Generation of carbonyl ylide dipoles from the Rh(II)-catalyzed cyclization of α-diazo-β-keto-1,5-diesters‡

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This paper is dedicated to Fritz Sauter on his 70th birthday

(received 27 Nov 00; accepted 29 Oct 01; published on the web 06 Nov 01)

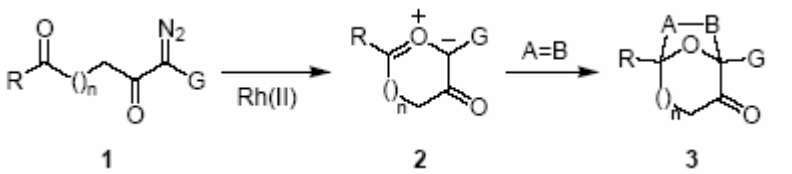
Abstract

The Rh(II)-catalyzed reaction of ethyl 2-diazo-3-[1-(ethoxycarbonyl)cyclopropyl]-3-oxo-propanecarboxylate with various dipolarophiles afforded dipolar cycloadducts in good yield. The reaction involves the formation of a rhodium carbenoid and subsequent transannular cyclization of the electrophilic carbon onto the remote ester carbonyl group to generate a five-membered cyclic carbonyl ylide which undergoes a subsequent dipolar cycloaddition reaction. In the absence of a trapping agent, a head to tail coupling of the 1,3-dipole intermediate occurs to give a dimer. Heating a benzene solution of the dimer at 80 ºC in the presence of various dipolarophiles gave the same cycloadducts as was obtained from the Rh(II)-catalyzed reaction.

Keywords: Rh(II) catalyzed reactions, dipolar cycloaddition reactions, transannular cyclization, carbonyl ylide

Introduction

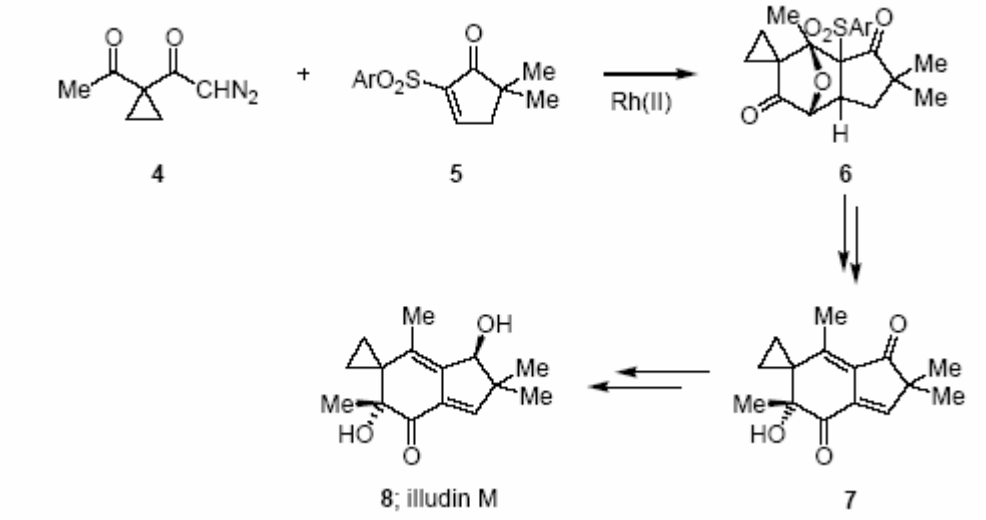
In recent studies,[1] we have described the formation of cyclic carbonyl ylide dipoles by a process involving cyclization of an electrophilic metallo carbenoid onto an adjacent carbonyl group.[2] The general reaction investigated is illustrated below; variations in chain length (n = 0, 1, 2) and nature of the activating group (G) were explored.[1,2] With limited exceptions,[3] alkyl and aryl ketones were employed, and dipole **2** was generated by the rhodium(II)-catalyzed decomposition of diazoalkane-dione **1** in benzene at 80 ºC (Scheme 1).[4]



1 2 3

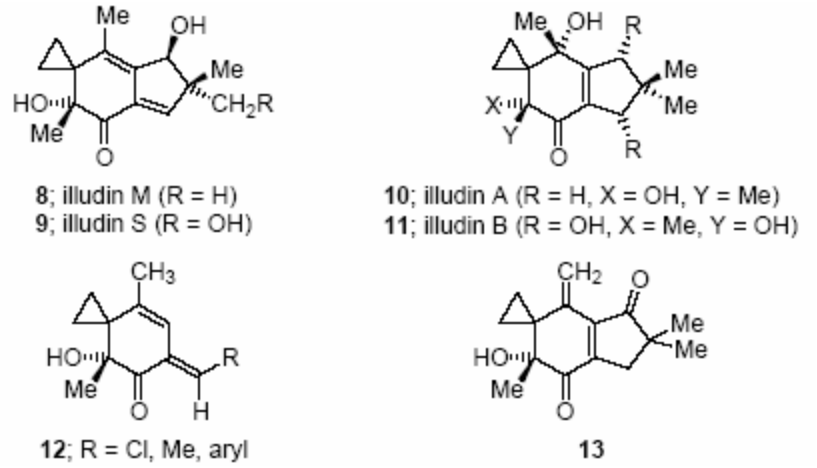
Scheme 1

This tandem cyclization-cycloaddition strategy was used as the key step in the synthesis of a number of natural products as it provides for the rapid assembly of the basic core unit of several target molecules having most of the functionality in place.[5-10] In an earlier study,we had reported on the use of a dipolar cycloaddition reaction of a cyclic carbonyl ylide dipole as the key step for the construction of (±)-illudin M (**8**) (Scheme 2).[11]



Scheme 2

Similar approaches have been independently reported by Kinder[12] and McMorris.[13] The illudins and certain derivatives have been evaluated for antitumor activity at the NCI and show selective toxicity for human myelocytic leukemia and other carcinoma cells of various species of origin.[14] Most of the existing illudin analogs (**9**-**13**) in the literature have been derived from the natural products. [15-17] The spirocyclopropane and α,β-unsaturated ketone moieties present in the illudin skeleton constitute a bis-electrophile that is undoubtedly responsible for the DNA damage. [18]

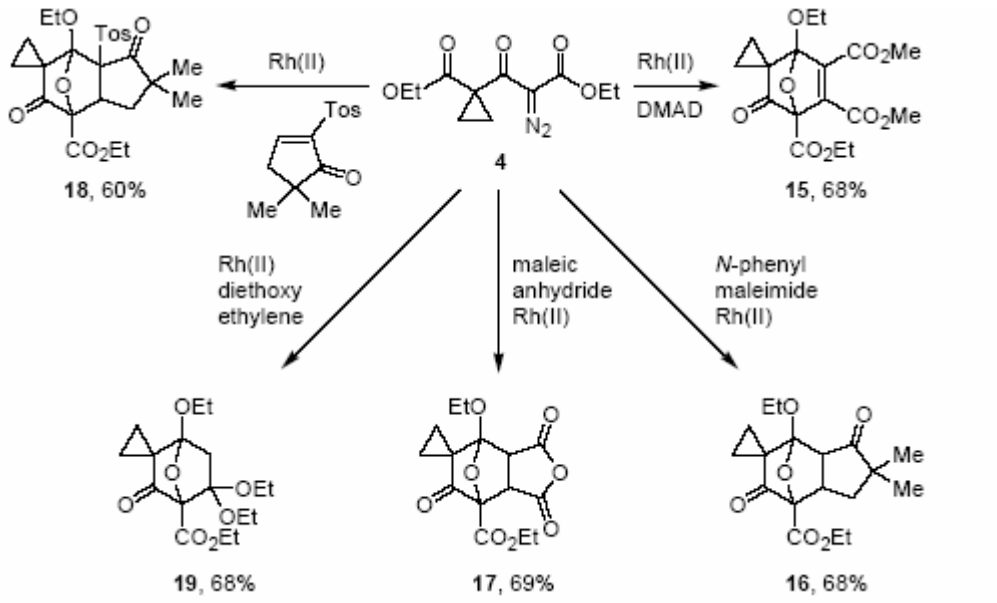


Some simpler illudin analogs such as the dehydroilludins M (**12**) as well as isodehydroilludin M (**13**) have recently been shown to possess high efficacy against a number of adenocarcinomas.[17,18] In an effort to increase the versatility of the cascade reaction of diazo

ketoesters and also to prepare additional illudin analogs for biological testing, we have undertaken a study of the effect of an interacting ester group on the efficiency of dipole formation. Details of these cyclizations are the subject of this paper.

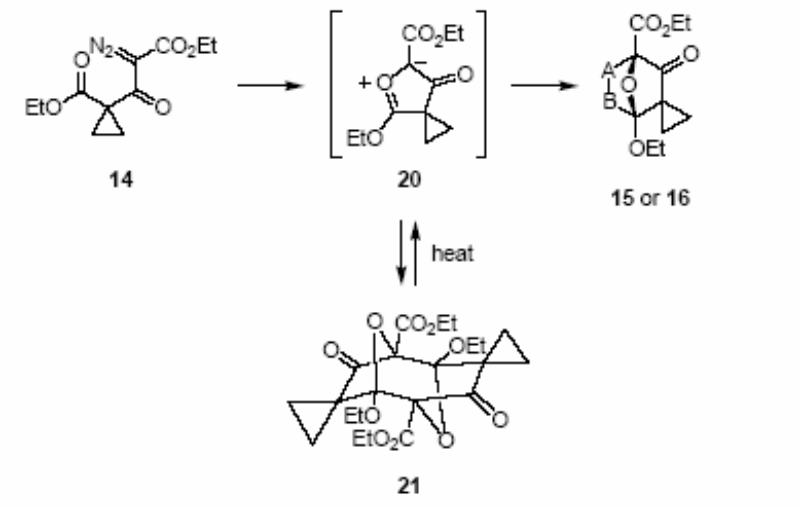
Results and Discussion

In order to apply the tandem cyclization-cycloaddition sequence to the eventual synthesis of ester analogs of the illudin family, we decided to first establish the viability of the dipolar cycloaddition using the cyclopropanated diazo ketoester **14** with a variety of acyclic and cyclic dipolarophiles. Indeed, the cycloaddition proceeded readily with dimethyl acetylenedicarboxylate, producing cycloadduct **15** in 68% yield (Scheme 3).



Scheme 3

Reaction with *N*-phenylmaleimide and maleic anhydride resulted in the formation of cycloadducts **16** and **17** in comparable yield. Earlier studies in our laboratory demonstrated that the bimolecular cycloaddition of cyclic carbonyl ylides with phenyl-sulfonyl-substituted alkenes was a remarkably efficient process.[20] MO calculations using the AM1 Hamiltonian reveal a small energy gap between the HOMO of the dipole and the LUMO of the phenylsulfonyl-substituted alkene. This led us to examine the reaction between **14** and 2-(4-methylphenyl)sulfonyl-5,5-dimethylcyclopentenone[11] which afforded the *exo*-cycloadduct **18** as the major diastereomer in 60% yield. The Rh(II)-catalyzed reaction of **14** with 1,1-diethoxyethylene was also studied and was found to produce cycloadduct **19** in 68% yield. This regiochemical selectivity is readily understandable on the basis of perturbation theory[19] and is also analogous to previous findings encountered in our laboratory.[20]



Scheme 4

All of the above results can be accommodated by a mechanism involving formation of a five-membered ring carbonyl ylide (*i.e.* **20**) derived by interaction of the initially formed rhodium carbenoid with a pair of electrons on the neighboring ester carbonyl group. In the absence of any added trapping agent, ylide **20** (Scheme 4) undergoes dimerization to produce the novel head to tail dimer **21** as a crystalline solid, mp 190–191 ºC, in 68% yield. The structure of **21** was unequivocally established by an X-ray crystal structure analysis[21] (Figure 1). A space group of $P2_1/c$, $Z = 4$ and density of 1.35 was found. The oxabicyclo portions of the dimer rest in an envelope conformation as expected from the sp^2-hybridization of the keto carbonyl groups at the 3 and 7-positions and the sp^2-like hybridization at the induced planarity of cyclopropane carbons. The packing diagram showed the absence of any strong intermolecular associations. The *anti*-relationship of the bridged ethers is understandable in terms of minimization of unfavorable dipole interactions in the transition state.

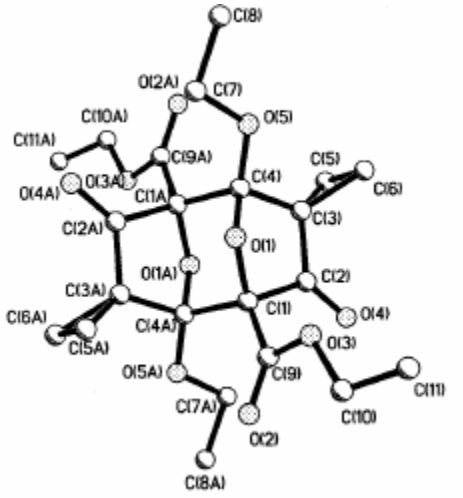
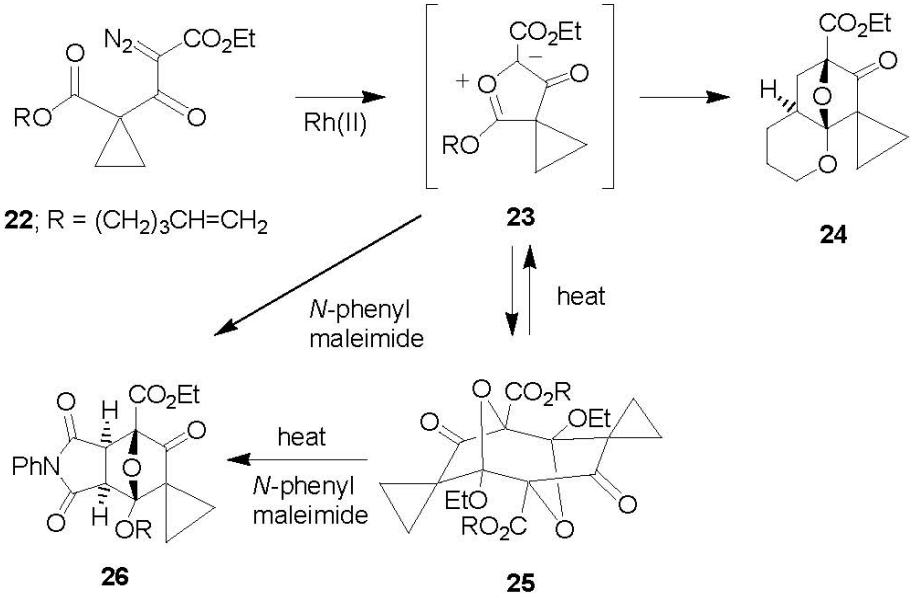


Figure 1. ORTEP Drawing of dimer **21**.

Heating dimer **21** in benzene at 80 ºC with DMAD or *N*-phenylmaleimide in the absence of the rhodium catalyst afforded the bimolecular cycloadducts **15** (70%) or **16** (75%) (Scheme 4).

More than likely, the push-pull nature of the alkoxy substituted carbonyl ylide enhances its stability thereby allowing the relatively rare dimerization reaction of the dipole to occur.[22]
Placement of a tethered π-bond on the diazo ester side chain was also examined. Thus, the Rh(II)-catalyzed decomposition of diazo ketodiester **22** in benzene at 80 ºC for 5 h furnished the expected intramolecular cycloadduct **24** as the exclusive product (60%). When the reaction was stopped after 1 h, however, a 1:1-mixture of cycloadduct **24** and dimer **25** was obtained in 84% yield. Further heating of the mixture at 80 ºC afforded additional quantities of cycloadduct **24** (Scheme 5). This transformation presumably involves C-C bond cleavage of the dimer followed by intramolecular trapping of the resultant carbonyl ylide intermediate **23**. Additional support for the involvement of dipole **23** comes from heating the 1:1-mixture of **24** and **25** in the presence of *N*-phenylmaleimide. Under these conditions, the bimolecular cycloadduct **26** was isolated in 38% yield.



Scheme 5

In conclusion, the Rh(II)-catalyzed cyclization/cycloaddition cascade of cyclopropyl-substituted diazo ketoesters bearing a neighboring alkoxycarbonyl group affords 1,3-dipolar cycloadducts in good yield. The regiochemical results encountered can be rationalized on the basis of FMO considerations. In the absence of any trapping agent, the initially formed dipole undergoes bimolecular coupling to produce a novel head to tail dimer. We are currently investigating further applications of the method outlined here as an approach to alkoxycarbonyl-substituted illudin derivatives.

Experimental Section

General Procedures. Melting points are uncorrected. Mass spectra were determined at an ionizing voltage of 70 eV. Unless otherwise noted, all reactions were performed in flame-dried glassware under an atmosphere of dry argon. Solutions were evaporated under reduced pressure

with a rotary evaporator and the residue was chromatographed on a silica gel column using an ethyl acetate/hexane mixture as the eluent unless specified otherwise. All solids were recrystallized from ethyl acetate/hexane for analytical data.

Ethyl 1-[2-diazo-3-(ethoxycarbonyl)propanoyl]-1-cyclopropanecarboxylate (14). To a solution containing 2.3 g (17 mmol) of 2-ethoxycarbonylacetic acid in 20 mL of CH_2Cl_2 at 0 ºC was slowly added 20 mL (42 mmol) of isopropyl magnesium chloride, and the reaction mixture was stirred at 0 ºC for 30 min. The solution was heated to 40 ºC and stirred for an additional 30 min. In a separate flask, 2.1 mL (24 mmol) of oxalyl chloride and 2 drops of DMF were slowly added to a solution of 2.5 g (16 mmol) of 1-(ethoxycarbonyl)-1-cyclopropanecarboxylic acid in 20 mL CH_2Cl_2. The solution was allowed to stir for 2 h at rt and was concentrated under reduced pressure, taken up in 5 mL CH_2Cl_2, and added to the above magnesium dianion solution. The resulting mixture was stirred at 0 ºC for 1h and then quenched with 50 mL of 50% HCl. The solution was extracted with CH_2Cl_2 and dried over $MgSO_4$. Purification of the crude residue by silica gel chromatography gave 2.0 g (55%) of ethyl 3-[1-(ethoxycarbonyl)cyclopropyl]-3-oxopropanecarboxylate as a clear oil. IR (neat): 1730, 1303, and 1168 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$): δ 1.17–1.24 (m, 10H), 3.98 (s, 2H), and 4.08–4.20 (m, 4H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 13.9, 14.0, 17.3, 21.3, 23.8, 34.6, 49.0, 61.3, 167.6, 170.6, 198.4. Anal. calcd. for $C_{11}H_{16}O_5$: C, 57.87; H, 7.07. Found: C, 57.81; H, 7.02.

To a stirred solution containing 1.0 g (4.4 mmol) of the above diethyl ester in 10 mL CH_3CN at 0 ºC was added 1.5 mL (11 mmol) of Et_3N. The reaction mixture was stirred at 0 ºC for 30 min, and then 1.0 g (5.0 mmol) of tosyl azide was added in one portion. The reaction mixture was stirred at rt overnight, the solvent was removed under reduced pressure and the crude oil was purified by silica gel chromatography to give 0.84 g (80%) of diazo ketodiester **14** as a yellow oil which was immediately used in the next step. IR (neat) 2128, 1730, 1645, 1374, and 1331 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$): δ 1.23 (3H, t, J = 7.1 Hz), 1.25 (3H, t, J = 7.1 Hz), 1.43 (2H, m), 1.55 (2H, m), 4.15 (2H, q, J = 7.1 Hz), and 4.27 (2H, q, J = 7.1 Hz); ^{13}C NMR (75 MHz, $CDCl_3$): δ 13.8, 14.0, 15.9, 33.9, 60.9, 61.3, 161.0, 170.3, 186.2.

4-Ethyl 5,6-dimethyl 4,7-epoxy-1-ethoxy-3-oxospiro[2.5]oct-5-ene-4,5,6-tricarboxylate (15). To a solution containing 0.3 mL (2.2 mmol) of dimethyl acetylenedicarboxylate and 2 mg of rhodium(II) acetate in 5 mL of refluxing benzene was added dropwise 0.1 g (0.4 mmol) of diazo ketodiester **14**. The reaction mixture was heated at reflux for 30 min, the solution was concentrated under reduced pressure, and the mixture was purified by silica gel chromatography to give 0.1 g (68%) of **15** as a clear oil. IR (neat): 1744, 1730, 1552, and 1339 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$): δ 1.08 (m, 2H), 1.20 (m, 1H), 1.26 (t, 3H, J = 7.0 Hz), 1.33 (t, 3H, J = 7.0 Hz), 1.52 (m, 1H), 3.70 (m, 2H), 3.81 (s, 3H), 3.86 (s, 3H), and 4.37 (m, 2H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 10.5, 12.0, 13.8, 14.7, 29.3, 52.5, 52.7, 62.6, 63.0, 88.1, 110.4, 141.6, 145.3, 160.7, 161.9, 162.3, 198.7. Anal. calcd. for $C_{17}H_{20}O_9$: C, 55.42; H, 5.48. Found: C, 55.35; H, 5.31.

7-Ethyl 4′,7′-epoxy-4′-ethoxy-1′,3′,6′-trioxo-2′-phenylperhydrospiro[cyclo-propane-1,5′-isoindole]-7′-carboxylate (16). To a solution containing 0.21 g (1.2 mmol) of *N*-phenylmaleimide and 2 mg of rhodium(II) acetate in 5 mL of refluxing benzene was added 0.11 g (0.5 mmol) of diazo ketodiester **14** dropwise. The reaction mixture was heated at reflux

for 45 min, and the solution was concentrated under reduced pressure. The residue was purified by silica gel chromatography to give 0.12 g (68%) of **16** as a white solid, mp 69–70 ºC. IR (neat): 1766, 1744, 1716, 1374, and 1324 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$): δ 1.22 (t, 3H, *J* = 7.0 Hz), 1.30 (d, 2H, *J* = 3.5 Hz), 1.35 (t, 3H, *J* = 7.1 Hz), 1.72 (m, 2H), 3.42 (d, 1H, *J* = 7.2 Hz), 3.63 (d, 1H, *J* = 7.2 Hz), 3.96 (q, 2H, *J* = 7.0 Hz), 4.39 (q, 2H, *J* = 7.1 Hz), and 7.43 (m, 5H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 13.8, 14.1, 15.7, 16.8, 37.6, 48.6, 50.7, 62.5, 62.7, 86.4, 108.7, 126.3, 129, 129.2, 131.4, 162.2, 171.2, 171.6, 200.6. Anal. calcd. for $C_{21}H_{21}NO_7$: C, 63.14; H, 5.30; N, 3.51. Found: C, 62.95; H, 5.40; N, 3.44.

7′-Ethyl 4′,7′-epoxy-4′-ethoxy-1′,3′,6′-trioxoperhydrospiro[cyclopropane-1,5′-isobenzofuran]-7′-carboxylate (17). To a solution containing 0.12 g (1.2 mmol) of maleic anhydride and 2 mg of rhodium(II) acetate in 5 mL of refluxing benzene was added dropwise 0.1 g (0.4 mmol) of diazo ketodiester **14**. The mixture was heated at reflux for 60 min, and the solution was concentrated under reduced pressure. The residue was purified by silica gel chromatography to give 0.09 g (69%) of **17** as a clear oil. IR (neat): 2950, 1750, 1745, and 1335 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$): δ 1.16 (m, 1H), 1.20 (t, 3H, *J* = 7.1 Hz), 1.24 (m, 1H), 1.34 (t, 3H, *J* = 7.1 Hz), 1.68 (m, 2H), 3.57 (d, 1H, *J* = 7.4 Hz), 3.83 (d, 1H, *J* = 7.4 Hz), 3.91 (q, 2H, *J* = 7.1 Hz), and 4.36 (q, 2H, *J* = 7.1 Hz); ^{13}C NMR (75 MHz, $CDCl_3$): δ 14.0, 14.3, 15.5, 17.2, 37.1, 49.8, 51.7, 62.9, 63.2, 86.5, 109.2, 161.5, 165.9, 167.1, 199.5. Anal. calcd. for $C_{15}H_{16}O_8$: C, 55.54; H, 4.98. Found: C, 55.42; H, 4.86.

7′-Ethyl 4′,7′-epoxy-4′-ethoxy-2′,2′-dimethyl-3′a-(4-methylphenyl)sulfonyl-3′,6′-dioxoperhydrospiro[cyclopropane-1,5′-indene]-7′-carboxylate (18). To a solution containing 0.2 g (0.8 mmol) of 5,5-dimethyl-2-(4-methylpheny)sulfonylcyclopent-2-en-one[11] and 2 mg of rhodium(II) acetate in 5 mL of refluxing benzene was added dropwise 0.1 g (0.4 mmol) of diazo ketodiester **14**. The mixture was heated at reflux for 60 min, the solution was concentrated under reduced pressure, and the residue was purified by silica gel chromatography to give 0.23 g (60%) of **18** as a clear oil. IR (neat): 2940, 1760, 1740, 1340, 1280 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$): δ 0.90 (m, 1H), 0.99 (s, 3H), 1.11 (s, 3H), 1.20 (t, 3H, *J* = 7.2 Hz), 1.3–1.4 (m, 1H), 1.35 (t, 3H, *J* = 7.2 Hz), 1.50 (m, 1H), 1.63 (m, 1H), 1.80 (m, 2H), 2.42 (s, 3H), 3.84 (d, 1H, *J* = 7.9 Hz), 4.21 (m, 2H), 4.40 (q, 2H, *J* = 7.2 Hz), 7.32 (m, 2H), and 7.68 (d, 2H, *J* = 8.2 Hz); ^{13}C NMR (75 MHz, $CDCl_3$): δ 13.8, 13.9, 15.9, 18.6, 21.7, 23.8, 24.1, 33.8, 37.7, 39.6, 46.6, 61.4, 64.1, 70.2, 83.6, 129.1, 129.6, 135.7, 145.1, 170.4, 170.9, 200.4, 210.4. Anal. calcd. for $C_{25}H_{30}O_8S$: C, 61.20; H, 6.17. Found: C, 61.06; H, 5.86.

5-Ethyl 5,8-epoxy-6,6,8-triethoxy-4-oxospiro[2.5]octane-5-carboxylate (19). To a solution containing 0.13 g (1.1 mmol) of diethoxyethylene and 2 mg of rhodium(II) acetate in 5 mL of refluxing benzene was added dropwise 0.13 g (0.53 mmol) of diazo ketodiester **14**. The mixture was heated at reflux for 60 min, and then the solution was concentrated under reduced pressure. The residue was purified by silica gel chromatography to give 0.12 g (68%) of **19** as a clear oil. IR (neat) 1773, 1744, 1339, and 1047 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$): δ 0.85 (m, 1H), 1.09 (t, 3H, *J* = 7.3 Hz), 1.22 (m, 6H), 1.2–1.4 (m, 2H), 1.33 (t, 3H, *J* = 7.1 Hz), 1.57 (m, 1H), 1.91 (d, 1H, *J* = 11.6 Hz), 2.63 (d, 1H, *J* = 11.6 Hz), 3.50 (m, 4H), 3.87 (m, 2H), and 4.28 (m, 2H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 14.0, 14.1, 14.2, 14.7, 15.0, 15.1, 36.3, 42.1, 57.8, 58.9, 59.9, 61.6, 92.2, 104.9, 107.9, 162.9, and 201.0. Anal. calcd. for $C_{17}H_{26}O_7$: C, 59.62; H, 7.66 Found: C, 59.54; H, 7.59.

5,11-Diethyl 5,12,6,11-diepoxy-6,12-diethoxy-4,10-dioxodispiro[2.3.2.3]dodecane-5,11-dicarboxylate (21). To a refluxing solution of rhodium(II) acetate in benzene was slowly added 0.1 g (0.4 mmol) diazo ketodiester **14** and the reaction was heated at reflux for 3 h until all the starting diazo compound had disappeared. The solvent was removed under reduced pressure and the crude white solid was recrystallized from a hexane/ethyl acetate (3:2) mixture to give 0.06 g (68%) of dimer **21**[21] as a white solid, mp 190–191 ºC. IR (neat) 2985, 1749, 1445, 1373, and 1280 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$): δ 1.10 (m, 1H), 1.2–1.3 (m, 4H), 1.4–1.5 (m, 4H), 1.65 (m, 1H), 3.80 (m, 1H), 4.20 (m, 1H), and 4.4–4.5 (m, 2H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 13.3, 13.9, 15.2, 17.8, 36.1, 61.0.0, 62.1, 90.8, 104.4, 162.4, 202.1. Anal. calcd. for $C_{22}H_{28}O_{10}$: C, 58.40; H, 6.24. Found: C, 58.26; H, 6.21.

Cycloadducts **15** (70%) and **16** (75%) were formed by heating a sample of dimer **21** (1 equiv) and the appropriate dipolarophile (2 equiv) in 5 mL of benzene at reflux for 2 h.

4-Pentenyl 1-[2-diazo-3-(ethoxycarbonyl)propanoyl]-1-cyclopropanecarboxylate (22). To a solution containing 4.0 g (30 mmol) of cyclopropane-1,1-dicarboxylic acid[23] and 3.2 mL (31 mmol) of 4-penten-1-ol in 100 mL of dry CH_2Cl_2 was added a solution of 7.4 g (36 mmol) of DCC and 0.95 g (7.8 mmol) of DMAP in 50 mL of dry CH_2Cl_2. A white precipitate immediately formed and the reaction mixture was allowed to stir at rt for an additional 12 h. The mixture was filtered, washed with 100 mL of a saturated NH_4Cl solution, and dried over $MgSO_4$. Concentration under reduced pressure gave 2.8 g (46%) of cyclopropane-1,1-dicarboxylic acid monopent-4-enyl ester.

To a solution containing 2.3 g (17 mmol) of 2-ethoxycarbonylacetic acid in 50 mL of CH_2Cl_2 at 0 ºC was slowly added 17 mL (34 mmol) of isopropyl magnesium chloride and the mixture was stirred at 0 ºC for 30 min. The solution was heated to 40 ºC for an additional 30 min. In a separate flask, 1.5 mL (17 mmol) of oxalyl chloride and 2 drops of DMF were slowly added to a solution of 2.8 g (14 mmol) of cyclopropane-1,1-di-carboxylic acid monopent-4-enyl ester in 50 of mL CH_2Cl_2. The solution was allowed to stir for 2 h at rt, concentrated under reduced pressure, taken up in 5 mL CH_2Cl_2, and added to the above magnesium dianion solution. The resulting mixture was stirred at 0 ºC for 1 h and was quenched with 50 mL of 50% hydrochloric acid. The solution was extracted with CH_2Cl_2, dried over $MgSO_4$, and the crude residue was purified by silica gel chromatography to give 1.8 g (46%) of pent-4-enyl 3-[1-(ethoxycarbonyl)cyclo-propyl]-3-propanecarboxylate as a clear oil. IR: 1737, 1637, and 1324 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$): δ 1.26 (t, 3H, J = 7.1 Hz), 1.60 (m, 4H), 1.74 (m, 2H), 2.12 (m, 2H), 3.94 (s, 2H), 4.1–4.2 (m, 4H), 5.01 (m, 2H), and 5.77 (m, 1H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 14.0, 21.1, 27.5, 29.8, 29.9, 34.5, 48.9, 61.0, 64.6, 115.4, 136.9, 167.5, 170.5, 198.3. Anal. calcd. for $C_{14}H_{20}O_5$: C, 62.66; H, 7.52. Found: C, 62.51; H, 7.40.

To a stirred solution of 1.0 g (3.7 mmol) of the above diester in 10 mL of CH_3CN at 0°C was added 1.3 mL (9.0 mmol) of Et_3N. The reaction mixture was stirred at 0 ºC for 30 min, and then 0.6 mL (4.6 mmol) of mesyl azide was added in one portion. The mixture was stirred at rt for 12 h, the solvent was removed under reduced pressure and the crude oil was purified by silica gel chromatography to give 0.95 g (87%) of diazo ketodiester **22** as a pale yellow oil which was immediately used in the next step. IR: (neat) 2128, 1723, and 1303 cm^{-1}; ^1H NMR (360 MHz, $CDCl_3$): δ 1.30 (t, 3H, J = 7.3 Hz), 1.44 (m, 2H), 1.56 (m, 2H), 1.71 (m, 2H), 2.08 (m, 2H), 4.09 (t, 2H, J = 6.7 Hz), 4.26 (q, 2H, J = 7.3 Hz), 5.03 (m, 2H), and 5.75 (m, 1H); ^{13}C NMR (75 MHz,

$CDCl_3$): δ 14.1, 14.2, 16.0, 27.5, 27.6, 29.8, 33.9, 61.4, 64.5, 115.1, 137.1, 161.0, 170.4, 186.2.

6′-Ethyl 6′,8′a-epoxyperhydrospiro[cyclopropane-1,8′-chromene]-6′-carboxylate (24). To a refluxing solution of benzene containing 2 mg of rhodium(II) acetate was added dropwise 0.48 g (1.6 mmol) of diazo ketodiester **22**. The mixture was heated at reflux for 5 h and the solution was concentrated under reduced pressure. The mixture was purified by silica gel chromatography to give 0.26 g (60%) of **24** as a white solid, mp 108–109 ºC. IR ($CHCl_3$): 1766, 1744, and 1339 cm^{-1}; ^1H NMR (360 MHz, $CDCl_3$): δ 0.82 (m, 1H), 1.00 (m, 1H), 1.17 (m, 2H), 1.28 (t, 3H, *J* = 7.1 Hz), 1.25–1.35 (m, 4H), 1.83 (m, 1H), 1.94 (m, 1H), 2.28 (m, 1H), 3.80 (m, 1H), 3.95 (m, 1H), and 4.27 (q, 2H, *J* = 7.1 Hz); ^{13}C NMR (75 MHz, $CDCl_3$): δ 12.4, 13.6, 14.1, 23.6, 28.7, 35.9, 36.5, 36.8, 61.8, 64.1, 84.8, 104.7, 166.1, 204.9. Anal. calcd. for $C_{14}H_{18}O_5$: C, 63.15; H, 6.81. Found: C, 63.10; H, 6.82.

When the above reaction was stopped after 1 h, a 1:1-mixture of cycloadduct **24** and 5,11-bis(pent-4-enyl)5,12,6,11-diepoxy-6,12-diethoxy-4,10 dioxodispiro[2.3.2.3]dodecane-5,11-dicarboxylate (**25**) was obtained in 84% yield. All of our attempts to isolate a pure sample of dimer **25** failed as a consequence of its lability on a silica gel column. Dimer **25** showed the following NMR signals: ^1H NMR (360 MHz, $CDCl_3$): δ 1.23 (t, 3H, *J* = 6.9 Hz), 1.25–1.35 (m, 4H), 1.85 (m, 2H), 2.15 (m, 2H), 3.84 (m, 1H), 4.17 (m, 1H), 4.26 (m, 2H), 5.00 (m, 2H) and 5.81 (m, 1H).

7′-(Pent-4-enyl) 4′,7′-epoxy-4′-ethoxy-1′,3′,6′-trioxo-2′-phenylperhydrospiro [cyclopropane-1,5′-isoindole]-7′-carboxylate (26). To a refluxing solution of benzene containing 2 mg of rhodium(II) acetate was added dropwise 0.1 g (0.4 mmol) of diazo ketodiester **22**. The mixture was heated at reflux for 60 min, the solution was cooled, filtered, and concentrated under reduced pressure. The mixture was slowly added to a refluxing solution of *N*-phenylmaleimide in 10 mL of benzene. After being heated at reflux for 1h, the solution was concentrated under reduced pressure and purified by silica gel chromatography to give 0.07 g (38%) of **26** as a white solid, mp 123–124 ºC. IR (neat) 2984, 1770, 1750, 1713, and 1385 cm^{-1}; ^1H-NMR (300 MHz, $CDCl_3$): δ 1.20 (m, 1H), 1.3–1.4 (m, 6H), 1.67 (m, 2H), 2.09 (m, 2H), 3.43 (d, 1H, *J* = 7.1 Hz), 3.64 (d, 1H, *J* = 7.1 Hz), 3.94 (m, 2H), 4.40 (q, 2H, *J* = 7.1 Hz), 4.90 (m, 2H), 5.73 (m, 1H), 7.24 (m, 2H), and 7.45 (m, 3H); ^{13}C-NMR (75 MHz, $CDCl_3$): δ 13.8, 14.1, 17.0, 29.3, 29.6, 37.6, 48.6, 50.8, 62.6, 66.3, 86.5, 115.2, 126.3, 129.0, 129.3, 129.4, 131.4, 137.6, 162.2, 171.2, 171.6, 200.6. Anal. calcd. for $C_{24}H_{25}NO_7$: C, 65.59; H,5.73; N, 3.19. Found: C, 65.48; H, 5.81; N, 3.20.

Acknowledgements

We gratefully acknowledge the National Institutes of Health (GM-59384) for generous support of this work.

References and Notes

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