# π-Facial Diastereoselection in [3 + 2]-Cycloadditions of Isomünchnone Dipoles

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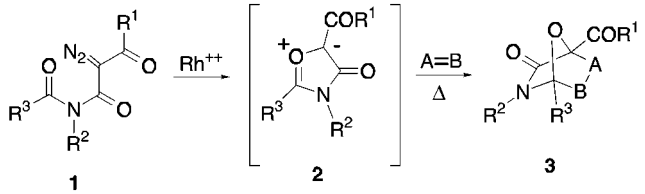
The Rh(II)-catalyzed reaction of 1-[diazo(methoxycarbonyl)acetyl]-2-oxopyrrolidine derivatives led to the formation of ring-fused isomünchnone betaines which are trapped with various dipolarophiles to give the corresponding [3 + 2]-cycloadducts in excellent yield. The cycloaddition reaction proceeded with high levels of diastereoselectivity leading to the predominant formation of the *exo* dipolar cycloadduct. The influence of substituents on the stereoselectivity of the reaction was investigated. Diastereotopic facial selectivity by the dipolarophile on the mesoionic betaine was found to depend upon the nature of the stereogenic center. Inclusion of substituents at *any* position of the fused five-membered ring was found to enhance *exo* selectivity. Isomünchnone dipoles derived from pyrrolidinones containing a carboalkoxy substituent in the 5-position of the ring afforded mainly *exo*−*syn* cycloadducts. In contrast, when a methyl group was present at the 3-position of the pyrrolidinone ring, the facial selectivity was reversed with the *exo*−*anti* adduct being the major product. A computational study was carried out to rationalize the observed product distribution.

Developing methods that efficiently construct stereochemically rich polyheterocyclic ring systems are of great interest in synthetic chemistry.[1] In recent years, much attention has been focused on reactions that affect formation of heterocycles through [3 + 2]-cycloadditions.[2] Among these, the dipolar cycloadditions of mesoionic compounds occupy a uniquely important position due to their synthetic as well as theoretical significance.[3−10] Our interest in the chemistry of mesoionic dipoles stems from studies in our laboratory dealing with the rhodium(II)-catalyzed reactions of α-diazo carbonyl compounds in the presence of various heteroatoms.[11] In earlier reports, we showed that the isomünchnone class of mesoionics can easily be generated from the Rh(II)-catalyzed reaction of α-diazo imides.[12] This mesoionic dipole was found to undergo cycloadditions with both electron-rich and electron-deficient dipolarophiles.[13] We were able to show that the dipolar cycloaddition of isomünchnones with alkenes also occurred intramolecularly and that the overall reaction represents an efficient way to synthesize complex polyheterocyclic ring systems.[14]




Stereocontrolled 1,3-dipolar cycloadditions hold considerable potential for the asymmetric synthesis of complex heterocyclic molecules.[15−17] One of today's challenges in this field is to control the regio-, diastereo-, and enantioselectivities of these reactions. Although some synthetic equivalents of metalated dipoles have been prepared, there are few examples known where Lewis acids control the stereo- and/or regioselectivity of dipolar cycloadditions[21,22] as is typically encountered with Diels−Alder chemistry.[23] High stereochemical control in [3 + 2]-cycloadditions has generally been secured by the use of chiral dipolarophiles[18] or chiral dipoles.[19,20] Most of

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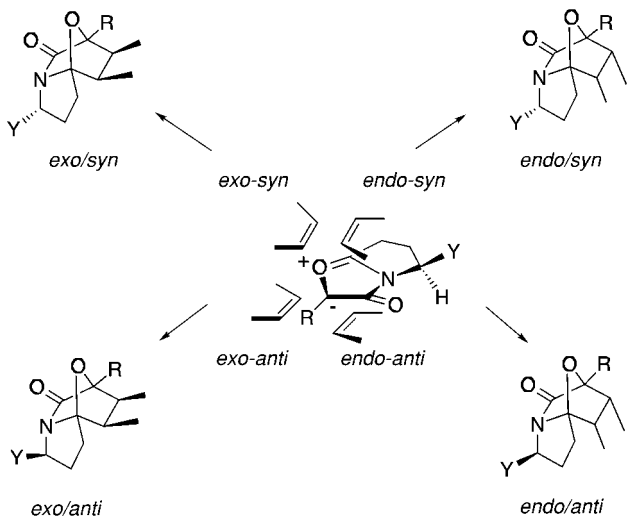
the available examples of asymmetric dipolar cycloadditions are limited to 1,3-dipoles such as nitrones,[19] nitrile oxides,[24] or azomethine ylides.[20] To the best of our knowledge, there have been no reports concerning substrate-controlled asymmetric 1,3-dipolar cycloadditions using isomünchnones as dipoles. Consequently, we initiated a study designed to examine the extent to which an asymmetric center on the mesoionic dipole can control diastereoselective cycloaddition of ring-fused isomünchnones with achiral dipolarophiles. In the present paper, we report on the effect various substituents have on the *exo*/*endo* and *syn*/*anti* selectivity of several isomünchnone betaines derived from cyclic amides.[25]




## Results and Discussion

The deprotonation of various pyrrolidinones with lithium bis(trimethylsilyl)amide followed by reaction with diazoethylmalonyl chloride[12] was found to be a general and high-yielding method for the preparation of the ester-stabilized diazo compounds needed in this study. Using this procedure, diazo imide **5** was prepared in a 80% yield from pyrrolidin-2-one (**4**). The related acetyl-substituted diazo imide **6** was synthesized by condensation of pyrrolidin-2-one with 2,2,6-trimethyl-4*H*-1,3-dioxin-4-one[26] followed by a subsequent diazo transfer using methanesulfonyl azide (1.5 equiv) and triethylamine (2.0 equiv)[27] in 81% overall yield (Scheme 1). Both of these diazo imides were decomposed by heating in benzene in the presence of an appropriate dipolarophile and a catalytic quantity of rhodium(II) perfluorobutyro amidate ($Rh_2(pfm)_4$). This choice of catalyst and solvent was found to be the best set of conditions for the tandem cyclization−cycloaddition reaction since it gives a near quantitative yield of cycloadduct (≥90%). Adduct ratios were determined by careful integration of the $^1$H-NMR spectra of the crude reaction mixture, and the results are shown in Scheme 2. The *endo* cycloadducts exhibit a signal for two aromatic protons at a field significantly higher ($\delta$ 7.13 ppm) than their *exo* counterparts ($\delta$ 7.23 ppm). In addition, the *exo* cycloadducts possess a vicinal coupling constant ($J$ = 6.6 Hz) for the two protons at the ring fusion smaller than do the *endo* cycloadducts ($J$ = 8.4 Hz). This diagnostic difference in the NMR[28] was encountered throughout the present study, and the stereochemical assignment was further verified by an X-ray analysis of one of the *exo* cycloadducts (*vide infra*). For some of the minor cycloadducts we had to rely on an analysis of trends in the NMR spectra in order to infer the stereochemistry.

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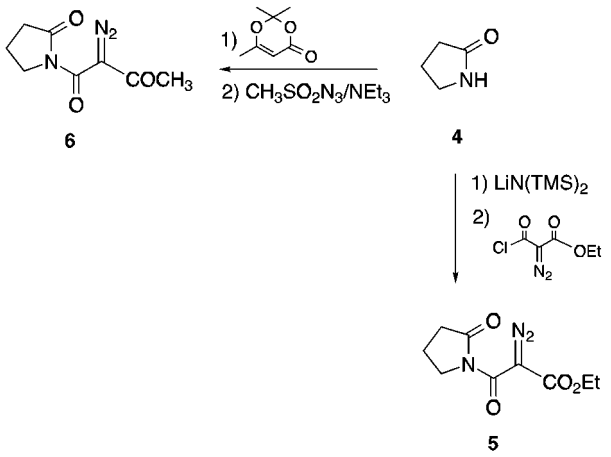
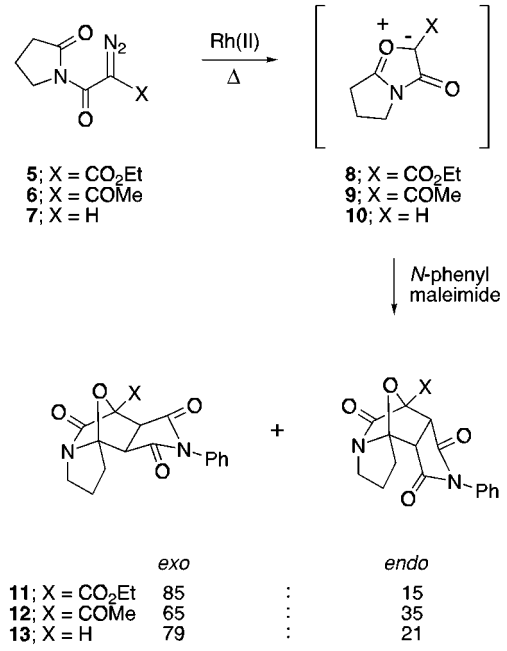
**Scheme 1**




**Scheme 2**



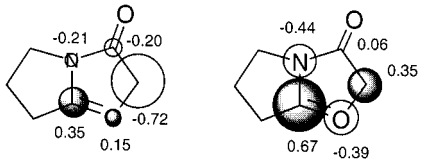

| | *exo* | | *endo* |
|---|---|---|---|
| **11**; X = $CO_2Et$ | 85 | : | 15 |
| **12**; X = COMe | 65 | : | 35 |
| **13**; X = H | 79 | : | 21 |

Kinetically controlled [4 + 2]-cycloadditions generally lead to the initial formation of the *endo* diastereomer[29] which often can be equilibrated to the thermodynamically more stable *exo* isomer. In keeping with previous studies of Diels−Alder cycloaddition reactions, it was assumed that the product distributions were kinetic. Experimental confirmation was provided by heating the dipolar adducts above the cycloaddition temperature. In no instance was there a hint of thermal equilibration. This result establishes that the 1,3-dipolar cycloaddition is not reversible under the reaction conditions used. In all of the cycloadditions, the dipolarophile reacts preferentially in an *exo* manner. However, the nature of the activating group X present on the mesoionic dipole can subtly affect the *exo*/*endo* ratio. Thus, the acetyl-substituted diazo imide **6** exhibits an *exo* preference lower than both the diazo imide ester **5** and the unsubstituted system **7**. Clearly, an all-embracing explanation that accounts for the variation in ratio is not obvious.

Attempts to rationalize the relative topical preference of [4 + 2]-cycloaddition reactions generally involve theoretical arguments.[30] In order to probe the geometric orientation and steric bulk of the substituent group X with respect to the topography of the isomünchnone cycloaddition reaction, we carried out some molecular orbital calculations. The mesoionic betaine intermediates involved (*i.e.*, **8**−**10**) were optimized using the RHF/$PM_3$ method, and the results are summarized in Table 1. Almost identical values were obtained by carrying out the calculations at the RHF/AM1 or *ab initio* RHF/3-21G level. The fused mesoionic system adopts a planar geometry. Both the HOMO and the LUMO show significant contributions from N(5) and the carbonyl ylide portion [C(1)−O(2)−C(3)], whereas C(4) corresponds to a nodal point in the LUMO. The HOMO possesses the largest orbital coefficient at C(3), while the LUMO is polarized toward C(1) for all the mesoionic dipoles examined. As expected, replacement of the hydrogen atom in **10** with the electron-withdrawing acetyl (**9**) or ester functionality (**8**) leads to a lowering of the HOMO and LUMO energies (Table 1). The orbital coefficients at the reactive centers are barely affected. The energies of both of the transition states and corresponding products were also determined for the reaction of isomünchnones **8**−**10** with *N*-methylmaleimide and were modeled at the RHF/AM1 and RHF/PM3 level using the Spartan software package.[31] A concerted transition state model based on a linear synchronous transit (LST)[32] was used as the initial input for the transition state geometry. Only one transition state was located for each reaction and was confirmed as a saddle point on the basis of frequency analysis. Regardless of the method, the optimized geometries show nearly synchronous bond formation, consistent with a concerted reaction. The calculated interatomic distances for the newly formed bonds are listed in Table 2 and generally show little variation.

The MO calculations suggest a slightly higher degree of asymmetry for the *exo* transition states, but the variation is quite small. The calculated difference in transition state energies ($H^{\ddagger}_{rel}$ (Table 2)) reflects the low *exo*/*endo* ratio observed for the keto system **9**, but tends to overemphasize the *exo* preference for the hydrogen-substituted system **10**. The ground state energies for the

**Table 1. HOMO/LUMO Energies and Orbital Coefficients**




**10** (HOMO) **10** (LUMO)

| | **8** (X = $CO_2Me$) | | **9** (X = COMe) | | **10** (X = H) | |
|---|---|---|---|---|---|---|
| | HOMO | LUMO | HOMO | LUMO | HOMO | LUMO |
| *E* (eV) | −8.7 | −0.9 | −8.6 | −0.9 | −8.0 | −0.5 |
| C(1) | 0.28 | 0.70 | 0.30 | 0.70 | 0.35 | 0.67 |
| O(2) | 0.17 | −0.39 | 0.16 | −0.39 | 0.15 | −0.39 |
| C(3) | −0.73 | 0.27 | −0.72 | 0.28 | −0.72 | 0.35 |
| C(4) | −0.17 | 0.02 | −0.18 | −0.02 | −0.20 | 0.06 |
| N(5) | −0.17 | −0.39 | −0.18 | −0.42 | −0.21 | −0.44 |

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(31) Spartan version 4.0; copyright 1995; Wavefunction, Inc.

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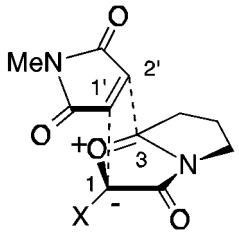
**Table 2. Calculated Transition State Parameters for the Cycloaddition of Isomünchnones 8−10**



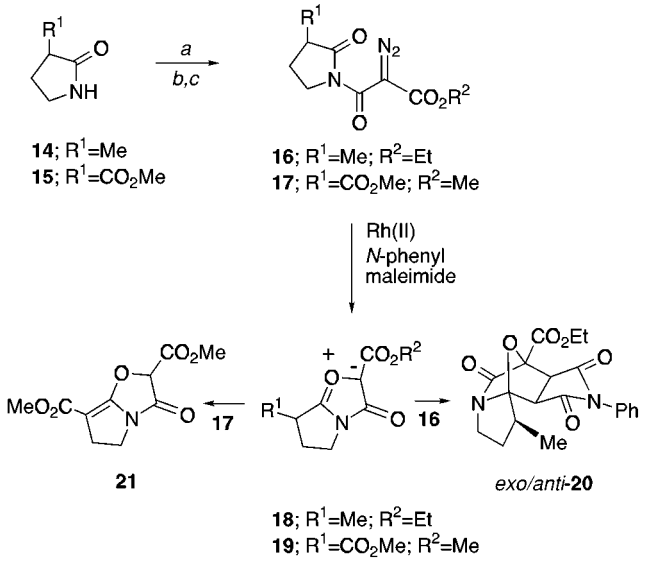
| | **8** → **11** (X = $CO_2Me$) | | **9** → **12** (X = COMe) | | **10** → **13** (X = H) | |
|---|---|---|---|---|---|---|
| | *exo* | *endo* | *exo* | *endo* | *exo* | *endo* |
| $H^{\ddagger}_{rel}$ (AM1)[a] | 0 | 0.8 | 0 | 0.1 | 0 | 2.9 |
| *d* (C(1)−C(1′)) (Å) | 2.19 | 2.21 | 2.19 | 2.20 | 2.29 | 2.24 |
| *d* (C(3)−C(2′)) (Å) | 2.29 | 2.26 | 2.29 | 2.26 | 2.41 | 2.37 |
| $H_{rel}$ (AM1)[b] | 0 | −0.2 | 0 | −0.1 | 0 | 1.5 |
| $H^{\ddagger}_{rel}$ (PM3)[a] | 0 | 1.1 | 0 | 0.7 | 0 | 2.4 |
| *d* (C(1)−C(1′)) (Å) | 2.21 | 2.23 | 2.22 | 2.24 | 2.12 | 2.15 |
| *d* (C(3)−C(2′)) (Å) | 2.36 | 2.32 | 2.36 | 2.32 | 2.59 | 2.51 |
| $H_{rel}$ (PM3)[b] | 0 | 1.4 | 0 | 1.2 | 0 | 2.4 |

[a] Transition state energy relative to the respective *exo* isomer in kcal/mol. [b] Ground state energies of the cycloadducts **11**−**13** relative to the respective *exo* isomer in kcal/mol.

*exo*/*endo* cycloadducts **11**−**13** were also determined (Table 2). While the PM3 method predicts that the *exo* isomer is more stable regardless of substitution, the energy differences are quite small when the AM1 Hamiltonian was used. Both semiempirical methods indicate that the *exo* isomer should be formed preferentially in a kinetically controlled process, which is in good agreement with the experimental findings. The qualitative agreement of the MO calculations with the experimental results for the isomünchnone reaction stands in contrast to the related cycloaddition chemistry of münchnones,[33] where semiempirical methods failed to account for the regio- and stereochemical findings.[34]

$\pi$-Facial selectivity in [4 + 2]-cycloadditions arises when the addends possess two diastereotopic reactive faces. Frequently, the presence of at least one center of chirality imparts sufficient perturbation to influence the diasterofacial selectivity.[30] Incorporation of a stereogenic center in the pyrrolidinone ring would be expected to exert a significant directing effect on these isomünchnone cycloadditions. Important factors that will need to be considered to rationalize the stereochemical outcome will include steric effects, complexation between the dipole and dipolarophile, secondary orbital interactions including tilting and torsional effects, as well as polarizability and electrostatic interactions. Prior to the present study, no experimental evidence was available concerning $\pi$-facial selectivity in isomünchnone cycloadditions. The first system we examined involved diazo imide **16** which was prepared in 65% yield from 3-methylpyrrolidin-2-one (**14**) by malonation[12] and subsequent diazo transfer. Treatment of **16** with $Rh_2(pfm)_4$ in the presence of *N*-phenylmaleimide afforded a single diastereomer (90%) whose structure was assigned as the *exo*−*anti* **20** isomer. The other possible diastereomers were present only in trace amounts (≤5%) and could not be isolated (Scheme 3).

**Scheme 3**[a]




[a] Reagents: (a) amide **14**, $LiN(SiMe_3)_2$, $EtO_2CC(N_2)COCl$; (b) amide **15**, $MeO_2CCH_2COCl$, Δ; (c) *p*-$NO_2C_6H_4SO_2N_3$, $NEt_3$.

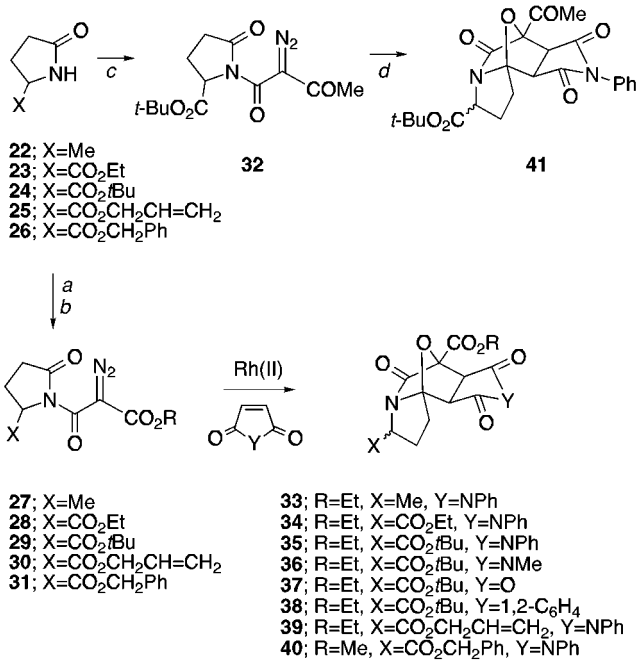
The absence of *endo* cycloadducts is probably related to an unfavorable steric interaction in the transition state for their formation. *Anti* attack by the dipolarophile is to be expected due to steric interaction of the incoming dipolarophile with the methyl group at C(3), which shields the *syn* face. This rationale is consistent with the MO calculations. Thus, the optimized *exo*−*anti* transition state for the reaction of **18** with *N*-methylmaleimide is favored over the *exo*−*syn* structure by 1.9 kcal/mol (AM1) [2.7 kcal/mol (PM3)]. The transition state energies reflect the relative stability of the *exo* cycloadducts, for which a $\Delta H$ of 1.1 kcal/mol (AM1) [1.4 kcal/mol (PM3)] in favor of the *exo*−*anti* adduct was calculated.

Stereoelectronic effects of polar functional groups on $\pi$-facial selectivity in Diels−Alder reactions have attracted considerable attention in recent years.[35−37] In a few of these cycloadditions, the dienophile reacts preferentially with the more sterically hindered *syn*face of the diene.[38] In order to probe whether the stereochemical

(33) (a) Maryanoff, C. A.; Turchi, I. J. *Heterocycles* **1993**, *35*, 649. (b) Coppola, B. P.; Noe, M. C.; Schwartz, D. J.; Abdon, R. L. H.; Trost, B. M. *Tetrahedron* **1994** *50*, 93.

(34) Avalos, M.; Babiano, R.; Cabanillas, A.; Cintas, P.; Jiménez, J. L.; Palacios, J. C.; Aguilar, M. A.; Corchado, J. C.; Espinosa-García, J. *J. Org. Chem*. **1996**, *61*, 7291. The same group, however, has been more successful applying MO calculations to cycloaddition reactions of thioisomünchnones; see: Avalos, M.; Babiano, R.; Diánez, M. J.; Espinosa, J.; Estrada, M. D.; Jiménez, J. L.; López-Castro, A.; Méndez, M. M.; Palacios, J. C. *Tetrahedron* **1992**, *48*, 4193.

**Scheme 4**[a]

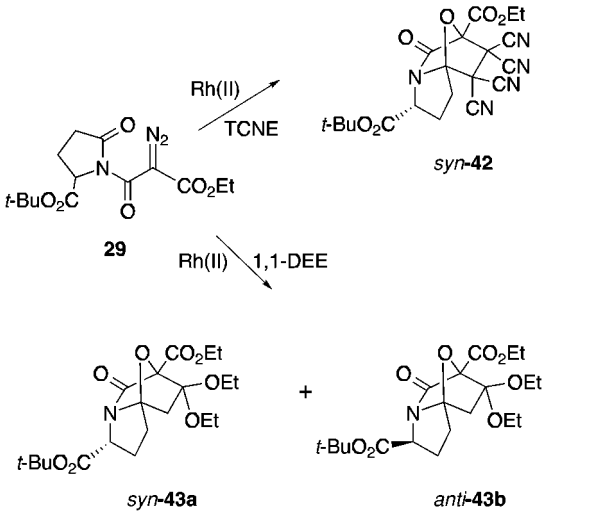



[a] Reagents: (a) amides **22**−**25**, $LiN(SiMe_3)_2$, THF, −78 °C, $EtO_2CC(N_2)COCl$; (b) amide **26**, $CH_3O_2CCH_2COCl$, Δ, $MsN_3$, $NEt_3$; (c) 2,2,6-trimethyl-1,3-dioxin-4-one, Δ, $MsN_3$, $NEt_3$; (d) $Rh_2(pfm)_4$, *N*-phenylmaleimide.

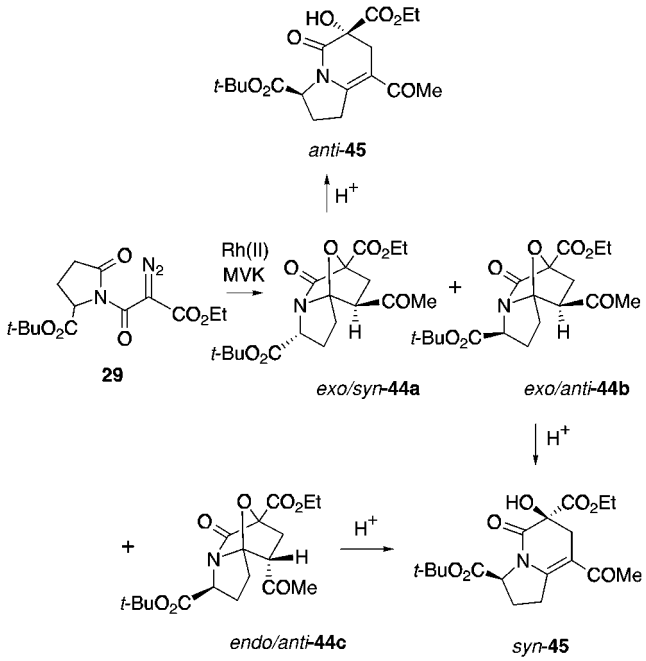
course of isomünchnone cycloadditions could be altered by electronic interaction with polar substituents, we prepared diazo ester **17** from the readily available 2-oxopyrrolidine-3-carboxylic acid methyl ester[39] (**15**) (Scheme 3). To our surprise, none of the expected dipolar cycloadduct was formed when **17** was treated with $Rh_2(pfm)_4$ in the presence of *N*-phenylmaleimide. Instead, the acidic proton at C(3) in the isomünchnone intermediate **19** was transferred, and the fused oxazolidinone **21** was isolated in 77% yield (Scheme 3).

We next turned our attention to the Rh(II)-catalyzed reaction of several diazo imides derived from 5-substituted pyrrolidin-2-ones. The stereogenic center in the isomünchnone dipole generated from this system is further removed from the reacting dipole, and thus a lesser steric effect is to be expected in the [3 + 2]-cycloaddition reaction. Chiral diazo imides **27**−**32** were prepared in good yield from readily available precursors. The Rh(II)-catalyzed decomposition of **27**−**32** in benzene in the presence of both cyclic (Scheme 4) and acyclic (Schemes 5 and 6) dipolarophiles resulted in the formation of the expected cycloadducts in nearly quantitative yield. Product distribution and yields are summarized in Table 3. The major product obtained in all cases

**Scheme 5**




**Scheme 6**




corresponded to the *exo* cycloadduct. The Rh(II)-catalyzed decomposition of the methyl-substituted derivative **27** afforded a 58:42 mixture of the *syn*/*anti exo* cycloadducts **33**. This result is not totally unexpected, since steric interaction of the incoming dipolarophile with the methyl group at C(5) is not significant for an *exo* transition state, and therefore, discrimination between the two diastereotopic faces is poor.

Fortunately, the situation changes when an ester group is located at the C(5) position. The reaction of diazo imides **28**−**32** with $Rh_2(pfm)_4$ and *N*-phenylmaleimide in refluxing benzene resulted in the formation of cycloadducts **34**−**35** and **39**−**41** with nearly complete *exo*/*endo* selectivity as well as high π-facial selectivity. NMR analysis of the crude reaction mixture indicated a near quantitative yield of cycloadducts, with one of the two *exo* adducts being formed as the dominant product in 90% isolated yield. *Endo* cycloadducts were formed in less than 3% yield. In view of the fact that the 5-methyl-substituted isomünchnone **27** did not discriminate between the two diastereotopic faces, the high stereoselectivity encountered with the ester-substituted analog is

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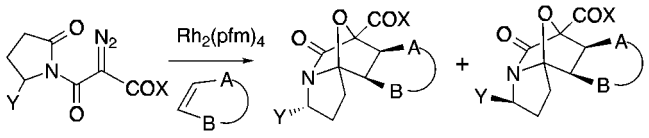
(37) (a) Macaulay, J. B.; Fallis, A. G. *J. Am. Chem. Soc.* **1990**, *112*, 1136. (b) Ishida, M.; Aoyama, T.; Beniya, Y.; Yamabe, S.; Kato, S.; Inagaki, S. *Bull. Chem. Soc. Jpn.* **1993**, *66*, 3430. (c) Ishida, M.; Beniya, Y.; Inagaki, S.; Kato, S. *J. Am. Chem. Soc.* **1990**, *112*, 8980. (d) Coxon, J. M.; McDonald, D. G. *Tetrahedron Lett.* **1992**, *33*, 651. (e) Ishida, M.; Kakita, S.; Inagaki, S. *Chem. Lett.* **1995**, 469.

(38) Datta, S. C.; Franck, R. W.; Tripathy, R.; Quigley, G. J.; Huang, L.; Chen, S.; Sihaed, A. *J. Am. Chem. Soc.* **1990**, *112*, 8472.

(39) (a) Lindstrom, K. L.; Crooks, S. L. *Synth. Commun.* **1990**, *20*, 2335. (b) Khouki, M.; Vaultier, M.; Carríe, R. *Tetrahedron Lett.* **1986**, *27*, 1031.

**Table 3. Product Distribution in the Cyclization−Cycloaddition Sequence of Diazo Imides 27−32**




*exo/syn* adduct *exo/anti* adduct

| substrate | Y | X | dipolarophile[a] | product | yield (%) | *exo/endo* | *syn/anti* |
|---|---|---|---|---|---|---|---|
| **27** | Me | OEt | NPM | **33** | 86 | ≥95:5 | 58:42[b] |
| **28** | $CO_2Et$ | OEt | NPM | **34** | 85 | ≥95:5 | 83:17 |
| **29** | $CO_2$-*t*-Bu | OEt | NPM | **35** | 84 | ≥95:5 | 90:10 |
| **29** | $CO_2$-*t*-Bu | OEt | NMM | **36** | 74[c] | ≥95:5 | 90:10 |
| **29** | $CO_2$-*t*-Bu | OEt | MA | **37** | 79[c] | ≥95:5 | 90:10 |
| **29** | $CO_2$-*t*-Bu | OEt | 1,4-NQ | **38** | 80 | ≥95:5 | 84:16 |
| **29** | $CO_2$-*t*-Bu | OEt | TCNE | **42** | 74[c] | | 77:23 |
| **29** | $CO_2$-*t*-Bu | OEt | MVK | **43** | 82 | 79:21 | 65:35[d] |
| **29** | $CO_2$-*t*-Bu | OEt | 1,1-DEE | **44** | 83 | | 65:35 |
| **30** | CO2allyl | OEt | NPM | **39** | 75[c] | ≥95:5 | 85:15 |
| **31** | $CO_2CH_2Ph$ | OMe | NPM | **40** | 91 | ≥95:5 | 87:13 |
| **32** | $CO_2$-*t*-Bu | Me | NPM | **41** | 95 | 92:8 | 88:12[d] |

[a] NPM = *N*-phenylmaleimide; NMM = *N*-methylmaleimide; MA = maleic anhydride; 1,4-NQ = 1,4-naphthoquinone; TCNE = tetracyanoethylene; MVK = methyl vinyl ketone; 1,1-DEE = 1,1-diethoxyethene. [b] The stereochemistry was not assigned. [c] Only the major cycloadduct was isolated. [d] *Syn*/*anti* ratio of the *exo* cycloadducts.

quite surprising. The unexpected *syn* preference was unambiguously established by an X-ray analysis of cycloadduct **35**.[40]

The nature of the ester group present at the 5-position of the pyrrolidinone ring showed little effect on the degree of diastereoselectivity, with the bulky *tert*-butyl ester **29** giving the best results. The cycloaddition reaction of benzyl ester **31** was examined in order to test the possiblity of $\pi$-stacking between the phenyl ring and the mesoionic system as a controlling factor, but no unusual effect was encountered. Interestingly, in the case of allyl ester **30**, intramolecular cycloaddition across the olefinic $\pi$-bond did not compete with bimolecular cycloaddition.

The scope and generality of the *syn*-directing effect of the ester group was established from a study of the cycloaddition of the *tert*-butyl ester **29** with a series of dipolarophiles (Schemes 4−6). High yields of the dipolar cycloadducts were obtained using electron-deficient (maleic anhydride, tetracyanoethylene, 1,4-naphthoquinone, methyl vinyl ketone) and electron-rich (1,1-diethoxyethylene) $\pi$-bonds. The regioselectivity observed using methyl vinyl ketone (Scheme 6) or 1,1-diethoxyethylene (Scheme 5) is consistent with FMO considerations.[41] The same stereochemical outcome was encountered for all the [3 + 2]-cycloadditions examined, regardless of the reaction partner. When unsymmetrical dipolarophiles were used, the *exo* adduct was formed in preference to the *endo* cycloadduct, which was only produced in trace quantities. A *syn*/*anti* ratio of *ca*. 9:1 was observed in all cases, in agreement with the results encountered when *N*-phenylmaleimide was used as the trapping reagent (Table 3). However, with methyl vinyl ketone, a 51:28:21 mixture of cycloadducts **44** was formed, with one of the diastereomers corresponding to the *endo* cycloadduct. The major *exo* adduct was assigned the *syn* stereochemistry in accordance with its NMR spectrum. Formation of the *endo* isomer occurs by *anti* attack of the dipolarophile on the mesoionic betaine intermediate. This stereochemical assignment was established by an acid-catalyzed rearrangement to give the fused bicyclic *anti*/*syn* ring-opened lactam **45**. Although the *exo*/*endo* stereochemical assignment is lost in the acid-catalyzed rearrangement, the *anti*/*syn* selectivity is reflected in the *anti*/*syn* ratio of lactam **45**. Formation of the same lactam from the minor *exo* adduct and the *endo* diastereomer indicates that both cycloadducts are derived from *anti* attack of the dipolarophile on the isomünchnone intermediate.

The above result is not surprising in view of the transition state geometry of the cycloaddition reaction. *Exo* approach of the dipolarophile proceeds with minimal steric interaction with the substituent group at C(5). The presence of the ester group promotes reaction at the sterically more hindered *syn* face of the dipole. Possible explanations to account for this *syn* selectivity involve favorable secondary orbital interactions,[42] electrostatic attraction,[30] or a Cieplak effect,[43] in which face selectivity is determined by a transition state bonding interaction between a developing $\sigma^*$ orbital and the carboalkoxy group. The *endo*−*syn* trajectory is severely hindered by steric interaction of the acetyl group of methyl vinyl ketone with the ester functionality at C(5), and therefore, the *endo*−*anti* cycloadduct is the only *endo* isomer formed. The lower $\pi$-facial selectivity encountered with 1,1-diethoxyethene (*i.e.*, **43**) (Scheme 4) probably originates from related steric interactions in the transition state. This dipolarophile encounters an unfavorable steric interaction in the *syn* transition state between the ester functionality and the ethoxy group. Another factor that may operate when 1,1-diethoxyethylene is used is that the cycloaddition may be subject to a stereoelectronic effect. The mesoionic dipole behaves as an electrophile in the reaction with 1,1-diethoxyethylene, and the electronic factors that result in a *syn* preference with electron-deficient dipolarophiles are no longer effective in a "*type III dipole controlled*" process.[41]

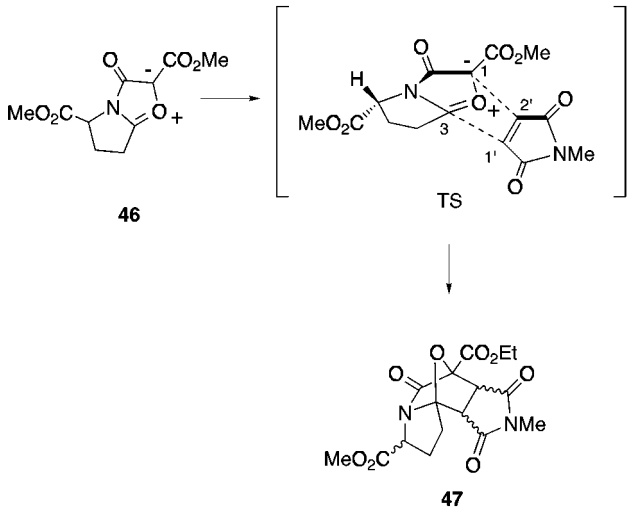
(40) The authors have deposited atomic coordinates for cycloadduct **35** with the Cambridge Crystallographic Data Centre. The coordinates can be obtained, on request, from the Director, Cambridge Crystallographic Centre, 12 Union Road, CB2 1EZ, UK.

(41) Padwa, A.; Hertzog, D. L. *Tetrahedron* **1993**, *49*, 2589.

(42) (a) Gleiter, R.; Ginsburg, D. *Pure Appl. Chem.* **1979**, *51*, 1301. (b) Ginsburg, D. *Tetrahedron* **1983**, *39*, 2095.

(43) (a) Cieplak, A. S. *J. Am. Chem. Soc.* **1981**, *103*, 4540. (b) Cieplak, A. S.; Tait, B. D.; Johnson, C. R. *J. Am. Chem. Soc.* **1989**, *111*, 8447.

**Table 4. Relative Transition State and Product Energies for the Reaction of 46 and *N*-Methylmaleimide[a]**



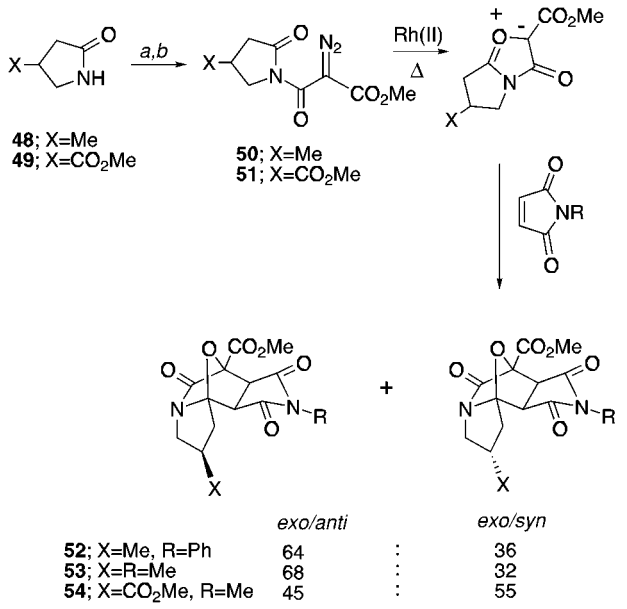

| | *exo−syn* | *exo−anti* | *endo−syn* | *endo−anti* |
|---|---|---|---|---|
| $H^{\ddagger}_{rel}$ (AM1)[b] | 0 | 0.7 | 2.4 | 1.3 |
| $H_{rel}$ (AM1)[c] | 0 | 0.4 | 0.4 | 0.4 |
| $H^{\ddagger}_{rel}$ (PM3)[b] | 0 | 0.1 | 2.3 | 1.2 |
| $H_{rel}$ (PM3)[c] | 0 | 1.6 | 1.3 | 3.1 |

[a] Calculated by RHF/PM3 or RHF/AM1 using the Spartan program package. [b] Transition state energies relative to the respective *exo−syn* isomer in kcal/mol. [c] Ground state energies of the cycloadducts **47** relative to the respective *exo−syn* isomer in kcal/mol.

More than likely, this mechanistic analysis also holds for the cycloaddition reaction of the acetyl-substituted diazoimido ester **32**. As was previously observed for achiral substrates, the acetyl-stabilized isomünchnone shows a reduced *exo*/*endo* selectivity compared to its ester analog **29**. In addition to the formation of two *exo* cycloadducts **41** (*syn*/*anti* = 88:12), the *endo−anti* isomer was also obtained, but only in 8% yield. The above examples clearly demonstrate that an ester functionality at C(5) acts as a stereodirecting group which guides the incoming dipolarophile to the sterically more congested *syn* face of the isomünchnone dipole. It should be noted that a related *syn*-directing effect of ester groups has been observed in several enolate alkylations[44] as well as Diels−Alder reactions.[45] This effect, however, is unprecedented in dipolar cycloaddition chemistry. Consequently, a computational study was initiated to rationalize the observed product distribution. The geometry of the four possible diastereomeric transition states from the reaction of isomünchnone **46** with *N*-methylmaleimide was optimized using both RHF/AM1 and RHF/PM3 methods. The relative energies are given in Table 4.

The calculated AM1 transition state energies nicely reflect the experimental observations. Although the PM3 Hamiltonian correctly predicts the *exo* selectivity, it fails to account for the observed *syn* preference in the *exo* transition state. It should be noted that the ground state energies of the cycloadducts do not correlate with the observed experimental diastereoselectivities. This observation eliminates the argument that the stereochemical preferences are the consequence of a product-like transition state. One possible explanation for the unusual contrasteric *syn*-directing effect of the ester group is that the *syn* face of the dipole exhibits enhanced electron density which is attributable to the electron-accepting ester functionality residing on this face. Such stereoelectronic effects have been invoked previously to explain $\pi$-facial selectivity in Diels−Alder cycloadditions as well as various electrophilic additions to $\pi$-systems.[46] On the other hand, when the structure of the mesoionic dipole or dipolarophile results in the formation of *endo* adducts, steric control is the dominant factor and the *anti* adduct becomes the preferred diastereomer. The general order (*exo−syn* > *exo−anti* > *endo−anti* > *endo−syn*) is nicely reflected in the calculated transition state energies using semiempirical methods.

**Scheme 7[a]**




[a] Reagents: (a) $CH_3O_2CCH_2COCl$, Δ; (b) $MsN_3$, $NEt_3$.

We also examined the tandem cyclization−cycloaddition chemistry of chiral diazo imides **50** and **51** which were readily prepared from pyrrolidinones **48** and **49** (Scheme 7).[47,48] In this case, placement of a substituent group at C(4) would be expected to result in modest $\pi$-facial selectivity, since the stereogenic center is too far removed from the dipole site to efficiently direct dipolarophile attack either *via* steric or electronic interactions. Indeed, the Rh(II)-catalyzed decomposition of **50** in the presence of *N*-methylmaleimide or *N*-phenylmaleimide afforded a 2:1 mixture of two *exo* cycloadducts. In view of the low diastereoselectivity, the relative configuration of the two products (**52** and **53**) was not established, but more than likely the major diastereomer stems from attack of the dipolarophile on the sterically less congested *anti* face of the isomünchnone dipole. The ester-substituted diazo imide **51** showed even lower $\pi$-facial selectivity with *N*-methylmaleimide (45:55). Presumably, the weak *syn*-directing effect of the ester group counteracts steric interactions in the transition state, thereby resulting in a relatively unselective reaction.

(44) (a) Graham, C. L.; McQuillin, F. J. *J. Chem. Soc.* **1963**, 4634. (b) Bottom, F. H.; McQuillin, F. J. *Tetrahedron Lett.* **1967**, 1975. (c) Rao, H. S. P.; Reddy, K. S.; Balasubrahmanyam, S. N. *Tetrahedron Lett.* **1994**, *35*, 1759.

(45) Sihida, M.; Tomohiro, S.; Shimzu, M.; Inagaki, S. *Chem. Lett.* **1995**, 739.

(46) (a) Fisher, M. J.; Hehre, W. J.; Kahn, S. D.; Overman, L. E. *J. Am. Chem. Soc.* **1988**, *110*, 4625. (b) Wu, Y.-D.; Li, Y.; Houk, K. N. *J. Am. Chem. Soc.* **1993** *58*, 4625.

(47) Gutsche, C. D.; Tao, I. Y. C. *J. Org. Chem.* **1967**, *32*, 1778.

(48) Wu, Y.-H.; Feldkamp, R. F.; Corrigan, J. R.; Rhodes, H. J. *J. Org. Chem.* **1961**, *26*, 1524.

In conclusion, the present study has helped define the stereochemical issues associated with the 1,3-dipolar cycloaddition of ring-fused isomünchnones. *Exo* transition states are generally preferred and the highest selectivities encountered occur when the reactive dipole contains an ester functionality. The inclusion of substituents at any position of the fused five-membered ring was found to enhance *exo* selectivity. Synthetically useful $\pi$-facial selectivities were achieved by incorporating a stereogenic center adjacent to C(2) of the dipole. Interestingly, a *contrasteric syn* addition of the dipolarophile occurred when an ester group was located adjacent to the nitrogen atom of the mesoionic ring system. The experimental results are reflected in the calculated transition state energies using semiempirical FMO methods. Experiments to determine the stereodirecting features of other substituents and to exploit the methodology in the stereocontrolled synthesis of chiral azapolycyclic systems are presently underway in our laboratories.

## Experimental Section

Melting points are uncorrected. Mass spectra were determined at an ionizing voltage of 70 eV. Unless otherwise noted, all reactions were performed under an atmosphere of dry argon in flame-dried glassware. 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. Methanesulfonyl azide and *p*-nitrobenzenesulfonyl azide were prepared according to previously published procedures.[49] Due to a very long relaxation time, the resonance for the carbon atom next to the diazo functional group was usually not detected for the diazo imides prepared in this study.

**General Procedure for the Preparation of α-Diazo Imides.** To a solution of the appropriate lactam (5.0 mmol) in THF (30 mL) was added lithium bis(trimethylsilyl)amide (1.0 equiv, 1.0 M in hexane) at −78 °C. The mixture was stirred at −78 °C for 30 min, and ethyldiazomalonyl chloride[12] (5.0 mmol) was added *via* syringe. The mixture was stirred at −78 °C for 10 min and allowed to warm to rt. Evaporation of the solvent afforded the crude diazo imide as orange oil, which was purified by silica gel column chromatography. An alternate method that was used involved heating a solution of the appropriate lactam (5.0 mmol) with methylmalonyl chloride (1.5 equiv) in benzene (30 mL) at reflux for 2.5−6 h. Evaporation of the solvent afforded the crude malonate as a colorless oil, which was purified by silica gel column chromatography. To a solution of the above malonate (2.0 mmol) in dichloromethane (25 mL) was added either mesyl azide or *p*-methylbenzenesulfonyl azide (1.1−1.5 equiv) and triethylamine (1.0−2.0 equiv). The mixure was stirred at rt for 2 h, and the insoluble precipitate that had formed in the reaction was removed by filtration. The solvent was removed under reduced pressure to give the diazo imide, which was purified by silica gel column chromatography.

**2-Diazo-3-(2-oxopyrrolidin-1-yl)-3-oxopropionic Acid Ethyl Ester (5).** A sample of pyrrolidin-2-one (**4**) (1.04 g, 12.2 mmol) and ethyldiazomalonyl chloride (2.16 g, 12.2 mmol) were allowed to react according to the general procedure. The crude residue was subjected to flash silica gel chromatography to give 2.2 g (80%) of **5** as a yellow oil: IR (neat) 2983, 2136, 1730, 1652, and 1126 $cm^{-1}$; $^1$H-NMR ($CDCl_3$, 300 MHz) $\delta$ 1.24 (t, 3H, $J$ = 7.2 Hz), 2.07 (m, 2H), 2.51 (t, 2H, $J$ = 7.8 Hz), 3.78 (t, 2H, $J$ = 7.2 Hz), and 4.20 (q, 2H, $J$ = 7.2 Hz); $^{13}$C-NMR ($CDCl_3$, 75 MHz) $\delta$ 14.1, 17.6, 32.6, 46.2, 61.5, 160.7, 160.9, and 173.9. Anal Calcd. for $C_9H_{11}N_3O_4$: C, 48.00; H, 4.92; N, 18.66. Found: C, 48.06; H, 4.92; N, 18.65.

**2-Diazo-3-(4-methyl-5-oxopyrrolidin-1-yl)-3-oxopropionic Acid Ethyl Ester (16).** A sample of 3-methylpyrrolidin-2-one (**14**) (700 mg, 7.1 mmol) and ethyldiazomalonyl chloride (1.4 g, 7.8 mmol) were allowed to react according to the general procedure. Flash silica gel chromatography of the crude residue gave 1.43 g (85%) of **16** as a bright yellow oil: IR (neat) 2138, 1732, 1651, 1125, 1029, and 878 $cm^{-1}$; $^1$H-NMR ($CDCl_3$, 300 MHz) $\delta$ 1.20 (d, 3H, $J$ = 5.7 Hz), 1.26 (t, 3H, $J$ = 7.2 Hz), 1.60−1.74 (m, 1H), 2.21−2.32 (m, 1H), 2.54−2.67 (m, 1H), 3.67 (ddd, 1H, $J$ =11.1, 9.6, and 7.2 Hz), 3.81 (ddd, 1H, $J$ = 11.1, 8.4, and 2.7 Hz), and 4.23 (q, 2H, $J$ = 7.2 Hz); $^{13}$C-NMR ($CDCl_3$, 75 MHz) $\delta$ 14.2, 15.2, 26.4, 38.6, 44.1, 61.6, 160.9, 161.0, and 176.5; HRMS calcd for $C_{10}H_{13}N_3O_4Li$ $(M + Li)^+$ 246.1066, found 246.1073.

**1-[(Methoxycarbonyl)acetyl]-2-oxopyrrolidine-3-carboxylic Acid Methyl Ester.** A sample of 2-oxopyrrolidine-3-carboxylic acid methyl ester (**15**)[39] (3.0 g, 21.0 mmol) and methylmalonyl chloride (3.2 g, 23.1 mmol) were allowed to react according to the general procedure for 5 h. Flash silica gel chromatography of the crude residue gave 4.68 g (92%) of the corresponding malonate as a colorless oil: IR (neat) 2951, 1733, 1690, 1435, 1151, and 990 $cm^{-1}$; $^1$H-NMR ($CDCl_3$, 300 MHz) $\delta$ 2.29−2.47 (m, 2H), 3.62 (dd, 1H, $J$ = 9.0 and 8.1 Hz), 3.71 (s, 3H), 3.79 (s, 3H), 3.82 (d, 1H, $J$ = 13.8 Hz), 3.93−4.09 (m, 2H), and 3.97 (d, 1H, $J$ = 13.8 Hz); $^{13}$C-NMR ($CDCl_3$, 75 MHz) $\delta$ 21.1, 43.5, 50.0, 52.1, 52.7, 165.9, 167.0, 168.4, and 170.4; HRMS calcd for $C_{10}H_{14}NO_6$ $(M + H)^+$ 244.0821, found 244.0816.

**1-[Diazo(methoxycarbonyl)acetyl]-2-oxopyrrolidine-3-carboxylic Acid Methyl Ester (17).** To a solution of the above malonate (1.4 g, 5.8 mmol) in dichloromethane (40 mL) at −10 °C was added *p*-nitrobenzenesulfonyl azide (2.0 g, 8.6 mmol) and triethylamine (1.2 g, 11.5 mmol). The mixture was stirred at −10 °C for 1 h and was stored at −20 °C overnight. The precipitate that had formed was filtered, and the solvent was removed under reduced pressure. The residue was subjected to flash silica gel chromatography to give 980 mg (63%) of diazo imide **17** as a bright yellow oil: IR (neat) 2135, 1756, 1697, 1646, 1041, and 750 $cm^{-1}$; $^1$H-NMR ($CDCl_3$, 300 MHz) $\delta$ 2.16−2.31 (m, 2H), 3.52 (dd, 1H, $J$ = 9.0 and 7.8 Hz), 3.63 (s, 3H), 3.64 (s, 3H), and 3.66−3.79 (m, 2H); $^{13}$C-NMR ($CDCl_3$, 75 MHz) $\delta$ 21.5, 44.3, 49.5, 52.2, 52.4, 70.0, 159.9, 160.9, 168.3, and 168.8; HRMS calcd for $C_{10}H_{12}N_3O_6$ $(M + H)^+$ 270.0726, found 270.0737.

**2-Diazo-3-(2-methyl-5-oxopyrrolidin-1-yl)-3-oxopropionic Acid Ethyl Ester (27).** A sample of 5-methylpyrrolidin-2-one (**22**) (730 mg, 7.4 mmol) and ethyldiazomalonyl chloride (1.4 g, 8.1 mmol) were allowed to react according to the general procedure. Flash silica gel chromatography of the crude residue gave 1.49 g (85%) of **27** as a bright yellow oil: IR (neat) 2139, 1733, 1652, 1371, 1133, and 1017 $cm^{-1}$; $^1$H-NMR ($CDCl_3$, 300 MHz) $\delta$ 1.22 (t, 3H, $J$ = 7.2 Hz), 1.27 (d, 3H, $J$ = 6.0 Hz), 1.59−1.69 (m, 1H), 2.15−2.25 (m, 1H), 2.34−2.53 (m, 2H), 4.18 (q, 2H, $J$ = 7.2 Hz), and 4.28−4.34 (m, 1H); $^{13}$C-NMR ($CDCl_3$, 75 MHz) $\delta$ 14.0, 19.7, 25.9, 31.4, 54.1, 61.4, 71.3, 160.9, 161.3, and 174.3. Anal. Calcd for $C_{10}H_{13}N_3O_4$: C, 50.21; H, 5.48; N, 17.56. Found: C, 49.91; H, 5.39; N, 17.55.

**1-[Diazo(ethoxycarbonyl)acetyl]-5-oxopyrrolidine-2-carboxylic Acid Ethyl Ester (28).** A sample of 5-oxopyrrolidine-2-carboxylic acid ethyl ester (**23**) (880 mg, 5.6 mmol) and ethyldiazomalonyl chloride (990 mg, 5.6 mmol) were allowed to react according to the general procedure. Addition of ethyl acetate to the crude mixture was followed by filtration of the solution through a plug of silica gel. Evaporation of the solvent gave 1.5 g (90%) of **28** as a yellow oil: IR (neat) 2129, 1752, 1652, 1197, and 1033 $cm^{-1}$; $^1$H-NMR ($CDCl_3$, 300 MHz) $\delta$ 1.27 (t, 3H, $J$ = 7.2 Hz), 1.29 (t, 3H, $J$ = 7.2 Hz), 2.07−2.13 (m, 1H), 2.37−2.72 (m, 3H), 4.21 (m, 2H), 4.26 (q, 2H, $J$ = 7.2 Hz), and 4.71 (dd, 1H, $J$ = 8.7 and 3.9 Hz); $^{13}$C-NMR ($CDCl_3$, 75 MHz) $\delta$ 13.9, 14.1, 21.9, 31.2, 58.6, 61.7, 61.8, 160.6, 170.5, 172.9, and 173.0; HRMS calcd for $C_{12}H_{16}N_3O_6$ $(M + H)^+$ 298.1039, found 298.1034.

**1-[Diazo(ethoxycarbonyl)acetyl]-5-oxopyrrolidine-2-carboxylic Acid *tert*-Butyl Ester (29).** A sample of 5-oxopyrrolidine-2-carboxylic acid *tert*-butyl ester[50] (**24**) (1.1 g, 6.0

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mmol) and ethyldiazomalonyl chloride (1.1 g, 6.0 mmol) were allowed to react according to the general procedure. Evaporation of the solvent gave 1.83 g (90%) of **29** as a yellow oil which crystallized on standing: mp 97−98 °C; IR (KBr) 2136, 1759, 1723, 1645, and 1154 $cm^{-1}$; $^1$H-NMR ($CDCl_3$, 300 MHz) $\delta$ 1.36 (t, 3H, $J$ = 7.2 Hz), 1.49 (s, 9H), 2.02−2.09 (m, 1H), 2.36−2.69 (m, 3H), 4.29 (q, 2H, $J$ = 7.2 Hz), and 4.63 (dd, 1H, $J$ = 8.7 and 4.5 Hz); $^{13}$C-NMR ($CDCl_3$, 75 MHz) $\delta$ 14.1, 21.9, 27.7, 31.2, 59.2, 61.6, 82.5, 160.5, 169.4, 172.9, and 173.0. Anal. Calcd for $C_{14}H_{19}N_3O_6$: C, 51.69; H, 5.89; N, 12.92. Found: C, 51.43; H, 5.86; N, 12.67.

**1-[Diazo(ethoxycarbonyl)acetyl]-5-oxopyrrolidine-2-carboxylic Acid Allyl Ester (30).** A sample of 5-oxopyrrolidine-2-carboxylic acid allyl ester[51] (**25**) (1.0 g, 6.0 mmol) and ethyldiazomalonyl chloride (1.1 g, 6.0 mmol) were allowed to react according to the general procedure. Flash silica gel chromatography of the crude residue gave 1.41 g (76%) of **30** as a yellow powder: mp 67−68 °C; IR (KBr) 2136, 1745, 1695, 1652, and 1183 $cm^{-1}$; $^1$H-NMR ($CDCl_3$, 300 MHz) $\delta$ 1.22 (t, 3H, $J$ = 7.2 Hz), 1.99−2.09 (m, 1H), 2.32−2.64 (m, 3H), 4.19 (q, 2H, $J$ = 7.2 Hz), 4.57 (dd, 2H, $J$ = 6.0 and 0.9 Hz), 4.67 (dd, 1H, $J$ = 8.4 and 3.9 Hz), 5.17 (dd, 1H, $J$ = 10.5 and 0.9 Hz), 5.26 (dd, 1H, $J$ = 15.6 and 0.9 Hz), and 5.75−5.88 (m, 1H); $^{13}$C-NMR ($CDCl_3$, 75 MHz) $\delta$ 13.9, 21.8, 31.0, 58.3, 61.5, 65.9, 118.7, 131.0, 160.4, 170.1, 172.7, and 172.8. Anal. Calcd for $C_{13}H_{15}N_3O_6$: C, 50.49; H, 4.89; N, 13.59. Found: C, 50.61; H, 4.89; N, 13.32.

**1-[(Methoxycarbonyl)acetyl]-5-oxopyrrolidine-2-carboxylic Acid Benzyl Ester.** A sample of 5-oxopyrrolidine-2-carboxylic acid benzyl ester (**26**)[51] (1.4 g, 6.4 mmol) and methyl malonyl chloride (1.3 g, 9.6 mmol) were allowed to react according to the general procedure for 6 h. Flash silica gel chromatography of the crude residue gave 1.76 g (82%) of the desired malonate as a colorless oil: IR (neat) 1748, 1699, 1393, and 745 $cm^{-1}$; $^1$H-NMR ($CDCl_3$, 300 MHz) $\delta$ 2.02−2.10, (m, 1H), 2.30−2.46 (m, 1H), 2.48−2.74 (m, 2H), 3.69 (s, 3H), 3.77 (d, 1H, $J$ = 16.5 Hz), 4.07 (d, 1H, $J$ = 16.5 Hz), 4.82 (dd, 1H, $J$ = 9.3 and 2.7 Hz), 5.18 (s, 2H), and 5.30−5.38 (s, 5H); $^{13}$C-NMR ($CDCl_3$, 75 MHz) $\delta$ 21.2, 31.4, 43.4, 52.2, 57.7, 67.3, 128.1, 128.4, 128.5, 134.9, 166.0, 167.1, 170.3, and 174.4; HRMS calcd for $C_{16}H_{18}NO_6$ $(M + H)^+$ 320.1134, found 320.1135.

**1-[Diazo(methoxycarbonyl)acetyl]-5-oxopyrrolidine-2-carboxylic Acid Benzyl Ester (31).** A sample of the above imide (800 mg, 2.5 mmol), mesyl azide (304 mg, 2.5 mmol), and triethylamine (250 mg, 2.5 mmol) were allowed to react according to the general procedure for 5 h at rt. Flash silica gel chromatography of the crude residue gave 813 mg (95%) of **31** as a viscous yellow oil: IR (neat) 2141, 1742, 1645, 1438, and 1037 $cm^{-1}$; $^1$H-NMR ($CDCl_3$, 300 MHz) $\delta$ 2.00−2.06 (m, 1H), 2.24−2.67 (m, 3H), 3.74 (s, 3H), 4.72 (dd, 1H, $J$ = 8.7 and 4.2 Hz), 5.14 (s, 2H), and 7.26−7.33 (m, 5H); $^{13}$C-NMR ($CDCl_3$, 75 MHz) $\delta$ 21.6, 30.9, 52.2, 58.3, 67.1, 127.8, 128.2, 128.3, 134.8, 160.1, 160.8, 170.1, and 172.7; HRMS calcd for $C_{16}H_{15}N_3O_5Li$ $(M + Li)^+$ 352.1121, found 352.1111.

**1-(1,3-Dioxobutyl)-5-oxopyrrolidine-2-carboxylic Acid *tert*-Butyl Ester.** A mixture of 5-oxopyrrolidine-2-carboxylic acid *tert*-butyl ester (**24**) (1.0 g, 5.4 mmol) and 2,2,6-trimethyl-1,3-dioxin-4-one (845 mg, 5.9 mmol) in toluene (20 mL) was placed in an oil bath at 160 °C and heated for 2.5 h. The solvent was removed under reduced pressure, and the oily residue was subjected to flash silica gel chromatography to give 1.30 g (90%) of the desired keto imide as a colorless oil: IR (neat) 1976, 2933, 1745, 1695, 1624, and 1154 $cm^{-1}$; $^1$H-NMR ($CDCl_3$, 300 MHz) $\delta$ 1.46 (s, 9H), 2.00−2.04 (m, 1H), 2.26 (s, 3H), 2.27−2.31 (m, 1H), 2.45−2.75 (m, 2H), 3.76 (d, 1H, $J$ = 16.2 Hz), 4.22 (d, 1H, $J$ = 16.2 Hz), and 4.64 (dd, 1H, $J$ = 9.3 and 1.5 Hz); $^{13}$C-NMR ($CDCl_3$, 75 MHz) $\delta$ 21.3, 27.8, 30.1, 31.6, 52.1, 58.5, 82.6, 166.7, 169.8, 174.8, and 200.8; HRMS calcd for $C_{13}H_{19}NO_5Li$ $(M + Li)^+$ 276.1423, found 276.1436.

**1-(2-Diazo-1,3-dioxobutyl)-5-oxopyrrolidine-2-carboxylic Acid *tert*-Butyl Ester (32).** A mixture of the above imide (1.3 g, 4.6 mmol), mesyl azide (620 mg, 5.1 mmol), and triethylamine (520 mg, 5.1 mmol) was allowed to react according to the general procedure for 3 h at rt. Flash silica gel chromatography of the crude residue gave 1.30 g (95%) of **32** as a viscous yellow oil: IR (neat) 2976, 2136, 1745, 1667, and 1147 $cm^{-1}$; $^1$H-NMR ($CDCl_3$, 300 MHz) $\delta$ 1.44 (s, 9H), 1.99−2.08 (m, 1H), 2.34−2.44 (m, 1H), 2.42 (s, 3H), 2.53−2.68 (m, 2H), and 4.62 (dd, 1H, $J$ = 8.7 and 5.1 Hz); $^{13}$C-NMR ($CDCl_3$, 75 MHz) $\delta$ 21.8, 27.8, 28.6, 31.5, 59.3, 82.8, 160.1, 169.5, 173.2, and 189.8. Anal. Calcd for $C_{13}H_{17}N_3O_5$: C, 52.88; H, 5.80; N, 14.23. Found: C, 52.62; H, 5.79; N, 14.10.

**3-(3-Methyl-5-oxopyrrolidin-1-yl)-3-oxopropionic Acid Methyl Ester.** A mixture of 4-methylpyrrolidin-2-one (**48**)[52] (2.2 g, 22 mmol) and methylmalonyl chloride (3.8 g, 28 mmol) was allowed to react according to the general procedure for 2.5 h. Flash silica gel chromatography of the crude residue gave 3.71 g (84%) of the desired imide as a colorless oil: IR (neat) 1738, 1695, 1339, 1211, 1014, and 898 $cm^{-1}$; $^1$H-NMR ($CDCl_3$, 400 MHz) $\delta$ 1.08 (d, 3H, $J$ = 6.4 Hz), 2.18 (dd, 1H, $J$ = 17.6 and 8.0 Hz), 2.31−2.46 (m, 1H), 2.65 (dd, 1H, $J$ = 17.6 and 8.0 Hz), 3.31 (dd, 1H, $J$ = 11.6 and, 6.8 Hz), 3.65 (s, 3H), 3.79 (d, 1H, $J$ = 16.4 Hz), 3.85 (d, 1H, $J$ = 16.4 Hz), and 3.92 (dd, 1H, $J$ = 11.6 and 7.6 Hz); $^{13}$C-NMR ($CDCl_3$, 100 MHz) $\delta$ 18.8, 25.4, 41.1, 43.7, 52.0, 52.1, 166.0, 167.5, and 175.1. Anal. Calcd for $C_9H_{13}NO_4$: C, 54.26; H, 6.58; N, 7.03. Found: C, 54.24; H, 6.60; N, 6.92.

**2-Diazo-3-(3-methyl-5-oxopyrrolidin-1-yl)-3-oxopropionic Acid Methyl Ester (50).** A mixture of the above imide (1.8 g, 8.8 mmol), mesyl azide (1.1 g, 8.8 mmol), and triethylamine (1.8 g, 18 mmol) was allowed to react according to the general procedure for 18 h at rt. Flash silica gel chromatography of the crude residue gave 1.73 g (87%) of **50** as a yellow oil: IR (neat) 2136, 1744, 1695, 1652, 1133, and 756 $cm^{-1}$; $^1$H-NMR ($CDCl_3$, 300 MHz) $\delta$ 1.14 (d, 3H, $J$ = 6.8 Hz), 2.18 (dd, 1H, $J$ = 17.6 and 7.2 Hz), 2.42−2.50 (m, 1H), 2.67 (dd, 1H, $J$ = 17.6 and 8.0 Hz), 3.39 (dd, 1H, $J$ = 10.8 and 6.8 Hz), 3.78 (s, 3H), and 3.88 (dd, 1H, $J$ = 10.8 and 7.2 Hz); $^{13}$C-NMR ($CDCl_3$, 75 MHz) $\delta$ 18.7, 26.0, 40.7, 52.5, 53.0, 160.6, 161.5, and 173.7. Anal. Calcd for $C_9H_{11}N_3O_4$: C, 48.00; H, 4.92; N, 18.66. Found: C, 48.05; H, 5.08; N, 18.83.

**1-[(Methoxycarbonyl)acetyl]-5-oxo-pyrrolidine-3-carboxylic Acid Methyl Ester.** A sample of 5-oxopyrrolidine-3-carboxylic acid methyl ester (**49**)[53] (2.0 g, 14 mmol) and methylmalonyl chloride (2.4 g, 18 mmol) were allowed to react according to the general procedure for 3 h. Flash silica gel chromatography of the crude residue gave 2.38 g (70%) of the desired imide as a colorless oil: IR (neat) 1752, 1695, 1439, 1125, and 848 $cm^{-1}$; $^1$H-NMR ($CDCl_3$, 300 MHz) $\delta$ 2.81 (dd, 1H, $J$ = 18.0 and 9.2 Hz), 2.93 (dd, 1H, $J$ = 18.0 and 7.2 Hz), 3.20−3.27 (m, 1H), 3.69 (s, 3H), 3.73 (s, 3H), 3.81 (d, 1H, $J$ = 16.4 Hz), 3.92 (d, 1H, $J$ = 16.4 Hz), 3.97 (dd, 1H, $J$ = 12.0 and 7.2 Hz), and 4.08 (dd, 1H, $J$ = 12.0 and 9.2 Hz); $^{13}$C-NMR ($CDCl_3$, 75 MHz) $\delta$ 34.6, 35.7, 43.6, 47.1, 52.3, 52.6, 165.9, 167.3, 172.2, and 172.9. Anal. Calcd for $C_{10}H_{13}NO_6$: C, 49.38; H, 5.39; N, 5.76. Found: C, 49.31; H, 5.33; N, 5.67.

**1-[Diazo(methoxycarbonyl)acetyl]-5-oxopyrrolidine-3-carboxylic Acid Methyl Ester (51).** A mixture of the above imide (1.1 g, 4.6 mmol), *p*-methylbenzenesulfonyl azide (920 mg, 4.6 mmol), and triethylamine (1.6 g, 16 mmol) was allowed to react according to the general procedure for 18 h at rt. Flash silica gel chromatography of the crude residue gave 1.1 g (86%) of **51** as a yellow oil: IR (neat) 2143, 1737, 1652, 1133, and 756 $cm^{-1}$; $^1$H-NMR ($CDCl_3$, 400 MHz) $\delta$ 2.79 (dd, 1H, $J$ = 18.0 and 8.8 Hz), 2.90 (dd, 1H, $J$ = 18.0 and 7.2 Hz), 3.26 (m, 1H), 3.74 (s, 3H), 3.79 (s, 3H), 3.99 (dd, 1H, $J$ = 11.6 and 6.8 Hz), and 4.05 (dd, 1H, $J$ = 11.6 and 8.4 Hz); $^{13}$C-NMR ($CDCl_3$, 100 MHz) $\delta$ 35.3, 35.4, 48.0, 52.5, 52.6, 160.3, 151.2, 171.5, and 172.0. Anal. Calcd for $C_{10}H_{11}N_3O_6$: C, 44.62; H, 4.12; N, 15.61. Found: C, 44.70; H, 4.18; N, 15.55.

**General Procedure for the Rhodium(II)-Catalyzed Reaction of α-Diazo Imides.** To a solution of the α-diazo imide (750 $\mu$mol) in benzene (10 mL) was added the appropriate dipolarophile (1.0−2.0 equiv), and the mixture was placed into an oil bath preheated to 90 °C. Rhodium perfluorobuty-

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roamidate [$Rh_2$(pfm)$_4$, 1 mg] was added, and the mixture was heated at reflux until the starting material was completely consumed. The solvent was removed under reduced pressure, and the crude cycloadduct was purified by flash silica gel chromatography.

**Tetrahydro-1,3,5-trioxo-2-phenyl-7*H*-4,9a-epoxy-1*H*-pyrrolo[3,4-*g*]indolizine-4-carboxylic Acid Ethyl Ester (11).** Diazo imide **5** (310 mg, 1.4 mmol) and *N*-phenylmaleimide (240 mg, 1.4 mmol) were allowed to react according to the general procedure. Proton NMR analysis of the crude product mixture showed the formation of two diastereomeric cycloadducts identified as *exo* **11a** and *endo* **11b** (90%, dr 85:15) which were separated by flash silica gel chromatography.

Cycloadduct *exo* **11a** (398 mg, 78%): mp 183−184 °C; IR (KBr) 1738, 1716, 1382, and 1204 cm$^{-1}$; $^1$H-NMR ($CDCl_3$, 300 MHz) $\delta$ 1.39 (t, 3H, $J$ = 7.2 Hz), 2.17−2.25 (m, 2H), 2.39−2.45 (m, 1H), 2.56−2.66 (m, 1H), 3.22 (m, 1H), 3.51 (d, 1H, $J$ = 6.9 Hz), 3.70−3.75 (m, 1H), 3.86 (d, 1H, $J$ = 6.9 Hz), 4.46 (q, 2H, $J$ = 7.2 Hz), 7.22 (d, 2H, $J$ = 7.2 Hz), and 7.29−7.49 (m, 3H); $^{13}$C-NMR ($CDCl_3$, 75 MHz) $\delta$ 14.1, 25.9, 26.7, 44.0, 47.9, 52.4, 62.8, 88.6, 103.7, 126.3, 129.0, 129.1, 131.1, 162.3, 169.1, 171.6, and 172.0. Anal. Calcd for $C_{19}H_{18}N_2O_6$: C, 61.62; H, 4.90; N, 7.56. Found: C, 61.50; H, 4.94; N, 7.51.

Cycloadduct *endo* **11b** (75 mg, 15%): mp 190−191 °C; IR (KBr) 1780, 1745, 1716, 1197, and 1119 cm$^{-1}$; $^1$H-NMR ($CDCl_3$, 300 MHz) $\delta$ 1.38 (t, 3H, $J$ = 7.2 Hz), 2.13−2.22 (m, 2H), 2.45−2.58 (m, 2H), 3.03 (m, 1H), 3.72 (d, 1H, $J$ = 8.4 Hz), 3.77−3.82 (m, 1H), 4.04 (d, 1H, $J$ = 8.4 Hz), 4.42 (q, 2H, $J$ = 7.2 Hz), 7.16 (m, 2H), and 7.41−7.51 (m, 3H); $^{13}$C-NMR ($CDCl_3$, 75 MHz) $\delta$ 14.0, 25.9, 27.9, 44.4, 48.8, 51.8, 63.0, 88.3, 103.3, 126.5, 129.0, 129.2, 131.1, 163.3, 168.6, 169.8, and 171.3. Anal. Calcd for $C_{19}H_{18}N_2O_6$: C, 61.62; H, 4.90; N, 7.56. Found: C, 61.69; H, 4.92; N, 7.61.

**Tetrahydro-9-methyl-1,3,5-trioxo-2-phenyl-7*H*-4,9a-epoxy-1*H*-pyrrolo[3,4-*g*]indolizine-4-carboxylic Acid Ethyl Ester (20).** Diazo imide **16** (400 mg, 1.7 mmol) and *N*-phenylmaleimide (290 mg, 1.7 mmol) were allowed to react according to the general procedure. Proton NMR analysis of the crude product mixture showed the predominant formation of cycloadduct *exo*−*anti* **20** (90%). Flash silica gel chromatography gave 552 mg (86%) of **20** as a white powder: mp 203−204 °C; IR (KBr) 1756, 1718, 1393, 1197, 1116, and 754 cm$^{-1}$; $^1$H-NMR ($CDCl_3$, 400 MHz) $\delta$ 1.15 (d, 3H, $J$ = 6.9 Hz), 1.35 (t, 3H, $J$ = 7.2 Hz), 1.78−1.87 (m, 1H), 2.18−2.26 (m, 1H), 2.84−2.92 (m, 1H), 3.05−3.13 (m, 1H), 3.42 (d, 1H, $J$ = 6.6. Hz), 3.63−3.70 (m, 1H), 3.82 (d, 1H, $J$ = 6.6 Hz), 4.39 (q, 2H, $J$ = 7.2 Hz), 7.19 (d, 2H, $J$ = 7.2 Hz), and 7.35−7.46 (m, 3H); $^{13}$C-NMR ($CDCl_3$, 75 MHz) $\delta$ 12.1, 14.0, 33.8, 34.6, 42.6, 47.8, 52.5, 62.5, 87.9, 103.3, 126.2, 128.9, 129.1, 131.1, 162.3, 169.0, 171.7, and 172.0. Anal. Calcd for $C_{20}H_{20}N_2O_6$: C, 62.49; H, 5.24; N, 7.29. Found: C, 62.52; H, 5.25; N, 7.28.

**3-Oxo-2,3,5,6-tetrahydropyrrolo[2,1-*b*]oxazole-2,7-dicarboxylic Acid Dimethyl Ester (21).** To a solution of diazo imide **17** (170 mg, 620 $\mu$mol) in benzene (5 mL) was added $Rh_2$(pfm)$_4$ (1 mg), and the mixture was stirred overnight under an atmosphere of argon. The solvent was removed under reduced pressure, and the residue was subjected to flash silica gel chromatography to give 115 mg (77%) of **21** as a colorless oil; IR (neat) 1762, 1646, 1450, 1377, 1107, and 721 cm$^{-1}$; $^1$H-NMR ($CDCl_3$, 400 MHz) $\delta$ 3.09−3.15 (m, 2H), 3.68 (s, 3H), 3.69−3.74 (m, 2H), 3.83 (s, 3H), and 5.51 (s, 1H); $^{13}$C-NMR ($CDCl_3$, 100 MHz) $\delta$ 30.1, 39.2, 51.2, 53.7, 80.7, 85.7, 159.5, 160.6, 163.3, and 163.9; HRMS calcd for $C_{10}H_{11}NO_6$ $(M + H)^+$ 242.0665, found 242.0662.

**Tetrahydro-7-methyl-1,3,5-trioxo-2-phenyl-7*H*-4,9a-epoxy-1*H*-pyrrolo-[3,4-*g*]indolizine-4-carboxylic Acid Ethyl Ester (33).** Diazo imide **27** (450 mg, 1.9 mmol) and *N*-phenylmaleimide (330 mg, 1.9 mmol) were allowed to react according to the general procedure. Proton NMR analysis of the crude product mixture showed the formation of two diastereomeric cycloadducts identified as *exo*−*syn* **33a** and *exo*−*anti* **33b** (90%, dr 58:42) which were separated by flash silica gel chromatography. The relative stereochemistry of these cycloadducts could not be assigned.

The major cycloadduct **33a** (357 mg, 49%): mp 219−220 °C; IR (KBr) 1749, 1713, 1206, 1136, and 1051 cm$^{-1}$; $^1$H-NMR ($CDCl_3$, 300 MHz) $\delta$ 1.29 (d, 3H, $J$ = 6.6 Hz), 1.40 (t, 3H, $J$ = 7.2 Hz), 1.85−1.89 (m, 1H), 2.29−2.49 (m, 2H), 2.76−2.82 (m, 1H), 3.50 (d, 1H, $J$ = 6.6 Hz), 3.90 (d, 1H, $J$ = 6.6 Hz), 4.07−4.11 (m, 1H), 4.45 (q, 2H, $J$ = 7.2 Hz), 7.24 (d, 2H, $J$ = 7.2 Hz), and 7.37−7.49 (m, 3H); $^{13}$C-NMR ($CDCl_3$, 75 MHz) $\delta$ 14.0, 20.5, 25.1, 33.2, 47.7, 52.6, 53.1, 62.6, 88.9, 103.5, 126.2, 128.9, 129.1, 131.1, 162.3, 168.6, 171.6, and 172.0. Anal. Calcd for $C_{20}H_{20}N_2O_6$: C, 62.49; H, 5.24; N, 7.29. Found: C, 62.50; H, 5.26; N, 7.28.

The minor cycloadduct **33b** (267 mg, 37%): mp 208−209 °C; IR (KBr) 1745, 1721, 1223, 1049, and 753 cm$^{-1}$; $^1$H-NMR ($CDCl_3$, 300 MHz) $\delta$ 1.39 (t, 3H, $J$ = 7.2 Hz), 1.46 (d, 3H, $J$ = 6.3 Hz), 1.87−2.04 (m, 1H), 2.35−2.51 (m, 2H), 2.62−2.80 (m, 1H), 3.47 (d, 1H, $J$ = 6.6 Hz), 3.81 (d, 1H, $J$ = 6.6 Hz), 3.83−3.87 (m, 1H), 4.43 (q, 2H, $J$ = 7.2 Hz), 7.22 (d, 2H, $J$ = 7.2 Hz), and 7.36−7.47 (m, 3H); $^{13}$C-NMR ($CDCl_3$, 75 MHz) $\delta$ 14.1, 17.5, 24.5, 34.4, 47.7, 52.5, 53.4, 62.7, 89.9, 104.9, 126.2, 129.0, 129.2, 131.1, 162.3, 166.6, 171.6, and 172.0. Anal. Calcd for $C_{20}H_{20}N_2O_6$: C, 62.49; H, 5.24; N, 7.29. Found: C, 62.41; H, 5.23; N, 7.23.

**Tetrahydro-1,3,5-trioxo-2-phenyl-7*H*-4,9a-epoxy-1*H*-pyrrolo[3,4-*g*]indolizine-4,7-dicarboxylic Acid Diethyl Ester (34).** Diazo imide **28** (360 mg, 1.2 mmol) and *N*-phenylmaleimide (210 mg, 1.2 mmol) were allowed to react according to the general procedure. Proton NMR analysis of the crude product mixture showed the formation of two diastereomeric cycloadducts identified as *exo*−*syn* **34a** and *exo*−*anti* **34b** (90%, dr 83:17) which were separated by flash silica gel chromatography.

Cycloadduct *exo*−*syn* **34a** (375 mg, 71%): mp 187−189 °C; IR (KBr) 1759, 1720, 1595, 1389, and 1040 cm$^{-1}$; $^1$H-NMR ($CDCl_3$, 300 MHz) $\delta$ 1.30 (t, 3H, $J$ = 7.2 Hz), 1.40 (t, 3H, $J$ = 7.2 Hz), 2.33−2.43 (m, 2H), 2.54−2.64 (m, 1H), 2.67−2.79 (m 1H), 3.87 (d, 1H, $J$ = 6.9 Hz), 3.92 (d, 1H, $J$ =6.9 Hz), 4.21 (q, 2H, $J$ = 7.2 Hz), 4.45 (q, 2H, $J$ = 7.2 Hz), 4.54 (d, 1H, $J$ = 8.1 Hz), 7.23 (m, 2H), and 7.39−7.51 (m, 3H); $^{13}$C-NMR ($CDCl_3$, 75 MHz) $\delta$ 14.0, 14.1, 25.5, 30.9, 47.9, 52.4, 56.8, 62.1, 62.9, 88.5, 104.0, 126.3, 129.0, 129.1, 131.1, 162.1, 167.7, 170.3, 171.4, and 172.0. Anal. Calcd for $C_{22}H_{22}N_2O_8$: C, 59.73; H, 5.01; N, 6.22. Found: C, 59.65; H, 4.96; N, 6.26.

Cycloadduct *exo*−*anti* **34b** (78 mg, 14%): mp 170−171 °C; IR (KBr) 1752, 1709, 1496, 1382, and 749 cm$^{-1}$; $^1$H-NMR ($CDCl_3$, 300 MHz) $\delta$ 1.25 (t, 3H, $J$ = 7.2 Hz), 1.37 (t, 3H, $J$ = 7.2 Hz), 2.13−2.30 (m, 2H), 2.32−2.46 (m, 2H), 3.58 (d, 1H, $J$ = 6.9 Hz), 3.85 (d, 1H, $J$ = 6.9 Hz), 4.20 (q, 2H, $J$ = 7.2 Hz), 4.28 (dd, 1H, $J$ = 7.9 and 2.1 Hz), 4.41 (q, 2H, $J$ = 7.2 Hz), 7.22 (m, 2H), and 7.39−7.51 (m, 3H); $^{13}$C-NMR ($CDCl_3$, 75 MHz) $\delta$ 13.9, 14.0, 23.6, 31.7, 47.6, 52.2, 56.0, 62.1, 62.7, 90.3, 103.9, 126.3, 129.0, 129.1, 131.1, 161.8, 166.5, 168.5, 171.5, and 172.0. Anal. Calcd for $C_{22}H_{22}N_2O_8$: C, 59.73; H, 5.01; N, 6.33. Found: C, 59.53; H, 5.03; N, 6.27.

**Tetrahydro-1,3,5-trioxo-2-phenyl-7*H*-4,9a-epoxy-1*H*-pyrrolo[3,4-*g*]indolizine-4,7-dicarboxylic Acid 4-Ethyl Ester 7-*tert*-Butyl Ester (35).** Diazo imide **29** (200 mg, 620 $\mu$mol) and *N*-phenylmaleimide (110 mg, 620 $\mu$mol) were allowed to react according to the general procedure. Proton NMR analysis of the crude product mixture showed the formation of two diastereomeric cycloadducts identified as *exo*−*syn* **35a** and *exo*−*anti* **35b** (90%, dr 90:10). Flash silica gel chromatography gave 242 mg (84%) of the major isomer *exo*−*syn* **35a** as a white powder: mp 191−192 °C; IR (KBr) 1752, 1709, 1496, 1389, and 1154 cm$^{-1}$; $^1$H-NMR ($CDCl_3$, 300 MHz) $\delta$ 1.40 (t, 3H, $J$ = 7.2 Hz), 1.46 (s, 9H), 2.25−2.75 (m, 4H), 3.92 (d, 1H, $J$ = 6.6 Hz), 3.94 (d, 1H, $J$ = 6.6 Hz), 4.39−4.50 (m, 2H), 4.45 (d, 1H, $J$ = 8.7 Hz), 7.24 (d, 2H, $J$ = 7.2 Hz), and 7.40−7.49 (m 3H); $^{13}$C-NMR ($CDCl_3$, 75 MHz) $\delta$ 14.0, 25.4, 27.9, 31.0, 47.9, 52.4, 57.5, 62.9, 82.9, 88.6, 104.0, 126.3, 129.0, 129.1, 131.2, 162.1, 167.5, 169.4, 171.5, and 172.1. Anal. Calcd for $C_{24}H_{26}N_2O_8$: C, 61.27; H, 5.27; N, 5.95. Found: C, 61.38; H, 5.60; N, 5.92.

Cycloadduct *exo*−*anti* **35b**: $^1$H-NMR ($CDCl_3$, 300 MHz) $\delta$ 1.41 (t, 3H, $J$ = 7.2 Hz), 1.49 (s, 9H), 2.25−2.75 (m, 4H), 3.55 (d, 1H, $J$ = 6.6 Hz), 3.86 (d, 1H, $J$ = 6.6 Hz), 4.22 (dd, 1H, $J$ = 8.4 and 1.5 Hz), 4.41−4.51 (m 2H), 7.24 (d, 2H, $J$ = 7.2 Hz), and 7.40−7.49 (m, 3H); $^{13}$C-NMR ($CDCl_3$, 75 MHz) $\delta$ 14.0, 23.5,

27.7, 31.5, 47.5, 52.3, 56.9, 62.8, 83.1, 104.0, 126.0, 129.0, 129.1, 131.4, 162.2, 167.5, 169.7, 171.4, and 172.0.

**Tetrahydro-1,3,5-trioxo-2-methyl-7*H*-4,9a-epoxy-1*H*-pyrrolo[3,4-*g*]indolizine-4,7-dicarboxylic Acid 4-Ethyl Ester 7-*tert*-Butyl Ester (36).** Diazo imide **29** (260 mg, 800 $\mu$mol) and *N*-methylmaleimide (90 mg, 800 $\mu$mol) were allowed to react according to the general procedure. Proton NMR analysis of the crude product mixture showed the formation of two diastereomeric cycloadducts identified as *exo*−*syn* **36a** and *exo*−*anti* **36b** (90%, dr 90:10). Flash silica gel chromatography gave 241 mg (74%) of the major adduct *exo*−*syn* **36a** isomer: mp 162−163 °C; IR (KBr) 1752, 1720, 1439, 1389, 1154, and 1047 cm$^{-1}$; $^1$H-NMR ($CDCl_3$, 400 MHz) $\delta$ 1.37 (t, 3H, $J$ = 7.2 Hz), 1.43 (s, 9H), 2.21−2.27 (m, 1H), 2.30 (ddd, 1H, $J$ = 14.8, 8.0, and 2.0 Hz), 2.45−2.55 (m, 1H), 2.61−2.69 (m, 1H), 2.93 (s, 3H), 3.70 (d, 1H, $J$ = 6.8 Hz), 3.76 (d, 1H, $J$ = 6.8 Hz), 4.37 (dd, 1H, $J$ = 6.8 and 1.6 Hz), and 4.37−4.45 (m, 2H); $^{13}$C-NMR ($CDCl_3$, 100 MHz) $\delta$ 14.0, 25.2, 25.3, 27.8, 30.9, 47.8, 52.4, 57.3, 62.7, 82.8, 88.1, 103.6, 162.2, 167.5, 169.4, 172.3, and 173.0. Anal. Calcd for $C_{19}H_{24}N_2O_8$: C, 55.88; H, 5.92; N, 6.86. Found: C, 55.90; H, 5.90; N, 6.83.

Cycloadduct *exo*−*anti* **36b**: $^1$H-NMR ($CDCl_3$, 400 MHz) $\delta$ 1.41 (t, 3H, $J$ = 7.2 Hz), 1.44 (s, 9H), 2.35−2.83 (m, 4H), 2.97 (s, 3H), 3.41 (d, 1H, $J$ = 6.8 Hz), 3.73 (d, 1H, $J$ = 6.8 Hz), 4.18 (dd 1 H, $J$ = 8.4 and 1.6 Hz), and 4.37−4.46 (m, 2H).

**Tetrahydro-1,3,5-trioxo-7*H*-4,9a-epoxy-1*H*-furano[3,4-*g*]indolizine-4,7-dicarboxylic Acid 4-Ethyl Ester 7-*tert*-Butyl Ester (37).** Diazo imide **29** (140 mg, 430 $\mu$mol) and maleic anhydride (40 mg, 430 $\mu$mol) were allowed to react according to the general procedure. Proton NMR analysis of the crude product mixture showed the formation of two diastereomeric cycloadducts identified as *exo*−*syn* **37a** and *exo*−*anti* **37b** (90%, dr 90:10). The major isomer *exo*−*syn* **37a** (134 mg, 79%) was a white powder: mp 136−137 °C; IR (KBr) 1780, 1732, 1695, 1368, and 1154 cm$^{-1}$; $^1$H-NMR ($CDCl_3$, 300 MHz) $\delta$ 1.41 (t, 3H, $J$ = 7.2 Hz), 1.48 (s, 9H), 2.29−2.72 (m, 4H), 4.08 (d, 1H, $J$ = 6.9 Hz), 4.12 (d, 1H, $J$ = 6.9 Hz), 4.46 (d, 1H, $J$ = 7.5 Hz), and 4.47 (q, 2H, $J$ = 7.2 Hz); $^{13}$C-NMR ($CDCl_3$, 75 MHz) $\delta$ 13.9, 25.2, 27.7, 30.8, 49.0, 53.8, 57.5, 63.1, 83.2, 88.8, 104.3, 161.3, 166.2, 166.5, 167.0, and 169.2. Anal. Calcd for $C_{18}H_{21}NO_9$: C, 54.68; H, 5.35; N, 3.54. Found: C, 54.48; H, 5.52; N, 3.27.

Cycloadduct *exo*−*anti* **37b**: $^1$H-NMR ($CDCl_3$, 300 MHz) $\delta$ 1.45 (s, 9H), 3.72 (d, 1H, $J$ = 7.2 Hz), 4.02 (d, 1H, $J$ = 7.2 Hz), and 4.22 (dd, 1H, $J$ = 8.1 and 1.5 Hz); $^{13}$C-NMR ($CDCl_3$, 75 MHz) $\delta$ 13.8, 23.4, 27.7, 31.1, 48.8, 53.6, 56.8, 62.9, 83.3, 88.8, 104.4, 161.1, 165.9, 167.8, and 168.1.

**Rh(II)-Catalyzed Decomposition of Diazoimide 29 in the Presence of 1,4-Naphthoquinone.** Diazo imide **29** (135 mg, 415 $\mu$mol) and 1,4-naphthoquinone (70 mg, 415 $\mu$mol) were allowed to react according to the general procedure. Proton NMR analysis of the crude product mixture showed the formation of two diastereomeric cycloadducts *exo*−*syn* **38a** and *exo*−*anti* **38b** (95%, dr 84:16) which were separated by flash silica gel chromatography.

Cycloadduct *exo*−*syn* **38a** (126 mg, 67%): mp 199−200 °C; IR (KBr) 1773, 1752, 1738, 1254, and 1154 cm$^{-1}$; $^1$H-NMR ($CDCl_3$, 300 MHz) $\delta$ 1.34 (t, 3H, $J$ = 7.2 Hz), 1.47 (s, 9H), 2.13 (dd, 1H, $J$ = 14.7 and 6.9 Hz), 2.24−2.43 (m, 2H), 2.71−2.75 (m, 1H), 3.90 (d, 1H, $J$ = 7.8 Hz), 3.99 (d, 1H, $J$ = 7.8 Hz), 4.30−4.40 (m, 2H), 4.40 (dd, 1H, $J$ = 8.4 and 1.5 Hz), 7.30−7.40 (m, 2H), 7.90 (m, 1H), and 7.94 (m, 1H); $^{13}$C-NMR ($CDCl_3$, 75 MHz) $\delta$ 13.9, 25.7, 27.8, 30.8, 52.0, 55.5, 57.7, 62.5, 82.7, 89.1, 104.9, 126.9, 134.7, 134.8, 135.9, 162.5, 168.1, 169.3, 191.6, and 191.7. Anal. Calcd for $C_{24}H_{25}NO_8$: C, 63.29; H, 5.53; N, 3.08. Found: C, 63.42; H, 5.39; N, 2.97.

Cycloadduct *exo*−*anti* **38b** (25 mg, 13%): mp 196−197 °C; IR (KBr) 1775, 1750, 1738, 1389, and 1154 cm$^{-1}$; $^1$H-NMR ($CDCl_3$, 300 MHz) $\delta$ 1.37 (t, 3H, $J$ = 7.2 Hz), 1.40 (s, 9H), 2.25−2.76 (m, 4H), 3.63 (d, 1H, $J$ = 7.8 Hz), 3.90 (d, 1H, $J$ = 7.8 Hz), 4.20 (dd, 1H, $J$ = 8.1 and 1.5 Hz), 4.33 (q, 2H, $J$ = 7.2 Hz), 7.72−7.75 (m, 2H), 7.91 (m, 1H), and 7.94 (m, 1H); $^{13}$C-NMR ($CDCl_3$, 75 MHz) $\delta$ 13.9, 23.8, 27.7, 31.1, 57.6, 56.2, 57.1, 62.4, 82.9, 89.0, 104.8, 126.9, 134.8, 134.9, 135.8, 162.3, 168.0, 169.1, 191.6, and 191.7. Anal. Calcd for $C_{24}H_{25}NO_8$: C, 63.29; H, 5.53; N, 3.08. Found: C, 63.17; H, 5.61; N, 3.11.

**Tetrahydro-1,3,5-trioxo-2-phenyl-7*H*-4,9a-epoxy-1*H*-pyrrolo[3,4-*g*]indolizine-4,7-dicarboxylic Acid 4-Ethyl Ester 7-Allyl Ester (39).** Diazo imide **30** (180 mg, 590 $\mu$mol) and *N*-phenylmaleimide (100 mg, 590 $\mu$mol) were allowed to react according to the general procedure. Proton NMR analysis of the crude product mixture showed the formation of two diastereomeric cycloadducts identified as *exo*−*syn* **39a** and *exo*−*anti* **39b** (90%, dr 85:15). Flash silica gel chromatography gave 199 mg (75%) of the major *exo*−*syn* **39a** isomer as a white powder: mp 154−155 °C; IR (KBr) 1763, 1714, 1455, 1200, 1145, and 754 cm$^{-1}$; $^1$H-NMR ($CDCl_3$, 400 MHz) $\delta$ 1.37 (t, 3H, $J$ = 7.2 Hz), 2.32−2.42 (m, 2H), 2.53−2.60 (m, 1H), 2.67−2.76 (m, 1H), 3.83 (d, 1H, $J$ = 6.8 Hz), 3.89 (d, 1H, $J$ = 6.8 Hz), 4.24−4.45 (m, 2H), 4.55 (d, 1H, $J$ = 8.4 Hz), 4.61−4.64 (m, 2H), 5.27 (d, 1H, $J$ = 11.6 Hz), 5.32 (d, 1H, $J$ = 17.2 Hz), 5.84−5.94 (m, 1H), 7.20−7.22 (m, 2H), and 7.35−7.45 (m, 3H); $^{13}$C-NMR ($CDCl_3$, 100 MHz) $\delta$ 13.9, 25.3, 30.7, 47.7, 52.3, 56.6, 62.8, 66.3, 88.3, 103.8, 119.4, 126.2, 128.9, 129.0, 130.9, 131.0, 161.9, 167.6, 169.8, 171.4, and 171.9. Anal. Calcd for $C_{23}H_{22}N_2O_8$: C, 60.79; H, 4.95; N, 6.03. Found: C, 60.77; H, 4.99; N, 5.99.

Cycloadduct *exo*−*anti* **39b** showed the following spectral properties: $^1$H-NMR ($CDCl_3$, 400 MHz) $\delta$ 1.35 (t, 3H, $J$ = 7.2 Hz), 3.56 (d, 1H, $J$ = 6.4 Hz), 3.83 (d, 1H, $J$ = 6.4 Hz), 4.58 (dd, 1H, $J$ = 8.4 and 2.0 Hz), and 4.23−5.34 (m, 2H); $^{13}$C-NMR ($CDCl_3$, 100 MHz) $\delta$ 14.0, 23.5, 31.7, 47.5, 52.2, 55.8, 62.7, 66.5, 119.1, 126.2, 127.8, 131.1, 167.7, and 168.2.

**Tetrahydro-1,3,5-trioxo-2-phenyl-7*H*-4,9a-epoxy-1*H*-pyrrolo[3,4-*g*]indolizine-4,7-dicarboxylic Acid 4-Ethyl Ester 7-Benzyl Ester (40).** Diazo imide **31** (130 mg, 380 $\mu$mol) and *N*-phenylmaleimide (72 mg, 410 $\mu$mol) were allowed to react according to the general procedure. Proton NMR analysis of the crude product mixture showed the formation of two diastereomeric cycloadducts identified as *exo*−*syn* **40a** and *exo*−*anti* **40b** (95%, dr 87:13) which were separated by flash silica gel chromatography.

Cycloadduct *exo*−*syn* **40a** (145 mg, 79%): mp 199−200 °C; IR (KBr) 1759, 1716, 1455, 1388, 1200, 1141, and 754 cm$^{-1}$; $^1$H-NMR ($CDCl_3$, 300 MHz) $\delta$ 2.32−2.76 (m, 4H), 3.83 (d, 1H, $J$ = 6.9 Hz), 3.91 (d, 1H, $J$ = 6.9 Hz), 3.98 (s, 3H), 4.62 (dd, 1H, $J$ = 7.2 and 1.2 Hz), 5.19 (s, 2H), 7.23 (d, 2H, $J$ = 7.2 Hz), and 7.35−7.51 (m, 8H); $^{13}$C-NMR ($CDCl_3$, 75 MHz) $\delta$ 25.3, 30.7, 47.8, 52.2, 53.2, 56.8, 67.6, 88.5, 103.9, 126.2, 128.5, 128.6, 128.9, 129.0, 131.0, 134.6, 162.4, 167.5, 169.9, 171.5, and 171.9. Anal. Calcd for $C_{26}H_{22}N_2O_8$: C, 63.67; H, 4.52; N, 5.71. Found: C, 63.62; H, 4.55; N, 5.64.

Cycloadduct *exo*−*anti* **40b** (21 mg, 12%): mp 193−194 °C; IR (KBr) 1760, 1716, 1388, 1196, 1141, and 753 cm$^{-1}$; $^1$H-NMR ($CDCl_3$, 300 MHz) $\delta$ 2.36−2.86 (m, 4H), 3.57 (d, 1H, $J$ = 6.9 Hz), 3.87 (d, 1H, $J$ = 6.9 Hz), 3.95 (s, 3H), 4.37 (dd, 1H, $J$ = 8.1 and 2.1 Hz), 5.19 (s, 2H), 7.23 (d, 2H, $J$ = 7.2 Hz), and 7.31−7.48 (m, 8H); $^{13}$C-NMR ($CDCl_3$, 75 MHz) $\delta$ 23.6, 31.8, 47.7, 52.2, 53.3, 56.0, 67.9, 90.5, 104.1, 126.3, 128.3, 128.5, 128.6, 129.0, 129.1, 131.1, 134.7, 162.2, 166.4, 168.3, 171.5, and 171.9. Anal. Calcd for $C_{26}H_{22}N_2O_8$: C, 63.67; H, 4.52; N, 5.71. Found: C, 63.51; H, 4.57; N, 5.60.

**4-Acetyltetrahydro-1,3,5-trioxo-2-phenyl-7*H*-4,9a-epoxy-1*H*-pyrrolo[3,4-*g*]indolizine-7-carboxylic Acid *tert*-Butyl Ester (41).** Diazo imide **32** (190 mg, 640 $\mu$mol) and *N*-phenylmaleimide (110 mg, 640 $\mu$mol) were allowed to react according to the general procedure. Proton NMR analysis of the crude product mixture showed the formation of three diastereomeric cycloadducts which were identified as *exo*−*syn* **41a**, *endo*−*anti* **41b**, and *exo*−*anti* **41c** (95%, dr 81:8:11) and were separated by flash silica gel chromatography.

Cycloadduct *exo*−*syn* **41a** (218 mg, 77%): mp 191−192 °C; IR (KBr) 1730, 1716, 1389, 1198, and 1147 cm$^{-1}$; $^1$H-NMR ($CDCl_3$, 300 MHz) $\delta$ 1.48 (s, 9H), 2.26−2.75 (m, 4H), 2.62 (s, 3H), 3.94 (d, 1H, $J$ = 6.9 Hz), 2.99 (d, 1H, $J$ = 6.9 Hz), 4.44 (dd, 1H, $J$ =8.1 and 1.2 Hz), 7.21 (d, 2H, $J$ = 7.2 Hz), and 7.26−7.47 (m, 3H); $^{13}$C-NMR ($CDCl_3$, 75 MHz) $\delta$ 25.2, 27.7, 27.8, 31.0, 48.0, 52.8, 57.2, 83.0, 93.3, 103.4, 126.2, 129.1, 129.3, 131.0, 168.0, 169.3, 171.7, 172.0, and 196.3. Anal. Calcd for $C_{23}H_{24}N_2O_7$: C, 62.72; H, 5.49; N, 6.36. Found: C, 62.56; H, 5.57; N, 6.29.

Cycloadduct *endo*−*anti* **41b** (22 mg, 8%): mp 194−195 °C; IR (KBr) 1733, 1714, 1702, 1389, and 1148 $cm^{-1}$; $^1$H-NMR ($CDCl_3$, 300 MHz) $\delta$ 1.44 (s, 9H), 2.26−2.75 (m, 4H), 2.66 (s, 3H), 3.82 (d, 1H, $J$ =8.4 Hz), 3.93 (d, 1H, $J$ = 8.4 Hz), 4.09 (dd, 1H, $J$ = 8.1 and 1.5 Hz), 7.13 (d, 2H, $J$ = 6.9 Hz), and 7.26−7.47 (m, 3H); $^{13}$C-NMR ($CDCl_3$, 75 MHz) $\delta$ 26.5, 27.6, 27.8, 32.2, 48.3, 54.1, 57.1, 83.1, 94.6, 103.4, 126.5, 129.2, 129.3, 131.0, 167.3, 167.6, 170.5, 171.8, and 197.0. Anal. Calcd for $C_{23}H_{24}N_2O_7$: C, 62.72; H, 5.49; N, 6.36. Found: C, 62.70; H, 5.49; N, 6.39.

Cycloadduct *exo*−*anti* **41c** (27 mg, 10%): mp 184−185 °C; IR (KBr) 1716, 1702, 1496, 1389, and 1154 $cm^{-1}$; $^1$H-NMR ($CDCl_3$, 300 MHz) $\delta$ 1.44 (s, 9H), 2.26−2.75 (m, 4H), 2.57 (s, 3H), 3.56 (d, 1H, $J$ = 6.6 Hz), 3.90 (d, 1H, $J$ = 6.6 Hz), 4.22 (dd, 1H, $J$ = 8.4 and 1.5 Hz), 7.29 (d, 2H, $J$ = 7.2 Hz), and 7.36−7.47 (m, 3H); $^{13}$C-NMR ($CDCl_3$, 75 MHz) $\delta$ 23.5, 27.8, 27.9, 32.1, 47.7, 52.7, 56.9, 83.3, 95.2, 103.7, 126.3, 129.1, 129.2, 131.0, 167.3, 167.5, 171.6, 171.9, and 196.0. Anal. Calcd for $C_{23}H_{24}N_2O_7$: C, 62.72; H, 5.49; N, 6.36. Found: C, 62.63; H, 5.50; N, 6.31.

**6-Oxo-8,8,9,9-tetracyano-10-oxa-5-azatricyclo-[5.2.1.0$^{1,5}$]decane-4,7-dicarboxylic Acid 4-*tert*-Butyl Ester 7-Ethyl Ester (42).** Diazo imide **29** (180 mg, 570 $\mu$mol) and tetracyanoethylene (70 mg, 570 $\mu$mol) were allowed to react according to the general procedure. Proton NMR analysis of the crude product mixture showed the predominant formation of the *syn* cycloadduct **42a** (90%, dr = 77:23). Recrystallization from dichloromethane/hexane gave 178 mg (74%) of **42a**: mp 149−150 °C; IR (KBr) 1776, 1745, 1695, 1375, and 1154 $cm^{-1}$; $^1$H-NMR ($CDCl_3$, 400 MHz) $\delta$ 1.48 (t, 3H, $J$ = 7.2 Hz), 1.49 (s, 9H), 2.64−4.65 (m, 4H), and 4.52−4.65 (m, 3H); $^{13}$C-NMR ($CDCl_3$, 75 MHz) $\delta$ 13.9, 26.8, 27.7, 28.9, 29.7, 59.6, 65.6, 84.8, 84.9, 107.1, 107.7, 108.2, 108.4, 108.8, 157.9, 163.2, and 166.1. Anal. Calcd for $C_{20}H_{19}N_5O_6$: C, 56.47; H, 4.50; N, 16.46. Found: C, 56.44; H, 4.39; N, 16.75.

**8,8-Diethoxy-6-oxo-10-oxa-5-azatricyclo[5.2.1.0$^{1,5}$]decane-4,7-dicarboxylic Acid 4-*tert*-Butyl Ester 7-Ethyl Ester (43).** Diazo imide **29** (200 mg, 610 $\mu$mol) and 1,1-diethoxyethene (120 mg, 1.0 mmol) were allowed to react according to the general procedure. Proton NMR analysis of the crude product mixture showed the formation of two diastereomeric cycloadducts identified as *syn* **43a** and *anti* **43b** (90%, dr 65:35) which were separated by flash silica gel chromatography.

Cycloadduct *syn* **43a** (177 mg, 56%): IR (neat) 1766, 1738, 1389, 1154, and 855 $cm^{-1}$; $^1$H-NMR ($CDCl_3$, 400 MHz) $\delta$ 1.13 (t, 3H, $J$ = 7.2 Hz), 1.16 (t, 3H, $J$ = 7.2 Hz), 1.30 (t, 3H, $J$ = 7.2 Hz), 1.42 (s, 9H), 2.07−2.22 (m, 2H), 2.29 (d, 1H, $J$ = 11.2 Hz), 2.29−2.43 (d, 2H), 2.49 (d, 1H, $J$ = 11.2 Hz), 3.42−3.55 (m, 2H), 3.62 (dq, 1H, $J$ = 9.6 and 7.2 Hz), 4.01 (dq, 1H, $J$ = 9.2 and 7.2 Hz), 4.25−4.37 (m, 2H), and 4.39 (d, 1H, $J$ = 7.2 Hz); $^{13}$C-NMR ($CDCl_3$, 100 MHz) $\delta$ 14.0, 14.8, 15.2, 27.5, 27.8, 30.2, 45.7, 57.3, 58.4, 59.4, 61.9, 82.1, 93.8, 101.6, 108.9, 163.0, 168.5, and 169.7; HRMS calcd for $C_{20}H_{32}NO_8$ $(M + H)^+$ 414.2128, found 414.2121.

Cycloadduct *anti* **43b** (83 mg, 27%): IR (neat) 1762, 1742, 1390, 1154, and 855 $cm^{-1}$; $^1$H-NMR ($CDCl_3$, 400 MHz) $\delta$ 1.13 (t, 3H, $J$ = 7.2 Hz, 1.17 (t, 3H, $J$ = 7.2 Hz), 1.30 (t, 3H, $J$ = 7.2 Hz), 1.42 (s, 9H), 2.04−2.10 (m, 1H), 2.15 (d, 1H, $J$ = 11.2 Hz), 2.32−2.49 (m, 3H), 2.43 (d, 1H, $J$ = 11.2 Hz), 3.42−3.56 (m, 2H), 3.64 (dq, 1H, $J$ = 9.6 and 7.2 Hz), 4.07 (dq, 1H, $J$ = 9.6 and 7.2 Hz), 4.14 (dd, 1H, $J$ = 8.0 and 2.0 Hz), and 4.27−4.40 (m, 2H); $^{13}$C-NMR ($CDCl_3$, 100 MHz) $\delta$ 14.1, 14.8, 15.2, 27.1, 27.8, 31.9, 46.2, 56.4, 58.5, 59.4, 61.7, 82.5, 95.9, 101.5, 108.8, 162.9, 166.8, and 168.5; HRMS calcd for $C_{20}H_{32}NO_8$ $(M + H)^+$ 414.2128, found 414.2133.

**9-Acetyl-6-oxo-10-oxa-5-azatricyclo[5.2.1.0$^{1,5}$]decane-4,7-dicarboxylic Acid 4-*tert*-Butyl Ester 7-Ethyl Ester (44).** Diazo imide **29** (320 mg, 970 $\mu$mol) and methyl vinyl ketone (140 mg, 1.9 mmol) were allowed to react according to the general procedure. Proton NMR analysis of the crude product mixture showed the formation of the three diastereomeric cycloadducts identified as *exo*−*syn* **44a**, *exo*−*anti* **44b**, and *endo*−*anti* **44c** (90%, dr 51:21:28) which were separated by flash silica gel chromatography.

Cycloadduct *exo*−*syn* **44a** (149 mg, 42%): IR (neat) 1773, 1752, 1730, 1453, 1154, 934, and 841 $cm^{-1}$; $^1$H-NMR ($CDCl_3$, 400 MHz) $\delta$ 1.35 (t, 3H, $J$ = 7.2 Hz), 1.46 (s, 9H), 2.17−2.31 (m, 2H), 2.22 (s, 3H), 2.39 (dd, 1H, $J$ = 13.2 and 4.4 Hz), 2.45−2.54 (m, 2H), 2.73 (dd, 1H, $J$ = 13.2 and 9.2 Hz), 3.58 (dd, 1H, $J$ = 9.2 and 4.4 Hz); 4.31−4.40 (m, 2H), and 4.40 (dd, 1H, $J$ = 7.2 and 2.0 Hz); $^{13}$C-NMR ($CDCl_3$, 100 MHz) $\delta$ 14.1, 26.6, 27.8, 29.0, 31.2, 32.1, 57.0, 62.3, 82.5, 86.3, 104.0, 164.8, 170.0, 171.1, and 205.0; HRMS calcd for $C_{18}H_{25}NO_7Li$ $(M + Li)^+$ 374.1791, found 374.1779.

Cycloadduct *exo*−*anti* **44b** (76 mg, 21%): IR (neat) 1752, 1738, 1389, 1126, and 848 $cm^{-1}$; $^1$H-NMR ($CDCl_3$, 400 MHz) $\delta$ 1.34 (t, 3H, $J$ = 7.2 Hz), 1.45 (s, 9H), 2.20 (s, 3H), 2.37−2.50 (m, 5H), 2.61 (dd, 1H, $J$ = 13.2 and 8.8 Hz), 3.21 (dd, 1H, $J$ = 8.8 and 4.4 Hz), 4.08 (dd, 1H, $J$ = 7.6 and 2.0 Hz), and 4.30−4.41 (m, 2H); $^{13}$C-NMR ($CDCl_3$, 100 MHz) $\delta$ 14.1, 25.0, 27.8, 28.6, 32.0, 32.2, 56.3, 57.3, 62.3, 82.9, 88.7, 104.1, 164.6, 167.9, 169.1, and 205.8; HRMS calcd for $C_{18}H_{25}NO_7Li$ $(M + Li)^+$ 374.1791, found 374.1776.

Cycloadduct *endo*−*anti* **44c** (67 mg, 19%): IR (neat) 1773, 1759, 1730, 1389, and 948 $cm^{-1}$; $^1$H-NMR ($CDCl_3$, 400 MHz) $\delta$ 1.34 (t, 3H, $J$ = 7.2 Hz), 1.46 (s, 9H), 2.20 (s, 3H), 2.21−2.50 (m, 4H), 2.65−2.73 (m, 2H), 3.31 (dd, 1H, $J$ = 10.8 and 5.7 Hz), 4.10 (dd, 1H, $J$ = 8.7 and 5.7 Hz), and 4.30−4.42 (m, 2H); $^{13}$C-NMR ($CDCl_3$, 100 MHz) $\delta$ 14.1, 26.5, 27.8, 30.2, 32.2, 32.3, 57.2, 57.4, 62.3, 82.6, 89.1, 104.0, 164.8, 168.3, 169.4, and 205.0. Anal. Calcd for $C_{18}H_{25}NO_7$: C, 58.85; H, 6.86; N, 3.81. Found: C, 58.60; H, 6.76; N, 3.74.

**(3*R**,6*R**)-8-Acetyl-6-hydroxy-5-oxo-1,2,3,5,6,7-hexahydroindolizine-3,6-dicarboxylic Acid 3-*tert*-Butyl Ester 6-Ethyl Ester (*anti* 45).** To a solution of *exo*−*syn* **44a** (75 mg, 200 $\mu$mol) in chloroform (2 mL) was added *p*-TsOH (1 mg), and the mixture was stirred at rt for 18 h. The solvent was removed under reduced pressure, and the residue was subjected to flash silica gel chromatography to give 67 mg (89%) of *anti* **45** as a colorless oil: IR (neat) 3438, 1738, 1695, 1602, and 1147 $cm^{-1}$; $^1$H-NMR ($CDCl_3$, 400 MHz) $\delta$ 1.26 (t, 3H, $J$ = 7.2 Hz), 1.41 (s, 9H), 2.06−2.13 (m, 1H), 2.25 (s, 3H), 2.25−2.35 (m, 1H), 2.90 (d, 1H, $J$ = 16.4 Hz), 2.97−3.06 (m, 1H), 3.24−3.33 (m, 1H), 3.28 (d, 1H, $J$ = 16.4 Hz), 4.20−4.30 (m, 1H), 4.59 (br s, 1H), and 4.60 (dd, 1H, $J$ = 9.2 and 2.8 Hz); $^{13}$C-NMR ($CDCl_3$, 100 MHz) $\delta$ 13.9, 26.5, 27.8, 29.2, 30.6, 33.0, 59.5, 63.0, 74.2, 82.4, 108.0, 150.4, 165.6, 168.9, 170.2, and 196.0; HRMS calcd for $C_{18}H_{26}NO_7$ $(M + H)^+$ 368.1709, found 368.1704.

**(3*R**,6*S**)-8-Acetyl-6-hydroxy-5-oxo-1,2,3,5,6,7-hexahydroindolizine-3,6-dicarboxylic Acid 3-*tert*-Butyl Ester 6-Ethyl Ester (*Syn* 45).** To a solution of *endo*−*anti* **44c** (50 mg, 140 $\mu$mol) in chloroform (2 mL) was added *p*-TsOH (1 mg), and the mixture was stirred at rt for 18 h. The solvent was removed under reduced pressure, and the residue was subjected to flash silica gel chromatography to give 46 mg (92%) of *syn* **45** as a colorless oil. The same product was also formed (85%) from the *exo*−*anti* **44b** isomer by treatment with *p*-TsOH: IR (neat) 3445, 1740, 1695, 1602, and 1368 $cm^{-1}$; $^1$H-NMR ($CDCl_3$, 400 MHz) $\delta$ 1.23 (t, 3H, $J$ = 7.2 Hz), 1.44 (s, 9H), 2.09−2.18 (m, 1H), 2.25 (s, 3H), 2.29−2.39 (m, 1H), 2.92 (dt, 1H, $J$ = 16.4 and 2.4 Hz), 2.97−3.11 (m, 1H), 3.20−3.31 (m, 1H), 3.32 (dt, 1H, $J$ = 16.4 and 1.6 Hz), 4.21 (q, 2H, $J$ = 7.2 Hz), 4.63 (dd, 1H, $J$ = 9.2 and 3.2 Hz), and 5.09 (brs, 1H); $^{13}$C-NMR ($CDCl_3$, 75 MHz) $\delta$ 14.0, 26.7, 27.8, 29.2, 30.5, 33.3, 59.5, 62.7, 74.3, 82.7, 107.8, 151.1, 166.4, 169.0, 170.0, and 196.0; HRMS calcd for $C_{18}H_{26}NO_7$ $(M + H)^+$ 368.1709, found 368.1720.

**Tetrahydro-8-methyl-1,3,5-trioxo-2-phenyl-7*H*-4,9a-epoxy-1*H*-pyrrolo[3,4-*g*]indolizine-4-carboxylic Acid Methyl Ester (52).** Diazo imide **50** (240 mg, 1.0 mmol) and *N*-phenylmaleimide (180 mg, 1.0 mmol) were allowed to react according to the general procedure. Proton NMR analysis of the crude product mixture showed the formation of two diastereomeric cycloadducts identified as *exo*−*syn* **52a** and *exo*−*anti* **52b** (95%, dr 36:64) which were separated by flash silica gel chromatography.

Cycloadduct *exo*−*syn* **52a** (123 mg, 32%): mp 198−199 °C; IR (KBr) 1766, 1745, 1709, 1476, 1389, 1197, and 1140 $cm^{-1}$; $^1$H-NMR ($CDCl_3$, 400 MHz) $\delta$ 1.17 (d, 3H, $J$ = 6.4 Hz), 2.24 (dd, 1H, $J$ = 14.8 and 11.2 Hz), 2.54 (dd, 1H, $J$ = 14.8 and 7.2 Hz), 2.60−2.74 (m, 1H), 2.80 (dd, 1H, $J$ = 11.6 and 10.4 Hz),

3.52 (d, 1H, $J$ = 6.8 Hz), 3.85 (dd, 1H, $J$ = 11.6 and 7.2 Hz), 3.87 (d, 1H, $J$ = 6.8 Hz), 3.97 (s, 3H), 7.23−7.25 (m, 2H), and 7.38−7.48 (m, 3H); $^{13}$C-NMR ($CDCl_3$, 100 MHz) $\delta$ 16.7, 34.7, 35.1, 47.9, 51.0, 52.8, 53.4, 88.0, 103.7, 126.3, 129.1, 129.2, 131.1, 162.8, 169.2, 171.6, and 171.9. Anal. Calcd for $C_{19}H_{18}N_2O_6$: C, 61.62; H, 4.90; N, 7.56. Found: C, 61.61; H, 4.96; N, 7.54.

Cycloadduct *exo*−*anti* **52b** (215 mg, 56%): mp 188−189 °C; IR (KBr) 1759, 1745, 1715, 1595, 1496, 1382, 1197, and 749 cm$^{-1}$; $^1$H-NMR ($CDCl_3$, 400 MHz) $\delta$ 1.18 (d, 3H, $J$ = 6.8 Hz), 2.06 (dd, 1H, $J$ = 14.0 and 6.4 Hz), 2.71−2.81 (m, 1H), 2.86 (dd, 1H, $J$ = 14.0 and 6.8 Hz), 3.21 (dd, 1H, $J$ = 11.2 and 7.2 Hz), 3.46 (dd, 1H, $J$ = 11.2 and 7.2 Hz), 3.51 (d, 1H, $J$ = 6.8 Hz), 3.83 (d, 1H, $J$ = 6.8 Hz), 3.96 (s, 3H), 7.21−7.24 (m, 2H), and 7.39−7.47 (m, 3H); $^{13}$C-NMR ($CDCl_3$, 100 MHz) $\delta$ 18.9, 33.3, 34.9, 47.8, 49.6, 52.5, 53.3, 89.6, 103.7, 126.3, 129.0, 129.2, 131.1, 162.7, 167.7, 171.6, and 171.9. Anal. Calcd for $C_{19}H_{18}N_2O_6$: C, 61.62; H, 4.90; N, 7.56. Found: C, 61.55; H, 4.95; N, 7.46.

**Tetrahydro-2,8-dimethyl-1,3,5-trioxo-7*H*-4,9a-epoxy-1*H*-pyrrolo[3,4-*g*]indolizine-4-carboxylic Acid Methyl Ester (53).** Diazo imide **50** (230 mg, 1.0 mmol) and *N*-methylmaleimide (110 mg, 1.0 mmol) were allowed to react according to the general procedure. Proton NMR analysis of the crude product mixture showed the formation of two diastereomeric cycloadducts identified as *exo*−*syn* **53a** and *exo*−*anti* **53b** (95%, dr 32:68) which were separated by flash silica gel chromatography.

Cycloadduct *exo*−*syn* **53a** (94 mg, 30%): mp 177−178 °C; IR (KBr) 1766, 1733, 1695, 1282, 1125, and 754 cm$^{-1}$; $^1$H-NMR ($CDCl_3$, 400 MHz) $\delta$ 1.13 (d, 3H, $J$ = 6.8 Hz), 2.16 (dd, 1H, $J$ = 15.2 and 10.8 Hz), 2.44 (dd, 1H, $J$ = 15.2 and 7.2 Hz), 2.50−2.64 (m, 1H), 2.74 (dd, 1H, $J$ = 11.6 and 10.8 Hz), 2.93 (s, 3H), 3.36 (d, 1H, $J$ = 6.8 Hz), 3.71 (d, 1H, $J$ = 6.8 Hz), 3.77 (dd, 1H, $J$ = 11.6 and 7.2 Hz), and 3.93 (s, 3H); $^{13}$C-NMR ($CDCl_3$, 100 MHz) $\delta$ 14.1, 16.6, 25.4, 34.6, 35.0, 47.8, 50.8, 52.7, 53.2, 87.6, 103.3, 162.8, 169.1, 172.4, and 172.8. Anal. Calcd for $C_{14}H_{16}N_2O_6$: C, 54.54; H, 5.23; N, 9.09. Found: C, 54.38; H, 5.21; N, 9.16.

Cycloadduct *exo*−*anti* **53b** (191 mg, 61%): mp 161−162 °C; IR (KBr) 1759, 1730, 1702, 1432, 1289, 1126, and 1054 cm$^{-1}$; $^1$H-NMR ($CDCl_3$, 400 MHz) $\delta$ 1.19 (d, 3H, $J$ = 6.8 Hz), 2.02 (dd, 1H, $J$ = 14.0 and 6.4 Hz), 2.72−2.79 (m, 1H), 2.84 (dd, 1H, $J$ = 14.0 and 6.8 Hz), 2.98 (s, 3H), 3.20 (dd, 1H, $J$ = 10.8 and 6.0 Hz), 3.37 (d, 1H, $J$ = 6.8 Hz) 3.45 (dd, 1H, $J$ = 10.8 and 6.8 Hz), 3.71 (d, 1H, $J$ = 6.8 Hz), and 3.99 (s, 3H); $^{13}$C-NMR ($CDCl_3$, 100 MHz) $\delta$ 18.8, 25.4, 33.3, 35.0, 47.7, 49.5, 52.5, 53.3, 89.3, 103.4, 162.8, 167.6, 172.4, and 172.8. Anal. Calcd for $C_{14}H_{16}N_2O_6$: C, 54.54; H, 4.23; N, 9.09. Found: C, 54.46; H, 5.18; N, 9.07.

**Tetrahydro-1,3,5-trioxo-2-methyl-7*H*-4,9a-epoxy-1*H*-pyrrolo[3,4-*g*]indolizine-4,8-dicarboxylic Acid Dimethyl Ester (54).** Diazo imide **51** (300 mg, 1.1 mmol) and *N*-methylmaleimide (120 mg, 1.1 mmol) were allowed to react according to the general procedure. Proton NMR analysis of the crude product mixture showed the formation of two diastereomeric cycloadducts identified as *exo*−*syn* **54a** and *exo*−*anti* **54b** (95%, dr 50:50) which were separated by flash silica gel chromatography.

Cycloadduct *exo*−*syn* **54a** (182 mg, 47%): mp 217−218 °C; IR (KBr) 1759, 1730, 1702, 1439, 1175, and 1133 cm$^{-1}$; $^1$H-NMR ($CDCl_3$, 400 MHz) $\delta$ 2.66 (dd, 1H, $J$ = 15.2 and 7.6 Hz), 2.89 (dd, 1H, $J$ = 15.2 and 10.0 Hz), 2.99 (s, 3H), 3.39−3.45 (m, 2H), 3.46 (d, 1H, $J$ = 6.8 Hz), 3.74 (d, 1H, $J$ = 6.8 Hz), 3.77 (s, 3H), 3.90−3.97 (m, 1H), and 3.99 (s, 3H); $^{13}$C-NMR ($CDCl_3$, 100 MHz) $\delta$ 25.5, 30.3, 43.5, 46.1, 47.7, 52.4, 52.6, 53.4, 87.9, 102.5, 162.6, 168.9, 171.4, 172.1, and 172.5. Anal. Calcd for $C_{15}H_{16}N_2O_8$: C, 51.14; H, 4.58; N, 7.95. Found: C, 51.04; H, 4.56; N, 7.92.

Cycloadduct *exo*−*anti* **54b** (178 mg, 46%): mp 209−210 °C; IR (KBr) 1759, 1738, 1695, 1439, 1376, 1225, and 1133 cm$^{-1}$; $^1$H-NMR ($CDCl_3$, 400 MHz) $\delta$ 2.78 (dd, 1H, $J$ = 15.6 and 4.4 Hz), 2.96 (dd, 1H, $J$ = 15.6 and 7.6 Hz), 2.98 (s, 3H), 3.39 (d, 1H, $J$ = 6.8 Hz), 3.40−3.46 (m, 2H), 3.72 (s, 3H), 3.73 (d, 1H, $J$ = 6.8 Hz), 3.97 (s, 3H), and 4.05−4.11 (m, 1H); $^{13}$C-NMR ($CDCl_3$, 100 MHz) $\delta$ 25.5, 29.9, 44.0, 45.4, 47.7, 52.4, 52.8, 53.3, 88.5, 102.5, 162.4, 168.3, 171.3, 172.1, and 172.6. Anal. Calcd for $C_{15}H_{16}N_2O_8$: C, 51.14; H, 4.58; N, 7.95. Found: C, 51.12; H, 4.44; N, 7.95.

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**Supporting Information Available:** $^1$H-NMR and $^{13}$C-NMR spectra for new compounds lacking analyses together with an ORTEP drawing for structure **35** (15 pages). This material is contained in libraries on microfiche, immediately follows this article in the microfilm version of the journal, and can be ordered from the ACS; see any current masthead page for ordering information.

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