Tandem Cyclization–Cycloaddition Reaction of Rhodium Carbenoids. Studies Dealing with the Geometric Requirements of Dipole Formation†

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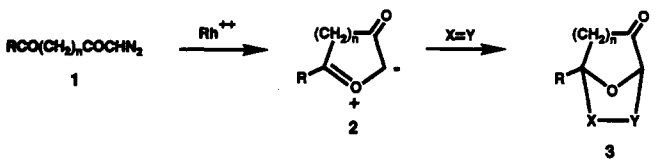
Received October 17, 1990

The carbenoid intermediate derived by the treatment of several 1-diazobutanediones with rhodium(II) acetate undergoes ready transannular cyclization onto the neighboring keto group to give five-membered ring carbonyl ylides. The dipole derived from ethyl 4-diazo-2-methyl-3-oxobutyrate was found to undergo a rapid proton transfer, producing 5-ethoxy-4-methyl-3-(2*H*)-furanone. When the position adjacent to the diazo carbonyl group is blocked with two substituent groups, however, smooth 1,3-dipolar cycloaddition occurs. The observed regioselectivity can be nicely accommodated in terms of frontier molecular orbital (FMO) theory. A type II FMO interaction is involved since carbonyl ylides possess one of the smallest HOMO–LUMO energy gaps of common 1,3-dipoles. The rhodium(II)-catalyzed reaction of 1-diazo-6-phenyl-2,6-hexanedione afforded a mixture of products. In addition to the expected cycloadduct, a product derived from the bimolecular addition of the rhodium carbenoid to benzene was obtained. The formation of a mixture of products in this case suggests that entropic factors have sufficiently retarded the rate of intramolecular cyclization so as to allow the bimolecular reaction with benzene to occur. No observable cycloadduct was obtained from the diazohexanedione system, thereby indicating that the longer tether was sufficient to shut down dipole formation.

The interaction of two reactive groups within the same molecule has always been of paramount concern to organic chemists.[1-5] Beyond the issue of bringing the two ends of the bifunctional substrate to within bonding distance, the task of cyclization is complicated by factors concerning the reactivity of the functional groups. Successful cyclization is markedly dependent on the compatibility of the two reacting partners and thus the prudent selection of functional groups is of utmost importance in the design of the cyclization reaction.[6-8] The geometric requirements of interaction can be evaluated through systems that have the reacting centers connected together by a few intervening atoms. This linkage provides a cyclic transition state, which imposes distinct restrictions upon the bond angles at the reacting centers.[4] Eschenmoser's classic experiments on the SN_2 reaction at carbon, for example, clearly established the requirement of a near linear arrangement of the nucleophile, carbon, and leaving group.[9]

Our own interest in the tandem intramolecular cyclization–cycloaddition strategy of α-diazo carbonyl compounds prompted us to address the issues of geometry and reactivity within the context of this reaction. In earlier papers we described the formation of bridged oxabicyclo[3.2.1]heptanes from the rhodium(II)-catalyzed reaction of 1-diazopentanediones.[10] The reaction involves the formation of a rhodium carbenoid and subsequent transannular cyclization of the electrophilic carbon onto the adjacent keto group to generate a cyclic carbonyl ylide, followed by 1,3-dipolar cycloaddition.[11] Of the many unexplored questions concerning the factors that govern the formation of carbonyl ylides by this method, one that is very easy to formulate focuses upon the course of the reaction as a function of the length of the tether that links the carbonyl and diazo ketone functionalities. Until now, the tether length has been restricted to cases where n = 2 (i.e., six-membered ring formation).[12] Because of the vast array of reaction pathways available to keto carbenoids and the demonstrated susceptibility of these intermediates to electronic effects,[13-16] we felt that a systematic study of the factors affecting carbonyl ylide formation should be initiated. In this paper we wish to detail our observations dealing with the effect of chain length on the tandem cyclization–cycloaddition reaction.



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Results and Discussion

Cyclization rates depend on the energy level of the open-chain initial state compared to the transition state resembling the cyclic product. Reactivity in cyclization reactions may be interpreted in terms of activation energy and the probability of end-to-end encounters. The activation energy is thought to reflect the strain energy of the ring to be formed, which is markedly dependent on ring

† Dedicated with respect and admiration to Professor Harry Wasserman, one of the leading pioneers in the area of heterocyclic chemistry, on the occasion of his 70th birthday.

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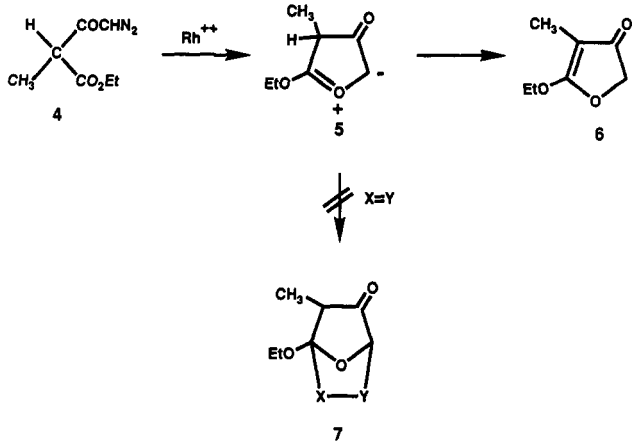
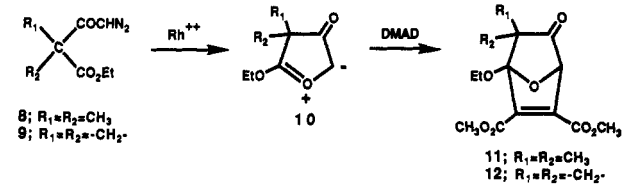
size as shown by strain energy data of the cycloalkanes.[17] The magnitudes of such strains have been evaluated by Allinger on the basis of force-field calculations.[18] The probability of the chain terminals coming close enough to each other for the reaction to occur decreases as the chain gets longer. 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 cyclic transition state. The ease of ring closure as a function of ring size generally increases on going from three- to five-membered rings and then decreases rapidly.[17] This observation would tend to suggest that five-membered ring carbonyl ylide formation should occur smoothly upon treatment of 1-diazobutanediones with rhodium(II) carboxylates. Indeed this was borne out by an examination of the rhodium(II) acetate catalyzed behavior of ethyl 4-diazo-2-methyl-3-oxobutyrate (4). Treatment of 4 with



4 5 6 7

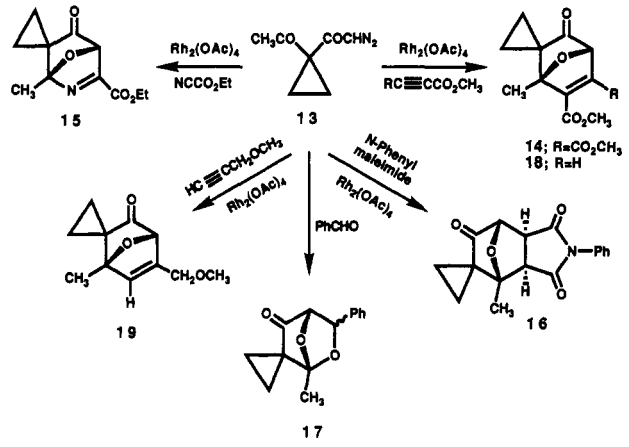
the rhodium(II) catalyst at 25 °C in methylene chloride afforded 5-ethoxy-4-methyl-3-(2*H*)-furanone (6) in 90% isolated yield. We believe that the mechanism by which 4 is converted into 6 involves rapid cyclization of the rhodium carbenoid onto the neighboring carbonyl group to give the five-ring carbonyl ylide 5, which undergoes a subsequent proton transfer.[19] All attempts to trap the suspected 1,3-dipole with a variety of dipolarophiles failed to produce a dipolar cycloadduct. Apparently the highly stabilized dipole 5 transfers a proton at a faster rate than bimolecular cycloaddition. The formation of furanone 6 comes as no real surprise since one of the characteristic reactions of carbonyl ylides derived from the reaction of α-diazoalkanes with ketones consists of an intramolecular proton transfer. The earliest example of this process was reported by Kharasch and co-workers in 1953,[20] and many related cases have been recorded since that time.[21] The overall reaction represents a novel route to the 3(2*H*)-furanone ring system and is now under further investigation.

When the α position of the 1-diazobutanedione skeleton was blocked with two substituent groups (i.e., 8 or 9), the rhodium-catalyzed cycloaddition with DMAD led to the carbonyl ylide cycloadducts 11 (85%) and 12 (55%), respectively.



8; R_1=R_2=CH_3
9; R_1=R_2=-CH_2-
10
11; R_1=R_2=CH_3
12; R_1=R_2=-CH_2-

We also studied the cyclization–cycloaddition chemistry of the cyclopropyl-substituted diazo ketone 13. Treatment of this material with rhodium(II) acetate at 25 °C in chloroform with dimethyl acetylenedicarboxylate afforded the expected cycloadduct 14 in 97% yield. Several different types of dipolarophiles were examined so as to establish the scope and generality of the process. The cycloaddition proceeded readily with *N*-phenylmaleimide and Mander's reagent,[24] giving rise to a single cycloadduct in both cases (i.e., 16 and 15). Treatment of 13 with benzaldehyde gave cycloadduct 17 in 86% yield as a 4:1 mixture of exo and endo isomers. Extension of the carbenoid cyclization–cycloaddition with methyl propiolate was also investigated, in order to probe the regiochemical aspects of the reaction. The only product isolated was cycloadduct 18. Interestingly, when methyl propargyl ether was used as the trapping agent, the alternate regioisomeric cycloadduct 19 was obtained as the exclusive product.



15 13 14; R=CO_2CH_3 18; R=H 19 16 17

The complete regiochemical crossover encountered with methyl propargyl ether can be rationalized on the basis of FMO considerations. Of the three categories described by Sustmann,[25] type II is particularly common for carbonyl ylides since they possess one of the smallest HOMO–LUMO energy gaps of the common 1,3-dipoles.[25] For carbonyl ylides, 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 on the carbonyl ylide derived from 13 clearly indicate that the largest coefficient in the LUMO resides on the carbon bearing the methyl group.[26] This site becomes linked with the less substituted carbon of the acetylenic group thereby accounting for the observed regiochemical results.

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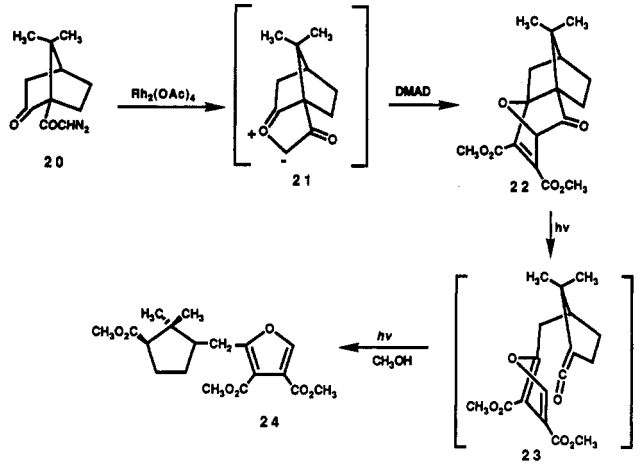
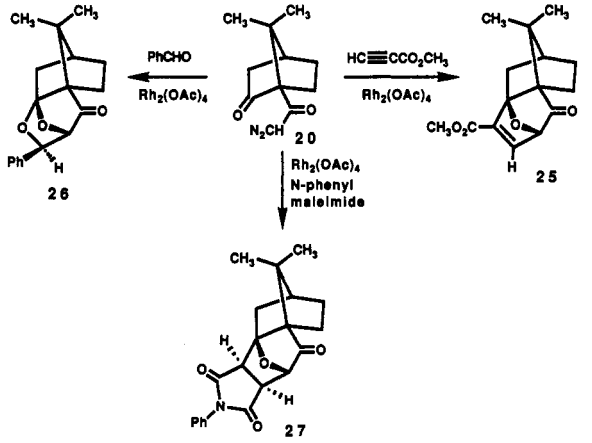
(26) Calculations were performed with the Ampac program (QCPE 506) using the AM1 Hamiltonian. The calculations show that the LUMO is located at −0.93 eV and the HOMO at −10.47 eV for the carbonyl ylide derived from 13 with coefficients of −0.62 (C_4) and −0.37 (C_2) in the LUMO.

As a consequence of the ready availability of ketopinic acid,[27] the rhodium-catalyzed behavior of 6-(diazoacetyl)-7,7-dimethylbicyclo[2.2.1]heptane (**20**) was also investigated. Treatment of **20** with a catalytic amount of rhodium(II) acetate at 25 °C in benzene with dimethyl acetylenedicarboxylate afforded cycloadduct **22** in 85% yield. The cycloaddition involves the five-ring dipole **21**



and proceeds with complete diastereofacial selectivity. We believe that approach from the α face of the dipole is the preferred process as a consequence of the severe steric interaction with the bridgehead *gem*-dimethyl group associated with β attack.[28] During the course of our studies with **22**, we had the opportunity to examine the photochemical behavior of this interesting bicyclic enone. Irradiation of a benzene solution of **22** for 2 h in methanol cleanly afforded furan **24** in 86% isolated yield. The formation of **24** can be readily accounted for by a Norrish type I cleavage followed by subsequent diradical fragmentation to give a transient furanyl ketene (i.e., **23**). This material rapidly reacts with methanol to give the observed product.[29]

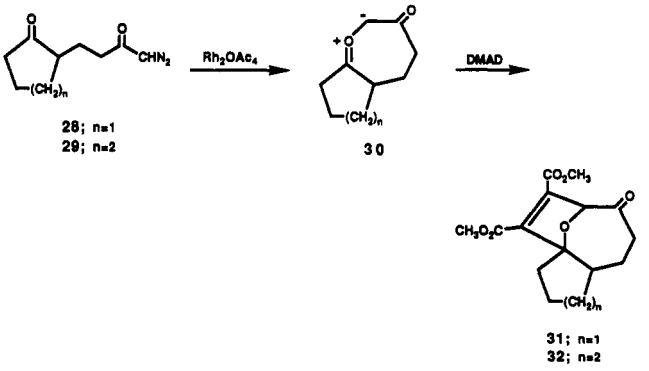
A similar tandem cyclization–cycloaddition sequence also occurred with methyl propiolate and produced the anticipated HOMO-controlled cycloadduct **25**. In addition to the high facial and regioselectivity of the cycloaddition, diazo ketone **20** also exhibits a high level of stereoselectivity. Cycloaddition of the metallocarbenoid derived from



20 was carried out in the presence of benzaldehyde. Bicyclic ketal **26** was the only product isolated in 66% overall yield. The stereochemical assignment (exo phenyl group) was made on the basis of its characteristic NMR spectrum, which showed the absence of coupling of the bridgehead hydrogen. This observation demands a dihedral angle close to 90°, which is expected for the exo-oriented isomer. The same selectivity was also found in the reaction of **20** with *N*-phenylmaleimide, which produced cycloadduct **27** (62%) that possessed a syn orientation of the oxa bridge and imide functionalities.

Rhodium carbenoids derived from α-diazo ketones are known to readily dimerize or react with nucleophiles.[30,31] Therefore, the success of intramolecular carbonyl ylide generation would be expected to be critically dependent on the relative rates of cyclization as compared to unproductive decomposition pathways. These rates are influenced by the choice of solvent, the nature of the carbonyl group, the temperature of the reaction, and the length and nature of the tether connecting the rhodium carbenoid with the carbonyl functionality. We assume that the length of the tether only influences the entropy of cyclization without affecting the rate of carbenoid formation. The primary spatial requirement for carbonyl ylide formation is that the distance between the two reacting centers should be sufficiently close so that effective overlap of the lone pair of electrons of the carbonyl group with the metallocarbenoid can occur. Good yields of cycloadducts have been obtained with both one and two methylene group tethers (i.e., five- and six-membered ring formation). The entropy of activation associated with the more flexible three (or four) methylene group tether (i.e., seven- or eight-membered ring formation) should be significantly more negative than that with the shorter tethers. In view of the stringent spatial requirements associated with the process, we thought it worthwhile to consider what effect a variation in the spatial proximity between the diazo ketone and carbonyl group would have on the course of the reaction. To this end, we investigated the rhodium(II)-catalyzed behavior of several 1-diazo-2,6-hexanediones.

As our first model we studied the reaction of 2-(4-diazo-3-oxobutyl)cyclopentenone (**28**) with rhodium(II) acetate in the presence of DMAD. The major product formed corresponded to cycloadduct **31**, which was obtained in 38% yield and was derived from the seven-membered ring carbonyl ylide intermediate **30**. An analogous result was encountered when diazo cycloheptanone **29** was used. The only product isolated corresponded to the seven-membered ring cycloadduct **32**, which was isolated in 50% yield.



We also examined the rhodium(II)-catalyzed behavior of 1-diazo-6-phenyl-2,6-hexanedione (**33**). As might be expected, the greater entropic constraints present by the

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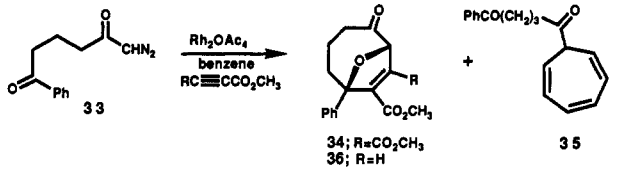
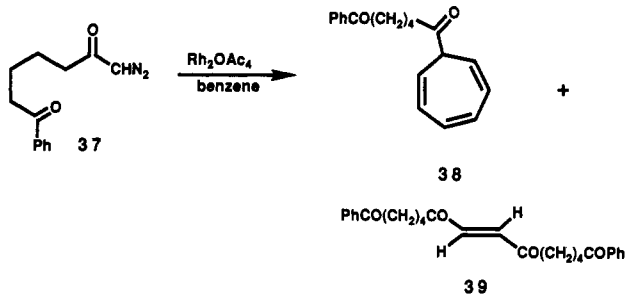
seven-membered ring ylide system might manifest itself in a lower reaction yield or no cycloaddition at all. We needed to determine whether the rhodium carbenoid was sufficiently stable to allow time to cyclize to the carbonyl ylide before allowing alternate side reactions to occur. When diazohexanedione **33** was treated with rhodium(II) acetate in the presence of DMAD in benzene, a 2:1 mixture of products was formed. The major product corresponded to the expected cycloadduct **34**. The minor component

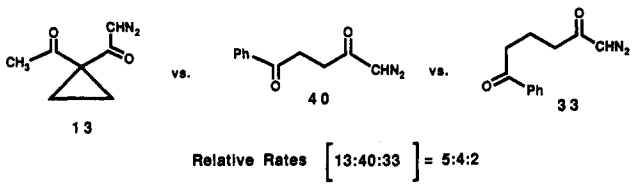


was assigned as cycloheptatriene **35** and is derived from a bimolecular addition of the rhodium carbenoid to benzene followed by ring tautomerization. A similar distribution of cycloaddition to solvent insertion resulted when methyl propiolate was used as the dipolarophile. The formation of a mixture of products in this case indicates that the additional methylene groups in **33** has sufficiently retarded the rate of intramolecular cyclization so as to allow the bimolecular reaction to occur. Changing the solvent to chloroform or dichloromethane did not result in an improved yield of cycloaddition. Evidently the additional entropy introduced by the longer tether was sufficient to slow down carbonyl ylide formation, thereby allowing other side reactions to occur.

Despite the decline in the efficiency of cyclization observed with diazohexanedione **33**, we were still interested in determining the upper limits to which this cyclization process could be carried. To this end, the precursor diazoheptanedione (i.e., **37**) to the eight-membered ring carbonyl ylide was prepared from benzoylpentenoic acid. When submitted to the cyclization–cycloaddition conditions, no products resulting from cycloaddition could be detected. Rather the products of solvent insertion (**38**) and dimerization (**39**) were obtained in 11% and 14% yield, respectively. As expected, the entropic factors required to cyclize an eight-membered ring carbonyl ylide were too significant to afford the desired product.



Armed with a better understanding of the effective range of the cyclization reaction, we felt that a qualitative measure of the relative rates of carbonyl ylide formation would be useful. The following competition experiments were performed to gauge the relative rates of cyclization. An equimolar mixture of diazo alkanedione **13** and 1-diazo-5-phenyl-2,5-pentanedione (**40**) was prepared and reacted in the presence of 1 equiv of DMAD to determine which cycloaddition product would predominate (i.e., five-membered or six-membered ring ylide). This experiment assumes that the rate of carbenoid formation and 1,3-dipolar cycloaddition are approximately the same but that the rate of cyclization to produce the dipole would differ. Product analysis (NMR) showed a near quantitative yield of cycloadducts with a 55/45 product distribution of five- to six-membered ring ylide favoring five-membered ring ylide formation by only 0.12 kcal/mol at 25 °C. The same competition between the six-membered and seven-membered ring ylides was performed with diazo ketones **40** and **33**. Reaction with DMAD afforded a 96% yield of the two cycloadducts in a 2:1 ratio favoring six-membered ring formation. This amounts to an energy difference of approximately 0.4 kcal/mol at 25 °C. Thus the facility of cyclization is quite similar with five-membered ring formation proceeding at the fastest rate.



In conclusion, the high efficiency of the rhodium carbenoid induced cyclization of diazobutane- and -hexanediones coupled with the simplicity of the procedure promises to provide an effective route to a variety of oxabicyclic ring systems. The success of the method is dependent on the relative rates of cyclization and unproductive decomposition pathways of the rhodium carbenoid. Although no activation parameters are available, the tandem cyclization–cycloaddition profile is in qualitative agreement with enthalpy and entropy considerations. We are continuing to explore the scope, generality, and synthetic applications of the rhodium(II) acetate induced cyclization–cycloaddition methodology and will report additional findings at a later date.

Experimental Section

Melting points are uncorrected. Ultraviolet absorption spectra were measured in 10-mm matching quartz cells. Flash silica gel chromatography was used to separate and purify the crude reaction mixtures.

Preparation and Rhodium(II)-Catalyzed Cyclization of Ethyl 4-Diazo-2-methyl-3-oxobutyrate (4). To a solution containing 2.1 g (12.8 mmol) of ethyl 3-chloro-2-methyl-3-oxopropiolate[32] in 50 mL of ether was added 50 mmol of an ethereal diazomethane solution at 0 °C. The resulting solution was slowly allowed to warm to room temperature and was kept at 25 °C for 12 h. The solvent was removed under reduced pressure and the crude residue was chromatographed on a silica gel column using a 3:1 hexane–ethyl acetate mixture as the eluent. The major fraction contained 1.54 g (71%) of ethyl 4-diazo-2-methyl-3-oxobutyrate (**4**) as a yellow oil, which was immediately used in the next step: IR (neat) 3110, 2995, 2120, 1740, 1650, 1460, 1370 and 1205 cm^{-1}; NMR (300 MHz, $CDCl_3$) δ 1.25 (t, 3 H, J = 7.2 Hz), 1.35 (d, 3 H, J = 7.2 Hz), 3.36 (d, 1 H, J = 7.2 Hz), 4.16 (q, 2 H, J = 7.2 Hz), and 5.44 (s, 1 H).

To a solution containing 170 mg (1.0 mmol) of the above diazo compound in 4 mL of methylene chloride was added a catalytic amount of rhodium(II) acetate dimer. Evolution of nitrogen occurred immediately and the mixture was stirred for an additional 30 min at 25 °C. The solvent was removed under reduced pressure and the resulting was purified to give 154 mg (90%) of 5-ethoxy-4-methyl-3(2*H*)-furanone[33] (**6**) as a white solid: mp 55–56 °C; IR (neat) 2995, 2945, 1700, 1610, 1445, 1390, 1350, 1145, and 1015 cm^{-1}; NMR (300 MHz, $CDCl_3$) δ 1.40 (t, 3 H, J = 7.2 Hz), 1.60 (s, 3 H), 4.42 (q, 2 H, J = 7.2 Hz), and 4.52 (s, 2 H).

Preparation and Rhodium(II) Acetate Catalyzed Reaction of Ethyl 4-Diazo-2,2-dimethyl-3-oxobutyrate (8) with Dimethyl Acetylenedicarboxylate. To a stirred solution containing 284 mg (2.0 mmol) of dimethyl acetylenedicarboxylate and a catalytic amount of rhodium(II) acetate dimer at 95 °C was

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slowly added 172 mg (0.93 mmol) of ethyl 4-diazo-2,2-dimethyl-3-oxobutyrate[34] (8) in 10 mL of benzene over a period of 2 h. The resulting solution was heated at reflux for an additional 30 min. Removal of the solvent under reduced pressure left a crude oil, which was purified to give 206 mg (74%) of 1-ethoxy-2,3-dicarbomethoxy-6,6-dimethyl-7-oxabicyclo[2.2.1]heptan-5-one (11) as a colorless oil: IR (neat) 2990, 2960, 1770, 1730, 1640, 1440, 1320, and 1250 cm^{-1}; NMR (300 MHz, $CDCl_3$) δ 1.10 (s, 3 H), 1.16 (s, 3 H), 1.22 (t, 3 H, J = 7.2 Hz), 3.76 (s, 3 H), 3.81 (s, 3 H), 3.93 (m, 2 H), and 5.90 (s, 1 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 15.2, 20.0, 21.4, 43.8, 52.7, 62.9, 80.0, 116.5, 138.9, 149.1, 160.7, 163.0, and 207.6; HRMS calcd for $C_{14}H_{18}O_7$ 298.1053, found 298.1052.

Preparation and Rhodium(II) Acetate Catalyzed Reaction of Ethyl 1-(2-Diazoacetyl)cyclopropanecarboxylate (9) with Dimethyl Acetylenedicarboxylate. A solution containing 2.0 g (12.7 mmol) of 1,1-cyclopropanedicarboxylic acid monoethyl ester[35] and 2.7 mL of thionyl chloride in 10 mL of methylene chloride was heated at reflux for 2 h. The solvent and excess thionyl chloride were removed under reduced pressure. The crude residue was dissolved in 100 mL of ether and this was added to 35 mmol of an ethereal diazomethane solution at 0 °C. The resulting solution was stirred overnight at 0 °C, and the solvent was removed under reduced pressure. The crude residue was purified to give 1.32 g (57%) of ethyl 1-(2-diazoacetyl)cyclopropanecarboxylate (9) as a yellow oil, which was immediately used in the next step without further purification: IR (neat) 3130, 2990, 2105, 1730, 1620, 1370, 1150, and 1085 cm^{-1}; NMR (300 MHz, $CDCl_3$) δ 1.23 (t, 3 H, J = 7.2 Hz), 1.3–1.7 (m, 4 H), 4.13 (q, 2 H, J = 7.2 Hz), and 6.49 (s, 1 H).

To a stirred solution containing 200 mg (1.4 mmol) of dimethyl acetylenedicarboxylate and a catalytic amount of rhodium(II) acetate dimer at 95 °C was added 121 mg (0.66 mol) of diazocyclopropane 9 in 10 mL of benzene over a 2-h period. The solution was heated at reflux for an additional 30 min, and the solvent was removed under reduced pressure. The residue was purified to give 80 mg (48%) of dimethyl 8-ethoxy-5,8-epoxy-4-oxo-6-spiro[2.5]octene-6,7-dicarboxylate (12) as a colorless oil: IR (neat) 2995, 2965, 1770, 1730, 1640, 1440, 1330, and 1250 cm^{-1}; NMR (300 MHz, $CDCl_3$) δ 0.99 (m, 2 H), 1.21 (t, 3 H, J = 7.2 Hz), 1.40 (m, 2 H), 3.78 (s, 3 H), 3.84 (s, 3 H), 3.97 (m, 2 H), and 5.09 (s, 1 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 10.7, 11.8, 15.2, 30.1, 52.7, 63.0, 80.6, 112.8, 138.8, 150.7, 160.7, 163.3 and 204.6; HRMS calcd for $C_{14}H_{16}O_7$ 296.0896, found 296.0899.

Preparation of 1-Acetyl-1-(diazoacetyl)cyclopropane (13). To a stirred solution containing 9.27 g (59.4 mmol) of 1-acetyl-1-carbethoxycyclopropane[36] in 35 mL of 95% ethanol at 0 °C was added 3.33 g (59.4 mmol) of powdered potassium hydroxide. Stirring was continued for 24 h, and the solution was allowed to warm to room temperature. The reaction mixture was concentrated under reduced pressure, and the residue was dissolved in water. The aqueous solution was extracted with ether and then carefully acidified at 0 °C to pH 1.0 with a 1.5 M aqueous hydrochloric acid solution. The aqueous phase was exhaustively extracted with ether. The combined organic extracts were dried over anhydrous sodium sulfate, filtered, and concentrated under reduced pressure to give 7.5 g (98%) of 1-acetylcyclopropanecarboxylic acid as a colorless oil: IR (neat) 3000, 1730, 1630, 1440, 1370, 1320, 1190, 1140, 940, 750, and 610 cm^{-1}; NMR (CCl_4, 90 MHz) δ 1.58 (s, 4 H), 2.40 (s, 3 H), and 9.78 (bs, 1 H).

To a stirred solution containing 2.24 g (17.5 mmol) of the above keto acid and 1.76 g (18.7 mmol) of methyl chloroformate in 80 mL of methylene chloride at 0 °C was slowly added 2.12 g (25.0 mmol) of triethylamine. The reaction was stirred for 3 h at 0 °C, filtered through Celite, and then treated with an ethereal solution containing 35 mmol of diazomethane. The solution was stirred at room temperature for 14 h and the excess diazomethane was removed under reduced pressure. Purification of the residue gave 1.62 g (70%) of 1-acetyl-1-(diazoacetyl)cyclopropane (13) as a bright yellow oil, which was used in the next step without further purification: IR (neat) 3110, 2120, 1710, 1380, 1170, 950, and 730 cm^{-1}; NMR ($CDCl_3$, 90 MHz) δ 1.43–1.58 (m, 4 H), 2.20 (s, 3 H), and 6.00 (s, 1 H); MS m/e 124 (base) 111, 95, 81, 67, and 65; HRMS calcd for $[C_7H_8O_2N_2]$ 124.0524, found 124.0527.

General Procedure for the Rhodium-Catalyzed Reaction of 1-Acetyl-1-(diazoacetyl)cyclopropane (13) with Various Dipolarophiles. To a stirred 0.2 M solution containing diazo cyclopropyl ketone 13 and 1.1–1.2 equiv of the appropriate dipolarophile was added a catalytic amount of rhodium(II) acetate dimer. A steady gas evolution was observed within 30 s, which continued for an additional 5–10 min. The catalyst was removed by filtration, and the solution was concentrated under reduced pressure. Purification was carried out by silica gel chromatography. The following reactions were carried out according to the above procedure.

Reaction of 1-Acetyl-1-(diazoacetyl)cyclopropane (13) with Dimethyl Acetylenedicarboxylate. A solution containing 210 mg (1.38 mmol) of diazo cyclopropyl ketone 13 and 210 mg (1.48 mmol) of dimethyl acetylenedicarboxylate in 5 mL of chloroform at 25 °C was treated with a trace of rhodium(II) acetate. The reaction was complete after 5 min, and the yield of the cycloadduct was determined as 97% based on NMR analysis. Purification of the residue gave a 73% isolated yield of spiro[2,3-dicarbomethoxy-4-methyl-7-oxabicyclo[2.2.1]-2-hepten-6-one-5,1′-cyclopropane] (14): mp 51–52 °C; IR ($CHCl_3$) 3020, 2980, 1780, 1740, 1640, 1450, 1400, 1340, 1280, 1160, 1090, 1040, 1000, 920, 870, and 820 cm^{-1}; NMR ($CDCl_3$, 300 MHz) δ 1.02 (s, 4 H), 1.41 (s, 3 H), 3.79 (s, 3 H), 3.84 (s, 3 H), and 5.05 (s, 1 H); ^{13}C NMR ($CDCl_3$, 300 MHz) δ 10.21, 11.28, 13.39, 30.36, 52.46, 83.46, 90.57, 138.27, 153.12, 161.09, 163.50, and 206.72; MS m/e 266 (M^+), 238, 207, 192, 174, 167, 166 (base), 137, 108, 91, and 59; HRMS calcd for $C_{13}H_{14}O_6$ 266.0790, found 266.0785. Anal. Calcd for $C_{13}H_{14}O_6$: C, 58.65; H, 5.30. Found: C, 58.38; H, 5.21.

Reaction of 1-Acetyl-1-(diazoacetyl)cyclopropane (13) with Ethyl Cyanoformate. A solution containing 250 mg (1.64 mmol) of diazo cyclopropyl ketone 13 and 180 mg (1.82 mmol) of ethyl cyanoformate at 25 °C in 5 mL of chloroform was treated with a trace of rhodium(II) acetate. The reaction was complete after 40 min, providing a 76% yield of the cycloadduct. An analytical sample was obtained by chromatography using a 25% ethyl acetate–hexane mixture to give spiro[3-carbethoxy-1-methyl-7-oxa-2-azabicyclo[2.2.1]-2-hepten-5-one-6,1′-cyclopropane] (15) as a colorless oil: IR (neat) 3000, 1780, 1740, 1620, 1460, 1420, 1360, 1320, 1260, 1190, 1120, 1010, 930, 860, and 750 cm^{-1}; NMR ($CDCl_3$, 360 MHz) δ 0.83–0.88 (m, 1 H), 0.91–1.05 (m, 2 H), 1.05–1.24 (m, 1 H), 1.36 (t, 3 H, J = 7.0 Hz), 1.69 (s, 3 H), 4.37 (q, 2 H, J = 7.0 Hz), and 5.23 (s, 1 H); MS m/e 223 (M^+) 194, 151 (100), 149, 135, 123, and 122; HRMS calcd for $C_{11}H_{13}NO_4$ 223.0844, found 223.0838. Anal. Calcd for $C_{11}H_{13}NO_4$: C, 59.19; H, 5.87, N, 6.27. Found: C, 59.96; H, 5.73, N, 6.11.

Reaction of 1-Acetyl-1-(diazoacetyl)cyclopropane (13) with *N*-Phenylmaleimide. A solution containing 220 mg (1.45 mmol) of diazo cyclopropyl ketone 13 and 270 mg (1.56 mmol) of *N*-phenylmaleimide at 25 °C in 5 mL of chloroform was treated with a trace of rhodium(II) acetate. The reaction was complete after 45 min, providing a 93% yield of a single cycloadduct. An analytical sample was obtained by chromatography using a 30% ethyl acetate–hexane mixture to give pure spiro[4,7-epoxy-4-methyl-2-phenyl-1,3,6-trioxopseudoisoindole-5,1′-cyclopropane] (16) as a white solid in 79% isolated yield: mp 167–168 °C; IR ($CHCl_3$) 1775, 1730, 1610, 1515, 1400, 1340, 1200, 1010, 880, and 850 cm^{-1}; NMR ($CDCl_3$, 300 MHz) δ 0.85–0.94 (m, 1 H), 1.12–1.21 (m, 1 H), 1.24–1.34 (m, 1 H), 1.40–1.51 (m, 1 H), 1.44 (s, 3 H), 3.20 (d, 1 H, J = 7.0 Hz), 3.40 (d, 1 H, J = 7.0 Hz), 4.92 (s, 1 H), and 7.24–7.50 (m, 5 H); MS m/e 297 (M^+), 267, 149, 124, and 69; HRMS calcd for $C_{17}H_{15}NO_4$ 297.1001, found 297.1012. Anal. Calcd for $C_{17}H_{15}NO_4$: C, 68.68; H, 5.09, N, 4.71. Found: C, 68.42, H, 5.03, N, 4.56.

Reaction of 1-Acetyl-1-(diazoacetyl)cyclopropane (13) with Benzaldehyde. A solution containing 120 mg (0.79 mmol) of diazo cyclopropyl ketone 13 and 100 mg (0.94 mmol) of benzaldehyde in 5 mL of chloroform at 25 °C was treated with a catalytic amount of rhodium(II) acetate. The reaction was finished after 10 min of stirring. Chromatography of the residue using a 15% ethyl acetate–hexane mixture gave rise to an inseparable 4:1 exo/endo mixture of the diastereoisomers of spiro[1-methyl-3-phenyl-2,7-dioxabicyclo[2.2.1]heptan-5-one-6,1′-cyclopropane] (17) in quantitative yield as a colorless oil: IR (neat) 3100, 1770, 1500, 1460, 1410, 1360, 1240, 1160, 1120, 1000, 920,

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(36) White, D. A. *Synth. Commun.* **1977**, *7*, 559.

900, 860, 810, 750, and 710 cm^{-1}; NMR ($CDCl_3$, 300 MHz) (major isomer) δ 1.02–1.58 (m, 4 H), 1.59 (s, 3 H), 4.57 (s, 1 H), 4.96 (s, 1 H), and 7.24–7.37 (m, 5 H); (minor isomer) δ 1.02–1.58 (m, 4 H), 1.59 (s, 3 H), 4.86 (d, 1 H, J = 4.0 Hz), 5.26 (d, 1 H, J = 4.0 Hz), and 7.24–7.37 (m, 5 H); MS m/e 230 (M^+), 124 (base), 106, 105, and 95; HRMS calcd for mixture $C_{14}H_{14}O_3$ 230.0943, found 230.0934. Anal. Calcd for mixture $C_{14}H_{14}O_3$: C, 73.03; H, 6.13. Found: C, 72.89; H, 6.04.

Reaction of 1-Acetyl-1-(diazoacetyl)cyclopropane (13) with Methyl Propiolate. A solution containing 220 mg (1.45 mmol) of diazo cyclopropyl ketone **13** and 130 mg (1.55 mmol) of methyl propiolate at 25 °C in 5 mL of chloroform was treated with a trace of rhodium(II) acetate. The reaction was complete after 30 min and the yield of the cycloadduct was determined as 72% on the basis of NMR analysis. The cycloadduct was purified to give (58%) spiro[2-carbomethoxy-1-methyl-7-oxabicyclo-[2.2.1]-2-hepten-5-one-6,1′-cyclopropane] (**18**) as a colorless oil: IR (neat) 3010, 2990, 1770, 1610, 1440, 1400, 1340, 1310, 1230, 1090, 1060, 1000, 970, 880, 780, and 740 cm^{-1}; NMR ($CDCl_3$, 360 MHz) δ 0.87–1.12 (m, 4 H), 1.52 (s, 3 H), 3.77 (s, 3 H), 4.82 (d, 1 H, J = 2.0 Hz), and 7.23 (d, 1 H, J = 2.0 Hz); MS (LRFAB) m/e 215, 208, 176 (base), 140, 109, 91, 77, 42, and 29; HRMS calcd for $C_{11}H_{12}O_4$ 208.0736, found 208.0734.

Reaction of 1-Acetyl-1-(diazoacetyl)cyclopropane (13) with Propargyl Methyl Ether. A solution containing 190 mg (1.25 mmol) of diazo cyclopropyl ketone **13** and 350 mg (5.0 mmol) of propargyl methyl ether at 25 °C in 5 mL of chloroform was treated with a trace of rhodium(II) acetate. The reaction was complete after 40 min to afford a 59% yield of the cycloadduct. An analytical sample was obtained by chromatography using a 25% ethyl acetate–hexane mixture to give spiro[2-(methylmethyl)-4-methyl-7-oxobicyclo[2.2.1]-2-hepten-6-one-5,1′-cyclopropane] (**19**) as a colorless oil: IR ($CHCl_3$) 3100, 2980, 1770, 1460, 1400, 1350, 1120, 1020, and 870 cm^{-1}: NMR ($CDCl_3$, 300 MHz) δ 0.53–1.31 (m, 4 H), 1.34 (s, 3 H), 3.32 (s, 3 H), 4.09 (dd, 1 H, J = 12.0 and 1.6 Hz), 4.17 (dd, 1 H, 12.0 and 1.6 Hz), 4.68 (s, 1 H), and 6.37 (d, 1 H, J = 1.6 Hz); MS m/e 194 (M^+) 179, 163, 151, 135, 126, 111, 96 (base), 95, 91, 77, and 67; HRMS calcd for $C_{11}H_{14}O_3$ 194.0943, found 194.0941. Anal. Calcd for $C_{11}H_{14}O_3$: C, 68.02; H, 7.27. Found: C, 67.92; H, 7.09.

General Procedure for Tandem Cyclization–Cycloaddition Reaction of 2-Oxo-1-apocamphane Diazo Ketone 20 with Various Dipolarophiles. A solution containing 2.18 g (12.0 mmol) of 2-oxo-1-apocamphanecarboxylic acid[28] and 1.02 mL (13.2 mmol) of methyl chloroformate in 30 mL of ether was treated with 1.85 mL (13.2 mmol) of triethylamine. After being stirred for 2 h under a nitrogen atmosphere, the solution was filtered and treated with an excess of diazomethane in ether at 0 °C. The reaction mixture was allowed to slowly warm to 25 °C over a 12-h interval. The solvent was removed under reduced pressure and the resulting oil was purified by chromatography using a 3:1 hexane–ethyl acetate mixture as the eluent to give 1.76 g (71%) of 2-oxo-1-apocamphane diazo ketone **20** as a yellow solid: mp 56–57 °C; IR (KBr) 2980, 2110, 1740, 1630, 1360, and 830 cm^{-1}; NMR ($CDCl_3$, 300 MHz) δ 1.08 (s, 3 H), 1.11 (s, 3 H), 1.34–1.45 (m, 1 H), 1.54–1.63 (m, 1 H), 1.95 (d, 1 H, J = 18.6 Hz), 2.03–2.12 (m, 2 H), 2.46–2.56 (m, 2 H), and 5.61 (s, 1 H). Anal. Calcd for $C_{11}H_{14}N_2O_2$: C, 64.06; H, 6.84; N, 13.58. Found: C, 64.34, H, 6.89; N, 13.42.

To a solution containing 1.0 mmol of diazo ketone **20**, 1.1 mmol of the appropriate dipolarophile, and 10 mL of benzene was added a trace amount of rhodium(II) acetate under a nitrogen atmosphere. Nitrogen evolution occurred upon stirring for 5 min at 25 °C, and the solution was stirred for another 2 h. After filtration, the solvent was removed under reduced pressure and the resulting residue was purified by chromatography using a 10:1 hexane–ethyl acetate mixture as the eluent. The following cycloadducts were prepared according to this procedure.

Rhodium(II) Acetate Catalyzed Reaction of 2-Oxo-1-apocamphane Diazo Ketone 20 with Dimethyl Acetylenedicarboxylate. The cycloaddition of diazo ketone **20** and dimethyl acetylenedicarboxylate afforded dimethyl 3,6-*exo*-epoxy-11,11-dimethyl-2-oxotricyclo[6.2.1.0^{1,6}]undec-4-en-4,5-dicarboxylate (**22**) in 85% yield as a white solid: mp 83–84 °C; IR (KBr) 2960, 2890, 1750, 1715, 1630, 1440, 1345, 1285, 1270, 1085, and 800 cm^{-1}; NMR ($CDCl_3$, 300 MHz) δ 1.08 (s, 3 H), 1.15 (s, 3 H), 1.29–1.36 (m, 2 H), 1.85–1.97 (m, 1 H), 2.00–2.11 (m, 3 H), 2.39 (dt, 1 H, J = 5.0 and 3.3 Hz), 3.71 (s, 3 H), 3.80 (s, 3 H), and 4.85 (s, 1 H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 21.0, 22.2, 26.6, 30.4, 34.2, 48.3, 52.4, 52.6, 53.4, 57.8, 86.9, 100.5, 140.4, 152.9, 161.3, 163.7, and 206.6; UV (methanol) 244 nm (ϵ 31 000) and 338 (2080); HRMS calcd for $C_{17}H_{20}O_6$ 320.1259, found 320.1261. Anal. Calcd for $C_{17}H_{20}O_6$: C, 63.74; H, 6.29. Found: C, 63.69; H, 6.08.

A solution containing 100 mg (0.31 mmol) of cycloadduct **22** in 40 mL of absolute methanol was degassed for 15 min under an argon atmosphere and was then irradiated for 2 h through a Pyrex filter. The solvent was removed under reduced pressure and the resulting oil was purified to give 110 mg (86% yield) of 2-[(3-carbomethoxy-2,2-dimethylcyclopentyl)methyl]-3,4-dicarbomethoxyfuran (**24**) as a colorless oil: IR (neat) 2960, 2890, 1730, 1605, 1560, 1300, 1205, 1160, 1060, and 770 cm^{-1}; NMR ($CDCl_3$, 300 MHz) δ 0.67 (s, 3 H), 1.06 (s, 3 H), 1.40–1.48 (m, 1 H), 1.57–1.76 (m, 2 H), 1.78–1.91 (m, 1 H), 1.96–2.08 (m, 1 H), 2.44 (t, 1 H, J = 9.3 Hz), 2.60 (dd, 1 H, J = 14.2 and 10.4 Hz), 2.89 (dd, 1 H, J = 14.2 and 4.2 Hz), 3.60 (s, 3 H), 3.75 (s, 3 H), 3.77 (s, 3 H), and 7.69 (s, 1 H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 16.35, 23.64, 26.30, 27.48, 27.84, 44.14, 49.81, 51.10, 51.63, 51.68, 54.91, 112.63, 118.59, 145.39, 162.10, 162.32, 163.22, and 174.01; UV (ethanol) 244 nm (ϵ 10 180); HRMS calcd for $C_{18}H_{24}O_7$ 352.1522, found 352.1521. Anal. Calcd for $C_{18}H_{24}O_7$: C, 61.35; H, 6.86. Found: C, 61.04; H, 6.72.

Rhodium(II) Acetate Catalyzed Reaction of 2-Oxo-1-apocamphane Diazo Ketone 20 with Methyl Propiolate. The reaction of diazo ketone **20** and methyl propiolate afforded methyl 3,6-*exo*-epoxy-11,11-dimethyl-2-oxotricyclo[6.2.1.0^{1,6}]undec-4-ene-5-carboxylate (**25**) in 53% yield as a white solid: mp 80–81 °C; IR (KBr) 2960, 1745, 1710, 1440, 1330, 1315, 1215, 1095, 1080, 1000, 870, and 625 cm^{-1}; NMR ($CDCl_3$, 360 MHz) δ 0.78 (ddd, 1 H, J = 13.0, 9.2, and 3.6 Hz), 1.07 (s, 3 H), 1.17 (s, 3 H), 1.57 (ddd, 1 H, J = 13.0, 9.2, and 4.7 Hz), 1.82 (m, 1 H), 1.99 (dd, 1 H, J = 4.7 and 4.1 Hz), 2.05 (ddd, 1 H, J = 13.0, 11.7, and 4.7), 2.25 (ddd, 1 H, J = 14.3, 3.3, and 3.1 Hz), 2.64 (d, 1 H, J = 14.3 Hz), 3.71 (s, 3 H), 4.59 (d, 1 H, J = 2.4 Hz), and 7.28 (d, 1 H, J = 2.4 Hz); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 21.2, 22.4, 26.7, 31.9, 33.1, 48.9, 51.8, 52.9, 57.9, 86.6, 98.2, 143.8, 146.5, 163.3, and 208.6. Anal. Calcd for $C_{15}H_{18}O_4$: C, 68.68; H, 6.92. Found: C, 68.55; H, 6.96.

Rhodium(II) Acetate Catalyzed Reaction of 2-Oxo-1-apocamphane Diazo Ketone (20) with Benzaldehyde. The reaction of diazo ketone **20** with benzaldehyde afforded 11,11-dimethyl-3,6-*exo*-epoxy-4-*exo*-phenyl-5-oxatricyclo[6.2.1.0^{1,6}]undecan-2-one (**26**) in 66% yield as a colorless oil: IR (neat) 2970, 1765, 1705, 1460, 1400, 1235, 1070, 985, and 715 cm^{-1}; NMR ($CDCl_3$, 300 MHz) δ 1.08 (s, 3 H), 1.17 (s, 3 H), 1.35–1.45 (m, 1 H), 1.83 (d, 1 H, J = 14.5 Hz), 1.84–2.02 (m, 4 H), 2.60 (dt, 1 H, J = 14.5 and 3.1 Hz), 4.33 (s, 1 H), 4.71 (s, 1 H), and 7.22–7.30 (m, 5 H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 21.6, 21.7, 21.8, 25.8, 27.0, 35.6, 47.8, 52.8, 65.4, 77.2, 89.6, 120.5, 126.4, 128.5, 138.6, and 209.0; HRMS calcd for $C_{18}H_{20}O_3$ 284.1412, found 284.1411. Anal. Calcd for $C_{18}H_{20}O_3$: C, 76.03; H, 7.09. Found: C, 75.97; H, 7.02.

Rhodium(II) Acetate Catalyzed Reaction of 2-Oxo-1-apocamphane Diazo Ketone 20 with *N*-Phenylmaleimide. The reaction of diazo ketone **20** with *N*-phenylmaleimide afforded 11,11-dimethyl-3,6-*exo*-epoxy-2-oxo-*N*-phenyltricyclo[6.2.1.0^{1,6}]-undecane-4,5-dicarboximide (**27**) in 62% yield as a white solid: mp 205–206 °C; IR (KBr) 2970, 1750, 1715, 1510, 1380, 1220, 1205, 1190, 830, 765, and 700 cm^{-1}; NMR ($CDCl_3$, 300 MHz) δ 1.08 (s, 3 H), 1.20 (s, 3 H), 1.20–1.40 (m, 2 H), 1.90–2.00 (m, 2 H), 2.07–2.17 (m, 1 H), 2.32 (d, 1 H, J = 14.9 Hz), 2.43 (dt, 1 H, J = 14.9, and 3.2 Hz), 3.17 (d, 1 H, J = 6.9 Hz), 3.32 (d, 1 H, J = 6.9 Hz), 4.66 (s, 1 H), and 7.18–7.43 (m, 5 H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 21.6, 22.5, 25.8, 26.9, 34.3, 46.4, 47.1, 47.7, 54.3, 65.0, 85.9, 98.4, 126.4, 128.8, 129.1, 131.6, 174.2, 175.2, and 209.2; HRMS calcd for $C_{21}H_{21}NO_4$ 351.1470, found 351.1479. Anal. Calcd for $C_{21}H_{21}NO_4$: C, 71.78; H, 6.02, N. 3.99. Found: C, 71.69; H, 5.83, N. 4.11.

Rhodium(II) Acetate Catalyzed Reaction of 2-(4-Diazo-3-oxobutyl)cyclopentanone (28) with Dimethyl Acetylenedicarboxylate. To a solution containing 1.8 g (11.5 mmol) of 3-(2-oxocyclopentanyl)propionic acid[37] in 100 mL of tetra-

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hydrofuran was added 1.1 mL (14.2 mmol) of methyl chloroformate followed by the slow addition of 2.4 mL (17.2 mmol) of triethylamine. The resulting solution was stirred at room temperature for 30 min, and the solid that formed was separated by filtration. The filtrate was added to 50 mmol of an ethereal diazomethane solution, and the mixture was stirred for 12 h at 0 °C. At the end of this time the solvent was removed under reduced pressure and the residue was purified to give 1.1 g (53%) of 2-(4-diazo-3-oxobutyl)cyclopentanone (**28**) as a yellow oil, which was used in the next step without further purification: IR (neat) 3100, 2980, 2880, 2120, 1735, 1640, 1380, and 1160 cm^{-1}; NMR (300 MHz, $CDCl_3$) 1.4–2.5 (m, 11 H) and 5.26 (s, 1 H).

To a solution containing 154 mg (0.86 mmol) of diazocyclopentanone **28** and 258 mg (1.82 mmol) of dimethyl acetylenedicarboxylate in 3 mL of methylene chloride was added a catalytic amount of rhodium(II) acetate dimer. A reaction occurred immediately with the vigorous evolution of nitrogen. The solution was allowed to stir for an additional 1 h at room temperature. The solvent was removed under reduced pressure, and the crude residue was purified to give 95 mg (38%) of a white solid, mp 74–75 °C, whose structure was assigned as dimethyl 1,4-epoxy-5-oxo-2-bicyclo[6.3.0]undecene-2,3-dicarboxylate (**31**): IR (neat) 2940, 1720, 1640, 1420, 1320, 1270, 1080, and 800 cm^{-1}; NMR (300 MHz, $CDCl_3$) δ 1.6–2.0 (m, 7 H), 2.1–2.5 (m, 3 H), 2.8–3.0 (m, 1 H), 3.73 (s, 3 H), 3.76 (s, 3 H), and 5.04 (s, 1 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 21.8, 22.8, 28.4, 35.5, 38.6, 48.7, 52.4, 52.5, 87.1, 100.6, 133.8, 143.1, 161.5, 163.4, and 209.3. Anal. Calcd for $C_{15}H_{18}O_6$: C, 61.22; H, 6.16. Found: C, 61.04; H, 6.12.

Preparation and Rhodium(II) Acetate Catalyzed Reaction of 2-(4-Diazo-3-oxobutyl)cyclohexanone (29) with Dimethyl Acetylenedicarboxylate. To a solution containing 200 mg (1.0 mmol) of diazo cyclohexanone[38] **29** and 305 mg (2.1 mmol) of dimethyl acetylenedicarboxylate in 4 mL of methylene chloride was added a catalytic amount of rhodium(II) acetate dimer. A reaction occurred immediately with the vigorous evolution of nitrogen. The solution was stirred for an additional 1 h at room temperature, the solvent was removed under reduced pressure, and the crude residue was purified to give 165 mg (50%) of a thick oil, which solidified upon standing and whose structure was assigned as dimethyl 1,4-epoxy-5-oxo-2-bicyclo[6.4.0]dodecene-2,3-dicarboxylate (**32**): mp 63–64 °C; IR (neat) 2950, 2870, 1730, 1660, 1440, 1330, and 1270 cm^{-1}; NMR (300 MHz, $CDCl_3$) δ 1.4–2.0 (m, 10 H), 2.1–2.3 (m, 2 H), 2.9–3.1 (m, 1 H), 3.76 (s, 3 H), 3.80 (s, 3 H), and 5.10 (s, 1 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 21.0, 25.2, 26.3, 26.5, 34.3, 39.1, 42.3, 52.36, 52.42, 87.7, 94.7, 132.4, 144.8, 161.3, 163.6, and 209.7. Anal. Calcd for $C_{16}H_{20}O_6$: C, 62.33; H, 6.54. Found: C, 62.19; H, 6.48.

General Procedure for the Trapping of the Carbonyl Ylide Derived from 1-Diazo-6-phenylhexane-2,6-dione (33) with Various Dipolarophiles. A suspension containing 3.0 g (15.6 mmol) of 4-benzoylbutyric acid in 100 mL of benzene was treated with 1.36 mL of oxalyl chloride, and the mixture was stirred under a nitrogen atmosphere until the solution became homogeneous. The reaction mixture was then added to a solution containing 100 mmol of diazomethane in 250 mL of ether at 0 °C. The solution was allowed to warm to 25 °C overnight, and the solvent was removed under reduced pressure. The resulting oil was purified to give 1.30 g (39%) of 1-diazo-6-phenylhexane-2,6-dione (**33**) as a yellow solid: mp 52–53 °C; IR (KBr) 3100, 2110, 1685, 1635, 1455, 1390, 1340, 740, and 695 cm^{-1}; NMR ($CDCl_3$, 300 MHz) δ 2.08 (pent, 2 H, J = 7.0 Hz), 2.46 (t, 2 H, J = 7.0 Hz), 3.06 (t, 2 H, J = 7.0 Hz), 5.29 (s, 1 H), 7.43–7.60 (m, 3 H), and 7.94–7.95 (m, 2 H). Anal. Calcd for $C_{12}H_{12}N_2O_2$: C, 66.65; H, 5.59; N, 12.95. Found: C, 66.73; H, 5.61; N, 12.89.

To a solution containing 1.0 mmol of 1-diazo-6-phenylhexane-2,6-dione (**33**), 1.1 mmol of the appropriate dipolarophile, and 10 mL of benzene was added 2 mg of rhodium(II) acetate under a nitrogen atmosphere. Nitrogen evolution occurred upon stirring for 5 min at room temperature, and the solution was stirred for another 2 h. After filtration, the solvent was removed under reduced pressure and the resulting residue was purified by chromatography using a 10:1 hexane–ethyl acetate mixture as the eluent. The following cycloadducts were prepared according to the above procedure.

Rhodium(II) Acetate Catalyzed Reaction of 1-Diazo-6-phenylhexane-2,6-dione (33) with Dimethyl Acetylenedicarboxylate. The first material isolated from the chromatographic separation was assigned as 1-(cyclohepta-2′,4′,6′-trienyl)-5-phenylpentane-1,5-dione (**35**) (22% yield) on the basis of its spectral properties: IR (neat) 2980, 2940, 2910, 1720, 1690, 1455, 1265, 1100, 1025, 805, and 700 cm^{-1}; NMR ($CDCl_3$, 300 MHz) δ 2.00 (pent, 2 H, J = 7.0 Hz), 2.35 (t, 1 H, J = 5.8 Hz), 2.64 (t, 2 H, J = 7.0 Hz), 2.97 (t, 2 H, J = 7.0 Hz), 4.97 (dd, 2 H, J = 8.1 and 5.8 Hz), 6.22 (dt, 2 H, J = 8.1 and 3.5 Hz), 6.50 (dt, 2 H, J = 3.5 Hz), 7.37–7.52 (m, 3 H), and 7.88–7.93 (m, 2 H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 18.26, 37.45, 40.60, 47.60, 105.65, 126.26, 128.04, 128.59, 129.70, 133.07, 136.81, 199.85, and 208.99; HRMS calcd for $C_{18}H_{18}O_2$ 266.1307, found 266.1305.

The second material isolated from the column was assigned as dimethyl 5-oxo-1-phenyl-9-oxabicyclo[4.2.1]non-2-ene-2,3-dicarboxylate (**34**) (45% yield): IR (neat) 2980, 1725, 1660, 1450, 1435, 1330, 1270, 1160, 1090, 970, 760, and 705 cm^{-1}; NMR ($CDCl_3$, 300 MHz) δ 1.75–1.83 (m, 1 H), 1.91–2.02 (m, 1 H), 2.29 (td, 1 H, J = 13.5 and 3.8 Hz), 2.51 (dd, 1 H, J = 14.6 and 5.9 Hz), 2.89 (d, 1 H, J = 13.5 Hz), 2.94 (d, 1 H, J = 3.5 Hz), 3.57 (s, 3 H), 3.74 (s, 3 H), 5.27 (s, 1 H), and 7.19–7.47 (m, 5 H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 20.4, 39.3, 43.6, 52.5, 52.6, 88.2, 96.1, 125.6, 128.4, 133.2, 140.1, 143.1, 161.1, 163.2, and 209.6; HRMS calcd for $C_{18}H_{18}O_6$ 330.1103, found 330.1116.

Rhodium(II) Acetate Catalyzed Reaction of 1-Diazo-6-phenylhexane-2,6-dione (33) with Methyl Propiolate. The first component isolated from the chromatography column was assigned as 1-(cyclohepta-2′,4′,6′-trienyl)-5-phenylpentane-1,5-dione (**35**) (24% yield). The second material isolated was identified as methyl 5-oxo-1-phenyl-9-oxabicyclo[4.2.1]non-2-ene-2-carboxylate (**36**) (43% yield): IR (neat) 3080, 2960, 2940, 1730, 1720, 1640, 1500, 1450, 1440, 1340, 1240, 1005 and 760 cm^{-1}; NMR ($CDCl_3$, 300 MHz) δ 1.49–1.63 (m, 1 H), 1.91 (dtd, 1 H, J = 15.1, 6.3, and 3.5 Hz), 2.33 (ddd, 1 H, J = 14.0, 13.5, and 3.8 Hz), 2.45 (dd, 1 H, J = 14.0 and 6.3 Hz), 2.89–2.99 (m, 2 H), 3.55 (s, 3 H), 5.15 (d, 1 H, J = 2.4 Hz), 6.75 (d, 1 H, J = 2.4 Hz), 7.18–7.32 (m, 3 H), and 7.45–7.49 (m, 2 H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 20.6, 37.9, 44.0, 51.8, 88.4, 93.7, 126.2, 127.9, 128.0, 136.7, 138.6, 141.6, 162.3, and 211.4; HRMS calcd for $C_{16}H_{16}O_4$ 272.1048, found 272.1044.

Preparation and Rhodium(II) Acetate Catalyzed Reaction of 1-Diazo-7-phenylheptane-2,7-dione (37) with Dimethyl Acetylenedicarboxylate. A solution containing 2.13 g (10.3 mmol) of 5-benzoylpentanoic acid[39] and 0.88 mL (11.4 mmol) of methyl chloroformate in 50 mL of ether was treated with 1.60 mL (11.4 mmol) of triethylamine. After being stirred for 2 h under a nitrogen atmosphere, the solution was filtered and was then treated with an excess of diazomethane in ether at 0 °C. The reaction mixture was allowed to warm to 25 °C over a 12-h period. The solvent was removed under reduced pressure and the resulting oil was purified to give 1.10 g (46%) of 1-diazo-7-phenylheptane-2,7-dione (**37**) as a yellow solid: mp 49–50 °C; IR (KBr) 3100, 2960, 2880, 2110, 1680, 1640, 1385, 1335, 740, and 705 cm^{-1}; NMR ($CDCl_3$, 90 MHz) δ 1.5–1.9 (m, 4 H), 2.36 (t, 2 H, J = 7.0 Hz), 2.98 (t, 2 H, J = 7.0 Hz), 5.26 (s, 1 H), 7.23–7.56 (m, 3 H), and 7.92–7.95 (m, 2 H). Anal. Calcd for $C_{13}H_{14}N_2O_2$: C, 67.81; H, 6.13; N, 12.17. Found: C, 67.63; H, 6.20; N, 12.07.

A solution containing 0.31 g (1.34 mmol) of diazoheptanedione **37** and 0.18 mL (1.47 mmol) of dimethyl acetylenedicarboxylate in 15 mL of benzene was treated with 2 mg of rhodium(II) acetate, and the mixture was stirred for 2 h at room temperature. The solution was filtered and the solvent was removed under reduced pressure. The crude NMR spectrum showed that no cycloadduct had been formed. The reaction mixture was chromatographed using a 10:1 hexane–ethyl acetate mixture as the eluent. The first material isolated from the column was assigned as 1-(cyclohepta-2′,4′,6′-trienyl)-6-phenylhexane-1,6-dione (**38**) (11% yield) on the basis of its spectral properties: IR (neat) 2970, 1685, 1600, 1450, 1260, 1100, 1020, 800, and 700 cm^{-1}; NMR ($CDCl_3$, 300 MHz) δ 1.62–1.72 (m, 4 H), 2.33 (t, 1 H, J = 5.7 Hz), 2.56 (t, 2 H, J = 6.8 Hz), 2.93 (t, 2 H, J = 6.8 Hz), 4.97 (dd, 2 H, J = 5.7 and 7.9

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Hz), 6.24 (dd, 2 H, J = 3.4 and 7.9 Hz), 6.51 (t, 2 H, J = 3.4 Hz), 7.36–7.52 (m, 3 H), 7.87–7.90 (m, 2 H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 23.42, 23.76, 38.31, 41.55, 47.61, 105.83, 126.21, 127.99, 128.57, 129.71, 132.98, 136.90, 199.91 and 201.11; HRMS calcd for $C_{19}H_{20}O_2$ 280.1463, found 280.1460.

The second fraction isolated was assigned as 1,14-diphenyl-7-tetradecane-1,6,9,14-tetrone (**39**) (14% yield): mp 135–136 °C; IR (KBr) 3420, 2970, 1685, 1690, 1640, 1620, 1390, 1270, and 1150 cm^{-1}; NMR ($CDCl_3$, 300 MHz) δ 1.69–1.73 (m, 8 H), 2.65 (t, 4 H, J = 6.7 Hz), 2.95 (t, 4 H, J = 6.7 Hz), 6.81 (s, 2 H), 7.35–7.50 (m, 6 H), and 7.86–7.89 (m, 4 H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 23.35, 23.54, 38.18, 41.43, 127.97, 128.58, 133.01, 136.20, 136.85, 199.72, and 200.12; HRMS calcd for $C_{26}H_{28}O_4$ 404.1987, found 404.1977.

Acknowledgment. We gratefully acknowledge support of this work by the National Institute of Health (CA-26751). The 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: ^{1}H NMR and ^{13}C NMR spectra (75 MHz) for all compounds with high resolution mass spectra (9 pages). Ordering information is given on any current masthead page.

Regioselective ϵ-Alkylation of 5-Acetoxy-1,3-alkadienes by Organocopper–Magnesium Reagents

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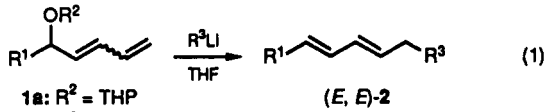
Received July 23, 1990

Treatment of the 5-acetoxy-1,3-alkadienes **1b** with dialkylcopper–magnesium complex $R_2Cu{\cdot}MgX$ prepared in tetrahydrofuran gave ϵ-alkylated products, i.e., conjugated (*E,E*)-alkadienes **2**, predominantly. In contrast, when **1b** was treated with the alkylcopper–magnesium reagent $RCuZ{\cdot}MgX$ prepared in diethyl ether, γ-alkylated 1,4-alkadienes **3** were the major products. The reaction of 6-acetoxy-2,4-tridecadiene (**14**) with *n*-BuMeCu·MgBr gave a 52:48 mixture of α- and ϵ-butylated products **15** and **16**, respectively. The conjugated (*E,E*)-alkadienes **21** possessing functional groups Y (Y = Br, AcO, Ac, HC≡C) at the ω-position were prepared in tetrahydrofuran by the same method.

Introduction

The regio- and stereoselective cross-coupling of allylic or dienylic derivatives with organometallic compounds to yield alkenes[1] and alkadienes[2] has been investigated. Earlier,[3] we reported the highly selective ϵ-alkylation of 5-(tetrahydropyranyloxy)-1,3-alkadienes **1a** by alkyllithiums (eq 1). Here, we report the results of a detailed study of similar ϵ-alkylations of 5-acetoxy-1,3-alkadienes **1b** by organocopper-mediated Grignard reagents.[4]



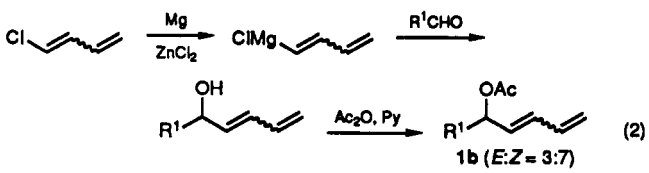
(1)

1a: R^2 = THP
1b: R^2 = Ac

(*E, E*)-**2**

Results and Discussions

Compound **1b** ($R^1 = n\text{-}C_7H_{15}$) was easily synthesized by acetylation of the alcohol obtained from the reaction of 1,3-butadienylmagnesium chloride[3,5] with *n*-octanal (eq 2).



(2)

1b (*E*:*Z* = 3:7)

The reaction of **1b** with organocopper–magnesium reagents, prepared in tetrahydrofuran (THF) or diethyl ether from Grignard reagents (RMgX) and either copper(I) iodide (CuI) or alkylcopper (RCu), was investigated (eq 3). The alkylation of **1b** by an organometallic reagent could, in theory, afford three sets of regioisomers, i.e., the products of α-, γ-, and ϵ-alkylation. A total of eight stereoisomers would be expected. The reaction products were separated by silica gel column chromatography. ^{1}H NMR analysis indicated that four isomeric products (*E,E*)-**2**, (*E,Z*)-**2**, (*E*)-**4**, and (*Z*)-**4**, were present (Table I). Neither α-alkylated products, i.e., (*E*)-**3** and (*Z*)-**3**, nor two of the possible ϵ-alkylated products, i.e., (*Z,E*)-**2** and (*Z,Z*)-**2** were

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