JOC The Journal of Organic Chemistry

Article

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Substrate-Dependent Divergent Outcomes from Catalytic Reactions of Silyl-Protected Enol Diazoacetates with Nitrile Oxides: Azabicyclo[3.1.0]hexanes or 5-Arylaminofuran-2(3*H*)-ones

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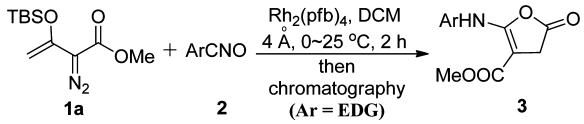
Supporting Information

ABSTRACT: Dirhodium(II)-catalyzed reactions of silyl-protected enol diazoacetates with nitrile oxides exhibit high nitrile oxide substituent dependence in the production rearrangement products via dipolar cycloaddition and either the Neber rearrangement or the Lossen rearrangement.

INTRODUCTION

Catalytically generated metal carbenes from rhodium-catalyzed reactions of diazo compounds are known mainly for their versatility in reactions that include cyclopropanation and cyclopropenation, ylide formation and rearrangements, and carbon−hydrogen insertion.[1,2] However, as we have recently demonstrated,[3,4] there are a variety of alternative metal carbene-dependent processes that offer intriguing possibilities for chemical syntheses. In order to understand metal carbene-dependent extensions in reactivity and selectivity, we have been investigating catalytic reactions of enol diazoacetates that include 3-(*tert*-butyldimethylsiloxy)-2-diazo-3-butenoates **1**,[4] a subset of vinyl diazoacetates that have been introduced and extensively studied by Davies and co-workers.[5] We recognized that dinitrogen extrusion by dirhodium(II) changes the polarity of the bound carbon from being electron-rich in the diazo compound to electron-deficient in the metal carbene.[6−8] Based on this principle, we have developed a novel formal [3 + 3] cycloaddition[7] and an alternative transformation for the functionalized pyrrole synthesis with nitrone.[8] Recently, we reported an unexpected catalytic reaction of enol diazoacetate **1a** with nitrile oxides having electron-donating substituents that form 5-arylaminofuran-2(3*H*)-one-4-carboxylates **3** in high yield (Scheme 1).[9] However, a constitutionally isomeric product was detected when nitrile oxides having halide or electron-withdrawing substituents were used. Spectral analyses were insufficient to completely identify the structure of this compound, so crystals of the product from the reaction with *o*-nitrobenzonitrile-*N*-oxide (**2g**) that resulted in the formation of only one isomer were used to obtain its X-ray structure (Figure 1). The constitutionally isomeric product is methyl 3-oxo-1-(*o*-nitrophenyl)-2-oxa-6-azabicyclo-[3.1.0]hexane-5-carboxylate **4g**. We report here the generality of this rearrangement reaction and the mechanism for its formation.

Scheme 1. 5-Arylaminofuran-2(3*H*)-one-4-carboxylates from Dirhodium(II)-Catalyzed Reactions of 1a with Nitrile Oxides Having Electron-Donating Substituents



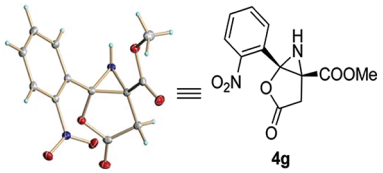


Figure 1. Crystal structure of the product **4g** from the dirhodium(II)-catalyzed reaction between **1a** and *o*-nitrobenzonitrile *N*-oxide **2g**.

RESULTS AND DISCUSSION

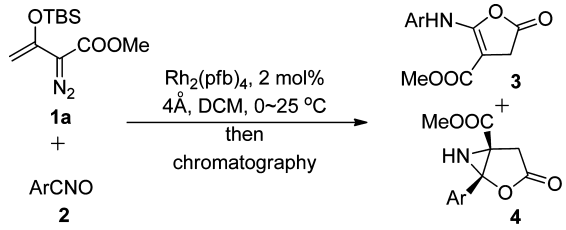
Examination of an array of monosubstituted benzonitrile oxides (Table 1) shows that aziridine derivatives, 3-oxo-1-aryl-2-oxa-6-azabicyclo[3.1.0]hexane-5-carboxylates **4**, result from reactions with benzonitrile *N*-oxides having electron-withdrawing substituents, whereas 5-arylaminofuran-2(3*H*)-one 4-carboxylates are the dominant products from reactions with benzonitrile *N*-oxides having electron-donating substituents. Both products result from rearrangement reactions that occur from the combination of enoldiazoacetate **1a** with the nitrile oxide in the presence of dirhodium(II) catalysts; in the absence of catalyst or the use of copper catalysts, TBS transfer from **1a** to the nitrile oxide occurs.[10]

We previously found that under the conditions used for reactions of **1a** with nitrile oxides, dinitrogen extrusion produces cyclopropene **5**, which undergoes subsequent uncatalyzed [2 + 3]-cycloaddition with nitrile oxides to form 2-oxa-3-azabicyclo[3.1.0]hex-3-ene **6**. Subsequent rearrangements of **6** lead to the formation of **3** (Lossen rearrangement)[9]

Received: April 5, 2012
Published: May 23, 2012

dx.doi.org/10.1021/jo3006733 | *J. Org. Chem.* 2012, 77, 5313−5317

Table 1. Nitrile Oxide Substituent Dependence in the Production Rearrangement Products[a]

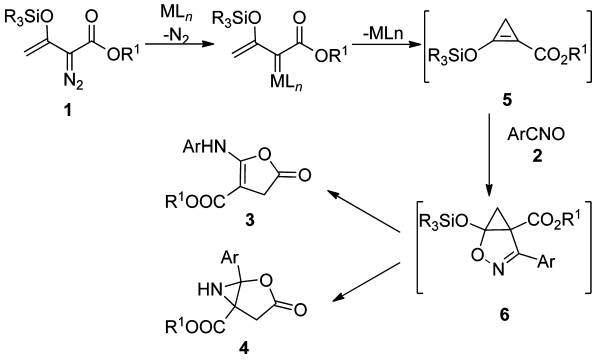


entry	Ar (2)	product	3:4[b]	yield[c] (%)
1	2-$MeOC_6H_4$ (**2a**)	**3a**	>95:5	92
2	4-MeC_6H_4 (**2b**)	**3b**, **4b**	90:10	84
3	4-FC_6H_4 (**2c**)	**3c**, **4c**	78:22	89
4	4-ClC_6H_4 (**2d**)	**3d**, **4d**	65:35	93
5	4-BrC_6H_4 (**2e**)	**3e**, **4e**	55:45	89
6	4-$AcOC_6H_4$ (**2f**)	**3f**, **4f**	39:61	81
7	2-$NO_2C_6H_4$ (**2g**)	**4g**	<5:95	90

[a]Reaction conditions: **1a** (1.2 mmol) in DCM (3.0 mL) was added over 1 h by syringe pump to mixture of 4 Å molecular sieves (100 mg), $Rh_2(pfb)_4$ (2.0 mol %), and nitrile oxide **2** (1.0 mmol) in DCM (5.0 mL) at 0 °C and stirred for 2 h at room temperature. After solvent removal, the product mixture was purified by chromatography on silica gel. [b]Determined by ^1H NMR of the reaction mixture. [c]Isolated yield of combined **3** and **4** based on limiting reagent **2**.

and, presumably, **4** (Scheme 2). We anticipated a substituent-dependent correlation between **3** and **4** if the pathways to them

Scheme 2. Divergent Outcomes from Catalytic Reactions of Silyl-Protected Enoldiazoacetates with Nitrile Oxides



are linked through **6**, and Figure 2 clearly shows linear correlation between the two processes (log [**3**]/[**4**] versus σ). The **6** → **3** conversion occurs through ring-opening of **6** (with aryl migration from carbon to nitrogen) to a ketenimine intermediate that has been intercepted and shown to undergo acid-catalyzed ring closure to **3**.[9] Could a similar ring-opening/ring closure process be occurring in the formation of **4** from **6**?

Analogous to the formation of **3** from **6**, the pathway to **4** is formally a cyclic analogue of the Neber reaction.[11] In this case ring-opening to an azirine intermediate (**7** in Scheme 3) would preface formation of the subsequent cyclization product **4**. Careful examination of the ^1H NMR data for the reaction mixture from $Rh_2(pfb)_4$ catalysis of **1a** with **2g** prior to chromatography[10] revealed that the chemical shifts of the CH_2 group protons of the product prior to chromatography were different from those of **4g**, suggesting that the initially formed reaction product is transformed into **4g** during chromatographic isolation. One possible explanation is that this pre-**4g** product is the *N*-TBS-bound aziridine **8** rather than **7**. However, the chemical shift of Si is consistent with oxygen attachment in **7** rather than nitrogen attachment in **8**.[10] Furthermore, catalysis in the formation of **4** occurs either when the product prior to chromatography is treated with saturated aqueous ammonium chloride or with silica gel during chromatography, which is also consistent with **7** as the pre-**4** product. Attempts to obtain pure crystalline **7** were not successful.

Using the combination of rhodium(II)-catalyzed formation of **7** followed by ammonium chloride promoted formation of **4**, reactions of **1a** with a series of nitrile oxides having electron-withdrawing groups were examined, and the results of this study are shown in Table 2. These reactions generate aziridine **4** as the sole product in 77−92% isolated yield. Even the *tert*-butyl ester of the enol diazoacetate (**1b**) gives comparable results. The same process and similar reactivity are observed with β-methyl-substituted enol diazoacetate **1c** that produces two diastereoisomers from its reaction with an equal amount of **2g** (Scheme 4, **4m**, 89% yield). Recognizing that stereocontrol occurs in the nitrile oxide dipolar addition step, we briefly investigated changes in R^1 and R^2 that could influence this selectivity. By increasing the size of the β-substituent of enol diazoacetates, very high diastereoselectivity (**4o**, dr >20:1) is achieved compared to increasing the size of the ester alkyl group (**4n**, dr 3:1, 83% yield). This rearrangement retains the stereochemical relationship of R^2 with the carboxylate group, and retention of configuration occurs in the formation of **4** from **7**.

Consistent with the proposed mechanism for this transformation, diastereocontrol is established in the intermolecular [3 + 2]-cycloaddition step that forms *cis*-**6** as the major product. Although the Neber rearrangement is ordinarily associated with the formation of azirines from oximes and their derivatives,[12] the formation of azirine **7** from **6** is formally the same process, and the overall scheme represents the first time that the Lossen and Neber rearrangements have been linked through one intermediate (**6**), especially with the strong correlation that is evident from the data in Figure 2.

In summary, we have discovered an unexpected duality of reactions whose outcome is substrate dependent. Occurring through unstable 2-oxa-3-azabicyclo[3.1.0]hex-3-ene **6** intermediates, electron-withdrawing substituents on the aryl group at the 4-position favor the Neber reaction, whereas electron-donating substituents direct product formation through the Lossen rearrangement. Good to excellent yields have been obtained, and direction to high diastereocontrol has been achieved in the formal Neber process. Evidence is provided that these two processes are interlinked, which has not been previously considered.

EXPERIMENTAL SECTION

General Information. Reactions were performed in oven-dried (140 °C) glassware under an atmosphere of dry N_2. Dichloromethane (DCM) was passed through a solvent column prior to use and was kept over 3 Å molecular sieves. Thin-layer chromatography (TLC) was carried out using silica gel plates; the developed chromatogram was analyzed by a UV lamp (254 nm). Liquid chromatography was performed using flash chromatography of the indicated system on silica gel (230−400 mesh). ^1H NMR and ^{13}C NMR spectra were recorded in $CDCl_3$ on a 400 MHz spectrometer; chemical shifts are reported in ppm with the solvent signals as reference, and coupling constants (J) are given in hertz. The peak information is described as follows: br = broad, s = singlet, d = doublet, t = triplet, q = quartet, m

dx.doi.org/10.1021/jo3006733 | J. Org. Chem. 2012, 77, 5313−5317

	Me	F	Cl	Br	OAc
3:**4**	9.00	3.55	1.86	1.22	0.64
log([**3**]/[**4**])	0.95	0.55	0.27	0.09	-0.19
σ	-0.17	0.06	0.23	0.23	0.31

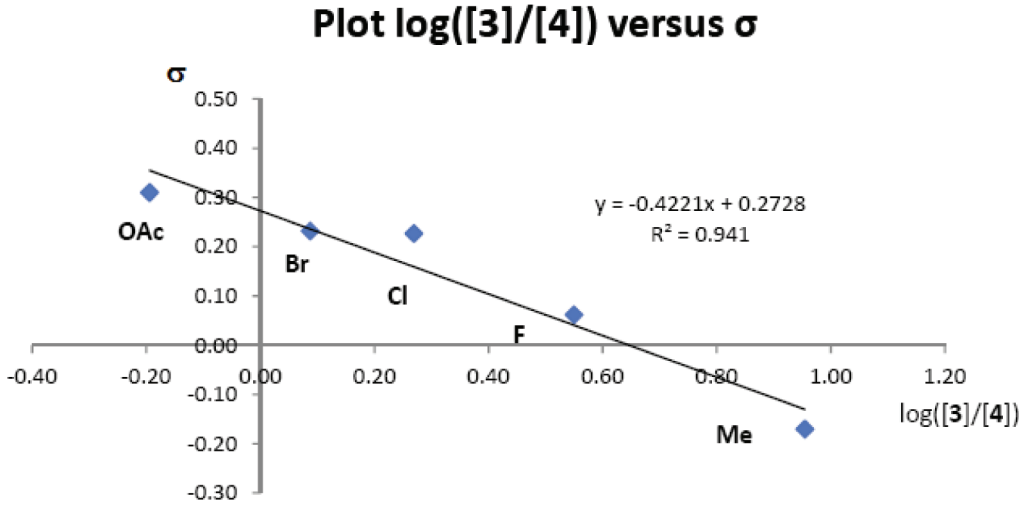


Figure 2. Plot of log([**3**]/[**4**]) vs σ: $\rho = -0.42$ ($R^2 = 0.94$).

Scheme 3. Mechanistic Possibilities for the Formation of 3-Oxo-1-aryl-2-oxa-6-azabicyclo[3.1.0]hexane-5-carboxylates (4)

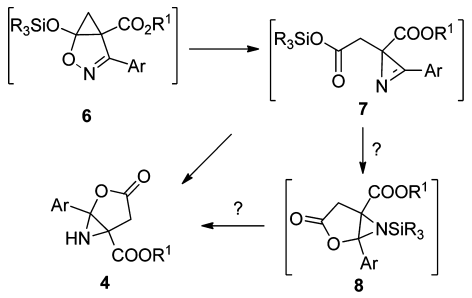
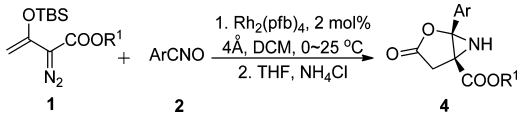


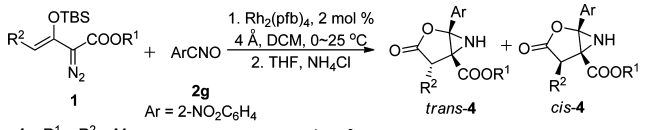
Table 2. Rhodium(II)-Catalyzed Reaction of Silyl-Protected Enoldiazoacetates with Nitrile Oxides[a]



entry	R^1 (**1**)	Ar (**2**)	product	yield[b] (%)
1	Me (**1a**)	2-$NO_2C_6H_4$ (**2g**)	**4g**	90
2	^{t}Bu (**1b**)	2-$NO_2C_6H_4$ (**2g**)	**4h**	92
3	Me (**1a**)	2,4-$(NO_2)_2C_6H_4$ (**2h**)	**4i**	81
4	^{t}Bu (**1b**)	2,4-$(NO_2)_2C_6H_4$ (**2h**)	**4j**	88
5	Me (**1a**)	2-$CF_3C_6H_4$ (**2i**)	**4k**	77
6	^{t}Bu (**1b**)	2-$CF_3C_6H_4$ (**2i**)	**4l**	82

[a]Reaction conditions: **1** (1.2 mmol) in DCM (3.0 mL) was added over 1 h via a syringe pump at 0 °C to mixture of 4 Å molecular sieves (100 mg), $Rh_2(pfb)_4$ (2.0 mol %), and nitrile oxide **2** (1.0 mmol) in DCM (5.0 mL) and stirred for another 2 h at room temperature. The crude product was hydrolyzed in THF (4.0 mL) with aqueous saturated ammonium chloride solution (2.0 mL) at 60 °C for 1−2 h. [b]Isolated yield of **4** based on limiting reagent **2**.

Scheme 4. Diastereoselectivity in Reactions of β-Substituted Enoldiazoacetates with *o*-Nitrobenzonitrile *N*-Oxide



1c, $R^1 = R^2$ = Me
1d, R^1 = Bn, R^2 = Me
1e, R^1 = Me, R^2 = Ph

$R^1 = R^2$ = Me, **4m** (*trans*:*cis* = 1:1), 89% yield.
R^1 = Bn, R^2 = Me, **4n** (*trans*:*cis* = 3:1), 83% yield.
R^1 = Me, R^2 = Ph, **4o** (*trans*:*cis* > 20:1), 57% yield.

= multiplet, comp = composite. High-resolution mass spectra (HRMS) were performed on a TOF-CS mass spectrometer using CsI as the standard. Copper hexafluorophosphate and other Lewis acids were purchased and used as received. Dirhodium tetraacetate was purchased. Other dirhodium catalysts[1a] and silyl-protected enol diazoacetates **1**[13] were synthesized according to literature procedures. Nitrile oxides **2** were synthesized according to the literature references.[14] The general procedure with corresponding data for the synthesis of 5-arylaminofuran-2(3*H*)-one-4-carboxylates (**3**) has been reported.[9]

General Procedure for the Synthesis of Azabicyclo[3.1.0]-hexanes (4). To an oven-dried flask containing a magnetic stirring bar, 4 Å molecular sieves (100 mg), $Rh_2(pfb)_4$ (2.0 mol %), and nitrile oxide **2** (1.0 mmol) in dichloromethane (5.0 mL) was added enol diazoacetate **1** (1.2 mmol) in dichloromethane (3.0 mL) over 1 h via a syringe pump at 0 °C. After addition was complete, the reaction solution was stirred for another 2 h at room temperature. Once the diazo compound was consumed (determined by a ^{1}H NMR spectrum of the crude reaction mixture), then DCM was removed under reduced pressure and THF (4.0 mL) was added; the resulting solution was stirred at 60 °C for 1−2 h with aqueous saturated ammonium chloride solution (2.0 mL). The hydrolyzed product was extracted with ether (5 mL × 3), and the combined organic phase was dried over anhydrous Na_2SO_4. After evaporation of the solvents (if necessary, the reaction mixture was subjected to ^{1}H NMR to determine the diastereoselectivity), the residue was purified by column chromatography on silica gel (eluent: hexanes/EtOAc = 10:1 to 2:1) to give the pure aziridine product **4** in high yield.

Methyl 3-oxo-1-(*p*-tolyl)-2-oxa-6-azabicyclo[3.1.0]hexane-5-carboxylate (4b): yellow oil; 21 mg, 8.4% yield; ^{1}H NMR (400 MHz,

dx.doi.org/10.1021/jo3006733 | J. Org. Chem. 2012, 77, 5313−5317

$CDCl_3$) δ (ppm) 7.38 (d, J = 8.0 Hz, 2H), 7.24 (d, J = 8.0 Hz, 2H), 3.70 (s, 3H), 3.57 (d, J = 20.0 Hz, 1H), 3.01 (d, J = 20.0 Hz, 1H), 2.91 (bs, 1H), 2.40 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) 172.67, 166.84, 140.77, 129.77, 127.64, 125.85, 81.54, 53.79, 46.18, 35.90, 21.74; HRMS (ESI) calcd for $C_{13}H_{14}NO_4$ $[M + H]^+$ 248.0917, found 248.0902.

Methyl 1-(4-fluorophenyl)-3-oxo-2-oxa-6-azabicyclo[3.1.0]-hexane-5-carboxylate (4c): white solid; mp 147−150 °C; 49 mg, 19.5% yield; ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) 7.50 (m, 2H), 7.11 (m, 2H), 3.68 (s, 3H), 3.57 (d, J = 20.0 Hz, 1H), 3.01 (d, J = 20.0 Hz, 1H), 2.99 (bs, 1); ^{13}C NMR (100 MHz, $CDCl_3$) 172.54, 166.69, 165.25 (d, J = 25.0 Hz), 129.94 (d, J = 8.0 Hz), 124.96 (d, J = 3.0 Hz), 116.21 (d, J = 22.0 Hz), 80.82, 53.85, 46.23, 35.82; HRMS (ESI) calcd for $C_{12}H_{11}FNO_4$ $[M + H]^+$ 252.0667, found 252.0671.

Methyl 1-(4-chlorophenyl)-3-oxo-2-oxa-6-azabicyclo[3.1.0]-hexane-5-carboxylate (4d): yellow solid; mp 135−136 °C; 87 mg, 32.5% yield; ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) 7.44 (q, J = 8.0 Hz, 4H), 3.72 (s, 3H), 3.61 (d, J = 20.0 Hz, 1H), 3.03 (d, J = 20.0 Hz, 1H), 2.91 (bs, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) 172.28, 166.58, 136.75, 129.36, 129.09, 127.52, 80.69, 53.94, 46.46, 35.85; HRMS (ESI) calcd for $C_{12}H_{11}ClNO_4$ $[M + H]^+$ 268.0371, found 268.0382.

Methyl 1-(4-bromophenyl)-3-oxo-2-oxa-6-azabicyclo[3.1.0]-hexane-5-carboxylate (4e): yellow solid; mp 148−150 °C; 138 mg, 44.4% yield; ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) 7.58 (d, J = 8.0 Hz, 2H), 7.39 (d, J = 8.0 Hz, 2H), 3.72 (s, 3H), 3.58 (d, J = 20.0 Hz, 1H), 3.03 (d, J = 20.0 Hz, 1H), 2.90 (bs, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) 172.26, 166.56, 132.32, 129.30, 128.04, 125.00, 80.74, 53.95, 46.46, 35.85; HRMS (ESI) calcd for $C_{12}H_{11}BrNO_4$ $[M + H]^+$ 311.9866, found 311.9874.

Methyl 1-(4-acetoxyphenyl)-3-oxo-2-oxa-6-azabicyclo[3.1.0]hexane-5-carboxylate (4f): yellow oil; 144 mg, 49.5% yield; ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) 7.54 (d, J = 8.0 Hz, 2H), 7.19 (d, J = 8.0 Hz, 2H), 3.73 (s, 3H), 3.58 (d, J = 20.0 Hz, 1H), 3.04 (d, J = 20.0 Hz, 1H), 2.89 (bs, 1H), 2.33 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) 171.97, 169.01, 166.22, 151.94, 128.55, 126.07, 121.93, 80.48, 53.52, 46.11, 35.53, 21.16; HRMS (ESI) calcd for $C_{14}H_{14}NO_6$ $[M + H]^+$ 292.0816, found 292.0833.

Methyl 1-(2-nitrophenyl)-3-oxo-2-oxa-6-azabicyclo[3.1.0]-hexane-5-carboxylate (4g): colorless crystal (after crystallization in DCM, EtOAc, and hexanes); mp 155−156 °C; 250 mg, 90% yield; ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) 8.17 (d, J = 8.0 Hz, 1H), 7.82−7.69 (comp, 3H), 3.74 (d, J = 16.0 Hz, 1H), 3.72 (s, 3H), 3.03 (d, J = 16.0 Hz, 1H), 2.80 (bs, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) 172.45, 167.54, 147.73, 134.48, 132.16, 131.91, 126.02, 124.91, 78.89, 54.07, 46.53, 34.99; HRMS (ESI) calcd for $C_{12}H_{11}N_2O_6$ $[M + H]^+$ 279.0612, found 279.0611.

***tert*-Butyl 1-(2-nitrophenyl)-3-oxo-2-oxa-6-azabicyclo[3.1.0]-hexane-5-carboxylate (4h):** brown oil; 294 mg, 92% yield; ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) 8.19 (d, J = 8.0 Hz, 1H), 7.80−7.67 (comp, 3H), 3.70 (d, J = 20.0 Hz, 1H), 2.97 (d, J = 20.0 Hz, 1H), 2.74 (bs, 1H), 1.28 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$) 172.60, 165.23, 147.11, 134.10, 131.64, 131.60, 125.49, 125.06, 84.15, 78.33, 46.83, 34.72, 27.53; HRMS (ESI) calcd for $C_{15}H_{17}N_2O_6$ $[M + H]^+$ 321.1081, found 321.1077.

Methyl 1-(2,4-dinitrophenyl)-3-oxo-2-oxa-6-azabicyclo[3.1.0]hexane-5-carboxylate (4i): yellow solid; mp 168−170 °C; 261 mg, 81% yield; ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) 8.95−8.09 (comp, 3H), 3.78 (d, J = 20.0 Hz, 1H), 3.72 (s, 3H), 3.07 (d, J = 16.0 Hz, 1H), 2.84 (bs, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) 171.90, 167.11, 149.48, 148.16, 133.76, 131.02, 128.36, 121.33, 54.26, 47.01, 34.98; HRMS (ESI) calcd for $C_{12}H_{10}N_3O_8$ $[M + H]^+$ 324.0462, found 324.0469.

***tert*-Butyl 1-(2,4-dinitrophenyl)-3-oxo-2-oxa-6-azabicyclo[3.1.0]hexane-5-carboxylate (4j):** dark brown oil; 321 mg, 88% yield; ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) 8.20−7.67 (comp, 3H), 3.70 (d, J = 20.0 Hz, 1H), 2.97 (d, J = 20.0 Hz, 1H), 2.74 (bs, 1H), 1.28 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$) 172.20, 165.49, 149.41, 147.89, 133.83, 131.59, 128.37, 121.22, 85.25, 47.67, 35.06, 28.02; HRMS (ESI) calcd for $C_{15}H_{16}N_3O_8$ $[M + H]^+$ 366.0932, found 366.09312.

Methyl 3-oxo-1-(2-(trifluoromethyl)phenyl)-2-oxa-6-azabicyclo[3.1.0]hexane-5-carboxylate (4k): brown oil; 231 mg, 77% yield; ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) 7.78−7.62 (comp, 4H), 3.71 (s, 3H), 3.56 (d, J = 20.0 Hz, 1H), 3.01 (d, J = 20.0 Hz, 1H), 2.85 (bs, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) 172.20, 167.23, 132.80, 131.56 (d, J = 5.0 Hz), 129.45 (q, J = 32.0 Hz), 127.81 (q, J = 5.0 Hz), 127.06, 125.38, 122.66, 79.67, 53.91, 46.02, 34.89; HRMS (ESI) calcd for $C_{13}H_{11}F_3NO_4$ $[M + H]^+$ 302.0635, found 302.0627.

***tert*-Butyl 3-oxo-1-(2-(trifluoromethyl)phenyl)-2-oxa-6-azabicyclo[3.1.0]hexane-5-carboxylate (4l):** brown oil; 281 mg, 82% yield; ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) 8.19 (d, J = 8.0 Hz, 1H), 7.80−7.67 (comp, 3H), 3.70 (d, J = 20.0 Hz, 1H), 2.97 (d, J = 20.0 Hz, 1H), 2.74 (bs, 1H), 1.28 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$) 172.68, 165.23, 132.58, 131.33 (d, J = 3.3 Hz), 129.74 (q, J = 32.0 Hz), 127.72 (q, J = 5.2 Hz), 127.4, 125.36, 122.64, 84.57, 79. 34, 46.70, 34.93, 27.93; HRMS (ESI) calcd for $C_{16}H_{17}F_3NO_4$ $[M + H]^+$ 344.1104, found 344.1107.

Methyl 4-methyl-1-(2-nitrophenyl)-3-oxo-2-oxa-6-azabicyclo[3.1.0]hexane-5-carboxylate (4m): *cis* + *trans*: 260 mg, 89% yield; *trans*:*cis* = 1:1 (*trans* and *cis* relative chemistry was determined by 1D-NoE experiment).[10] ***trans*-4 m**: yellow oil; ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) 8.14 (d, J = 8.0 Hz, 1H), 7.80−7.67 (comp, 3H), 3.85 (q, J = 8.0 Hz, 1H), 3.72 (s, 3H), 2.80 (bs, 1H), 1.48 (d, J = 8.0 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) 175.42, 167.65, 147.73, 134.46, 132.12, 131.91, 125.95, 124.94, 77.30, 54.05, 50.30, 39.82, 11.86. ***cis*-4 m**: yellow solid; mp 117−119 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) 8.14 (d, J = 8.0 Hz, 1H), 7.80−7.67 (comp, 3H), 3.85 (q, J = 8.0 Hz, 1H), 3.72 (s, 3H), 2.80 (bs, 1H), 1.48 (d, J = 8.0 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) 176.78, 167.65, 147.75, 134.36, 132.21, 131.99, 125.78, 125.37, 79.46, 53.66, 49.05, 43.35, 14.21; HRMS (ESI) calcd for $C_{13}H_{13}N_2O_6$ $[M + H]^+$ 293.0768, found 293.0771.

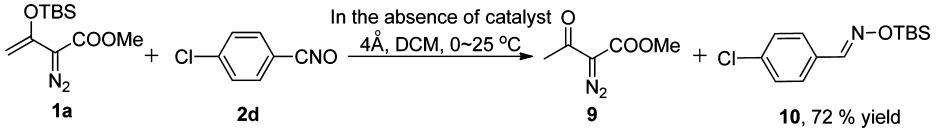
Benzyl 4-methyl-1-(2-nitrophenyl)-3-oxo-2-oxa-6-azabicyclo[3.1.0]hexane-5-carboxylate (4n): *cis* + *trans*: 305 mg, 83% yield; *trans*:*cis* = 3:1 (*trans* and *cis* relative chemistry was determined by comparison the analogue ^{1}H NMR specrta with **4m**). ***trans*-4n**: yellow oil; ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) 8.08 (d, J = 8.0 Hz, 1H), 7.75−7.14 (comp, 8H), 5.16 (d, J = 12.0 Hz, 1H), 5.01 (d, J = 12.0 Hz, 1H), 3.91 (q, J = 8.0 Hz, 1H), 2.65 (bs, 1H), 1.47 (d, J = 8.0 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) 175.35, 166.89, 147.57, 134.72, 134.32, 131.97, 131.79, 129.11, 129.04, 128.73, 125.98, 124.98, 77.25, 68.81, 50.41, 39.83, 11.90. ***cis*-4n**: yellow oil; ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) 8.06 (d, J = 8.0 Hz, 1H), 7.69−7.08 (comp, 8H), 5.09 (d, J = 12.0 Hz, 1H), 4.97 (d, J = 12.0 Hz, 1H), 3.18 (q, J = 8.0 Hz, 1H), 2.80 (bs, 1H), 1.82 (d, J = 8.0 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) 176.83, 166.69, 147.55, 134.53, 134.62, 132.09, 131.83, 129.09, 129.01, 128.86, 125.97, 125.80, 79.45, 68.61, 49.01, 43.47, 14.18; HRMS (ESI) calcd for $C_{19}H_{17}N_2O_6$ $[M + H]^+$ 369.1081, found 369.1062.

Methyl 1-(2-nitrophenyl)-3-oxo-4-phenyl-2-oxa-6-azabicyclo[3.1.0]hexane-5-carboxylate (4o): white solid; mp 189−191 °C; 202 mg, 57% yield; *trans*:*cis* > 20:1 (*trans* and *cis* relative chemistry was determined by 1D-NoE experiment); ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) 8.19 (d, J = 8.0 Hz, 1H), 7.75−7.38 (comp, 8H), 5.14 (s, 1H), 3.72 (s, 3H), 2.80 (bs, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) 172.84, 167.39, 147.72, 134.53, 133.25, 132.24, 131.97, 129.69, 129.18, 128.71, 126.06, 124.79, 54.20, 50.78, 50.19; HRMS (ESI) calcd for $C_{18}H_{15}N_2O_6$ $[M + H]^+$ 355.0925, found 355.0905.

General Procedure for Rearrangement Reactions of TIPS-Protected Enoldiazoacetate 1 with Nitrile Oxides 2g. To an oven-dried flask containing a magnetic stirring bar, 4 Å molecular sieves (100 mg), $Rh_2(pfb)_4$ (2.0 mol %), and nitrile oxide **2g** (1.0 mmol) in dichloromethane (5.0 mL) was added enol diazoacetate **1** (1.2 mmol) in dichloromethane (3.0 mL) over 1 h via a syringe pump at 0 °C. After addition was complete, the reaction solution was stirred for another 2 h at room temperature, and then DCM was removed under reduced pressure and the crude reaction mixture was subjected to NMR analysis: 100% conversion to 7; ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) 8.23−7.78 (comp, 4H), 3.73 (s, 3H), 3.43 (d, J = 16.0 Hz, 1H), 2.97 (d, J = 16.0 Hz, 1H), 1.24 (m, 3H), 1.02 (m, 18H); ^{13}C

dx.doi.org/10.1021/jo3006733 | J. Org. Chem. 2012, 77, 5313−5317

NMR (100 MHz, $CDCl_3$) δ (ppm) 171.87, 170.80, 163.72, 147.98, 134.21, 133.97, 132.49, 125.50, 119.50, 53.19, 40.59, 38.72, 18.04, 18.03, 12.25; ^{29}Si NMR (99 MHz, $CDCl_3$) δ (ppm) 22.73.



Control Reaction of Enoldiazoacetate 1a with 4-Chlorobenzonitrile Oxide (2d) in the Absence of Catalyst. *4-Chlorobenzaldehyde O-(tert-Butyldimethylsilyl) Oxime (**10**).* To an oven-dried flask containing a magnetic stirring bar, 4 Å molecular sieves (100 mg), and nitrile oxide **2d** (1.0 mmol) in dichloromethane (5.0 mL) was added diazo compound **1a** (1.2 mmol) in dichloromethane (3.0 mL) over 1 h via a syringe pump at 0 °C. After addition was complete, the reaction solution was stirred overnight at room temperature. The crude product was purified by column chromatography on silica gel (eluent: hexanes/EtOAc = 30:1 to 10:1) to give the hydrolyzed diazo compound **9** and TBS protected oxime **10**: colorless oil; 193 mg, 72% yield of **10**); ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) 8.18 (s, 1H), 7.55 (d, J = 8.0 Hz, 2H), 7.34 (d, J = 8.0 Hz, 2H), 1.00 (s, 9H), 0.25 (s, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm) 152.47, 136.00, 131.62, 129.32, 128.59, 26.49, 18.68; HRMS (ESI) calcd for $C_{13}H_{21}ClNOSi$ $[M + H]^+$ 270.1075, found 270.1093.

■ ASSOCIATED CONTENT

Ⓢ Supporting Information

Product characterization (^{1}H and ^{13}C spectra) and X-ray diffraction analysis data of **4g**. This material is available free of charge via the Internet at http://pubs.acs.org.

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Notes

The authors declare no competing financial interest.

■ ACKNOWLEDGMENTS

The support of the National Institutes of Health (GM 46503) for this research is gratefully acknowledged.

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