Rhodium(II) Acetate Induced Intramolecular Dipolar Cycloadditions of *o*-Carboalkoxy-α-diazoacetophenone Derivatives

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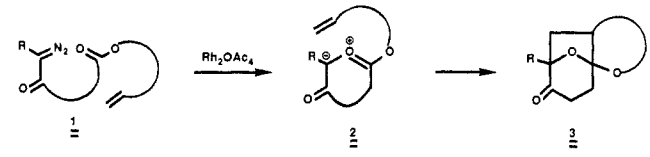
Abstract: Several *o*-carboalkoxy-α-diazoacetophenone derivatives were prepared, and their rhodium(II) acetate catalyzed behavior was studied. The results are consistent with a mechanism in which the key step involves intramolecular cyclization of the keto carbenoid onto the oxygen atom of the ester carbonyl to give a resonance-stabilized six-membered carbonyl ylide intermediate. The ylide dipole is then trapped internally by the neighboring double bond to give the cyclohepta[1,2-*b*]furanone ring system. Support for the carbonyl ylide intermediate was obtained by carrying out the rhodium-catalyzed reaction in the presence of dimethyl acetylenedicarboxylate. The formation of the intramolecular cycloadduct was completely suppressed and instead a bimolecular 1,3-dipolar cycloadduct was obtained. Reaction of the diazo ketone derived from 7-carboxyphthalide was also studied and was found to undergo internal cyclization with rhodium(II) acetate to give a six-ring carbonyl ylide that is subsequently converted to 7-carboxyphthalide.

In recent years there has been a growing interest in the use of carbonyl ylides as 1,3-dipoles for total synthesis.[1-6] Their dipolar cycloaddition to olefinic, acetylenic, and hetero-multiple-bonded dipolarophiles has been well documented.[7] The intramolecular trapping of carbonyl ylides by π bonds represents a useful method for the synthesis of some novel carbocyclic ring systems.[2-10] An attractive feature of this reaction is the opportunity to control the stereochemistry of the product at several centers.[11,12] The addition of a carbene onto the oxygen atom of a carbonyl group represents one of the simplest routes for the generation of these 1,3-dipoles.[13-23] There have been a number of reports in the literature

Scheme I



where $Rh_2(OAc)_4$ was found to be an exceptionally effective catalyst for keto carbenoid generation.[24,25] Formation of a carbonyl ylide by attack of a rhodium carbenoid intermediate onto the lone pair of electrons of the carbonyl group represents a synthetically useful approach to this dipole.[26] Although examples of intramolecular dipolar cycloadditions shown in general in Scheme I are known,[27] the reaction has not been widely exploited in synthesis. Hence, we became interested in exploring the potential of the rhodium carbenoid induced intramolecular cycloadditions as a general route to oxabicyclo[3.2.1]octanones of type **3**.[28] In this paper we present results that show that the cyclic six-membered-ring carbonyl ylides, produced from *o*-((alkyl-2-enoxy)carbonyl)-α-diazoacetophenones, undergo smooth intramolecular cycloaddition with a C–C double bond suitably located within the molecule. The resulting product represents a multiply functionalized rigid bicyclic system that is capable of subsequent synthetic elaboration.

Results and Discussion

Transition-metal-mediated carbon–carbon bond-forming reactions from various diazo precursors have been extensively utilized in carbocylic synthesis. A general review of intramolecular diazo carbonyl reactions appeared in 1979,[29] and since then many further

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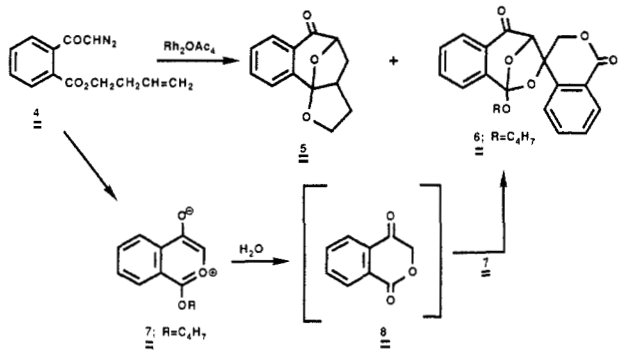
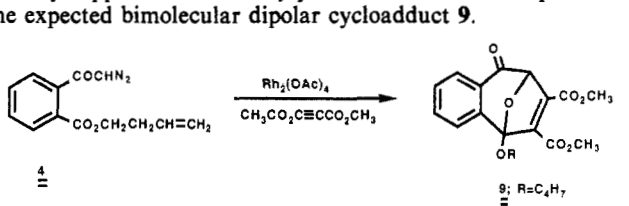
publications on transition-metal-catalyzed reactions have extended the scope of this methodology.[30-34] The use of diazo carbonyl precursors to prepare heterocyclic rings, on the other hand, has been limited.[35] To facilitate investigation of the fundamental aspects of the carbenoid cycloaddition reaction, we utilized substrates devoid of unnecessary functionality. Our synthetic objective was to construct substrates of general type **1** (Scheme I) in which the carbonyl group to undergo reaction is tethered to the α-diazo ketone with a carbon chain long enough to allow for carbonyl ylide generation and intramolecular cycloaddition.

As our first model we chose to investigate the tandem cyclization–cycloaddition reactions of several α-diazoacetophenone derivatives. The synthesis of diazo ketone **4** consisted of treating



phthalic anhydride with 1-buten-4-ol followed by conversion of the resulting acid to the diazo ketone in the usual fashion. Treatment of **4** with a catalytic quantity of rhodium(II) acetate at 25 °C in benzene afforded cyclohepta[1,2-*b*]furanone **5** in 87% yield (NMR($CDCl_3$, 360 MHz) δ 1.15–1.25 (m, 1 H), 1.55–1.68 (m, 3 H), 1.96–2.67 (m, 1 H), 3.90 (dt, 1 H, J = 8.3 and 5.7 Hz), 4.17 (dt, 1 H, J = 8.3 and 6.8 Hz), 4.79 (dd, 1 H, J = 7.4 and 2.0 Hz), 6.90–8.14 (m, 4 H)). In addition to cycloadduct **5**, a 10% yield of spiroisochromandione **6** was also obtained. This material could be prepared in larger quantities by adding a sample of 1*H*-2-benzopyran-1,4(3*H*)-dione **8** to the initial reaction mixture.

The above results are consistent with a mechanism in which the key step involves intramolecular cyclization of the keto carbenoid onto the oxygen atom of the ester carbonyl to give a resonance-stabilized six-membered carbonyl ylide intermediate (**7**). The ylide dipole is then trapped internally by the neighboring double bond to give the internal cycloadduct **5**. The formation of **6** can be rationalized in terms of a competitive hydrolysis of **7** to **8** which is followed by a dipolar cycloaddition reaction with **7** across the carbonyl group to produce **6**.[36] Support for the above suggestion was obtained by carrying out the reaction of **4** in the presence of excess dimethyl acetylenedicarboxylate (DMAD). Under these conditions the formation of compounds **5** and **6** was entirely suppressed. The only product obtained corresponds to the expected bimolecular dipolar cycloadduct **9**.



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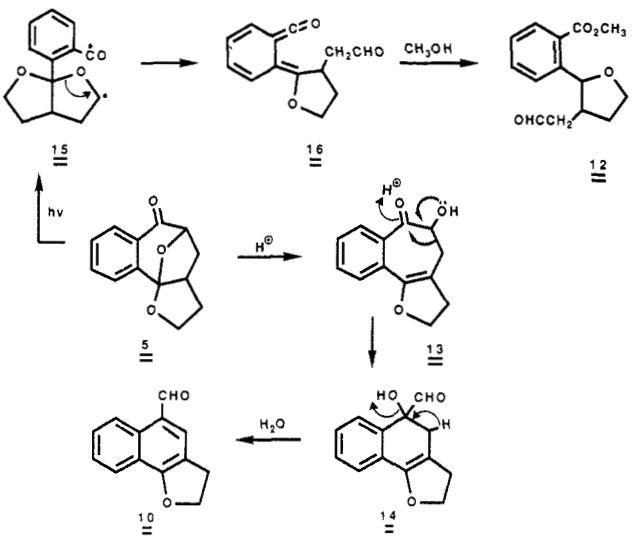
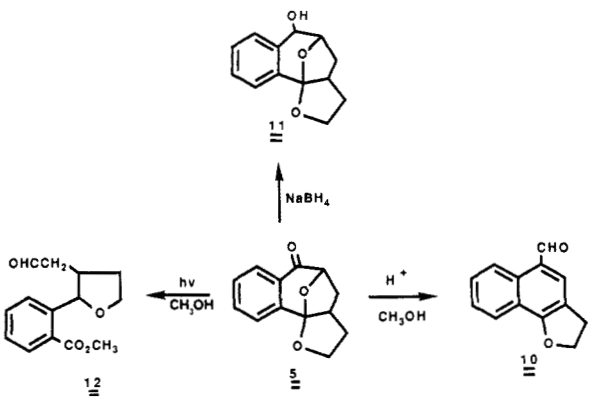
(36) We assume that a small amount of water is present in the reaction mixture which induced the hydrolysis of dipole **7** to **8**.

Scheme II

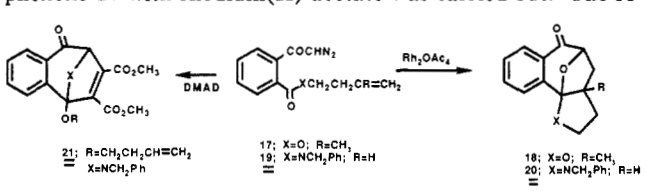


During the course of our studies we found that cycloadduct **5** undergoes some unusual rearrangement reactions. Treatment of **5** with hydrochloric acid in methanol gave 2,3-dihydronaphtho-[1,2-*b*]furan-5-carboxaldehyde (**10**) in 85% yield. Sodium borohydride reduction of **5** gave the expected alcohol **11**. On irradiation in methanol, however, a novel rearrangement occurred producing methyl (tetrahydrofuranyl)benzoate **12** in 73% yield.



The unexpected conversion of **5** to **10** can be rationalized in terms of an initial protonation on the bridged ether oxygen followed by ring opening and proton loss to give **13** as a transient species. This compound then undergoes a subsequent acid-induced rearrangement to **14** followed by loss of water to produce **10** (see Scheme II). The formation of benzoate **12** on irradiation of **5** is readily explicable in terms of a photoinduced Norrish type I ring cleavage of **5** to give diradical **15**. Fragmentation of this species produces ketene **16**, which reacts with methanol to give benzoate **12**.

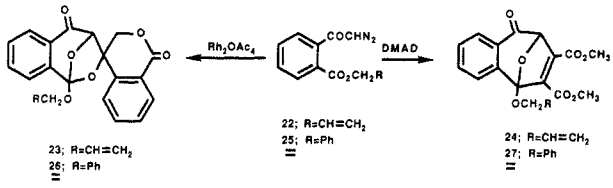
We also studied the cyclization–cycloaddition chemistry of a number of closely related systems so as to establish the generality of the reaction. The NMR spectrum of cycloadduct **5** was a bit complicated since a number of overlapping peaks were present. In order to simplify the spectrum, the reaction of diazoacetophenone **17** with rhodium(II) acetate was carried out. The re-



action proceeded quite smoothly, producing cycloadduct **18** in 80% yield (NMR ($CDCl_3$, 360 MHz) δ 0.40 (s, 3 H), 1.31 (dd, 1 H, J = 12 and 1.4 Hz), 1.40 (ddd, 1 H, J = 12.0, 8.0, and 4.3 Hz), 1.80 (ddd, 1 H, J = 12.0, 8.4, and 8.0 Hz), 2.09 (dd, 1 H, J =

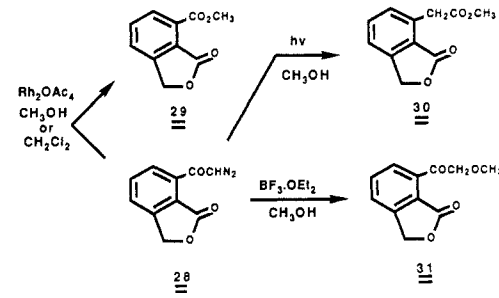
12.2 and 9.0 Hz), 3.94 (q, 1 H, J = 8.0 Hz), 4.20 (ddd, 1 H, J = 12.2, 8.7, and 4.3 Hz), 4.77 (dd, 1 H, J = 9.0 and 1.4 Hz), 7.01 (dt, 1 H, J = 9.0 and 1.6 Hz), 7.12 (dt, 1 H, J = 9.0 and 1.6 Hz), 7.53 (dd, 1 H, J = 9.0 and 1.2 Hz), 8.14 (dd, 1 H, J = 9.0 and 1.2 Hz)). The metal-catalyzed reaction of the closely related diazo amide **19** was also examined and we found that an analogous reaction occurred. In the presence of DMAD the intramolecular cycloaddition reaction of **19** was completely suppressed and only the expected dipolar cycloadduct **21** was isolated in high yield.

The primary spatial requirement for intramolecular dipolar cycloaddition is that the distance between the two reacting centers should be sufficiently close so that effective overlap of the 1,3-dipole with the dipolarophile occurs. For concerted cycloaddition to take place, the atoms of the dipolarophile should be arranged in such a way as to allow their p orbitals to lie in a plane parallel to the plane of the 1,3-dipole. In view of the stringent spatial requirements associated with process outlined in Scheme I, we thought it worthwhile to consider what effect a variation in the spatial proximity between the carbonyl ylide and the π bond would have on the course of the reaction. To this end we investigated the rhodium(II)-catalyzed reaction of diazoacetophenone **22**. The

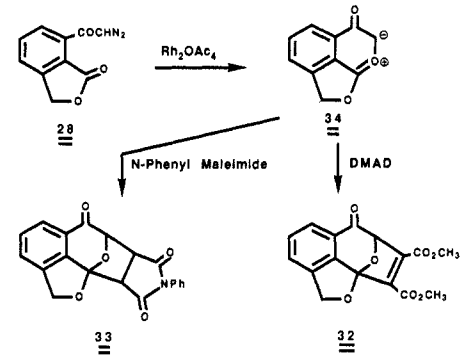


only product obtained from treating **22** with rhodium(II) acetate was 1-(3-propenyloxy)spiro[1,4-epoxy-2-benzoxepin-3(1*H*)-4′-isochroman]-1′,5(4*H*)-dione (**23**). This product was identified on the basis of its characteristic 360-MHz NMR spectrum ($CDCl_3$), which showed a set of doublets at δ 4.51 and 4.61 (J = 10.6 Hz), a multiplet at δ 4.60 (2 H), a singlet at 5.20, and a vinylic set of hydrogens at δ 5.31 (qd, J = 10.5 and 1.5 Hz), 5.48 (qd, J = 18.0 and 1.5 Hz), and 6.08 (m) in addition to the aromatic protons. All attempts to detect an intramolecular cycloadduct from the rhodium-catalyzed reaction of **22** failed. The initially generated carbonyl ylide derived from **22** could be trapped, however, with dimethyl acetylenedicarboxylate to give the normal bimolecular cycloadduct **24**. A similar set of reactions was also encountered with diazo ketone **25**. Inspection of molecular models of the carbonyl ylide derived from **22** indicates that the "two-plane orientation approach" of the 1,3-dipole and allyl π system is impossible as a result of the geometric restrictions imposed on the system. Consequently, the normal mode of 1,3-dipolar cycloaddition cannot occur. The most reasonable mechanism to account for the formation of **23** (or **26**) is to assume that the transient dipole is hydrolyzed to benzopyrandione **8**, which then undergoes cycloaddition across the carbonyl group to produce **23**. Benzopyrylium oxides are known to undergo 1,3-dipolar cycloaddition across carbonyl π bonds,[37] thereby providing good support for the suggested mechanism.

In order to obtain additional information on the rhodium-catalyzed formation of carbonyl ylides from diazo ketones and esters, we decided to study the chemistry of a simpler system. Diazo ketone **28** was synthesized from the known carboxylic acid.[38] Treatment of this material with a catalytic quantity of rhodium(II) acetate in methanol at room temperature produced 7-carbomethoxyphthalide **29** in 92% isolated yield. Most remarkably, this same ester was formed in 90% yield when the reaction was carried out in benzene or methylene chloride with or without an equivalent amount of methanol. In contrast to this finding, the photolysis of **28** in methanol afforded the expected Arndt–Eistert product **30**, while treatment of **28** with BF_3·OEt_2 gave methoxy ketone **31** in high yield.

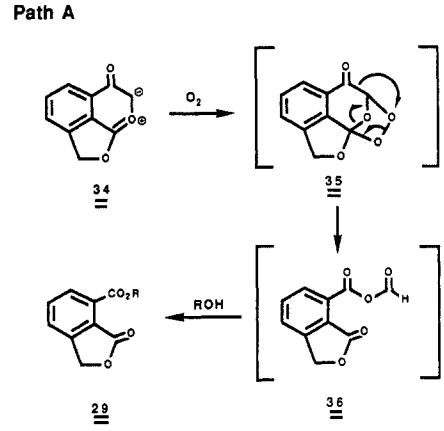


When the reaction of **28** with rhodium(II) acetate was carried out in the presence of DMAD or *N*-phenylmaleimide, the formation of 7-carbomethoxyphthalide **29** is entirely suppressed. The only produced obtained corresponds to the bimolecular cycloadduct **32** (or **33**). The formation of **32** (or **33**) is consistent with a



mechanism in which the key step involves intramolecular cyclization of the keto carbenoid onto the oxygen atom of the adjacent ester carbonyl to give a resonance-stabilized six-membered carbonyl ylide intermediate (i.e., **34**). In the presence of a trapping reagent the ylide dipole undergoes 3 + 2 cycloaddition to give the observed product.

The mechanism by which carbonyl ylide **34** is converted to 7-carbomethoxyphthalide **29** is of considerable interest. Two fundamentally different pathways seem possible. One path (A)



involves addition of oxygen across the ylide dipole to give a transient peroxide (i.e., **35**) which undergoes a subsequent Baeyer–Villiger rearrangement to the mixed anhydride **36**. This species would readily be converted to **29** in the presence of methanol. Other six-membered heteroaromatic betaines have been found to undergo similar cycloadditions with oxygen[39-42] and provide reasonable chemical precedent for this mechanism.

The second possibility (path B) involves protonation of the carbonyl ylide to give **37**, which reacts further with water to give the ring opened substrate **38**. Alternatively, **37** could react with

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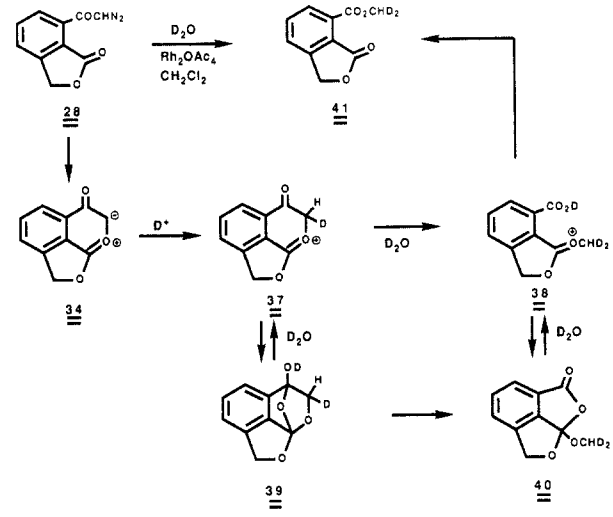
water to produce the cyclic orthoformate **39**, which, in turn, can undergo ring opening to afford **40**. This species would exist in equilibrium with **38**. Once **38** is formed it will readily undergo intramolecular alkylation to give 7-carbomethoxyphthalide **29**.

Path B



If mechanism A was correct, treatment of **28** with rhodium(II) acetate in the presence of ethanol or 2-propanol should result in the formation of the ethyl or isopropyl esters. This is not the case as only the methyl ester was obtained in both solvents. Additional support for path B was obtained by carrying out the metal-catalyzed reaction in either CH_3OD or a CH_2Cl_2–D_2O mixture. Under these conditions the only product obtained corresponded to the dideuterio ester **41**. The isolation of **41** and the complete absence of the ethyl or isopropyl ester provide strong support for path B.

In conclusion, the rhodium acetate catalyzed cyclization–cycloaddition reaction of *o*-carboalkoxy-α-diazoacetophenone derivatives has been demonstrated to be a mild and efficient method for preparing cyclohepta[1,2-*b*]furanones in excellent yield. The metal-catalyzed reactions of these *o*-carboalkoxy-α-diazoacetophenone derivatives should be useful for the construction of a variety of heterocylic ring systems. Work is currently under way utilizing this methodology for the synthesis of the perhydroazulene ring system.

Experimental Section

Melting points were determined on a Thomas-Hoover capillary melting point apparatus and are uncorrected. Infrared spectra were run on a Perkin-Elmer Model 283 infrared spectrometer. Proton NMR spectra were obtained on a Varian EM-390 and Nicolet NMC-360 spectrometer. ^{13}C NMR spectra were recorded on an IBM NB 200 SY FT spectrometer. Microanalyses were performed at Atlantic Microlabs, Atlanta, GA. Mass spectra were determined with a VG MM-7070S mass spectrometer at an ionizing voltage of 70 eV.

Preparation of *o*-((But-3-enoxy)carbonyl)-α-diazoacetophenone (4). A solution containing 0.1 mol of 1-buten-4-ol and phthalic anhydride in 10 mL of pyridine and 30 mL of benzene was heated at 100 °C for 2 h. Upon cooling, the solution was poured into an ice–water mixture, acidified with concentrated hydrochloric acid, and extracted with chloroform. The combined chloroform extracts were washed with a 5% aqueous sodium carbonate solution. Acidification of the aqueous solution with hydrochloric acid followed by extraction with chloroform gave *o*-((but-3-enoxy)carbonyl)benzoic acid in 98% yield as a colorless oil: IR (neat) 2500–3500, 1720, 1600, 1580, 1490, 1450, 1420, 1380, 1300, 1140, 1070, 920 cm^{-1}; NMR (CCl_4, 90 MHz) δ 2.43 (q, 2 H, *J* = 7.5 Hz), 4.33 (t, 2 H, *J* = 7.5 Hz), 4.90–5.25 (m, 2 H), 5.57–6.10 (m, 1 H), 7.23–7.93 (4 H, m), 11.93 (1 H, s). Anal. Calcd for $C_{12}H_{12}O_4$: C, 65.44; H, 5.49. Found: C, 65.32; H, 5.26.

A solution containing 1 mmol of the above carboxylic acid and 1.5 mmol of thionyl chloride was heated at reflux for 1 h with the exclusion of moisture until the evolution of gas ceased. The excess thionyl chloride was removed by distillation under reduced pressure to give *o*-((but-3-enoxy)carbonyl)benzoyl chloride in 98% yield as a colorless oil: IR (neat) 3095, 3000, 2970, 2900, 1800, 1750, 1650, 1600, 1580, 1450, 1390, 1280, 1200, 1140, 1090, 900, 850 cm^{-1}; NMR (CCl_4, 60 MHz) δ 2.47 (q, 2 H, *J* = 6.4 Hz), 4.37 (t, 2 H, *J* = 6.4 Hz), 4.93–5.37 (m, 2 H), 5.53–6.23 (m, 1 H), 7.50–8.07 (m, 4 H).

A solution containing 50 mmol of the above acid chloride in 40 mL of ether was added dropwise to a solution containing 75 mmol of diazomethane in 250 mL of ether at 0 °C. The solution was allowed to warm to room temperature overnight. The solvent was removed by evaporation under reduced pressure, and the residue was subjected to silica gel chromatography using an ethyl acetate–hexane mixture was the eluent to give *o*-((but-3-enoxy)carbonyl)-α-diazoacetophenone (**4**) in 95% yield as a yellow oil: IR (neat) 3100, 2980, 2900, 2100, 1740, 1630, 1600, 1590, 1500, 1360, 1280, 1230, 1130, 1100, 1020, 930, 880, 780, 750 cm^{-1}; NMR (CCl_4, 60 MHz) δ 2.43 (q, 2 H, *J* = 7.0 Hz), 4.27 (t, 2 H, *J* = 7.0 Hz), 4.87–5.30 (m, 2 H), 5.65 (s, 1 H), 5.53–6.23 (m, 1 H), 7.30–8.30 (m, 4 H).

Reaction of *o*-((But-3-enoxy)carbonyl)-α-diazoacetophenone (4) with Rhodium(II) Acetate Dimer. A solution containing 3 mmol of **4** in 30 mL of benzene was treated with a catalytic amount of rhodium(II) acetate dimer under a nitrogen atmosphere. Nitrogen evolution occurred upon stirring for 5 min at room temperature. After 30 min of stirring at 25 °C, the solvent was removed under reduced pressure, and the residue was subjected to silica gel chromatography using an ethyl acetate–hexane mixture as the eluent. The major fraction isolated was identified as 3,3a,4,5-tetrahydro-5,10b-epoxy-10b*H*-benzo[6,7]cyclohepta[1,2-*b*]furan-6(2*H*)-one (**5**) (87% yield): mp 87–88 °C; IR (KBr) 1705, 1605, 1460, 1370, 1330, 1290, 1045, 1010, 780 cm^{-1}; NMR (benzene-d_6, 360 MHz) δ 1.15–1.25 (m, 1 H), 1.55–1.68 (m, 3 H), 1.96–2.67 (m, 1 H), 3.90 (dt, 1 H, *J* = 8.3 and 5.7 Hz), 4.17 (dt, 1 H, *J* = 8.3 and 6.8 Hz), 4.79 (dd, 1 H, *J* = 7.4 and 2.0 Hz), 6.90–8.14 (m, 4 H); ^{13}C NMR ($CDCl_3$, 50 MHz) δ 32.8, 33.2, 47.1, 71.8, 82.6, 114.2, 121.9, 126.9, 128.5, 129.6, 133.9, 195.9. Anal. Calcd for $C_{13}H_{12}O_3$: C, 72.20; H, 5.60. Found: C, 72.27; H, 5.62.

The minor product was assigned the structure of 1-(3-butenyloxy)-spiro[1,4-epoxy-2-benzoxepin-3(1*H*),4′-isochroman]-1′,5(4*H*)-dione (**6**) (10%) on the basis of its spectral properties: mp 172–173 °C; IR (KBr) 1750, 1715, 1610, 1470, 1390, 1300, 1250, 1200, 1090, 1050, 940, 780 cm^{-1}; NMR ($CDCl_3$, 360 MHz) δ 2.56 (tq, 2 H, *J* = 6.6 and 1.3 Hz), 4.05 (td, 1 H, *J* = 9.1 and 6.6 Hz), 4.12 (td, 1 H, *J* = 9.1 and 6.6 Hz), 4.52 (d, 1 H, *J* = 10.7 Hz), 4.62 (d, 1 H, *J* = 10.7), 5.14 (qd, 1 H, *J* = 10.1 and 1.6 Hz), 5.17 (s, 1 H), 5.22 (qd, 1 H, *J* = 17.2 and 1.6 Hz) 5.93 (m, 1 H), 6.41 (dd, 1 H, *J* = 7.9 and 1.2 Hz), 7.26 (dt, 1 H, *J* = 8.0 and 1.2 Hz), 7.39 (dt, 1 H, *J* = 8.0 and 1.2 Hz), 7.54 (dt, 1 H, *J* = 8.0 and 1.2 Hz), 7.73 (dt, 1 H, *J* = 8.0 and 1.2 Hz), 7.81 (t, 2 H, *J* = 7.9 Hz), 8.06 (d, 1 H, *J* = 8.0 Hz). Anal. Cald for $C_{22}H_{18}O_6$: C, 69.83; H, 4.80. Found: C, 69.71; H, 4.84.

Chemical Transformations of 3,3a,4,5-Tetrahydro-5,10b-epoxy-10b*H*-benzo[6,7]cyclohepta[1,2-*b*]furan-6(2*H*)-one (5). To a solution containing 40 mg of sodium borohydride in 10 mL of tetrahydrofuran was added a solution containing 0.45 mmol of **5** in 5 mL of tetrahydrofuran under a nitrogen atmosphere. After the addition was complete, the mixture was heated at reflux for 2 h. To this solution was added 10 mL of water, and the aqueous mixture was extracted with ether. The ethereal solution was dried over anhydrous magnesium sulfate, and the solvent was removed under reduced pressure. The residue was recrystallized from an ether–hexane mixture, and the major product obtained was assigned as 2,3,3a,4,5,6-hexahydro-5,10b-epoxy-10b*H*-benzo[6,7]cyclohepta[1,2-*b*]-furan-6-ol (**11**) (95% yield): mp 129–130 °C; IR (KBr) 3470, 1585, 1490, 1470, 1415, 1370, 1330, 1310, 1275, 1200, 1150, 1050, 1020, 1005, 950, 815, 770 cm^{-1}; NMR ($CDCl_3$, 360 MHz) δ 1.88–2.00 (m, 2 H), 2.16 (d, 1 H, *J* = 7.0 Hz), 2.22–2.58 (m, 1 H), 2.42–2.58 (m, 2 H), 4.30 (td, 1 H, *J* = 8.5 and 7.4 Hz), 4.50 (qd, 1 H, *J* = 8.7 and 3.9 Hz), 4.76 (ddd, 1 H, *J* = 8.6, 6.4, and 1.1 Hz), 5.22 (t, 1 H, *J* = 6.4 Hz), 7.18–7.37 (m, 3 H), 7.44 (d, 1 H, *J* = 7.6 Hz). Anal. Calcd for $C_{13}H_{14}O_3$: C, 71.53; H, 6.48. Found: C, 71.58; H, 6.51.

A solution containing 100 mg of **5** in 5 mL of methanol and 10 mL of concentrated hydrochloric acid was heated at reflux for 3 days. The reaction mixture was extracted with ether, and the ethereal extracts were washed with an aqueous sodium carbonate solution. After drying over anhydrous magnesium sulfate, the solvent was removed under reduced pressure. The resulting residue was subjected to silica gel chromatography using a 10% ethyl acetate–hexane mixture as the eluent. The major fraction (62%) contained a yellow solid, mp 101–102 °C, whose structure was assigned as 2,3-dihydronaphtho[1,2-*b*]furan-5-carboxaldehyde (**10**) on the basis of its spectral data: IR (KBr) 3070, 2980, 2940, 2860, 2760, 1690, 1600, 1580, 1460, 1405, 1350, 1290, 1180, 1110, 1080, 1000, 940, 860, 790, 780, 750 cm^{-1}; NMR ($CDCl_3$, 360 MHz) δ 3.69(T, 2 H, *J* = 9.1 Hz), 4.85 (t, 2 H, *J* = 9.1 Hz), 7.52 (dt, 1 H, *J* = 6.0 and 1.1 Hz), 7.58 (dt, 1 H, *J* = 6.0 and 1.1 Hz), 7.85 (s, 1 H), 7.92 (d, 1 H, *J* = 11.0 Hz), 7.98 (d, 1 H, *J* = 11.0 Hz), 10.20 (s, 1 H); ^{13}C NMR ($CDCl_3$, 50 MHz) δ 30.3, 72.9, 117.9, 121.8, 126.8, 128.3,

128.5, 129.3, 131.5, 133.2, 141.0, 157.0, 192.8; UV (ethanol) 264 (ε 32 900), 380 (ε 4440). Anal. Calcd for $C_{13}H_{10}O_2$: C, 78.06; H, 5.10. Found: C, 77.97; H, 5.12.

Irradiation of 3,3a,4,5-Tetrahydro-5,10b-epoxy-10b*H*-benzo[6,7]-cyclohepta[1,2-*b*]furan-6(2*H*)-one (5). A solution containing 100 mg of **5** in 150 mL of methanol was irradiated with an internal water-cooled mercury arc lamp (Hanovia Type L, 450 W) with a uranium filter for 11 h. Removal of the solvent under reduced pressure left an oily residue, which was subjected to silica gel chromatography using an ethyl acetate–hexane mixture as the eluent. The major fraction was a colorless oil (83% yield) whose structure was assigned as methyl 2-[3-(2-oxoethyl)-2-tetrahydrofuranyl]benzoate (**12**) on the basis of its spectroscopic data: IR (neat) 2980, 2890, 1725, 1610, 1580, 1455, 1440, 1300, 1265, 1140, 1070 cm^{-1}; NMR ($CDCl_3$, 360 MHz) δ 1.71 (dtd, 1 H, J = 12.7, 12.6, and 5.1 Hz), 1.93 (ddd, 1 H, J = 17.0, 8.9, and 2.3 Hz), 2.10 (ddd, 1 H, J = 17.0, 5.0, and 1.3 Hz), 2.40 (dtd, 1 H, J = 12.7, 12.6, and 5.1 Hz), 3.36 (m, 1 H), 3.89 (s, 3 H), 3.91 (q, 1 H, J = 8.0 Hz), 4.19 (ddd, 1 H, J = 8.2, 8.2, and 5.2 Hz), 5.61 (d, 1 H, J = 6.7 Hz), 7.34 (dt, 1 H, J = 6.7 and 1.4 Hz), 7.53 (dt, 1 H, J = 6.7 and 1.4 Hz), 7.70 (d, 1 H, J = 6.7 Hz), 7.94 (dd, 1 H, J = 6.7 and 1.4 Hz), 9.47 (t, 1 H, J = 1.4 Hz). Anal. Calcd for $C_{14}H_{16}O_4$: C, 77.75; H, 7.46. Found: C, 77.82; H, 7.39.

Preparation and Rhodium(II) Acetate Catalyzed Reaction of *o*-((3-Methylbut-3-enoxy)carbonyl)-α-diazoacetophenone (17). A solution containing 0.1 mmol of 2-methyl-4-buten-1-ol and phthalic anhydride in 10 mL of pyridine and 30 mL of benzene was heated at 100 °C for 2 h. Standard workup gave *o*-((3-methylbut-3-enoxy)carbonyl)benzoic acid as a colorless oil in 98% yield: IR (neat) 3000, 2680, 2550, 1720, 1600, 1590, 1500, 1450, 1420, 1380, 1250, 1140, 1080, 900, 780 cm^{-1}; NMR (CCl_4, 90 MHz) δ 1.73 (s, 3 H), 2.37 (t, 2 H, J = 7.2 Hz), 4.33 (t, 2 H, J = 7.2 Hz), 4.73 (s, 2 H), 7.37–7.87 (m, 4 H), 11.30 (s, 1 H). Anal. Calcd for $C_{13}H_{14}O_4$: C, 66.65; H, 6.02. Found: C, 66.57; H, 5.87.

To a stirred solution containing 0.025 mol of dicyclohexylcarbodiimide in 60 mL of ether under a dry nitrogen atmosphere was added 0.025 mol of the above carboxylic acid. After stirring for 4 h, the mixture was added over 15 min to an ice-cold solution containing 0.0375 mol of diazomethane in 100 mL of ether. The solution was maintained at 0 °C for 4 h and was then filtered in order to remove undissolved material. The filtrate was evaporated under reduced pressure, and the residual oil was subjected to silica gel chromatography using an ethyl acetate–hexane mixture as the eluent to give *o*-(((3-methylbut-3-en)oxy)carbonyl)-α-diazoacetophenone (**17**) (50% yield) as a yellow oil: IR (neat) 3100, 2980, 2120, 1740, 1640, 1600, 1580, 1500, 1450, 1360, 1260, 1230, 1130, 1110, 1060, 1020, 900, 770 cm^{-1}; NMR (CCl_4, 60 MHz) δ 1.73 (s, 3 H), 2.30 (t, 2 H, J = 6.0 Hz), 4.20 (t, 2 H, J = 6.0 Hz), 4.67 (s, 2 H), 5.53 (s, 1 H), 7.13–7.63 (m, 4 H).

Treatment of **17** with rhodium(II) acetate followed by standard workup gave 3,3a,4,5-tetrahydro-3a-methyl-5,10b-epoxy-10b*H*-benzo-[6,7]cyclohepta[1,2-b]furan-6[2*H*]-one (**18**) (80% yield) as a colorless oil: IR (neat) 3080, 2960, 2900, 2880, 1700, 1610, 1460, 1390, 1370, 1300, 1280, 1210, 1180, 1120, 1090, 1050, 990, 950, 770 cm^{-1}; NMR (benzene-d_6, 360 MHz) δ 0.40 (s, 3 H), 1.31 (dd, 1 H, J = 12.1 and 1.4 Hz), 1.40 (ddd, 1 H, J = 12.1, 8.1 and 4.3 Hz), 1.80 (ddd, 1 H, J = 12.1, 8.4, and 8.1 Hz), 2.09 (dd, 1 H, J = 12.2 and 9.0 Hz), 3.94 (q, 1 H, J = 8.1 Hz), 4.20 (ddd, 1 H, J = 12.1, 8.7, and 4.3 Hz), 4.77 (dd, 1 H, J = 9.0 and 1.4 Hz), 7.01 (dt, 1 H, J = 9.0 and 1.6 Hz), 7.12 (dt, 1 H, J = 9.0 and 1.6 Hz), 7.53 (dd, 1 H, J = 9.0 and 1.2 Hz), 8.14 (dd, 1 H, J = 9.0 and 1.2 Hz). Anal. Calcd for $C_{14}H_{14}O_3$: C, 73.02; H, 6.14. Found: C, 72.87; H, 6.14.

To a solution containing 40 mg of sodium borohydride in 10 mL of tetrahydrofuran was added a solution of **17** in 5 mL of tetrahydrofuran under a nitrogen atmosphere. Standard workup gave 2,3,3a,4,5,6-hexahydro-3a-methyl-5,10b-epoxy-10b*H*-benzo[6,7]cyclohepta[1,2-*b*]furan-6-ol in 90% yield as a colorless solid: mp 87–88 °C; IR (KBr) 3440, 2980, 2900, 1595, 1460, 1390, 1370, 1310, 1290, 1230, 1160, 1080, 1030, 950, 760, 670 cm^{-1}; NMR ($CDCl_3$, 360 MHz) δ 0.75 (s, 3 H), 1.09–2.00 (m, 2 H), 2.01 (d, 1 H, J = 1.7 Hz), 2.25 (dd, 1 H, J = 13.3 and 8.0 Hz), 2.37 (td, 1 H, J = 11.9 and 9.8 Hz), 4.29 (ddd, 1 H, J = 9.7, 8.6, and 7.4 Hz), 4.44 (ddd, 1 H, J = 12.0, 8.6, and 2.6 Hz), 4.68 (ddd, 1 H, J = 8.0, 5.6, and 1.7 Hz), 5.23 (t, 1 H, J = 6.1 Hz), 7.18–7.37 (m, 3 H), 7.36 (d, 1 H, J = 7.6 Hz). Anal. Calcd for $C_{14}H_{16}O_3$: C, 72.38; H, 6.96. Found: C, 72.46; H, 6.95.

Preparation and Rhodium(II) Acetate Reaction of *N*-Benzyl-*N*-(3-butenyl)-*o*-(diazoacetyl)benzamide (19). A solution containing 3.0 g of 4-bromobut-1-ene and 9.5 g of benzylamine in a sealed tube under a nitrogen atmosphere was heated at 140 °C for 4 h. The reaction mixture was cooled and then poured into a 10% sodium hydroxide solution. The aqueous mixture was extracted with ether, and the ether extracts were washed with water and dried over anhydrous magnesium sulfate. The solvent was removed uner reduced pressure, and the residue was fractionally distilled to give *N*-benzyl-*N*-(3-butenyl)amine in 68% yield as a colorless liquid: bp 76–80 °C (2 mm); IR (neat) 3075, 3040, 2930, 2920, 1650, 1610, 1450, 1430, 1120, 915, 900, 860 cm^{-1}; NMR ($CDCl_3$, 90 MHz) δ 1.34 (bs, 1 H), 2.22 (q, 2 H, J = 7.0 Hz) 2.73 (t, 2 H, J = 7.0 Hz), 3.82 (s, 2 H), 4.95–5.22 (m, 2 H), 5.54–6.10 (m, 1 H), 7.32 (s, 5 H).

A solution containing 1.62 g of phthalic anhydride in 30 mL of ether was heated at reflux and a solution containing 2.0 g of N-benzyl-*N*-(3-butenyl)amine in 10 mL of ether was added dropwise. The reaction mixture was heated at reflux for an additional 2 h. Upon cooling, the mixture was extracted with a 10% sodium carbonate solution. The aqueous extracts were acidified with concentrated hydrochloric acid and extracted with ether. The ether layer was washed with water and then dried over anhydrous magnesium sulfate. The solvent was removed under reduced pressure to leave behind *N*-benzyl-*N*-(3-butenyl)phthalamic acid as a viscous oil in 54% yield: IR (neat) 1725, 1640, 1605, 1505, 1460, 1440, 1380, 1265, 1150, 1080, 1040, 1010, 930, 810, 785, 750 cm^{-1}; NMR ($CDCl_3$, 90 MHz) δ 2.06 (q, 1 H, J = 8.0 Hz), 2.40 (q, 1 H, J = 8.0 Hz), 3.04 (q, 1 H, J = 8.0 Hz), 3.52 (t, 1 H, J = 8.0 Hz), 4.18 (d, 1 H, J = 11.0 Hz), 4.62–5.22 (m, 3 H), 5.20–6.04 (m, 1 H), 7.02–7.67 (m, 8 H), 7.95–8.22 (m, 1 H), 10.43 (bs, 1 H). Anal. Calcd for $C_{19}H_{19}NO_3$: C, 73.76; H, 6.19; N, 4.53. Found: C, 73.58; H, 6.06; N, 4.38.

The above acid was converted to *N*-benzyl-*N*-(3-butenyl)-*o*-(diazoacetyl)benzamide (**19**) in the standard way in 42% yield: IR (neat) 2940, 2870, 2120, 1735, 1645, 1600, 1500, 1455, 1430, 1365, 1300, 1280, 1085, 925, 790, 775 cm^{-1}; NMR (CCl_4, 90 MHz) δ 1.85–2.50 (m, 2 H), 2.72–3.48 (m, 2 H), 4.04 (s, 2 H), 4.50–5.12 (m, 2 H), 5.14–5.72 (m, 1 H), 5.85 (s, 1 H), 6.75–7.45 (m, 9 H). Treatment of this material with rhodium(II) acetate gave 1-benzyl-1,2,3,3a,4,5-hexahydro-6*H*-5,10b-epoxybenzo[6,7]cyclohepta[1,2-*b*]pyrrol-6-one (**20**) in 87% yield as a colorless solid: mp 117–118 °C; IR (KBr) 3080, 3040, 2990, 2850, 1710, 1605, 1500, 1460, 1375, 1320, 1300, 1270, 1250, 1160, 1075, 990, 960, 880, 790, 760 cm^{-1}; NMR (benzene-d_6, 360 MHz) δ 1.04 (bt, 1 H, J = 9.2 Hz), 1.63 (ddd, 1 H, J = 13.3, 8.25, and 5.2 Hz), 1.70–1.87 (m, 2 H), 2.22–2.32 (m, 1 H), 2.81 (td, 1 H, J = 10.2 and 8.4 Hz), 3.02 (dt, 1 H, J = 14.7 Hz), 3.70 (d, 1 H, J = 14.7 Hz), 4.30 (d, 1 H, J = 14.7 Hz), 4.88 (d, 1 H, J = 8.3 Hz), 7.00 (dft, 1 H, J = 8.0 and 1.2 Hz), 7.10–7.20 (m, 4 H), 7.24 (dt, 1 H, J = 8.0 and 1.2 Hz), 7.40 (d, 1 H, J = 8.0 Hz), 7.68 (d, 1 H, J = 8.0 Hz), 8.22 (d, 1 H, J = 8.0 Hz). Anal. Calcd for $C_{20}H_{19}NO_2$: C, 78.66; H, 6.27; N, 4.58. Found: C, 78.54; H, 6.31; N, 4.51.

Preparation and Rhodium(II) Acetate Catalyzed Reaction of *o*-((Prop-2-enoxy)carbonyl)-α-diazoacetophenone (22). Treatment of phthalic anhydride with allyl alcohol in the standard fashion afforded *o*-((prop-2-enoxy)carbonyl)benzoic acid (98% yield) as a colorless oil: IR (neat) 3000, 2680, 2560, 1740, 1600, 1580, 1500, 1420, 1370, 1280, 1140, 1080, 950, 780, 650 cm^{-1}; NMR (CCl_4, 90 MHz) δ 4.87 (d, 2 H, J = 6.0 Hz), 5.03–5.43 (m, 2 H), 5.67–6.13 (m, 1 H), 7.37–7.53 (m, 4 H), 12.53 (s, 1 H). Anal. Calcd for $C_{11}H_{10}O_4$: C, 64.07; H, 4.89. Found: C, 63.96; H, 4.71.

A sample of the above acid was converted to *o*-((prop-2-enoxy)-carbonyl)-α-diazoacetophenone (**22**) using the cyclohexylcarbodiimide method in 50% yield: IR (neat) 3100, 2950, 2100, 1730, 1630, 1600, 1590, 1490, 1450, 1370, 1280, 1230, 1140, 1000, 1020, 880, 780 cm^{-1}; NMR (CCl_4, 60 MHz) δ 4.66 (d, 2 H, J = 6.0 Hz), 5.37 (s, 1 H), 5.40–5.62 (m, 2 H), 5.75–6.30 (m, 1 H), 7.17–7.33 (m, 4 H). Treatment of this diazo ketone with rhodium(II) acetate gave 1-(3-propenyloxy)-spiro[1,4-epoxy-2-benzoxepin-3(1*H*),4′isochroman]-1′,5(4*H*)-dione (**23**) in 50% yield as a colorless solid: mp 204–205 °C; IR (KBr) 1750, 1715, 1600, 1460, 1585, 1300, 1280, 1190, 1080, 770 cm^{-1}; NMR ($CDCl_3$, 360 MHz) δ 4.51 (d, 1 H, J = 10.6 Hz), 4.61 (d, 1 H, J = 10.6 Hz), 4.50–4.70 (m, 2 H), 5.20 (s, 1 H), 5.31 (qd, 1 H, J = 10.5 and 1.5 Hz), 5.48 (qd, 1 H, J = 18.0 and 1.5 Hz), 6.08 (m, 1 H), 6.41 (d, 1 H, J = 7.5 Hz), 7.26 (dt, 1 H, J = 8.0 and 1.2 Hz), 7.39 (dt, 1 H, J = 8.0 and 1.2 Hz), 7.55 (dt, 1 H, J = 8.0 and 1.2 Hz), 7.74 (dt, 1 H, J = 8.0 and 1.2 Hz), 7.83 (dt, 1 H, J = 8.0 and 1.2 Hz), 7.85 (s, 1 H), 8.07 (dd, 1 H, J = 8.0 and 1.2 Hz). Anal. Calcd for $C_{21}H_{16}O_6$: C, 69.22; H, 4.44. Found: C, 69.18; H, 4.37.

Preparation and Reaction of *o*-(Benzyloxycarbonyl)-α-diazoacetophenone (25) with Rhodium(II) Acetate. Treatment of phthalic anhydride and benzyl alcohol in the standard fashion afforded *o*-(benzyloxycarbonyl)benzoic acid as a crystalline solid: mp 103–104 °C; 84% yield; IR (KBr) 2800–3100, 1700, 1600, 1500, 1450, 1420, 1380, 1250–1350, 1150, 1090, 1020, 970, 930, 700 cm^{-1}; NMR ($CDCl_3$, 90 MHz) δ 5.37 (s, 2 H), 7.13–7.97 (m, 9 H), 11.33 (s, 1 H). Anal. Calcd for $C_{15}H_{12}O_4$: C, 70.30; H, 4.72. Found: C, 70.19; H, 4.58.

This material was converted to *o*-(benzyloxycarbonyl)-α-diazoacetophenone (**25**) (50% yield) in the standard manner using cyclohexylcarbodiimide: IR (neat) 3100, 2960, 2100, 1740, 1630, 1600, 1580, 1505,

1460, 1350, 1230, 1140, 1100, 1050, 1020, 970, 920, 880, 750 cm^{-1}; NMR (CCl_4, 90 MHz) δ 5.20 (s, 2 H), 5.38 (s, 1 H), 7.08–7.42 (m, 8 H), 7.55–7.78 (m, 1 H). Treatment of **25** with rhodium(II) acetate gave two products after column chromatography. The major product was isolated in 65% yield and was assigned the structure of 1-(3-benzyloxy)spiro[1,4-epoxy-2-benzoxepin-3(1*H*)-4′-isochroman]-1′,5(4*H*)-dione (**26**): mp 202–203 °C; IR (KBr) 1740, 1710, 1610, 1470, 1385, 1295, 1260, 1190, 1080, 1050, 935, 775, 740 cm^{-1}; NMR ($CDCl_3$, 360 MHz) δ 4.60 (d, 1 H, J = 10.7 Hz), 4.70 (d, 1 H, J = 10.7 Hz), 5.05 (d, 1 H, J = 11.1 Hz), 5.13 (d, 1 H, J = 11.1 Hz), 5.24 (s, 1 H), 6.44 (d, 1 H, J = 8.0 Hz), 7.23–7.58 (m, 8 H), 7.73 (dt, 1 H, J = 8.0 and 1.2 Hz), 7.84 (d, 2 H, J = 8.0 Hz), 8.08 (d, 1 H, J = 8.0 Hz); ^{13}C NMR ($CDCl_3$, 50 MHz) δ 190.0, 162.8, 141.9, 137.0, 136.2, 134.8, 133.9, 130.9, 130.0, 129.6, 129.5, 128.5, 128.1, 127.8, 126.3, 123.8, 123.2, 119.3, 83.9, 75.8, 70.44, 64.8. Anal. Calcd for $C_{25}H_{18}O_6$: C, 72.46; H, 4.38. Found: C, 72.39; H, 4.25.

The minor product was a dimeric material (10%): mp 134–135 °C; IR (KBr) 1715, 1600, 1505, 1460, 1380, 1300, 1260, 1170, 1150, 1070, 1055, 950, 810, 760, 700 cm^{-1}; NMR (acetone-d_6, 360 MHz) δ 4.47 (s, 1 H), 4.62 (d, 1 H), 4.62 (d, 1 H, J = 12.5 Hz), 4.91 (d, 1 H, J = 12.5 Hz), 4.92 (s, 1 H), 5.06 (d, 1 H, J = 18 Hz), 5.12 (d, 1 H, J = 18.0 Hz), 7.04 (d, 1 H, J = 8.0 Hz), 7.26–7.68 (m, 15 H), 7.78 (d, 1 H, J = 8.0 Hz), 8.07 (d, 1 H, J = 8.00 Hz); ^{13}C NMR ($CDCl_3$, 50 MHz) δ 59.5, 66.0, 66.3, 66.8, 80.3, 104.4, 124.6, 126.7, 127.0, 127.5, 127.9, 128.1, 128.2, 128.4, 128.9, 129.4, 129.5, 129.9, 130.2, 131.5, 132.4, 133.3, 135.4, 137.6, 140.6, 165.5, 191.8. Anal. Calcd for $C_{32}H_{24}O_6$: C, 76.17; H, 4.80. Found: C, 76.32; H, 4.83.

General Procedure for the Bimolecular Trapping of the Carbonyl Ylides Derived from Diazoacetophenone Derivatives with Dimethyl Acetylenedicarboxylate. A solution containing 1.5 mmol of the appropriate diazo ketone and 3 mmol of dimethyl acetylenedicarboxylate in 30 mL of benzene was treated with a catalytic amount of rhodium(II) acetate dimer under a nitrogen atmosphere at room temperature. Nitrogen evolution could be observed after 5 min and the reaction was complete after 30 min. The solvent was removed by evaporation under reduced pressure and the residue was purified by silica gel chromatography using an ethyl acetate–hexane mixture as the eluent. In this manner the following compounds were obtained:

Dimethyl 5-(butenyloxy)-8,9-dihydro-9-oxo-5,8-epoxy-5*H*-benzocycloheptene-6,7-dicarboxylate (9): clear oil, 70% yield; IR (neat) 3080, 2960, 2910, 1750, 1670, 1610, 1450, 1190–1350, 1140, 1090, 1040, 960, 930, 830, 810, 770, 710, 650 cm^{-1}; NMR ($CDCl_3$, 360 MHz) δ 2.29–2.46 (m, 2 H), 3.16 (s, 3 H), 3.33 (s, 3 H), 3.85 (td, 1 H, J = 9.4 and 6.7 Hz), 4.07 (td, 1 H, J = 9.4 and 6.7 Hz), 5.04 (qd, 1 H, J = 10.2 and 1.1 Hz), 5.10 (qd, 1 H, J = 17.3 and 1.5 Hz), 5.45 (s, 1 H), 5.78–5.90 (m, 1 H), 6.90 (dt, 1 H, J = 8.0 and 1.2 Hz), 7.15 (dt, 1 H, J = 8.0 and 1.2 Hz), 7.65 (dd, 1 H, J = 8.0 and 1.2 Hz), 7.90 (dd, 1 H, J = 8.0 and 1.2 Hz). Anal. Calcd for $C_{19}H_{18}O_7$: C, 63.67; H, 5.07. Found: C, 63.78; H, 5.10.

Dimethyl 5-[(3-butenyl)(phenylmethyl)amino]-8,9-dihydro-9-oxo-5,8-epoxy-5*H*-benzocycloheptene-6,7-dicarboxylate (21): colorless oil, 65% yield; IR (neat) 3080, 3040, 2960, 1730, 1650, 1605, 1505, 1460, 1440, 1310, 1270, 1220, 1140, 1080, 1020, 980, 970, 930, 780, 770, 760, 755, 710 cm^{-1}; NMR ($CDCl_3$, 90 MHz) δ 1.70–2.22 (m, 2H), 2.82 (t, 2 H, J = 7.0 Hz), 3.45 (s, 3 H), 3.64 (s, 3 H), 3.92 (d, 1 H, J = 16.0 Hz), 4.38 (d, 1 H, J = 16.0 Hz), 4.64 (dd, 1 H, J = 7.0 and 1.5 Hz), 4.75 (s, 1 H), 5.22 (s, 1 H), 5.15–5.62 (m, 1 H), 6.80–7.92 (m, 9 H). Anal. Calcd for $C_{26}H_{25}NO_6$: C, 69.78; H, 5.63; N, 3.13. Found: C, 69.69; H, 5.78; N, 3.03.

Dimethyl 5-(prop-2-enoxy)-8,9-dihydro-9-oxo-5,8-epoxy-5*H*-benzocycloheptene-6,7-dicarboxylate (24): colorless oil, 84% yield; IR (neat) 3080, 3020, 2960, 2890, 2860, 1730, 1660, 1600, 1460, 1440, 1370, 1250, 1220, 1140, 1080, 1020, 980, 770, 710, 650 cm^{-1}; NMR (CCl_4, 90 MHz) δ 3.73 (s, 3 H), 3.76 (s, 3 H), 4.07–4.57 (m, 2 H), 5.20 (dt, 2 H, J = 10.5 and 1.5 Hz), 5.27 (s, 1 H), 5.70–6.20 (m, 1 H), 7.30–7.50 (m, 3 H), 7.73–7.90 (m, 1 H). Anal. Calcd for $C_{18}H_{16}O_7$: C, 62.78; H, 4.69. Found: C, 62.86; H, 4.70.

Dimethyl 5-(benzyloxy)-8,9-dihydro-9-oxo-5,8-epoxy-5*H*-benzocycloheptene-6,7-dicarboxylate (27): colorless oil, 74% yield; IR (neat) 3080, 3050, 3020, 2960, 1740, 1670, 1605, 1505, 1460, 1440, 1190–1350, 1150, 1080, 1030, 980, 650 cm^{-1}; NMR (CCl_4, 90 MHz) δ 3.68 (s, 3 H), 3.73 (s, 3 H), 4.75 (d, 1 H, J = 12.0 Hz), 5.04 (d, 1 H, J = 12.0 Hz), 5.32 (s, 1 H), 7.12–7.55 (m, 8 H), 7.72–7.92 (m, 1 H). Anal. Calcd for $C_{22}H_{18}O_7$: C, 66.99; H, 4.61. Found: C, 66.88; H, 4.65.

Preparation of 7-(2-Diazo-1-ethanoyl)phthalide (28). A mixture containing 1.0 g of phthalide-7-carboxylic acid[38] and 6.4 mL of thionyl chloride in 25 mL of dry benzene was heated at reflux for 3 h. A portion of the solvent was removed under reduced pressure and crystallization was induced by the addition of hexane. The colorless needles that formed were recrystallized from benzene–hexane to give 0.8 g (67%) of phthalide-7-carbonyl chloride as a crystalline product: mp 93–94 °C (lit.[38] mp 95–96 °C); IR (KBr) 3090, 1785, 1765, 1610, 1600, 1440, 1190, 1050, 825, 720 cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz) δ 5.36 (s, 2 H), 7.58–7.76 (m, 3 H); ^{13}C NMR ($CDCl_3$, 300 MHz) δ 68.90, 123.30, 124.84, 129.38, 131.58, 133.73, 147.72, 166.16, 168.01.

A solution containing 500 mg of the above acid chloride in 25 mL of dry tetrahydrofuran was treated with 0.3 g of diazomethane in 20 mL of ether at 0 °C. The solution was allowed to warm to 25 °C and was stirred for 12 h. The solvent was removed under reduced pressure and the residue was subjected to silica gel chromatography using a hexane–ethyl acetate mixture as the eluent to give 0.37 g (73%) of 7-(2-diazo-1-ethanoyl)phthalide (**28**) as a white crystalline solid: mp 125–126 °C; IR (KBr) 3120, 2105, 1740, 1600, 1570, 1360, 1300, 1190, 1050 cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz) δ 5.32 (s, 2 H), 6.51 (s, 1 H), 7.58–7.90 (m, 3 H); ^{13}C NMR ($CDCl_3$, 300 MHz) δ 58.8, 69.1, 122.0, 124.8, 129.4, 134.2, 137.7 147.8, 169.5, 184.8; UV (95% ethanol) 292 nm (ϵ 8400), 214 (ϵ 21 000). Anal. Calcd for $C_{10}H_6N_2O_3$: C, 59.41; H, 2.99; N, 13.86. Found: C, 59.32; H, 3.06; N, 13.79.

Reaction of 7-(2-Diazo-1-ethanoyl)phthalide (28) with Rhodium(II) Acetate. A solution containing 202 mg of 7-(2-diazo-1-ethanoyl)-phthalide (28) in 15 mL of methanol was treated with a catalytic quantity of rhodium(II) acetate at 25 °C, and the solution was stirred for 3 h. After this time the mixture was filtered and the solvent was removed under reduced pressure to give 190 mg (94%) of methyl phthalide-7-carboxylate (**29**) as a white crystalline solid: mp 104–105 °C (lit.[43] mp 106–108 °C); IR (KBr) 2970, 1755, 1725, 1600, 1430, 1390, 1230, 1000 cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz) δ 3.86 (s, 3 H), 5.22 (s, 2 H), 7.56–7.64 (m, 3 H); ^{13}C NMR ($CDCl_3$, 300 MHz) δ 52.83, 68.78, 123.33, 124.77, 129.45, 131.61, 133.81, 147.68, 166.15, 168.0.

The structure of this material was verified by comparison with an independently synthesized sample. A solution containing 100 mg of diazomethane in 25 mL of ether was added to a solution containing 260 mg of phthalide-7-carboxylic acid[38] in 10 mL of ether at 0 °C. The resulting solution was allowed to warm to 25 °C and was stirred for 12 h. The excess diazomethane was quenched with acetic acid, and the solvent was removed under reduced pressure to give a yellow solid, which was recrystallized from benzene–hexane to give 280 mg (97%) of a white crystalline solid: mp 104–105 °C; identical in every detail with a sample of **29** prepared from diazo ketone **28**. The same product was formed when benzene or methylene chloride was used as the solvent with or without an equivalent of methanol.

Photolysis of 7-(2-Diazo-1-ethanoyl)phthalide (28) in Methanol. A solution containing 333 mg of **28** in 175 mL of methanol was irradiated for 1.5 h under an argon atmosphere using a 450-W Hanovia mercury arc lamp in a Pyrex photolysis well. The solvent was removed under reduced pressure and the residue was subjected to silica gel chromatography using a hexane–ethyl acetate mixture as the eluent to give 330 mg (86%) of the expected Arndt–Eistert product **30**: mp 89–90 °C; IR (KBr) 3020, 2960, 2930, 2860, 1755, 1735, 1605, 1365, 1265, 1210, 1080, 1005 cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz) δ 3.68 (s, 3 H), 4.13 (s, 2 H), 5.25 (s, 2 H), 7.32–7.57 (m, 3 H); ^{13}C NMR ($CDCl_3$, 300 MHz) δ 35.7, 52.1, 69.1, 121.1, 123.6, 130.8, 134.0, 134.7, 147.2, 170.7, 171.1. Anal. Calcd for $C_{11}H_{10}O_4$: C, 63.96; H, 4.92. Found: C, 63.91; H, 4.72.

Reaction of 7-(2-Diazo-1-ethanoyl)phthalide (28) with Boron Trifluoride Etherate in the Presence of Methanol. A solution containing 410 mg of **28** in 100 mL of dry methanol under a nitrogen atmosphere was treated with 20 mg of boron trifluoride etherate, and the mixture was stirred at 25 °C for 1.5 h. The solvent was removed under reduced pressure and the residue was subjected to silica gel chromatography using a hexane–ethyl acetate mixture as the eluent to give 392 mg (95%) of methoxymethyl phthalide-7-carboxylate (**31**) as a white crystalline solid: mp 75–76 °C; IR (KBr) 2995, 2950, 2910, 2830, 1750, 1710, 1600, 1450, 1135, 1060, 1005 cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz) δ 3.45 (s, 3 H), 4.71 (s, 2 H), 5.37 (s, 2 H), 7.59–7.76 (m, 3 H); ^{13}C NMR ($CDCl_3$, 300 MHz) δ 59.2, 69.5, 77.4, 122.9, 124.7, 128.5, 134.3, 137.2, 147.0, 169.4, 201.7. Anal. Calcd for $C_{11}H_{10}O_4$: C, 64.07; H, 4.89. Found: C, 64.16; H, 4.97.

Reaction of 7-(2-Diazo-1-ethanoyl)phthalide (28) with Rhodium(II) Acetate in the Presence of a Trapping Agent. A solution containing 158 mg of **28** and 133 mg of dimethyl acetylenedicarboxylate in 10 mL of dichloromethane was treated with a catalytic amount of rhodium(II) acetate, and the mixture was stirred at 25 °C for 3 h. The mixture was filtered and the solvent was removed under reduced pressure. The residue was subjected to silica gel chromatography and the major fraction contained 210 mg (85%) of the expected dipolar cycloadduct **32**: mp 124–125 °C; IR (KBr) 3020, 2985, 1740, 1720, 1660, 1620, 1600, 1440, 1295, 1265, 1175, 970, 955, 805 cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz) δ 3.26 (s, 3 H), 3.35 (s, 3 H), 5.27 (s, 1 H), 5.37 (d, 1 H, J = 12.5 Hz),

(43) Wenkert, E.; Johnston, D. B. R.; Dave, K. G. *J. Org. Chem.* **1964**, *29*, 2534.

5.58 (d, 1 H, J = 12.4 Hz), 7.47-7.65 (m, 3 H); ^{13}C NMR ($CDCl_3$, 300 MHz) δ 52.68, 52.85, 78.77, 85.08, 115.75, 123.61, 125.28, 127.39, 131.98, 134.80, 138.06, 142.59, 147.16, 161.00, 162.81, 186.96. Anal. Calcd for $C_{16}H_{12}O_7$: C, 60.76; H, 3.82. Found: C, 60.81; H, 3.84.

A solution containing 350 mg of **28** and 400 mg of *N*-phenylmaleimide in 20 mL of methylene chloride was treated with a catalytic amount of rhodium(II) acetate at 25 °C. The mixture was stirred for 12 h and filtered through Celite, and the solvent was removed under reduced pressure. The resulting residue was subjected to silica gel chromatography using a hexane–ethyl acetate mixture as the eluent, and the major fraction contained 470 mg (79%) of the expected dipolar cycloadduct **33**: mp 174-175 °C; IR (KBr) 3080, 2950, 2890, 1725, 1605, 1510, 1400, 1205, 1015, 795, 715 cm^{-1}; ^{1}H NMR ($CDCl_3$, 300 MHz) δ 4.04 (d, 1 H, J = 9.5 Hz), 4.27 (t, 1 H, J = 9.5 Hz), 5.09 (d, 1 H, J = 9.3 Hz), 5.34 (d, 1 H, J = 12.6 Hz), 5.70 (d, 1 H, J = 12.6 Hz), 6.63 (m, 2 H), 7.26-7.94 (m, 6 H); ^{13}C NMR ($CDCl_3$, 300 MHz) δ 46.3, 52.4, 77.1, 80.7, 124.1, 125.6, 125.7, 128.0, 128.3, 128.4, 129.1, 130.8, 132.0, 132.7, 143.3, 171.6, 172.3, 190.5. Anal. Calcd for $C_{20}H_{13}NO_5$: C, 69.16; H, 3.77; N, 4.03. Found: C, 69.09; H, 3.80; N, 4.01.

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Free Energies of Transfer of Carbon Acids and Their Conjugate Carbanions from Water to Me_2SO–Water Mixtures

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Abstract: Free energies (or solvent activity coefficients) of transfer of nitromethane, phenylnitromethane, acetylacetone, 1,3-indandione, 9-carbomethoxyfluorene, and 9-cyanofluorene from water to various Me_2SO–water mixtures were determined from partitioning experiments between *n*-heptane and the solvent of interest. In combination with the pK_a values of the various carbon acids in the different solvents and the solvent activity coefficients of the hydronium ion taken from the literature, free energies of transfer of the respective carbanions were also calculated. These latter values are of particular relevance with respect to recent suggestions that solvent effects on the intrinsic barriers of proton-transfer reactions may be understood in terms of nonsynchronous solvation/desolvation effects of the ions involved in these reactions (principle of nonperfect synchronization). The availability of free energies of transfer of the carbon acids and their conjugate bases also allows a better understanding of the solvent effects on the pK_a values of the carbon acids.

The reactivity of carbanions acting as bases or nucleophiles is generally substantially affected by the solvent although the degree of their dependence varies greatly with the nature of the carbanion. One may distinguish three major categories of carbanions with respect to solvent effects on their reactivity. In the first are the carbanions whose basicity and nucleophilic reactivity increase dramatically upon transfer from water to Me_2SO. These are ions in which the negative charge is highly localized on an oxygen atom, as is the case with enolate and nitronate ions. The second category consists of carbanions whose reactivity is also significantly solvent dependent but in the direction of *decreased* basicity in Me_2SO compared with water. Typical examples would be highly delocalized carbanions derived from aromatic hydrocarbons. The third category comprises carbanions with pK_a values that are about the same in water and Me_2SO, such as the malononitrile anion. Table I summarizes pK_a values for some representative examples.

In a first approximation the pK_a differences shown in Table I can be attributed to differences in the solvation of the respective carbanions in the two solvents. Thus, the sharp increase in pK_a upon transfer from water to Me_2SO for the nitroalkanes, diketones, and diesters may primarily be seen to be the consequence of the loss of hydrogen bonding solvation of the nitronate and enolate ions. This contrasts with the carbanions derived from the aromatic hydrocarbons, which seem to be better solvated in the dipolar aprotic solvent than in water, and hence their pK_a decreases.

For a more accurate assessment of the effect of solvation on carbanion reactivity, a more quantitative evaluation of solvation energies is needed than that provided by mere comparisons of the solvent effects on pK_a values. This is because the pK_a changes are not only the result of the solvent effect on the stability of the carbanion but on the stability of the carbon acid and the hydronium ion as well.

Table I. pK_a Values for Some Carbon Acids in Water and Me_2SO

carbon acid	pK_a		carbon acid	pK_a	
	H_2O	Me_2SO		H_2O	Me_2SO
CH_3NO_2	10.2[a]	17.2[b]	$CH_2(CN)_2$	11.1[g]	11.0[h]
$PhCH_2NO_2$	6.88[c]	12.03[d]	4-$NO_2C_6H_4CH_2CN$	13.4[i]	12.3[j]
$CH_2(COCH_3)_2$	9.0[a]	13.4[b]	9-COOMe-fluorene	15.8[k,l]	10.35[m]
$CH_2(COOEt)_2$	13.3[a]	16.4[b]	9-CN-fluorene	10.71[n,p]	8.3[m]
$CH_3CH(NO_2)_2$	5.2[e]	6.6[f]			

[a] Pearson, R. G.; Dillon, R. L. *J. Am. Chem. Soc.* **1953**, *75*, 2439. [b] Olmstead, W. N.; Bordwell, F. G. *J. Org. Chem.* **1980**, *45*, 3299. [c] Reference 16a. [d] Keeffe, J. R.; Morey, J.; Palmer, C. A.; Lee, J. C. *J. Am. Chem. Soc.* **1979**, *101*, 1295. [e] Bell, R. P.; Tranter, R. L. *Proc. R. Soc. London, Ser. A* **1974**, *337*, 578. [f] Cox, B. G.; Gibson, A. *Faraday Symp. Chem. Soc.* **1975**, *10*, 107. [g] Bowden, K.; Stewart, R. *Tetrahedron* **1965**, *21*, 261. [h] Ritchie, C. D.; Uschold, R. E. *J. Am. Chem. Soc.* **1967**, *89*, 2752. [i] Stearns, R. S.; Wheland, G. W. *J. Am. Chem. Soc.* **1947**, *69*, 2025. [j] Bordwell, F. G., cited by: Walters, E. *J. Phys. Chem.* **1977**, *81*, 1995. [k] Ritchie, C. D. *J. Am. Chem. Soc.* **1969**, *91*, 6749. [l] In MeOH. [m] Bordwell, F. G.; Branca, J. C.; Hughes, D. L.; Olmstead, W. N. *J. Org. Chem.* **1980**, *45*, 3305. [n] Reference 4a. [p] In 10% Me_2SO–90% water.

Adopting the formalism used by Parker[1] one can express the change in pK_a upon transfer from water(W) to Me_2SO(D) as eq 1. $^W\gamma^D_{C^-}$, $^W\gamma^D_{H^+}$, and $^W\gamma^D_{CH}$ are the solvent activity coefficients

$$^W\Delta^D pK_a = \log {}^W\gamma^D_{C^-} + \log {}^W\gamma^D_{H^+} - \log {}^W\gamma^D_{CH} \quad (1)$$

for the transfer of the carbanion, the hydronium ion, and the carbon acid, respectively, from water to Me_2SO. Alternatively, one may express eq 1 in terms of free energies as eq 2, with the

$$^W\delta^D\Delta G^\circ = {}^W\delta^D G_{tr}(C^-) + {}^W\delta^D\Delta G_{tr}(H^+) - {}^W\delta^D\Delta G_{tr}(CH) \quad (2)$$

(1) Parker, A. J. *Chem. Rev.* **1969**, *69*, 1.

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