JOC Article

Divergence of Carbonyl Ylide Reactions as a Function of Diazocarbonyl Compound and Aldehyde Substituent: Dioxolanes, Dioxolenes, and Epoxides

Albert E. Russell,[†] Jonathan Brekan,[‡] Luisa Gronenberg,[‡] and Michael P. Doyle*[,†,‡]

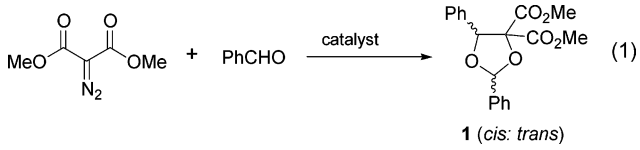
Department of Chemistry and Biochemistry, University of Maryland, College Park, Maryland, 20742, and Department of Chemistry, University of Arizona, Tuscon, Arizona 85721

mdoyle3@umd.edu

Received April 9, 2004

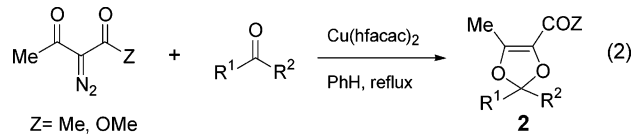
The products from dirhodium(II) acetate-catalyzed reactions between diazocarbonyl compounds and a series of benzaldehydes demonstrate the extent of competition between intramolecular and intermolecular trapping of carbonyl ylide intermediates and the electronic effects that govern these transformations. With dimethyl diazomalonate, competition exists between dioxolane and epoxide formation so that with *p*-anisaldehyde only epoxide formation is observed and with *p*-nitrobenzaldehyde only 1,3-dioxolane products are formed. With methyl diazoacetoacetate, intramolecular trapping of the intermediate carbonyl ylide results in the sole production of dioxolenes. However, the vinyldiazoacetate analogue of methyl diazoacetoacetate, as its *tert*-butyldimethlsilyloxy derivative, only produces epoxides in its reactions with substituted benzaldehydes.

Reactions of carbonyl ylides formed from diazocarbonyl compounds present a dichotomy of results.[1−3] Investigations by Huisgen and de March with dimethyl diazomalonate revealed that in reactions with benzaldehyde a mixture of isomeric 1,3-dioxolanes was formed (eq 1) with $Rh_2(OAc)_4$ (2 mol %, 75 °C, 72% of 55:45 **1**), $Cu(acac)_2$ (1 mol %, 125 °C, 82% of 55:45 **1**), and CuOTf (25 °C, 87% of 71:29 **1**), but only with $Cu(acac)_2$ was there any trace of epoxide (7%).[4] A similar outcome, that of dioxolane formation without evidence of epoxide production, was obtained in extensive investigations of the reactions of diazoacetates with benzaldehyde and substituted benzaldehydes.[5] With alkyl diazoacetates and 3-diazo-2,4-pentanedione in copper-catalyzed reactions, dioxolene formation is the sole outcome (eq 2),[6] presumably because of intramolecular trapping of the intermediate carbonyl ylide. These observations have led to extensive applications of carbonyl ylides involving [3 + 2]-cycloaddition (Scheme 1),[1−3,7−11] all without competition with epoxide formation. Contrast this then with the outcome of dirhodium(II) acetate-catalyzed reactions of phenyldiazoacetates, vinyldiazoacetates with a broad selection of aldehydes in which only stereospecific epoxide formation was observed (eq 3).[12,13] Recently, stereoselective epoxide formation has been achieved from cyclic diazoamides.[14]



(1)

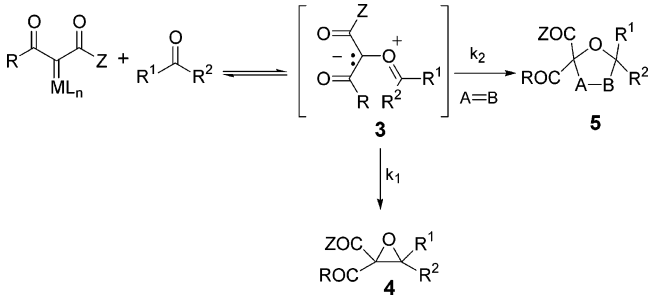
1 (*cis: trans*)



(2)

2

SCHEME 1

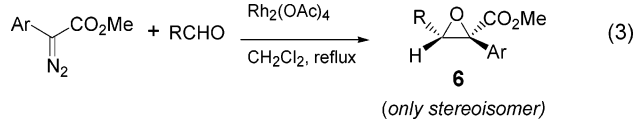


[†] University of Maryland.
[‡] University of Arizona.

(1) Doyle, M. P.; McKervey, M. A.; Ye, T. *Modern Catalytic Methods for Organic Synthesis with Diazo Compounds*; John Wiley and Sons: New York, 1998.
(2) (a) Padwa, A.; Hornbuckle, S. F. *Chem. Rev.* **1991**, *91*, 223. (b) Padwa, A.; Weingarten, M. D. *Chem. Rev.* **1996**, *96*, 223.
(3) Hodgson, D. M.; Pirard, Y. T. M.; Stupple, P. A. *Chem. Soc. Rev.* **2001**, *30*, 50.
(4) de March, P.; Huisgen, R. *J. Am. Chem. Soc.* **1982**, *104*, 4952.
(5) Doyle, M. P.; Forbes, D. C.; Protopopova, M. N.; Stanley, S. A.; Vasbinder, M. M.; Xavier, K. R. *J. Org. Chem.* **1997**, *62*, 7210.
(6) Alonso, M. E.; del Carmen García, M.; Chitty, A. W. *J. Org. Chem.* **1985**, *50*, 3445.
(7) Huisgen, R.; de March, P. *J. Am. Chem. Soc.* **1982**, *104*, 4953.
(8) (a) Alt, M.; Maas, G. *Tetrahedron* **1994**, *50*, 7435. (b) Alt, M.; Maas, G. *Chem. Ber.* **1994**, *127*, 1537.
(9) (a) Padwa, A.; Snyder, J. P.; Curtis, E. A.; Sheehan, S. M.; Worsencroft, K. M.; Kappe, C. O. *J. Am. Chem. Soc.* **2000**, *122*, 8155. (b) Padwa, A.; Zhang, Z. J.; Zhi, L. *J. Org. Chem.* **2000**, *65*, 5223.
(10) Hodgson, D. M.; Glen, R.; Grant, G. H.; Redgrave, A. J. *J. Org. Chem.* **2002**, *67*.
(11) Kitagaki, S.; Anada, M.; Kataoka, O.; Matsumo, K.; Umeda, C.; Watanabe, N.; Hashimoto, S. *J. Am. Chem. Soc.* **1999**, *121*, 1417.
(12) Doyle, M. P.; Hu, W.; Timmons, D. J. *Org. Lett.* **2001**, *3*, 933.
(13) Davies, H. M. L.; DeMeese, J. *Tetrahedron Lett.* **2001**, *42*, 6803.

10.1021/jo049403y CCC: $27.50
Published on Web 07/07/2004

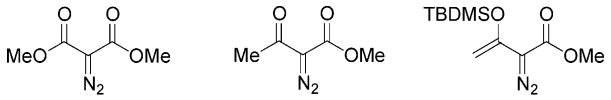
On the basis of these results, carbonyl ylide intermediates (Scheme 1) are precursors to both epoxide and cycloaddition products, but the factors that govern product selectivity are not evident. We now report results that define electronic factors that control this selectivity.



(3)

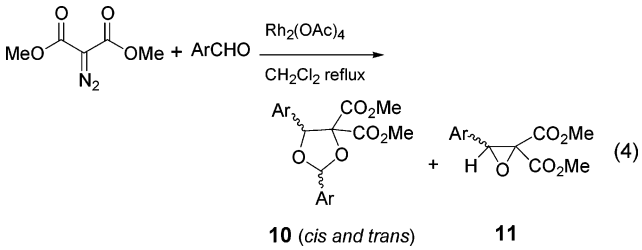
Results and Discussion

To determine the influence of structure on product selectivity, we employed three diazocarbonyl compounds (**7**−**9**), each addressing a specific potentiality in reactions with a series of aldehydes. In the first case, dimethyl diazomalonate (**7**) was selected because of its prior uses for ylide generation, albeit under harsher conditions than those employed in this study.[4,7] Davies has previously



7 **8** **9**

reported[15] from competitive cyclopropanation reactions that electrophilic effects observed with diazomalonate fall between those of phenyldiazoacetate and ethyl diazoacetate, and we have reported that in reactions with aldehydes phenyldiazoacetate forms epoxides[12] and diazoacetates form dioxolanes.[5] In the present study with dimethyl diazomalonate (**7**), using only 1 equiv of an aromatic aldehyde for $Rh_2(OAc)_4$-catalyzed reactions in refluxing dichloromethane, both dioxolane (**10**) and epoxide (**11**) products (eq 4) were obtained in relative amounts that were dependent on the aldehyde substituent (Table 1).



10 (*cis and trans*) **11**

(4)

Product yields were good, despite the requirement of 2 equiv of aldehyde for the formation of **10**. The amount of aldehyde employed, as expected on the basis of the proposed mechanism,[12] changed the ratio of **10**/**11**, so when 2.0 equiv of benzaldehyde was used, the ratio of **10**/**11** increased from 44:56 to 81:19, and with 5.0 equiv the ratio was 91:9 in favor of the dioxolane. Figure 1 describes the degree of change in the product distribution of epoxide and dioxolane relative to the concentration of aldehyde employed. Extreme cases were omitted because there was either no epoxide formation (*p*-trifluoromethylbenzaldehyde, *p*-nitrobenzaldehyde) or no dioxolane formation (*p*-anisaldehyde) at higher concentrations of aldehyde. When 2.0 or 5.0 equiv of *p*-trifluoromethylbenzaldehyde was employed, epoxidation was not evident, and only dioxolane formation occurred. More evident was the transition that occurred when a moderately electron-withdrawing substituent was attached to benzaldehyde such as in *p*-chlorobenzaldehyde. When 1.0 equiv of *p*-chlorobenzaldehyde was used, the ratio of dioxolane to epoxide was similar to that of benzaldehyde, 57:43. An increase in the amount of *p*-chlorobenzaldehyde to 2.0 equiv changed the ratio drastically in favor of the dioxolane 87:13. A 5-fold increase in the molar amount of *p*-chlorobenzaldehyde resulted in almost exclusive dioxolane formation (95:5 in favor of the dioxolane). Product yields decreased as the relative amount of aldehyde was increased which, we believe, was the result of complexation between the aldehyde and the dirhodium(II) acetate catalyst.[16] When 5.0 equiv of *p*-anisaldehyde was employed under the standard reaction conditions with diazomalonate, only starting materials were recovered. Even when the reaction of *p*-anisaldehyde with dimethyl diazomalonate was performed in refluxing 1,2-dichloroethane with 5.0 equiv of *p*-anisaldehyde, product formation did not occur. Stereochemical assignments for the *cis*-isomer were made through NOE correlations with *cis*-**10e** (2.1% between hydrogens on C-2 and C-4, for example).

TABLE 1. Product Formation from $Rh_2(OAc)_4$-Catalyzed Reactions of Dimethyl Diazomalonate with Substituted Benzaldehydes[a]

entry	Ar =	isolated yield,[b] % **10** + **11**	**10**/**11**[c]	*cis*-**10**/ *trans*-**10**[c]
a	*p*-$MeOC_6H_4$	62	0:100	
b	*p*-MeC_6H_4	52	20:80	1.4:1
c	C_6H_5	53	44:56	1.4:1
d	*p*-ClC_6H_4	54	57:43	1.6:1
e	*p*-$F_3CC_6H_4$	50	80:20	1.5:1
f	*p*-$NO_2C_6H_4$	47	100:0	1.7:1

[a] Reactions performed in refluxing dichloromethane with 1.0 mol % $Rh_2(OAc)_4$ and a molar equivalent amount of aldehyde, based on diazomalonate. [b] Isolated weight yield of chromatographically pure **10** + **11**. [c] Determined by ^1H NMR analyses prior to chromatographic purification.

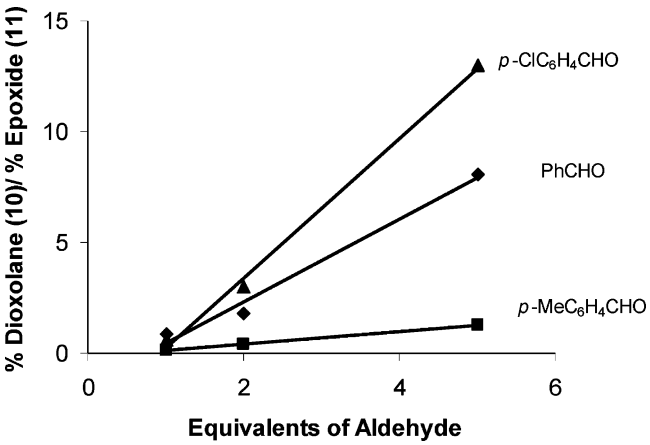


FIGURE 1. Comparison of product distribution versus aldehyde equivalents.

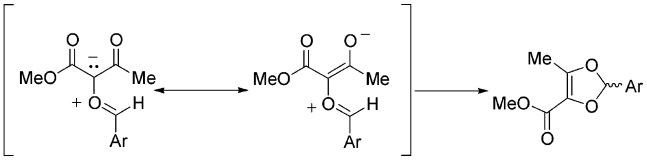
(14) Muthusamy, S.; Gunanathan, C.; Nethaji, M. *Synlett* **2004**, *4*, 639.
(15) Davies, H. M. L.; Panaro, S. A. *Tetrahedron* **2000**, *56*, 4871.
(16) Doyle, M. P.; Valenzuela, M. V.; Huang, P. L. *PNAS* **2004**, *15*, 5391.

TABLE 2. Dioxolene (12) Formation from $Rh_2(OAc)_4$-Catalyzed Reactions of Methyl Diazoacetoacetate and Substituted Benzaldehydes[a]

entry	Ar =	isolated yield,[b] % **12**
a	*p*-$MeOC_6H_4$	57
b	*p*-MeC_6H_4	56
c	C_6H_5	50 (84)[c] (75)[d]
d	*p*-$NO_2C_6H_4$	65
e	*p*-FC_6H_4	75[e]

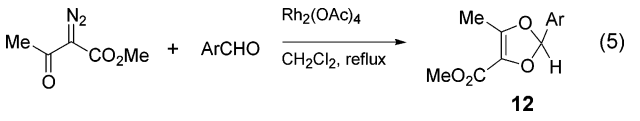
[a] Reactions performed in refluxing dichloromethane with 1.0 mol %$Rh_2(OAc)_4$ and an equivalent amount of aldehyde, based on diazomalonate. [b] Isolated weight yield of chromatographically pure **12**. [c] Isolated yield of dioxolene from reaction with 2.0 equiv of aldehyde. [d] Isolated yield of dioxolene from reaction with 5.0 equiv of aldehyde. [e] Product **e** decomposes readily upon standing.

SCHEME 2



The crossover from exclusive epoxide to exclusive dioxolane formation as the benzaldehyde substituent is changed from *p*-MeO to *p*-NO_2 is quite striking. When *p*-anisaldehyde is employed (Table 1, **a**) epoxidation is the only process that occurs. Stabilization of the intermediate ylide (**3**) may account for its diminished relative reactivity toward a second molecule of *p*-anisaldehyde. With *p*-trifluoromethylbenzaldehyde on the other hand, epoxidation is diminished and dioxolane formation is favored (Table 1, **e**). When *p*-nitrobenzaldehyde is employed (Table 1, **f**), a complete reversal from epoxide to dioxolane is observed, apparently due to destabilization of the intermediate ylide.

In terms of the rate of diazo decomposition, the reactivity difference between diazoacetoacetates and diazomalonates is minimal.[1] However, there is a stark difference in product formation from reactions performed with these compounds. Intramolecular trapping of an intermediate carbonyl ylide is the dominant chemical process for diazoacetoacetates. As reported by Alonso, dioxolene formation occurs exclusively and in moderate to high yields in reactions between methyl diazoacetoacetate and selected aldehydes[17] or ketones.[6] Our results (eq 5) using only 1.0 equiv of a substituted benzaldehyde and methyl diazoacetoacetate confirm the exclusive formation of dioxolene (**12**), even in reactions with *p*-anisaldehyde. In the case of benzaldehyde (Table 2, **c**), the yield of dioxolene is increased by employing 2 equiv of aldehyde. However, no dioxolane formation occurs in the presence of 2.0 or 5.0 equiv of benzaldehyde. The greater nucleophilicity of the keto carbonyl oxygen is the probable cause for this pathway (Scheme 2).



(5)

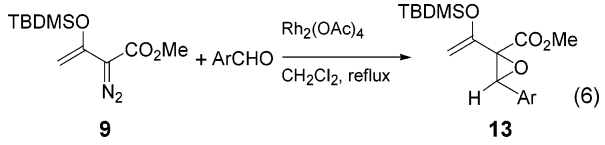
(17) (a) Alonso, M. E.; Chitty, A. W. *Tetrahedron Lett.* **1981**, *22*, 4181. (b) Alonso, M. E.; Jano, P. *J. Heterocycl. Chem.* **1980**, *17*, 721.

TABLE 3. Epoxide (13) Formation from $Rh_2(OAc)_4$-Catalyzed Reactions of Methyl 3-(*tert*-Butyldimethylsilyloxy)-2-diazo-3-butenoate (9) and Aldehydes[a]

entry	Ar =	isolated yield,[b] % **13**
a	*p*-$MeOC_6H_4$	52
b	*p*-MeC_6H_4	43
c	C_6H_5	50 (12)[c] (16)[d]
d	*p*-ClC_6H_4	30
e	*trans*-PhCH=CH	67
f	2-naphthyl	60
g	*trans*-$C_5H_{11}CH$=CH	51
h	3,4-$CH_2(O)_2C_6H_3$	32
i	*p*-$NO_2C_6H_4$	0

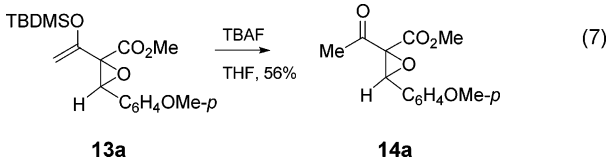
[a] Reactions performed in refluxing dichloromethane with 1.0 mol % $Rh_2(OAc)_4$ and an equivalent amount of aldehyde, based on **9**. [b] Isolated weight yield of chromatographically pure **13**. [c] Reaction conducted with 2.0 equiv of PhCHO. [d] Reaction conducted with 5.0 equiv of PhCHO.

Reactions with vinyl ether **9** were conducted to further understand the electronic and structural properties that govern product formation. Diazo decomposition of **9**, catalyzed by $Rh_2(OAc)_4$ in the presence of 1.0 equiv of a broad selection of aldehydes, resulted solely in epoxide formation without evidence of any side product including dihydrofuran (eq 6).[13] Isolated yields (Table 3) were



(6)

modest, owing in part to decomposition of **13** upon chromatographic purification, but reactions were clean, and only one epoxide diastereoisomer was formed. Access to the α-keto epoxide was achieved by simple tetrabutylammonium fluoride (TBAF) deprotection of the product of *p*-anisaldehyde and vinyl diazoacetate **9** (eq 7). The α-keto epoxide, which is formally the product from epoxidation of methyl diazoacetoacetate, was generated in 56% yield.



(7)

In conclusion, epoxides, dioxolanes, or dioxolenes are generated from diazocarbonyl compounds based on careful selection of the reaction conditions and starting materials. We are able to direct the decomposition of diazomalonates to produce epoxide or dioxolane by influencing the stability of the intermediate carbonyl ylide. The internal carbonyl oxygen of diazoacetoacetates on the other hand, circumvents pathways to either epoxide or dioxolane. Vinyldiazoacetate **9** retains the electrophilic control required for the collapse of the intermediate ylide to form the corresponding epoxide.

Experimental Section

Representative Procedure for Diazo Decomposition with Dimethyl Diazomalonate. To an oven-dried 25 mL two-necked round-bottom flask equipped with a condenser was added 4.4 mg (0.010 mmol) of dirhodium(II) acetate. The flask was sealed with a septum and purged with nitrogen. Under an atmosphere of nitrogen, 10 mL of dichloromethane was added. Neat aldehyde (1.0 mmol) was then added via syringe. The mixture was brought to reflux, and a 0.20 M solution of dimethyl diazomalonate[18] (158 mg, 1.0 mmol in 5.0 mL dichloromethane) was added over the course of 1 h via syringe pump. After the addition was complete, the reaction mixture was allowed to reflux for an additional 1 h. The mixture was then filtered through a plug of silica, and the solvent was removed under reduced pressure.

Dimethyl 2,5-Di(*p*-tolyl)-1,3-dioxolane-4,4-dicarboxylate (10b): ^{1}H NMR ($CDCl_3$, 400 MHz) (*cis*-**10b**) δ 7.66 (d, J = 8.0 Hz, 4H), 7.37 (d, J = 8.0 Hz, 4H), 6.00 (s, 1H), 5.83 (s, 1H) 3.77 (s, 3H), 3.38 (s, 3H), 2.36 (s, 6H); ^{13}C NMR ($CDCl_3$, 100 MHz) 172.1, 168.4, 144.6, 140.2, 138.5, 132.2, 131.2, 128.9, 128.77, 127.82, 105.3, 86.9, 83.7 53.5, 52.6, 21.7, 21.4; HRMS for $C_{21}H_{22}O_6$ (*cis*-**10b**) [M + 1] calcd 371.14, found 371.1495; HRMS for $C_{13}H_{14}O_5$ (**11b**) [M + 1] 251.08, found 251.0919. Compound *cis*-**10b** was isolated as an inseparable mixture with **11b** after repeated attempts at purification via flash chromatography and prep-TLC (**11b**/*cis*-**10b** ratio 3.3:1): ^{1}H NMR ($CDCl_3$, 400 MHz) (*trans*-**10b**) δ 7.35 (t, J = 8.0 Hz, 4H), 7.17 (t, J = 8.0 Hz, 4H), 6.76 (s, 1H), 5.81 (s, 1H) 3.79 (s, 3H), 3.29 (s, 3H), 2.36 (s, 3H), 2.33 (s, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz) 167.4, 167.1, 139.2, 138.4, 134.7, 132.1, 129.1, 128.9, 126.7, 126.2, 106.4, 88.2, 81.9, 53.2, 52.4, 21.3, 21.2; HRMS for $C_{21}H_{22}O_6$ [M + 1] calcd 371.14, found 371.1501.

Dimethyl 2,5-di(*p*-chlorophenyl)-1,3-dioxolane-4,4-dicarboxylate (10d): ^{1}H NMR ($CDCl_3$, 250 MHz) (*cis*-**10d**) δ 7.77 (d, J = 8.5 Hz, 2H), 7.46 (m, 4H), 7.35 (d, J = 8.5 Hz, 2H) 6.06 (s, 1H), 5.86 (s, 1H) 3.89 (s, 3H), 3.29 (s, 3H); ^{13}C NMR ($CDCl_3$, 62.5 MHz) 168.0, 166.7, 136.3, 134.8, 133.4, 132.5, 129.3, 128.8, 128.4, 128.2, 104.7, 86.8, 83.2, 53.4, 52.5; HRMS for $C_{19}H_{16}Cl_2O_6$ [M + 1] calcd 411.03, found 411.0392; ^{1}H NMR ($CDCl_3$, 250 MHz) (*trans*-**10d**) δ 7.48−7.31 (m, 8H, aromatic), 6.75 (s, 1H), 5.77 (s, 1H) 3.81 (s, 3H), 3.32 (s, 3H); ^{13}C NMR ($CDCl_3$, 62.5 MHz) 166.9, 166.6, 135.9, 135.5, 134.7, 133.3, 128.7, 128.4, 128.1, 127.6, 105.7, 88.1, 81.3, 53.4, 52.6; HRMS for $C_{19}H_{16}Cl_2O_6$ [M + 1] calcd 411.03, found 411.0392.

Dimethyl 2,5-di(*p*-trifluoromethylphenyl)-1,3-dioxolane-4,4-dicarboxylate (10e): ^{1}H NMR ($CDCl_3$, 250 MHz) (*cis*-**10e**) δ 7.95 (d, J = 8.0 Hz, 2H), 7.73 (d, J = 8.0 Hz, 2H), 7.64 (dd, J = 11.5, 9 Hz, 4H), 6.15 (s, 1H), 5.96 (s, 1H), 3.91 (s, 3H), 3.22 (s, 3H); ^{13}C NMR ($CDCl_3$, 62.5 MHz) 167.8, 166.4, 138.6, 137.9, 132.7, 132.1, 131.4, 130.9, 128.3, 127.3, 125.6, 125.5, 104.6, 86.9, 83.2, 53.5, 52.5; HRMS for $C_{21}H_{16}F_6O_6$ [M + 1] calcd 479.09, found 479.0931; ^{1}H NMR ($CDCl_3$, 250 MHz) (*trans*-**10e**) δ 7.67−7.65 (m, 8H), 6.85 (s, 1H), 5.84 (s, 1H) 3.83 (s, 3H), 3.28 (s, 3H); ^{13}C NMR ($CDCl_3$, 62.5 MHz) 166.7, 166.3, 141.1, 138.6, 131.9, 131.5, 131.3, 130.9, 127.1, 126.6, 125.6, 125.5, 105.6, 88.2, 81.4, 53.5, 52.6; HRMS for $C_{21}H_{16}F_6O_6$ [M + 1] calcd 479.09, found 479.0931.

Dimethyl 2,5-Di(*p*-nitrophenyl)-1,3-dioxolane-4,4-dicarboxylate (10f): ^{1}H NMR ($CDCl_3$, 250 MHz) (*cis*-**10f**) δ 8.35 (d, J = 9.0 Hz, 2H), 8.24 (d, J = 8.75 Hz, 2H), 8.01 (d, J = 8.75 Hz, 2H), 7.72 (d, J = 8.5 Hz, 2H) 6.21 (s, 1H), 6.00 (s, 1H), 3.94 (s, 3H), 3.27 (s, 3H); ^{13}C NMR ($CDCl_3$, 62.5 MHz) 167.5, 166.1, 149.2, 148.3, 141.1, 140.6, 128.9, 127.8, 123.8, 123.4, 104.1, 86.9, 83.0, 53.8, 52.8; HRMS for $C_{19}H_{16}N_2O_{10}$ [M + 1] calcd 433.08, found 433.0884; ^{1}H NMR ($CDCl_3$, 250 MHz) (*trans*-**10f**) δ 8.23 (q, J = 9.0 Hz, 4H), 7.72 (d, J = 8.5 Hz, 4H), 6.88 (s, 1H), 5.85 (s, 1H) 3.86 (s, 3H), 3.33 (s, 3H); ^{13}C NMR ($CDCl_3$, 62.5 MHz) 166.4, 166.0, 148.8, 148.2, 143.7, 141.4, 127.7, 127.2, 123.9, 123.4, 105.2, 88.2, 81.2, 53.7, 52.8; HRMS for $C_{19}H_{16}N_2O_{10}$ [M + 1] calcd 479.09, found 479.0931. When the reaction was carried out with 2.0 equiv of *p*-nitrobenzaldehyde the ratio **10a**/**11a** = 100:0 (6.0% yield). When the reaction was carried out with 5.0 equiv of *p*-nitrobenzaldehyde no reaction occurred. The limited solubility of *p*-nitrobenzaldehyde at higher molar amounts is a probable cause for its lowered reactivity at 2.0 and 5.0 equiv.

Dimethyl 3-(*p*-methoxyphenyl)oxirane-2,2-dicarboxylate (11a): ^{1}H NMR ($CDCl_3$, 250 MHz) δ 7.24 (d, J = 8.5 Hz, 2H), 6.87 (d, J = 8.5 Hz, 2H), 4.52 (s, 1H), 3.86 (s, 3H), 3.79 (s, 3H), 3.60 (s, 3H); ^{13}C NMR ($CDCl_3$, 62.5 MHz) 165.8, 164.0, 160.2, 127.3, 123.6, 113.8, 63.1, 62.2, 55.1, 53.4, 52.5; HRMS for $C_{13}H_{14}O_6$ [M + 1] calcd 267.08, found 267.0870. When the reaction was carried out with 2.0 equiv of *p*-anisaldehyde the ratio of **10a**/**11a** = 0:100 (20% yield). When the reaction was carried out with 5.0 equiv of *p*-anisaldehyde no reaction occurred.

Dimethyl 3-(*p*-tolyl)oxirane-2,2-dicarboxylate (11b): ^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.17 (q, J = 8.0 Hz, 4H), 4.53 (s, 1H), 3.86 (s, 3H), 3.59 (s, 3H), 2.33(s, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz) 165.8, 164.0, 139.1, 129.1, 128.8, 125.9, 63.1, 62.3, 53.4, 52.5, 21.2; HRMS for $C_{13}H_{14}O_5$ [M + 1] calcd 251.08, found 251.0925. When the reaction was carried out with 2.0 equiv of *p*-tolualdehyde the ratio of **10a**/**11a** = 36:64 (17% yield). When the reaction was carried out with 5.0 equiv of *p*-tolualdehyde the ratio **10a**/**11a** = 51:49 (14% yield).

Dimethyl 3-phenyloxirane-2,2-dicarboxylate (11c): ^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.25 (s, 5H), 4.50 (s, 1H), 3.80 (s, 3H), 3.3.49 (s, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz) 165.8, 164.0, 131.8, 129.2, 128.4, 126.0, 63.1, 62.3, 53.5, 52.5; HRMS for $C_{12}H_{12}O_5$ [M + 1] calcd 237.07, found 237.0763; HRMS for $C_{18}H_{19}O_6$ [M + 1] calcd 342.11, found 342.1107. The product was obtained as an inseparable mixture with dimethyl 2,5-diphenyl-1,3-dioxolane-4,4 dicarboxylate (*cis*-**10c** and *trans*-**10c**). Repeated attempts at product separation by flash chromatography or prep-TLC were unsuccessful. Spectral details are available in the Supporting Information. When the reaction was carried out with 2.0 equiv of benzaldehyde the ratio of **10a**/**11a** = 75:25 (35% yield). When the reaction was carried out with 5.0 equiv of benzaldehyde the ratio of **10a**/**11a** = 91:9 (20% yield).

Dimethyl 3-(*p*-chlorophenyl)oxirane-2,2-dicarboxylate (11d): ^{1}H NMR ($CDCl_3$, 250 MHz) δ 7.30 (q, J = 8.5 Hz), 4.54 (s, 1H), 3.88 (s, 3H), 3.60 (s, 3H); ^{13}C NMR ($CDCl_3$, 62.5 MHz): 165.5, 163.7, 135.2, 130.4, 128.7, 127.5, 63.0, 61.6, 53.6, 52.7; HRMS for $C_{12}H_{11}ClO_5$ [M + 1] calcd 271.03, found 271.0374. When the reaction was carried out with 2.0 equiv of *p*-chlorobenzaldehyde the ratio of **10a**/**11a** = 83:17 (28% yield). When the reaction was carried out with 5.0 equiv of *p*-chlorobenzaldehyde the ratio of **10a**/**11a** = 95:5 (4% yield).

Dimethyl 3-(*p*-trifluoromethylphenyl)oxirane-2,2-dicarboxylate (11e): ^{1}H NMR ($CDCl_3$, 250 MHz) δ 7.68−7.58 (m, 2H), 7.47 (d, J = 7.8 Hz), 4.62 (s, 1H), 3.89 (s, 3H), 3.59 (s, 3H); ^{13}C NMR ($CDCl_3$, 62.5 MHz) 165.4, 163.6, 135.9, 131.5, 131.3, 126.6, 90.3, 63.0, 61.4, 53.7, 52.8; HRMS for $C_{13}H_{11}F_3O_5$ [M + 1] calcd 305.06, found 305.0641. Compound **11e** was isolated as an inseparable mixture with *cis*-**10e** after repeated attempts at purification via flash chromatography and prep-TLC (**11e**/**10e** ratio 1.6:1). When the reaction was carried out with 2.0 equiv of *p*-trifluoromethylbenzaldehyde the ratio of **10a**/**11a** = 100:0 (39% yield). When the reaction was carried out with 5.0 equiv of *p*-trifluoromethylbenzaldehyde the ratio of **10a**/**11a** = 100:0 (14% yield).

Representative Procedure for Diazo Decomposition Reaction with Methyl Diazoacetoacetate. To an oven-dried 25 mL two-necked round-bottom flask equipped with a condenser was added 4.4 mg (0.01 mmol) of dirhodium(II) acetate. The flask was sealed with a septum and purged with nitrogen. Under an atmosphere of nitrogen, 10 mL of dichloromethane was added. Neat aldehyde (1.0 mmol) was then added

(18) Tullis, J. S.; Helquist, P. *Org. Synth.* **1997**, *74*, 229.

via syringe. The mixture was brought to reflux, and 5 mL of a 0.20 M solution of methyl diazoacetoacetate[19] (142 mg, 1.0 mmol in 5.0 mL dichloromethane) was added over the course of 1 h via syringe pump. After the addition was complete, the reaction mixture was allowed to reflux for an additional 2.5 h. The mixture was then filtered through a plug of silica and solvent removed via rotary evaporation. The crude oil was purified via flash chromatography (20:1 hexanes/ethyl acetate, 1% triethylamine). It should be noted that these compounds decompose readily in the presence of excess moisture and care should be taken to store them in a dry place.

Methyl 5-methyl-2-(*p*-methoxyphenyl)-1,3-dioxole-4-carboxylate (12a): ^{1}H NMR ($CDCl_3$, 300 MHz) δ 7.47 (d, J = 9.0 Hz, 2H), 6.93 (d, J = 9.0 Hz, 2H), 6.62 (s, 1H), 3.82 (s, 6H), 2.26 (s, 3H); ^{13}C NMR ($CDCl_3$, 75 MHz) 161.1, 149.2, 131.9, 128.0, 127.2, 114.3, 113.9, 108.0, 55.3, 51.5, 11.3; HRMS for $C_{13}H_{14}O_5$ [M + 1] calcd 251.08, found 251.0921.

Methyl 5-methyl-2-(*p*-tolyl)-1,3-dioxole-4-carboxylate (12b): ^{1}H NMR ($CDCl_3$, 300 MHz) δ 7.43 (d, J = 8.0 Hz, 2H), 7.23 (d, J = 9.0 Hz, 2H), 6.69 (s, 1H), 3.82 (s, 3H), 2.38 (s, 3H), 2.26 (s, 3H); ^{13}C NMR ($CDCl_3$, 75 MHz) 161.0, 149.2, 140.2, 133.0, 129.2, 127.2, 126.4, 107.9, 51.6, 21.3, 11.4; HRMS for $C_{13}H_{14}O_4$ [M + 1] calcd 235.09, found 235.0975.

Methyl 5-methyl-2-phenyl-1,3-dioxole-4-carboxylate (12c): ^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.43 (d, J = 8.0 Hz, 2H), 7.51−7.39 (m, 2H), 7.38−7.29 (m, 3H), 6.60 (s, 1H), 3.70 (s, 3H), 2.16 (s, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz) 160.7, 148.9, 135.7, 129.9, 128.3, 127.0, 126.2, 107.6, 51.3, 11.1; HRMS for $C_{12}H_{12}O_4$ [M + 1] calcd 220.07, found 220.0736.

Methyl 5-methyl-2-(*p*-nitrophenyl)-1,3-dioxole-4-carboxylate (12d): ^{1}H NMR ($CDCl_3$, 300 MHz) δ 8.29 (d, J = 4.8 Hz, 2H), 7.74 (d, J = 4.8 Hz, 2H), 6.80 (s, 1H), 3.84 (s, 3H), 2.28 (s, 3H); ^{13}C NMR ($CDCl_3$, 75 MHz) 160.5, 148.6, 142.6, 143.8, 127.3, 127.1, 123.7 105.7, 51.7, 11.2; HRMS for $C_{12}H_{11}NO_6$ [M + 1] calcd 266.06, found 266.0660.

Methyl 5-methyl-2-(*p*-fluorophenyl)-1,3-dioxole-4-carboxylate (12e): ^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.45 (dd, J = 6.0 Hz, 2H), 7.06 (t, J = 8.8 Hz, 2H), 6.63 (s, 1H), 3.76 (s, 3H), 2.20 (s, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz) 162.5, 160.8, 149.0, 128.5, 128.4, 127.2, 115.7, 115.4, 51.5, 11.2. This compound decomposed readily upon standing. Repeated attempts at column chromatography all resulted in product decomposition.

Representative Procedure for Diazo Decomposition Reaction with Methyl 3-(*tert*-Butyldimethylsilanoxy)-2-diazobut-3-enoate. To an oven-dried 25 mL two-necked round-bottom flask equipped with a condenser was added 4.4 mg (0.010 mmol, 0.010 equiv) of dirhodium(II) acetate. The flask was sealed with a septum and purged with nitrogen. Under an atmosphere of nitrogen, 10 mL of dichloromethane was added. Neat aldehyde (1.0 mmol, 1.0 equiv) was then added via syringe. The mixture was brought to reflux, and a 0.20 M solution of methyl 3-(*tert*-butyldimethylsilanoxy)-2-diazobut-3-enoate[20] (256 mg, 1.0 mmol, 1.0 equiv in 5 mL of dichloromethane) was added over the course of 1 h via syringe pump. After the addition was complete, the reaction mixture was allowed to reflux for an additional 1 h. The mixture was then filtered through a plug of silica, and the solvent was removed under reduced pressure.

Methyl 2-(1-*tert*-butyldimethylsilanoxy-1-vinyl)-3-(*p*-methoxyphenyl)-2,3-epoxypropanoate (13a): ^{1}H NMR ($CDCl_3$, 300 MHz) δ 7.24 (d, J = 8.8 Hz, 2H), 6.85 (d, J = 8.8 Hz, 2H), 4.60 (d, J = 2.2 Hz, 1H), 4.50 (d, J = 2.2 Hz, 1H), 4.32 (s, 1H), 3.79 (s, 3H), 3.53 (s, 3H), 0.95 (s, 9H), 0.22 (d, J = 1.9 Hz, 6H); ^{13}C NMR ($CDCl_3$, 75 MHz) 166.4, 159.6, 151.7, 127.1, 125.4, 113.5, 94.7, 66.6, 61.5, 55.1, 51.9, 25.4, 18.0, −4.9, −5.2; HRMS for $C_{19}H_{28}O_5Si$ [M + 1] calcd 364.17, [M + 1] found 365.1787.

Methyl 2-[1-(*tert*-butyldimethylsilanoxy)vinyl]-3-(*p*-tolyl)-2,3- epoxypropanoate (13b): ^{1}H NMR ($CDCl_3$, 300 MHz) δ 7.20 (d, J = 8 Hz, 2H), 7.12 (d, J = 8 Hz, 2H), 4.61 (d, J = 2 Hz, 1H), 4.50 (d, J = 2 Hz, 1H), 4.33 (s, 1H), 3.52 (s, 3H) 2.32 (s, 3H), 0.95 (s, 9H), 0.22 (d, J = 1.9 Hz, 6H); ^{13}C NMR ($CDCl_3$, 75 MHz) 166.4, 151.8, 138.1, 130.5, 128.8, 125.8, 94.8, 66.6, 61.8, 51.9, 25.5, 21.1, 18.0, −4.8, −5.1; HRMS for $C_{19}H_{28}O_4Si$ [M + 1] calcd 349.18, [M + 1] found 349.1846.

Methyl 2-[1-(*tert*-butyldimethylsilanoxy)vinyl]-3-phenyl-2,3-epoxypropanoate (13c): ^{1}H NMR ($CDCl_3$, 300 MHz) δ 7.31 (s, 5H), 4.62 (d, J = 2.4 Hz, 1H), 4.52 (d, J = 2.4 Hz, 1H), 4.37 (s, 1H), 3.50 (s, 3H), 0.95 (s, 9H), 0.23 (d, J = 1.9 Hz, 6H); ^{13}C NMR ($CDCl_3$, 75 MHz) 166.3, 151.6, 133.6, 128.4, 128.2, 125.9, 95.0, 66.6, 61.6, 52.0, 25.5, 18.1, −4.8, −5.1; HRMS for $C_{18}H_{26}O_4Si$ [M + 1] calcd 335.16, [M + 1] found 335.1664. When the reaction was conducted with 2.0 or 5.0 equiv of benzaldehyde only epoxide was formed.

Methyl 2-[1-(*tert*-butyldimethylsilanoxy)vinyl]-3-(*p*-chlorophenyl)-2,3-epoxypropanoate (13d): ^{1}H NMR ($CDCl_3$, 300 MHz) δ 7.49−7.19 (m, 4H), 4.61 (d, J = 2.4 Hz, 1H), 4.52 (d, J = 2.4 Hz, 1H), 4.34 (s, 1H), 3.52 (s, 3H), 0.95 (s, 9H), 0.22 (d, J = 3.6 Hz, 6H); ^{13}C NMR ($CDCl_3$, 75 MHz) 166.1, 151.3, 134.3, 132.2, 128.5, 127.3, 95.2, 66.6, 61.0, 52.2, 25.5, 18.1, −4.8, −5.1; HRMS for $C_{18}H_{25}ClO_4Si$ [M + 1] calcd 369.12, [M + 1] found 369.1284.

Methyl 2-[1-(*tert*-butyldimethylsilanoxy)vinyl]-3-styryl-2,3-epoxypropanoate (13e): ^{1}H NMR δ 7.42−7.20 (m, 5H), 6.86 (d, J = 16 Hz, 1H), 5.96 (q, J = 7.8 Hz, 1H), 4.58 (d, J = 2.2 Hz, 1H), 4.46 (d, J = 2.2 Hz, 1H), 3.92 (d, J = 8.4 Hz, 1H), 3.79 (s, 3H), 0.94 (s, 9H), 0.21 (d, J = 1.6 Hz, 6H); ^{13}C NMR ($CDCl_3$, 75 MHz) 167.3, 152.1, 136.9, 135.7, 129.7, 126.4, 125.6, 121.7, 94.5, 65.2, 62.5, 53.4, 25.1, 18.1, −4.8, −5.0; HRMS for $C_{20}H_{28}O_4Si$ [M + 1] calcd 361.17, [M + 1] found 361.1830.

Methyl 2-[1-(*tert*-butyldimethylsilanoxy)vinyl]-3-naphthyl-2,3-epoxypropanoate (13f): ^{1}H NMR ($CDCl_3$, 300 MHz) δ 7.76−7.91 (m, 4H), 7.39−7.54 (m, 3H) 4.66 (d, J = 2.4 Hz, 1H), 4.60−4.49 (m, 2H), 3.44 (s, 3H), 0.97 (s, 9H), 0.25 (d, J = 1.5 Hz, 6H); ^{13}C NMR ($CDCl_3$, 75 MHz) 166.3, 151.6, 133.1, 132.9, 131.1, 128.0, 127.9, 126.2, 125.4, 123.3, 95.1, 66.9, 61.8, 52.0, 25.5, 18.1, −4.7, −5.0; HRMS for $C_{22}H_{28}O_4Si$ [M + 1] calcd 385.18, [M + 1] found 385.1838.

Methyl 2-[1-(*tert*-butyldimethylsilanoxy)vinyl]-3-((1*E*)-hept-1-enyl)-2,3-epoxypropanoate (13g): ^{1}H NMR ($CDCl_3$, 300 MHz) δ 6.20−5.88 (m, 1H), 5.17 (dd, J = 7.98 Hz, 1H), 4.49 (d, J = 2.2 Hz, 1H), 4.39 (d, J = 2.2 Hz, 1H), 3.76 (s, 3H), 3.68 (d, J = 7.8 Hz, 1H), 2.10−1.95 (m, 2H), 1.51−1.15 (m, 6H), 0.88−0.95 (m, 12H), 0.15 (d, J = 1.8 Hz, 6H); ^{13}C NMR ($CDCl_3$, 75 MHz) 167.4, 152.2, 140.1, 122.4, 94.4, 64.8, 62.2, 52.3, 32.3, 31.1, 28.3, 25.5, 22.4, 18.0, 13.9, −4.9, −5.1; HRMS for $C_{19}H_{34}O_4Si$ [M + 1] calcd 355.22, [M + 1] found 355.2303.

Methyl 2-[1-(*tert*-butyldimethylsilanoxy)vinyl]-3-benzo-3,5-diox-5-yl-2,3-epoxypropanoate (13h): ^{1}H NMR ($CDCl_3$, 300 MHz) δ 6.83−6.65 (m, 3H), 5.89 (s, 2H), 4.55 (d, J = 2.3 Hz, 1H), 4.45 (d, 2H, J = 2.3 Hz, 1H), 4.24 (s, 1H), 3.53 (s, 3H), 0.91 (s, 9H), 0.18 (d, J = 2.0 Hz, 6H); ^{13}C NMR ($CDCl_3$, 75 MHz) 166.3, 151.6, 147.7, 147.7, 127.4, 119.7, 108.1, 106.2, 101.1, 94.8, 66.6, 61.7, 52.1, 25.5, 18.0, −4.8, −5.1; HRMS for $C_{19}H_{26}O_6Si$ [M + 1] calcd 379.15, [M + 1] found 379.1571.

Synthesis of 2-Acetyl-3-(*p*-methoxyphenyl)oxirane-2-carboxylate (14a). To a crude reaction mixture containing **13a** was added 200 μL of a 1 M solution of TBAF in THF and the solution stirred for 15 min. The solution was passed through a short silica plug and concentrated under reduced pressure. The product was purified by flash chromatography: ^{1}H NMR ($CDCl_3$, 300 MHz) δ 7.23 (d, J = 9 Hz, 2H), 6.87 (d, J = 9 Hz, 2H), 4.36 (s, 1H), 3.80 (s, 3H), 3.59 (s, 3H), 2.31 (s, 3H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 164.6, 160.3, 128.0, 127.4, 123.8, 113.9, 68.6, 62.2, 55.2, 52.5, 25.3; HRMS for $C_{13}H_{14}O_5$ [M + 1] calcd 251.08, found 251.0917.

Acknowledgment. This research was initiated at the University of Arizona with undergraduate students J.B. and L.G. We are grateful to the National Science

(19) Davies, H. M. L.; Cantrell, W. R., Jr.; Romines, K. R.; Baum, J. S. *Org. Synth.* **1991**, *70*, 93.

(20) Davies, H. M.; Ahmed, G.; Churchill, M. *J. Am. Chem. Soc.* **1996**, *118*, 10774.

Foundation and to the National Institutes of Health (GM46503) for their support of this research. L.G. acknowledges the support of Pfizer, Inc., for a 2003 Pfizer Summer Undergraduate Research Fellowship in Synthetic Organic Chemistry.

Supporting Information Available: Carbon and proton spectra for reaction products. This material is available free of charge via the Internet at http://pubs.acs.org.

JO049403Y