1104.

Preparation and Rhodium(II) Acetate Catalyzed Reaction of 5-Diazo-1-[2-(2-propenylphenyl)]-2,4-pentanedione (14). Freshly ground magnesium metal (4.75 g, 196 mmol) was placed in a 500-mL three-necked round-bottomed flask fitted with a reflux condenser and an addition funnel. A solution containing 15.3 mL (131 mmol) or *o*-bromochlorobenzene in 175 mL of ether was added at such a rate so as to maintain a gentle reflux. After the addition was complete, reflux was maintained for an additional hour. After being cooled to 25 °C, the Grignard solution was cannelated into a solution containing 23 mL (0.27 mol) of allyl bromide in 200 mL of ether, and the mixture was stirred overnight at 25 °C. The reaction was quenched with a saturated NH_4Cl solution, washed twice with water and once with a brine solution, and dried over anhydrous Na_2SO_4. The solvent was removed under reduced pressure, and the product was distilled to give 15.0 g of 1-chloro-2-(2-propenyl)benzene (11) as a colorless liquid (75% yield): bp 88–90 °C (54 mm); IR (neat) 1835, 1445, 1000, 920, 750, and 640 cm^{-1}; NMR (CCl_4, 90 MHz) δ 3.48 (d, 2 H, J = 6.5 Hz), 4.80–5.20 (m, 2 H), 5.63–6.18 (m, 1 H), and 6.83–7.43 (m, 4 H).

A 0.5-g (20-mmol) freshly ground sample of magnesium metal was placed in a 100-mL round-bottomed flask, and then a solution containing 1.52 g (10 mmol) of the above chloride in 30 mL of THF was added. The mixture was heated at reflux under N_2 for 24 h. While the Grignard solution was cooling to 25 °C, a solution containing 1.0 g (10 mmol) of succinic anhydride in 25 mL of THF was prepared and cooled to −78 °C. The Grignard solution was added via syringe to the anhydride solution at −78 °C. The reaction mixture was allowed to slowly warm up to 25 °C. The reaction was quenched with 10% HCl and was then extracted with ether. The combined ether extracts were washed with a 10% NaOH solution, the basic aqueous layer was acidified with concentrated HCl, and the product was extracted with ether. The ether layer was washed with brine and dried over anhydrous Na_2SO_4. The solvent was removed under reduced pressure, and the crude product was chromatographed on silica using methanol as the eluent to give 1.55 g (78% yield) of 4-oxo-4-[2-(2-propenyl)phenyl]butanoic as a pale yellow oil: IR (KBr) 1715, 1695, 1640, 1360, 1175, 925, and 765 cm^{-1}; NMR ($CDCl_3$, 90 MHz) δ 2.65 (t, 2 H, J = 7 Hz), 3.15 (t, 2 H, J = 7 Hz), 3.55 (d, 2 H, J = 7 Hz), 4.80–5.17 (m, 2 H), 5.72–6.22 (m, 1 H), 7.05–7.95 (m, 4 H), and 11.80 (br s, 1 H).

A solution containing 2.79 g (14.1 mmol) of the above acid in 50 mL of THF was treated with 1.1 mL (15 mmol) of methyl chloroformate and 2.0 mL (14.1 mmol) of Et_3N. After being stirred at 25 °C for 6 h, the solution was filtered and treated with 34 mmol of freshly prepared diazomethane at 0 °C and was then allowed to warm to 25 °C overnight. The solvent was removed under reduced pressure, and the residue was chromatographed on silica gel to give 2.1 g (65%) of the methyl ester: IR (neat) 1745, 1695, 1580, 1360, 1225, and 765 cm^{-1}; NMR (CCl_4, 90 MHz) δ 2.60 (t, 2 H, J = 7.0 Hz), 3.08 (t, 2 H, J = 7.0 Hz), 3.55 (d, 2 H, J = 8.4 Hz), 3.62 (s, 3 H), 4.82–5.13 (m, 2 H), 5.70–6.18 (m, 1 H), 7.10–7.47 (m, 3 H), and 7.56–7.78 (m, 1 H).

The second product eluted from the column contained 1.0 g (29% yield) of the desired diazo ketone 14 as a pale yellow oil: IR (neat) 1740, 1695, 1575, 1490, 1350, 1035, 1000, and 765 cm^{-1}; NMR (CCl_4, 90 MHz) δ 2.60 (t, 2 H, J = 6.0 Hz), 3.08 (t, 2 H, J = 6.0 Hz), 3.54 (br d, 2 H, J = 6.5 Hz), 4.78–4.98 (m, 1 H), 4.98–5.19 (m, 1 H), 5.32 (s, 1 H), 5.68–6.22 (m, 1 H), 7.05–7.48 (m, 3 H), and 7.54–7.87 (m, 1 H).

To a solution containing 193 mg (0.795 mmol) of diazo ketone 14 in 10 mL of dry benzene was added 2 mg of rhodium(II) acetate dimer. The mixture was stirred under N_2 for 4 h at 25 °C, the solution was filtered, and the solvent was removed under reduced pressure. The crude product was chromatographed on silica gel to give 168 mg (98% yield) of cycloadduct 16 as colorless crystals: mp 110–111 °C; IR (KBr) 1725, 1615, 1490, 1235, 1190, 1030, 995, and 775 cm^{-1}; NMR ($CDCl_3$, 300 MHz) δ 2.06 (ddd, 1 H, J = 13.1, 7.0, and 3.4 Hz), 2.19 (ddd, 1 H, J = 13.5, 7.7, and 5.8 Hz), 2.40 (dd, 1 H, J = 13.5 and 9.2 Hz), 2.54–2.74 (m, 2 H), 2.76–2.92 (m, 2 H), 3.10 (tt, 1 H, J = 9.3 and 5.9 Hz), 3.41 (dd, 1 H, J = 16.7 and 9.6 Hz), 4.52 (d, 1 H, J = 7.8 Hz), and 7.18–7.46 (m, 4 H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 32.1, 33.2, 38.4, 39.7, 45.9, 85.6, 94.1, 123.6, 125.1, 127.0, 129.9, 140.6, 144.5, and 207.9. Anal. Calcd for $C_{14}H_{14}O_2$: C, 78.48; H, 6.59. Found: C, 78.42; H, 6.37.

Preparation and Rhodium(II) Acetate Catalyzed Reaction of 5-Diazo-1-[2-(2-methyl-2-propenyl)phenyl]-2,4-pentanedione (15). Freshly ground magnesium metal (6.4 g, 260 mmol) was placed in a 500-mL three-necked round-bottomed flask that was fitted with a dropping funnel and a reflux condenser. The apparatus was then flame-dried under a stream of dry N_2. A solution containing 29 mL (250 mmol) of *o*-bromochlorobenzene in 150 mL of ether was added over 45 min so as to maintain a gentle reflux. The mixture was stirred at 25 °C overnight and was then heated at reflux for 1 h. A solution containing 25 mL (250 mmol) of freshly distilled methallyl chloride in 50 mL of ether was added dropwise over 1 h at reflux, and the reaction mixture was maintained at reflux for 24 h. The reaction mixture was then allowed to cool to 25 °C and was quenched with an aqueous NH_4Cl solution. The ether layer was washed with water and brine and then dried over anhydrous Na_2SO_4. The solvent was removed, and the residue was distilled under reduced pressure to give 13.5 g (33%) of 1-chloro-2-(2-methyl-2-propenyl)benzene as a colorless liquid: bp 79–81 °C (18 mm); IR (neat) 1955, 1810, 1650, 1380, 1130, 1055, and 685 cm^{-1}; NMR (CCl_4, 90 MHz) δ 1.71 (s, 3 H), 3.42 (s, 2 H), 4.63 (br s, 1 H), 4.83 (br s, 1 H), and 6.96–7.40 (m, 4 H).

A 1.0-g (41-mmol) sample of freshly ground magnesium metal was placed in a 100-mL round-bottomed flask, and a solution

containing 5.0 g (30 mmol) of the above chloride and 20 mg of anthracene in 25 mL of THF was heated at reflux for 24 h. As the Grignard solution was cooled to 25 °C, a solution containing 3.0 g of succinic anhydride (30 mmol) in 200 mL of THF was prepared and cooled to −78 °C. The Grignard solution was transferred via syringe to the cooled anhydride solution. The reaction mixture was allowed to warm to 25 °C overnight and was then quenched with 10% HCl and extracted with ether. The organic phase was washed with 10% NaOH, and then the basic aqueous layer was acidified with concentrated HCl and extracted with ether. The ether layer was washed with water and brine and then dried over anhydrous Na_2SO_4. The solvent was removed under reduced pressure, and the crude product was chromatographed on silica gel to give 4.73 g (68% yield) of 4-oxo-4-[2-(2-methyl-2-propenyl)phenyl]butanoic acid as a pale yellow oil: IR (neat) 1695, 1650, 1575, 1360, 1175, 760, and 705 cm^{-1}; NMR ($CDCl_3$, 90 MHz) δ 1.66 (s, 3 H), 2.72 (t, 2 H, J = 6.0 Hz), 3.14 (t, 2 H, J = 6.0 Hz), 3.53 (br s, 2 H), 4.45 (br s, 1 H), 4.78 (br s, 1 H), 7.03–7.49 (m, 3 H), 7.52–7.71 (m, 1 H), and 11.80 (br s, 1 H).

A solution containing 2.63 g (11 mmol) of the above acid in 100 mL of ether was treated with 0.85 mL (11 mmol) of methyl chloroformate and 1.5 mL (11 mmol) of Et_3N. The resulting white suspension was stirred at 25 °C for 8 h and was then filtered and treated with 25 mmol of freshly prepared diazomethane at 0 °C. The yellow solution was allowed to stir overnight, and then the solvent was removed under reduced pressure and the residue was chromatographed on silica gel. The first product isolated from the column was identified as the methyl ester and consisted of a yellow oil (625 mg, 23% yield): IR (neat) 1740, 1695, 1575, 1260, 1220, 980, 950, and 705 cm^{-1}; NMR (CCl_4, 90 MHz) δ 1.65 (s, 3 H), 2.58 (t, 2 H, J = 7.0 Hz), 3.05 (t, 2 H, J = 7.0 Hz), 3.50 (br s, 2 H), 3.64 (s, 3 H), 4.45 (br s, 1 H), 4.72 (br s, 1 H), 6.94–7.46 (m, 3 H), and 7.53–7.70 (m, 1 H).

The second material isolated contained 925 mg (33%) of a pale yellow oil which was identified as diazo ketone **15**: IR (neat) 2120, 1750, 1705, 1335, 1250, 1225, 770, and 715 cm^{-1}; NMR (CCl_4, 90 MHz) δ 1.67 (br s, 3 H), 2.60 (t, 2 H, J = 6.6 Hz), 3.08 (t, 2 H, J = 6.6 Hz), 3.52 (br s, 2 H), 4.45 (br s, 1 H), 4.73 (br s, 1 H), 5.30 (s, 1 H), 7.03–7.48 (m, 3 H), and 7.57–7.78 (m, 1 H).

A solution containing 310 mg (1.2 mmol) of **15** in 12 mL of benzene was treated with a catalytic amount of rhodium(II) acetate dimer for 6 h. The solution was filtered, and the solvent was removed under reduced pressure. The crude residue was chromatographed on silica gel to give 240 mg of cycloadduct **17** as a colorless crystalline solid (88% yield): mp 127–128 °C; IR (KBr) 1725, 1465, 1305, 1230, 875, and 770 cm^{-1}; NMR ($CDCl_3$, 300 MHz) δ 1.29 (s, 3 H), 1.90 (d, 1 H, J = 13.5 Hz), 2.17 (ddd, 1 H, J = 13.5, 7.1, and 3.1 Hz), 2.56–2.70 (m, 3 H), 2.7–2.9 (m, 1 H), 2.88 (d, 1 H, J = 15.9 Hz), 3.21 (d, 1 H, J = 15.9 Hz), 4.48 (d, 1 H, J = 8.6 Hz), and 7.16–7.41 (m, 4 H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 23.5, 25.9, 32.4, 43.2, 48.9, 53.4, 84.0, 94.3, 123.8, 125.2, 126.8, 129.9, 140.0, 144.0, and 207.6. Anal. Calcd for $C_{15}H_{16}O_2$: C, 78.92; H, 7.06. Found: 78.84; H, 6.93.

Preparation and Rhodium-Catalyzed Reaction of Methyl 2-Diazo-5-oxo-5-(2-allylphenyl)pentanoate (18). To a mixture containing 1.8 mL (10 mmol) of tetravinyltin in 30 mL of ether was slowly added 28 mL of 1.4 M methyllithium at 0 °C. After being stirred for 30 min, the resulting solution was cannulated into a solution containing 3.2 g (22 mmol) of *o*-allylbenzaldehyde in 40 mL of ether at 0 °C. After being stirred for 2 h at rt, the mixture was poured into a 1.0 N HCl solution. The aqueous phase was extracted with ether and the organic layer was dried over $MgSO_4$. The solvent was removed under reduced pressure, and the crude residue was chromatographed on a silica gel column to give 3.4 g (90%) of 1-(2-allylphenyl)-2-propen-1-ol as a colorless oil: IR (neat) 3334, 1638, 1451, 991, 920, and 758 cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz) δ 1.90 (s, 1 H), 3.48 (d, 2 H, J = 6.1 Hz), 4.95–5.50 (m, 5 H), 5.90–6.15 (m, 2 H), and 7.10–7.50 (m, 4 H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 36.4, 70.9, 114.6, 115.7, 126.5, 127.5, 129.6, 136.8, 137.2, 139.6, and 140.2. Anal. Calcd for $C_{12}H_{14}O$: C, 82.72; H, 8.10. Found: C, 82.69; H, 8.13.

To a solution containing 2.7 g (15.5 mmol) of the above alcohol in 50 mL of CH_2Cl_2 was slowly added 6.5 g (30 mmol) of PCC at 0 °C. After the mixture was stirred for 2 h, 100 mL of ether was added, and the resulting mixture was passed through a short pad of silica gel. The solvent was removed under reduced pressure, and the crude residue was chromatographed on a silica gel column to give 1.21 g (45%) of *o*-allylphenyl vinyl ketone as a colorless liquid: IR (neat) 1661, 1402, 1231, 993, 962, and 758 cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz) δ 3.51 (d, 2 H, J = 6.3 Hz), 4.95–5.10 (m, 2 H), 5.85–6.20 (m, 3 H), 6.75 (dd, 1 H, J = 17.4 and 10.2 Hz), and 7.20–7.45 (m, 4 H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 37.2, 115.8, 125.6, 128.2, 130.4, 130.6, 131.2, 136.5, 136.8, 137.7, 138.9, and 196.3.

In addition, 0.34 g (13%) of 3-(*o*-allylphenyl)propenal was also obtained as a colorless liquid: IR (neat) 1684, 1622, 1128, 918, and 754 cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz) δ 3.55 (d, 2 H, J = 5.7 Hz), 4.95 (d, 1 H, J = 17.1 Hz), 5.10 (d, 1 H, J = 10.2 Hz), 6.60–6.75 (m, 1 H), 6.66 (dd, 1 H, J = 15.5 and 7.8 Hz), 7.20–7.40 (m, 3 H), 7.61 (d, 1 H, J = 7.8 Hz), 7.75 (d, 1 H, J = 15.6), and 9.69 (d, 1 H, J = 7.8 Hz); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 37.3, 116.5, 126.9, 127.0, 129.7, 130.6, 131.1, 132.7, 136.2, 139.3, 150.1, and 193.8.

A mixture containing 1.3 g (7.6 mmol) of *o*-allylphenyl vinyl ketone, 5 mL of methyl acetoacetate, and 200 mg of $Ni(AcAc)_2$ was heated at 90 °C for 20 h. The solvent was removed under reduced pressure, and the crude product was chromatographed on a silica gel column to give 1.80 g (83%) of methyl 2-acetyl-5-oxo-5-(*o*-allylphenyl)pentanoate as a colorless oil: IR (neat) 1744, 1717, 1688, 1360, 1248, 1151, and 756 cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz) δ 2.20–2.30 (m, 5 H), 2.93 (d, 2 H, J = 7.2 Hz), 3.58–3.65 (m, 3 H), 3.73 (s, 3 H), 4.90–5.05 (m, 2 H), 5.86–6.02 (m, 1 H), 7.22–7.30 (m, 2 H), 7.40 (t, 1 H, J = 7.5 Hz), and 7.56 (d, 1 H, J = 7.5 Hz); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 22.1, 28.9, 37.6, 38.4, 52.2, 57.9, 115.5, 126.0, 128.0, 131.0, 131.2, 137.2, 137.8, 139.2, 169.8, 202.6, and 203.0. Anal. Calcd for $C_{17}H_{20}O_4$: C, 70.82; H, 6.99. Found: C, 70.72; H, 7.06.

A mixture containing 800 mg (2.88 mmol) of the above compound, 706 mg (5.6 mmol) of methanesulfonyl azide, and 1.1 mL (8 mmol) of Et_3N in 6 mL of CH_3CN was stirred at rt for 2 h. The solvent was removed under reduced pressure, and the crude residue was chromatographed on a silica gel column to give 460 mg of recovered starting material and 201 mg (63%) of methyl 2-diazo-5-oxo-5-(*o*-allylphenyl)pentanoate (**18**) as a yellow oil: IR (neat) 2091, 1696, 1437, 1333, 1111, and 740 cm^{-1}; ^1H NMR ($CDCl_3$, 360 MHz) δ 2.70 (t, 2 H, J = 6.5 Hz), 3.17 (t, 2 H, J = 6.5 Hz), 3.62 (d, 2 H, J = 6.5 Hz), 3.75 (s, 3 H), 4.95–5.04 (m, 2 H), 5.80–6.00 (m, 1 H), 7.25–7.35 (m, 2 H), 7.42 (t, 1 H, J = 7.5 Hz), and 7.76 (d, 1 H, J = 7.5); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 18.6, 37.8, 39.5, 51.7, 115.5, 126.1, 128.3, 131.2, 131.5, 137.2, 137.6, 139.5, 167.7, and 202.9.

To a solution containing 242 mg (0.9 mmol) of **18** in 10 mL of CH_2Cl_2 was added a catalytic amount of rhodium(II) acetate. After the mixture was stirred for 5 h at rt, the solvent was removed under reduced pressure and the crude residue was chromatographed on a silica gel column to give 173 mg (80%) of methyl 2,4a-oxy-3,4,9,9a-tetrahydro-1*H*-fluorene-2-carboxylate (**20**) as a white solid, mp 97–98 °C: IR (neat) 1738, 1269, 1105, 1070, and 762 cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz) δ 1.85–1.95 (m, 1 H), 2.00–2.08 (m, 1 H), 2.10–2.25 (m, 2 H), 2.33–2.43 (m, 2 H), 2.70–2.80 (m, 2 H), 3.05–3.18 (m, 1 H), 3.78 (s, 3 H), 7.20–7.30 (m, 3 H), and 7.44 (d, 1 H, J = 7.2 Hz); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 30.5, 33.5, 38.2, 43.3, 48.8, 52.1, 86.9, 96.8, 124.3, 125.0, 126.3, 129.7, 136.9, 147.0, and 171.8. Anal. Calcd for $C_{15}H_{16}O_3$: C, 73.75; H, 6.60. Found: C, 73.70; H, 6.56.

To a mixture containing 298 mg (1.1 mmol) of **18** in 5 mL of CH_2Cl_2 was added 332 mg (2.3 mmol) of DMAD followed by the addition of a catalytic amount of rhodium(II) acetate. After the mixture was stirred for 1 h at rt, the solvent was removed under reduced pressure, and the crude residue was chromatographed on a silica gel column to give 359 mg (85%) of trimethyl 4-(*o*-allylphenyl)-7-oxabicyclo[2.2.1]-2-heptene-1,2,3-tricarboxylate (**21**) as a clear oil: IR (neat) 1752, 1640, 1437, 1263, 778, and 756 cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz) δ 1.90–2.00 (m, 1 H), 2.18–2.28 (m, 1 H), 2.36–2.46 (m, 1 H), 2.54–2.64 (m, 1 H), 3.40–3.68 (m, 5 H), 3.80 (s, 3 H), 3.86 (s, 3 H), 4.98–5.08 (m, 2 H), 5.84–5.98 (m, 1 H), 7.20–7.35 (m, 3 H), and 7.43 (d, 1 H, J = 7.2 Hz); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 29.7, 31.3, 37.6, 52.1, 52.5, 52.7, 88.3, 92.5, 115.6, 125.7, 128.4, 129.1, 130.6, 132.2, 137.9, 139.5, 140.8, 146.6, 162.1, 162.9, and 167.6. Anal. Calcd for $C_{21}H_{20}O_7$: C, 65.27; H, 5.73. Found: C, 65.26; H, 5.63.

Preparation and Rhodium(II) Acetate Reaction of Ethyl 2-Oxo-7-heptenyl Diazopropanedioate (22). A solution con-

taining 4.0 g (20.9 mmol) of 1-bromo-6-hepten-2-one and 8.95 g (132 mmol) of sodium formate in 60 mL of 95% ethanol was heated at reflux for 15 h. The solvent was removed under reduced pressure, and the resulting residue was taken up in 50 mL of water. The aqueous solution was extracted with CH_2Cl_2, and the combined organic extracts were washed with 50 mL of brine and dried over anhydrous $MgSO_4$. The solvent was removed under reduced pressure, and the resulting residue was subjected to flash silica gel chromatography to give 2.05 g (75%) of 1-hydroxy-6-hepten-2-one as a light yellow oil: IR (neat) 1940, 1735, 1440, 1420, and 1070 cm^{-1}; NMR ($CDCl_3$, 90 MHz) δ 1.80 (m, 2 H), 2.05 (t, 2 H, J = 7.5 Hz), 2.42 (t, 2 H, J = 7.5 Hz), 3.25 (t, 1 H, J = 4.5 Hz) 4.30 (d, 2 H, J = 4.5 Hz), 5.10 (m, 2 H), and 5.75 (m, 1 H).

A solution containing 0.75 g (5.86 mmol) of this compound and 0.82 g (6.15 mmol) of ethyl hydrogen malonate in 10 mL of CH_2Cl_2 was treated with 1.33 g with (6.44 mmol) of dicyclohexylcarbodiimide and 70 mg (0.586 mmol) of 4-(dimethylamino)pyridine at 0 °C. The solution was allowed to warm to rt and was further stirred for an additional 15 h. The solution was filtered so as to remove dicyclohexylurea, and the filtrate was concentrated under reduced pressure. The resulting residue was subjected to flash silica gel chromatography to give 1.04 g (74%) of ethyl 2-oxo-7-heptenyl propanedioate as a clear oil: IR (neat) 1765, 1745, 1420, and 1150 cm^{-1}; NMR ($CDCl_3$, 90 MHz) δ 1.32 (t, 3 H, J = 7.0 Hz, 3 H), 1.75 (m, 2 H), 2.05 (m, 2 H), 2.46 (t, 2 H, J = 6.5 Hz), 3.55 (s, 2 H), 4.30 (q, 2 H, J = 7.0 Hz), 4.80 (s, 2 H), 5.05 (m, 2 H), and 5.75 (m, 1 H).

To a solution containing 0.5 g (2.06 mmol) of the above compound and 0.49 g (2.17 mmol) of *p*-acetamidobenzenesulfonyl azide in 7 mL of CH_3CN was added 0.52 g (5.15 mmol) of Et_3N at 0 °C. The solution was stirred at 0 °C for 1 h and at 25 °C for 2 h. The solvent was removed under reduced pressure, and the resulting residue was taken up in 5 mL of CH_2Cl_2. After filtration, the solvent was removed under reduced pressure and the crude product was purified by flash silica gel chromatography to give 320 mg (60%) of ethyl 2-oxo-7-heptenyl diazopropanedioate (**22**) as a light yellow oil: IR (neat) 2135, 1765, 1735, 1380, and 1335 cm^{-1}; NMR ($CDCl_3$, 90 MHz) δ 1.32 (t, 3 H, J 7.0 Hz), 1.75 (m, 2 H), 2.00 (m, 2 H), 2.48 (t, 2 H, J = 7.2 Hz) 4.35 (q, 2 H, J = 7.0 Hz), 4.82 (s, 2 H), 5.05 (m, 2 H), and 5.80 (m, 1 H).

A solution containing 60 mg (0.233 mmol) of the above diazo ketone in 3 mL of benzene was treated with a catalytic amount of rhodium(II) acetate. The solution was placed in a 90 °C preheated oil bath and was heated until N_2 evolution had ceased (ca. 30 min). After being cooled to rt, the solution was filtered through a pad of Celite, and the solvent was removed under reduced pressure. The resulting residue was subjected to flash silica gel chromatography to give 35 mg (67%) of ethyl decahydro-1*H*-7-carboxy-3a,7-oxy-5-oxaazulen-6-one (**23**) as a clear oil: IR (neat) 1775, 1760, 1330, and 1245 cm^{-1}; NMR ($CDCl_3$, 300 MHz) δ 1.32 (t, 3 H, J = 7.12 Hz), 1.53 (m, 2 H), 1.75 (m, 1 H), 1.96 (m, 2 H), 2.05 (m, 1 H), 2.24 (dd, 1 H, J = 12.5 and 5.9 Hz), 2.70 (m, 1 H), 2.78 (dd, 1 H, J = 12.5 and 9.1 Hz), 4.16 (d, 1 H, J = 10.6 Hz), 4.32 (m, 2 H), and 4.69 (d, 1 H, J = 10.6 Hz). Anal. Calcd for $C_{12}H_{16}O_5$: C, 59.99; H, 6.71. Found: C, 59.87; H, 6.58.

Preparation and Rhodium(II) Acetate Catalyzed Reaction of 2-Propenyl [2-(1-Oxo-1-phenylethyl)] Diazopropanedioate (24). A solution containing 1.0 g (7.34 mmol) of 2-hydroxyacetophenone and 1.26 g (8.80 mmol) of 2-propenyl hydrogen malonate in 15 mL of CH_2Cl_2 was treated with 1.67 g (8.07 mmol) of dicyclohexylcarbodiimide and 0.1 g (0.734 mmol) of 4-(dimethylamino)pyridine at 0 °C. The solution was allowed to warm to rt and was further stirred for an additional 15 h. The mixture was filtered in order to remove dicyclohexylurea, and the filtrate was concentrated under reduced pressure. The resulting residue was subjected to flash chromatography to give 0.4 g (23%) of 2-propenyl [2-(1-oxo-1-phenylethyl)] propanedioate as a clear oil: IR (neat) 1765, 1745, 1460, 1380, and 1160 cm^{-1}; NMR ($CDCl_3$, 90 MHz) δ 3.60 (s, 2 H), 4.70 (m, 2 H), 5.75 (m, 1 H), and 7.80 (m, 5 H).

To a solution containing 163 mg (0.622 mmol) of the above compound and 156 mg (0.684 mmol) of *p*-acetamidobenzenesulfonyl azide in 3 mL of CH_3CN was added 0.22 mL (1.55 mmol) of Et_3N at 0 °C. The solution was allowed to warm to rt and was further stirred for 2 h. The mixture was concentrated under reduced pressure, and the residue was taken up in 5 mL of CH_2Cl_2. After filtration, the crude product was purified by flash silica gel chromatography to give 120 mg (67%) of 2-propenyl [2-(1-oxo-1-phenylethyl)] diazopropanedioate (**24**) as a yellow oil: IR (neat) 2160, 1770, 1755, 1385, 1350, and 1110 cm^{-1}; NMR ($CDCl_3$, 90 MHz) δ 4.80 (d, 2 H, J = 6.0 Hz), 5.32 (m, 2 H), 5.50 (s, 2 H), 5.85 (m, 1 H), and 7.80 (m, 5 H).

All efforts to isolate an internal cycloadduct from the reaction of **24** with Rh_2OAc_4 failed. However, a bimolecular cycloadduct with DMAD could be obtained. A solution containing 40 mg (0.138 mmol) of **24** and 27 mg (0.153 mmol) of *N*-phenylmaleimide in 1.5 mL of benzene was treated with a catalytic amount of rhodium(II) acetate. The solution was placed in a 90 °C preheated oil bath and was heated until gas evolution had ceased (ca. 20 min). After being cooled to rt, the solution was filtered through a pad of Celite, and the solvent was removed under reduced pressure. The crude solid was recrystallized from CH_2Cl_2–hexane to give 36 mg (58%) of the expected bimolecular dipolar cycloadduct **25** as a white solid: mp 182–183 °C; IR (KBr) 1780, 1735, 1510, 1300, and 1215 cm^{-1}; NMR ($CDCl_3$, 300 MHz) δ 3.95 (d, 1 H, J = 7.35 Hz), 4.32 (d, 1 H, J = 7.35 Hz), 4.67 (d, 1 H, J = 11.20), 4.85 (d, 1 H, J = 11.20), 4.97 (d, 1 H, J = 5.75), 5.32 (dd, 1 H, J = 12.8 and 1.12 Hz), 5.50 (dd, 1 H, J = 12.8 and 1.25 Hz), 6.21 (m, 1 H), and 7.35 (m, 10 H). Anal. Calcd for $C_{24}H_{10}NO_7$: C, 66.51; H, 4.42; N, 3.23. Found: C, 66.34; H, 4.19; N, 3.12.

Preparation and Rhodium-Catalyzed Reaction of Allyl 2-Diazo-3-[2-(α-tetralonyl)]propionate (26). A mixture containing 1.8 g (11.5 mmol) of 2-methylene-α-tetralone, 1.42 g (10 mmol) of allyl acetoactate, and 200 mg of $Ni(AcAc)_2$ in 10 mL of benzene was heated at 90 °C for 40 h. The solvent was removed under reduced pressure, and the crude residue was purified by silica gel chromatography to give 2.5 g (84%) of allyl 2-acetyl-3-[2-(α-tetralonyl)]propionate as a colorless oil: IR (neat) 1717, 1682, 1601, 1360, 1221, and 774 cm^{-1}; ^1H NMR ($CDCl_3$, 360 MHz) δ 1.85–2.15 (m, 2 H), 2.18–2.28 (m, 1 H), 2.30–2.40 (m, 4 H), 2.44–2.54 (m, 1 H), 2.95–3.05 (m, 2 H), 3.90–4.05 (m, 1 H), 4.61 (d, 2 H, J = 5.7 Hz), 5.20–5.37 (m, 2 H), 5.80–5.95 (m, 1 H), 7.20–7.45 (m, 3 H), and 7.90–8.00 (m, 1 H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 28.1 (28.2), 28.5 (28.6), 28.8 (29.0), 29.5 (29.6), 44.6 (45.0), 56.7 (57.6), 65.6, 118.7, 126.3, 126.9, 127.0, 128.5, 131.3, 133.1, 143.5, 168.9 (169.2), 199.3 (199.6), and 202.6 (202.9). Anal. Calcd for $C_{18}H_{20}O_4$: C, 71.98; H, 6.71. Found: C, 72.07; H, 6.75.

A mixture containing 500 mg (1.7 mmol) of the above compound, 430 mg (3.3 mmol) of methanesulfonyl azide, and 0.7 mL (5.0 mmol) of Et_3N in 4 mL of CH_3CN was stirred at rt for 5 h. The solvent was removed under reduced pressure, and the crude residue was purified by silica gel chromatography to give 196 mg of recovered starting material and 260 mg (90%) of allyl 2-diazo-3-[2-(α-tetralonyl)]propionate (**26**) as a yellow oil: IR (neat) 2093, 1686, 1601, 1456, 1317, 1124, and 739 cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz) δ 1.90–2.05 (m, 1 H), 2.22–2.35 (m, 1 H), 2.56–2.68 (m, 1 H), 2.70–2.90 (m, 2 H), 2.95–3.15 (m, 2 H), 4.65 (d, 2 H, J = 5.7 Hz), 5.20–5.40 (m, 2H), 5.80–6.00 (m, 1H), 7.20–7.38 (m, 2 H), 7.46 (d, 1 H, J = 7.5 Hz), and 7.99 (d, 1 H, J = 7.5 Hz); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 24.5, 28.7, 28.9, 47.0, 65.0, 117.7, 126.5, 127.1, 128.6, 132.16, 132.19, 133.3, 143.8, 167.2, and 199.2.

To a solution containing 214 mg (0.8 mmol) of **26** in 2 mL of CH_2Cl_2 was added 214 mg (1.5 mmol) of DMAD in 2 mL of CH_2Cl_2 followed by the addition of catalytic amount of rhodium(II) acetate. After the mixture was stirred at rt for 2 h, the solvent was removed under reduced pressure, and the crude residue was chromatographed on a silica gel column to give 265 mg (89%) of 2-allyl 3,4-dimethyl 2,4a-oxy-1,9,10,10a-tetrahydrophenanthrene-2,3,4-tricarboxylate (**29**) as a colorless oil: IR (neat) 1746, 1435, 1238, 1128, and 756 cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz) δ 1.60–1.72 (m, 1 H), 1.98–2.08 (m, 2 H), 2.23–2.35 (m, 2 H), 2.75–2.90 (m, 2 H), 3.58 (s, 3 H), 3.78 (s, 3 H), 4.65–4.80 (m, 2 H), 5.22–5.40 (m, 2 H), 5.85–6.00 (m, 1 H), 7.10–7.25 (m, 3 H), and 7.36 (d, 1 H, J = 7.8 Hz); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 27.9, 29.5, 37.6, 39.7, 52.1, 52.4, 66.4, 88.1, 90.3, 119.1, 126.4, 128.5, 129.0, 129.4, 130.2, 131.3, 139.3, 142.6, 146.6, 162.2, 163.4, and 166.8. Anal. Calcd for $C_{22}H_{22}O_7$: C, 66.31; H, 5.57. Found: C, 66.23; H, 5.61.

To a solution containing 230 mg (0.8 mmol) of **26** in 10 mL of CH_2Cl_2 was added a catalytic amount of rhodium(II) acetate. After the mixture was stirred for 3 h at rt, the solvent was removed under reduced pressure, and the crude residue was chromatographed on a silica gel column to give 35 mg (17%) of allyl

2,3,4,5-tetrahydronaphthol[1,2-*b*]furan-2-carboxylate (**28**) as a clear oil: IR (neat) 1740, 1194, 1065, 1032, and 764 cm^{-1}; ^1H NMR ($CDCl_3$, 360 MHz) δ 2.39 (t, 2 H, J = 7.9 Hz), 2.90–3.00 (m, 3 H), 3.10–3.20 (m, 1 H), 4.70 (d, 2 H, J = 5.8 Hz), 5.16 (dd, 1 H, J = 10.8 and 6.8 Hz), 5.26 (dd, 1 H, J = 10.1 and 1.1 Hz), 5.36 (dd, 1 H, J = 16.9 and 1.1 Hz), 5.88–6.00 (m, 1 H), and 7.10–7.35 (m, 4 H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 21.9, 28.4, 37.4, 65.7, 77.9, 107.8, 118.6, 120.4, 126.3, 127.1, 127.3, 127.6, 131.6, 135.8, 150.1, and 171.5. Anal. Calcd for $C_{16}H_{16}O_3$: C, 74.98; H, 6.29. Found: C, 74.96; H, 6.27.

Preparation and Rhodium-Catalyzed Reaction of 3-Butenyl 2-Diazo-3-[2-(α-tetralonyl)]propionate (27). A mixture containing 1.8 g (11.5 mmol) of 2-methylene-α-tetralone, 1.56 g (10 mmol) of 3-butenyl acetoacetate, and 200 mg of $Ni(AcAc)_2$ in 10 mL of benzene was heated at 90 °C for 23 h. The solvent was removed under reduced pressure, and the crude residue was chromatographed on a silica gel column to give 2.59 g (83%) of 3-butenyl 2-acetyl-3-[2-(α-tetralonyl)]propionate as a colorless oil: IR (neat) 1717, 1684, 1601, 1221, 920, and 743 cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz) δ 1.80–2.12 (m, 2 H), 2.16–2.25 (m, 1 H), 2.30 (s, 3 H), 2.32–2.55 (m, 4 H), 2.90–3.10 (m, 2 H), 3.85–4.05 (m, 1 H), 4.15–4.25 (m, 2 H), 5.00–5.15 (m, 2 H), 5.75–5.80 (m, 1 H), 7.18–7.30 (m, 2 H), 7.45 (t, 1 H, J = 7.5 Hz), and 7.95–8.00 (m, 1 H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 27.9 (28.0), 28.35 (28.43), 28.75 (28.83), 29.3 (29.5), 32.5, 44.6 (44.9), 56.5 (57.5), 63.9, 117.1, 126.2, 126.8, 128.4, 131.8, 133.0, 133.4, 143.4, 169.1 (169.3), 199.1 (199.4), and 202.4 (202.7). Anal. Calcd for $C_{19}H_{22}O_4$: C, 72.59; H, 7.11. Found: C, 72.79; H, 7.06.

A mixture containing 506 mg (1.66 mmol) of the above compound, 410 mg (3.2 mmol) of methanesulfonyl azide, and 0.7 mL (5 mmol) of Et_3N was stirred at rt for 4 h. The solvent was removed under reduced pressure, and the crude residue was chromatographed on a silica gel column to give 191 mg of recovered starting material and 272 mg (91%) of 3-butenyl 2-diazo-3-[2-(α-tetralonyl)]propionate (**27**) as a yellow oil: IR (neat) 2093, 1686, 1317, 1124, and 739 cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz) δ 1.85–2.00 (m, 1 H), 2.18–2.28 (m, 1 H), 2.30–2.40 (m, 2 H), 2.50–2.60 (m, 1 H), 2.65–2.80 (m, 2 H), 2.92–3.10 (m, 2 H), 4.15 (t, 2 H, J = 6.9 Hz), 5.00–5.15 (m, 2 H), 5.65–5.80 (m, 1 H), 7.18–7.45 (m, 3 H), and 7.97 (d, 1 H, J = 8.1 Hz); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 24.5, 28.7, 28.9, 33.2, 47.0, 63.5, 117.1, 126.5, 127.1, 128.6, 132.2, 133.3, 133.7, 143.8, 167.5, and 199.2.

To a mixture containing 204 mg (0.7 mmol) of **27** in 2 mL of CH_2Cl_2 was added 196 mg (1.4 mmol) of DMAD in 2 mL of CH_2Cl_2 followed by the addition of a catalytic amount of rhodium(II) acetate. After the mixture was stirred overnight, the solvent was removed under reduced pressure, and the crude residue was chromatographed on a silica gel column to give 254 mg (90%) of 2-(2-butenyl) 3,4-dimethyl 2,4a-oxy-1,9,10,10a-tetrahydrophenanthrene-2,3,4-tricarboxylate (**30**) as a colorless oil: IR (neat) 1752, 1240, 1130, 1022, 980, and 756 cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz) δ 1.58–1.72 (m, 1 H), 1.97–2.05 (m, 1 H), 2.10–2.18 (m, 1 H), 2.20–2.32 (m, 2 H), 2.38–2.48 (m, 2 H), 2.75–2.80 (m, 2 H), 3.58 (s, 3 H), 3.79 (s, 3 H), 4.18–4.45 (m, 2 H), 5.03–5.25 (m, 2 H), 5.68–5.82 (m, 1 H), 7.10–7.22 (m, 3 H), and 7.38 (d, 1 H, J = 7.5 Hz); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 27.9, 29.5, 32.6, 37.6, 39.7, 52.1, 52.3, 64.8, 88.1, 90.2, 117.4, 126.3, 128.4, 128.9, 129.4, 130.2, 133.3, 139.3, 142.6, 146.4, 162.2, 163.3, and 167.0. Anal. Calcd for $C_{23}H_{24}O_7$: C, 66.98; H, 5.87. Found: C. 67.17; H, 6.01.

Preparation and Rhodium(II) Acetate Catalyzed Reaction of 5-Diazo-1-phenyl-9-decene-1,4,6-trione (33). To a stirred suspension containing 120 mg of anhydrous tin(II) chloride in 4 mL of dry CH_2Cl_2 was added a solution containing 1.46 g of 5-diazo-1-phenyl-1,4-pentanedione[35] in 4 mL of CH_2Cl_2 at 25 °C under N_2. A solution containing 0.55 g of 4-pentenal[57] in 4 mL of CH_2Cl_2 was added dropwise over a period of 2 min. After N_2 evolution had ceased, the reaction mixture was filtered through a silica gel column using CH_2Cl_2 as the eluent. The solvent was removed under reduced pressure, and the residue was rechromatographed on silica gel to give 0.71 g (42%) of 1-phenyl-9-decene-1,4,6-trione as a pale orange oil: IR (neat) 1725, 1690, 1600, 1450, 1360, 1215, 920, and 695 cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz) (keto form) δ 2.33–2.37 (m, 2 H), 2.65 (t, 2 H, J = 7.2 Hz), 2.91 (t, 2 H, J = 6.4 Hz), 3.30 (t, 2 H, J = 6.4 Hz), 3.69 (s, 2 H), 4.95–5.08 (m, 2 H), 5.74–5.84 (m, 1 H), 7.42–7.47 (m, 2 H), 7.52–7.58 (m, 1 H), and 7.94–7.98 (m, 2 H); (enol form) δ 2.33–2.37 (m, 4 H), 2.78 (t, 2 H, J = 6.8 Hz), 3.31 (t, 2 H, J = 6.8 Hz), 4.95–5.08 (m, 2 H), 5.58 (s, 1 H), 5.74–5.84 (m, 1 H), 7.42–7.47 (m, 2 H), 7.52–7.58 (m, 1 H), and 7.94–7.98 (m, 2 H).

To a stirred solution containing 176 mg (0.68 mmol) of the above compound and 166 mg (0.69 mmol) of *p*-acetamidobenzenesulfonyl azide in 15 mL of CH_3CN at 0 °C was added 0.28 mL (2.04 mmol) of Et_3N. The solution was stirred for 2 min and was then filtered through a silica gel column using CH_2Cl_2 as the eluent. The solvent was removed under reduced pressure. The resulting residue was repurified via silica gel chromatography to give 62 mg (32%) of 5-diazo-1-phenyl-9-decene-1,4,6-trione (**33**) as a yellow oil: IR (neat) 2130, 1690, 1670, 1240, 930, and 700 cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz) δ 2.33 (q, 2 H, J = 7.3 Hz), 2.89 (t, 2 H, J = 7.3 Hz), 3.09 (t, 2 H, J = 6.0 Hz), 3.32 (t, 2 H, J = 6.0 Hz), 4.91–5.02 (m, 2 H), 5.69–5.81 (m, 1 H), 7.39 (t, 2 H, J = 7.6 Hz), 7.47–7.52 (m, 1 H), and 7.92 (d, 2 H, J = 7.6 Hz).

A solution containing 98 mg (0.34 mmol) of the above diazo ketone in 7 mL of dry benzene was treated with 5 mg of rhodium(II) acetate for 1 h at 60 °C. The solution was filtered and concentrated under reduced pressure. The crude residue was subjected to silica gel flash chromatography to give 72 mg (81%) of 1-(1,4-dioxo-4-phenylbutanyl)bicyclo[3.1.0]hexan-2-one (**34**): IR (neat) 1720, 1685, 1675, 1590, 1440, 1030, and 690 cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz) δ 1.41 (dd, 1 H, J = 5.6 and 4.4 Hz), 1.91–1.99 (m, 1 H), 2.05 (dd, 1 H, J = 7.9 and 4.2 Hz), 2.13–2.27 (m, 3 H), 2.62 (dt, 1 H, J = 7.9 and 5.4 Hz), 3.11–3.42 (m, 4 H), 7.36–7.41 (m, 2 H), 7.46–7.51 (m, 1 H), and 7.88–7.92 (m, 2 H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 21.0, 25.3, 32.2, 34.2, 35.9, 36.1, 45.5, 128.0, 128.5, 133.0, 136.7, 198.5, 203.1, and 209.6; HRMS calcd for $C_{16}H_{16}O_3$ 256.1099, found 256.1101.

A solution containing 168 mg (0.59 mmol) of **33** and 80 μL (0.65 mmol) of DMAD in 6 mL of dry benzene was treated with 5 mg of rhodium(II) acetate for 1 h at 60 °C. The solution was filtered and concentrated under reduced pressure. NMR analysis of the reaction mixture indicated the presence of a 68% yield of dimethyl 4-oxo-5-(1-oxo-4-pentenyl)-1-phenyl-8-oxabicyclo[3.2.1]oct-6-ene-6,7-dicarboxylate (**35**). Unfortunately, a pure sample could not be isolated by chromatography due to its rapid decomposition: ^1H NMR ($CDCl_3$, 300 MHz) δ 2.34 (q, 2 H, J = 7.3 Hz), 2.51–2.60 (m, 1 H), 2.78 (t, 2 H, J = 7.3 Hz), 2.79–2.82 (m, 1 H), 2.87–3.00 (m, 2 H), 3.56 (s, 3 H), 3.81 (s, 3 H), 4.92–5.04 (m, 2 H), 5.64–5.92 (m, 1 H), and 7.31–7.48 (m, 5 H). In addition to **35**, a 15% yield of bicyclo[3.1.0]hexan-2-one **34** was also present in the crude reaction mixture.

Preparation and Rhodium(II) Acetate Catalyzed Reaction of 5-Diazo-1-phenyl-10-undecene-1,4,6-trione (39). To a stirred suspension containing 290 mg of anhydrous tin(II) chloride in 15 mL of dry CH_2Cl_2 was added a solution containing 3.0 g of 5-diazo-1-phenyl-1,4-pentanedione[35] in 9 mL of CH_2Cl_2 at 25 °C under N_2. To this mixture was added a solution containing 1.35 g of 5-hexenal in 3 mL of CH_2Cl_2 over a period of 2 min. After N_2 evolution had ceased, the reaction mixture was filtered through a silica gel column using CH_2Cl_2 as the eluent. The solvent was removed under reduced pressure, and the residue was rechromatographed on silica gel to give 1.86 g (49%) of 1-phenyl-10-undecene-1,4,6-trione as a pale orange oil: IR (neat) 1730, 1700, 1690, 1455, 1135, 920, and 700 cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz) (enol form) δ 1.64 (q, 2 H, J = 7.4 Hz), 2.01 (q, 2 H, J = 7.4 Hz), 2.20 (t, 2 H, J = 7.4 Hz), 2.73 (t, 2 H, J = 6.8 Hz), 3.25 (t, 2 H, J = 6.8 Hz), 4.90–4.99 (m, 2 H), 5.52 (s, 1 H), 5.66–5.76 (m, 1 H), 7.37–7.42 (m, 2 H), 7.50–7.52 (m, 1 H), and 7.82–7.93 (m, 2 H); (keto form) δ 1.64 (q, 2 H, J = 7.4 Hz), 2.01 (q, 2 H, J = 7.4 Hz), 2.49 (t, 2 H, J = 7.4 Hz), 2.86 (t, 2 H, J = 6.4 Hz), 3.23 (t, 2 H, J = 6.4 Hz), 3.63 (s, 2 H), 4.90–4.99 (m, 2 H), 5.66–5.76 (m, 1 H), 7.37–7.42 (m, 2 H), 7.50–7.52 (m, 1 H), and 7.82–7.93 (m, 2 H).

To a stirred solution containing 740 mg (2.71 mmol) of the above diketone and 720 mg (2.98 mmol) of *p*-acetamidobenzenesulfonyl azide in 10 mL of CH_3CN at 0 °C was added 1.14 mL of Et_3N. The solution was stirred for 2 min and was then filtered and concentrated under reduced pressure. The resulting residue was purified via silica gel chromatography to give 740 mg (91%) of 5-diazo-1-phenyl-10-undecene-1,4,6-trione (**39**) as a yellow solid: mp 59–60 °C; IR (KBr) 2140, 1690, 1650, 1370, 1185, and

(57) Coates, R. M.; Senter, P. D.; Baker, W. R. *J. Org. Chem.* 1982, *47*, 3597.

915 cm^{-1}; ^{1}H NMR ($CDCl_3$, 300 MHz) δ 1.70 (q, 2 H, J = 7.3 Hz), 2.04 (q, 2 H, J = 7.3 Hz), 2.66 (t, 2 H, J = 7.3 Hz), 3.09 (t, 2 H, J = 6.0 Hz) 3.32 (t, 2 H, J = 6.0 Hz), 4.91–5.00 (m, 2 H), 5.65–5.78 (m, 1 H), 7.41 (t, 2 H, J = 7.3 Hz), 7.49 (t, 1 H, J = 7.3 Hz), and 7.93 (d, 2 H, J = 7.3 Hz).

A solution containing 152 mg (0.51 mmol) of **39** in 7 mL of dry benzene was treated with 5 mg of rhodium(II) acetate for 1 h at 60 °C. The solution was filtered and concentrated under reduced pressure. The crude residue was examined by proton NMR spectroscopy and showed none of the expected internal cycloadduct or cyclopropanation product. All attempts to isolate any characterizable product failed. The rhodium(II) catalyzed decomposition was also carried out in the presence of DMAD. A solution containing 153 mg (0.51 mmol) of **39** and 130 μL (1.03 mmol) of DMAD in 6 mL of dry benzene was treated with 5 mg of rhodium(II) acetate for 1 h at 60 °C. The solution was filtered and concentrated under reduced pressure. NMR analysis of the reaction mixture indicated the presence of a 46% yield of dimethyl 4-oxo-5-(1-oxo-5-hexenyl)-1-phenyl-8-oxabicyclo[3.2.1]oct-6-ene-6,7-dicarboxylate (**40**). Unfortunately, a pure sample could not be isolated by chromatography due to its rapid decomposition: ^{1}H NMR ($CDCl_3$, 300 MHz) δ 1.70 (quint, 2 H, J = 7.3 Hz), 1.99 (q, 2 H, J = 7.3 Hz), 2.46 (dt, 1 H, J = 18.0 and 7.2 Hz), 2.58–2.77 (m, 3 H), 2.90–2.99 (m, 2 H), 3.56 (s, 3 H), 3.81 (s, 3 H), 4.87–4.97 (m, 2 H), 5.63–5.78 (m, 1 H), and 7.32–7.50 (m, 5 H).

Acknowledgment. We gratefully acknowledge support of this work by the National Institutes of Health (CA-26751). Use of the high-field NMR spectrometer used in these studies was made possible through equipment grants from the NIH and NSF.

Supplementary Material Available: NMR spectra of **8**, **9**, **11**, **13**, and **34** to indicate purity (8 pages). This material is contained in many libraries on microfiche, immediately follows this article in the microfilm version of the journal, and can be ordered from the ACS; see any current masthead page for ordering information.

Notes

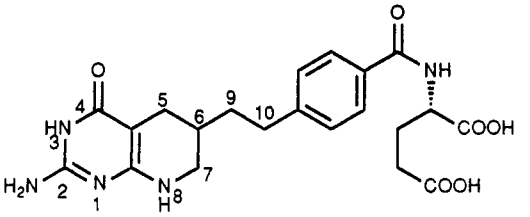
Further Acyclic Analogues of 5,10-Dideaza-5,6,7,8-tetrahydrofolic Acid

Edward C. Taylor* and Paul Gillespie

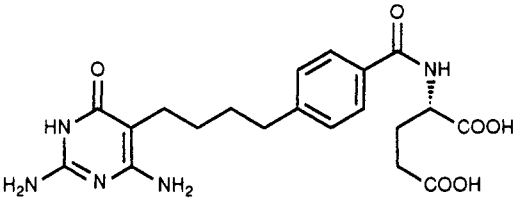
Department of Chemistry, Princeton University, Princeton, New Jersey 08544

Received February 21, 1992

5,10-Dideaza-5,6,7,8-tetrahydrofolic acid (DDATHF, lometrexol, **1**) is an antitumor agent with a novel site of action as an inhibitor of glycinamide ribonucleotide formyltransferase (EC 2.1.2.1) in the purine de novo biosynthetic pathway.[1] In vitro studies have shown that DDATHF inhibits the growth of a large number of cancer cell lines, and in vivo studies have shown it to be effective against a range of solid tumors, including lung, mammary, and colon tumors.[2] Early syntheses of DDATHF[3] relied on catalytic hydrogenation to reduce the pyridine ring and led to the formation of a mixture of diastereomers epimeric at C-6 which were then separated via recrystallization of camphor-D-sulfonic acid salts; a chiral synthesis of the drug has recently been developed.[4] We recently reported the preparation of 7-desmethylene-DDATHF (**2**),[5] an acyclic analogue of the parent compound which lacks the C-6 chiral center by virtue of deletion of the C-7 methylene group and which exhibited excellent in vitro cytotoxicity. An alternate strategy for removing the C-6 chiral center would be deletion of the C-5 methylene group, and we have now prepared several representatives of this isomeric 5-desmethylene system. In this note we describe our synthetic route to these compounds and several problems and unexpected reactions which were encountered in the course of this work.



1



2

Our initial approach was to use a Wittig reaction between a suitably substituted 5-formylpyrimidine (**7**) and the phosphonium ylide generated from (3-(4-(methoxycarbonyl)phenyl)propyl)triphenylphosphonium iodide (**12**) (Scheme I). One of the chlorine substituents in 2-amino-4,6-dichloro-5-formylpyrimidine (**3**) was displaced by *N*-methylbenzylamine to give chloropyrimidine **4**, and the second was displaced using sodium methoxide to give compound **5**. It was planned to protect the remaining amino group as a 2,5-dimethylpyrrole so that the substrate for the Wittig reaction would have no remaining acidic hydrogens. When compound **5** was heated at 140 °C with hexane-2,5-dione in the presence of catalytic *p*-toluenesulfonic acid, two products were isolated in low yield. In addition to the desired product (**7**), the decarbonylated derivative **6** was obtained. Decarbonylation of formyl-

(1) (a) Moran, R. G.; Baldwin, S. W.; Taylor, E. C.; Shih, C. *J. Biol. Chem.* **1989**, *264*, 21047. (b) Baldwin, S. W.; Tse, A.; Gossett, L. S.; Taylor, E. C.; Rosowsky, A.; Shih, C.; Moran, R. G. *Biochemistry* **1991**, *30*, 1997.

(2) Taylor, E. C. *J. Heterocycl. Chem.* **1990**, *27*, 1.

(3) (a) Taylor, E. C.; Harrington, P. J.; Fletcher, S. R.; Beardsley, G. P.; Moran, R. G. *J. Med. Chem.* **1985**, *28*, 914. (b) Boschelli, D. H.; Webber, S.; Whiteley, J. M.; Oronsky, A. L.; Kerwar, S. S. *Arch. Biochem. Biophys.* **1988**, *265*, 43. (c) Piper, J. R.; McCaleb, G. S.; Montgomery, J. A.; Kisliuk, R. L.; Gaumont, Y.; Thorndike, J.; Sirotnak, F. M. *J. Med. Chem.* **1988**, *31*, 2164. (d) Taylor, E. C.; Wong, G. S. K. *J. Org. Chem.* **1989**, *54*, 3618. (e) Taylor, E. C.; Harrington, P. M. *J. Org. Chem.* **1989**, *55*, 3222.

(4) Barnett, C. J.; Wilson, T. M. *Tetrahedron Lett.* **1989**, *30*, 6291.

(5) Taylor, E. C.; Harrington, P. M.; Shih, C. *Heterocycles* **1989**, *28*, 1169.

0022-3263/92/1957-5757$03.00/0