# RHODIUM(II) CATALYZED CYCLIZATION OF DIAZO THIOCARBONYL COMPOUNDS FOR HETEROCYCLIC SYNTHESIS†

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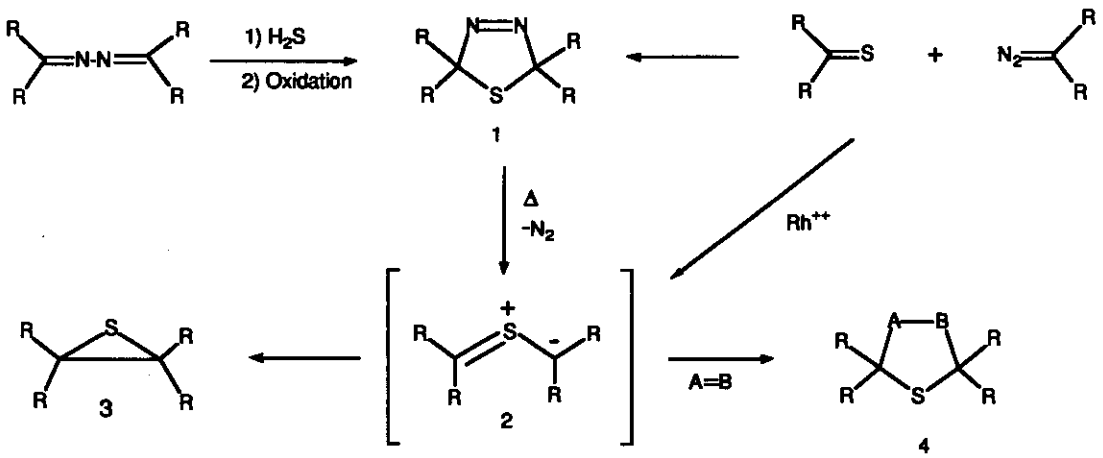
**Abstract** - The mesoionic thioisomünchnone system was prepared from the rhodium(II) acetate catalyzed cyclization of a diazothioamide and was found to undergo smooth 1,3-dipolar cycloaddition with *N*-phenylmaleimide. In contrast to this system, the rhodium(II) reaction of an α-diazo-β-oxo ester containing a thiocarbonyl group produced a cyclic thiocarbonyl ylide which extruded sulfur from a transient episulfide intermediate.

Thiocarbonyl ylides have been the subject of much interest in recent years due to their potential role as intermediates in a variety of reactions including the formation of episulfides[1] and novel heterocyclic ring systems.[2] The first recognition of the existence of thiocarbonyl ylides appears to have been made by Knott in 1955 in conjunction with considerations of the contributions of this segment to the electronic make-up of certain dyestuffs.[3] Thiocarbonyl ylide formation can be achieved by several different pathways. The most flexible and general route involves the $\Delta^3$-1,2,4-thiadiazoline ring system (**1**) as the dipole precursor.[4] Mild thermolysis of (**1**) extrudes nitrogen and produces the thiocarbonyl ylide (**2**) *via* a 1,3-dipolar cycloreversion.[5] Two generalized routes to the precursor (**1**) are shown in Scheme I.[6-8] Thiocarbonyl ylide (**2**) generated as a reactive and short-lived intermediate has been trapped by various dipolarophiles, and kinetic analysis of the reaction has also unambiguously established the transitory existence of intermediate (**2**). The predicted conrotatory ring closure occurs to give episulfide (**3**) in the absence of trapping agents. 1,3-Dipolar cycloaddition of **2** proceeds with retention of configuration as predicted.[9]

Other methods for thiocarbonyl ylide generation involve the addition of thioketones to oxiranes,[10] the photorearrangement of aryl vinyl sulfides,[11,12] the desilylation of α-bromo-*bis*(trimethylsilylmethyl) sulfide,[13] and the release of disiloxane from *bis*(trimethylsilylmethyl) sulfoxide.[14] The reaction of keto carbenoids with π-bonds which possess a lone pair of electrons is rapidly gaining prominence as an extremely efficient method for dipole generation.[15] Previous papers from these laboratories have outlined a

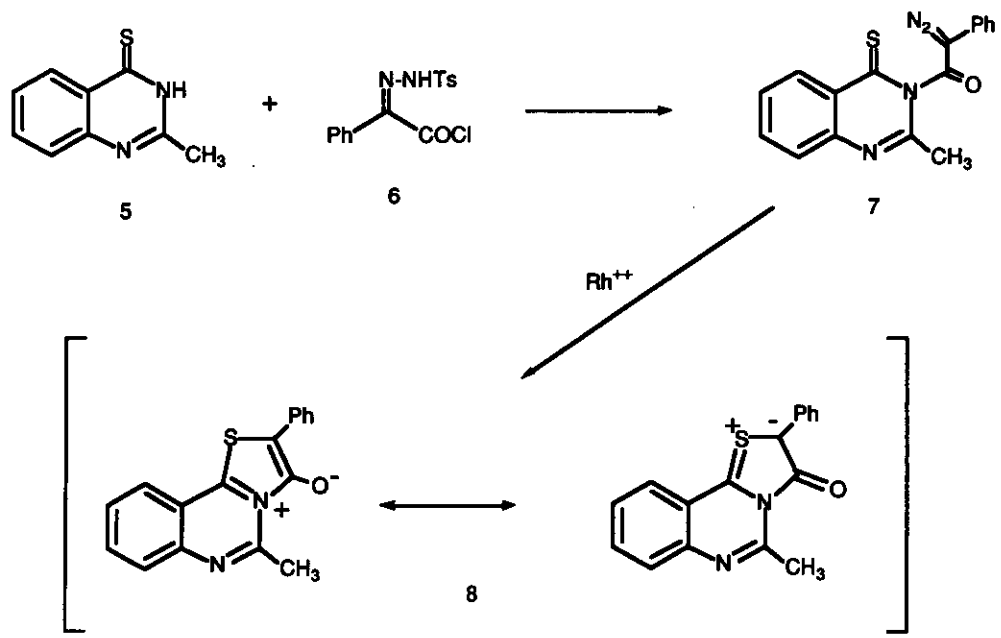
Scheme I



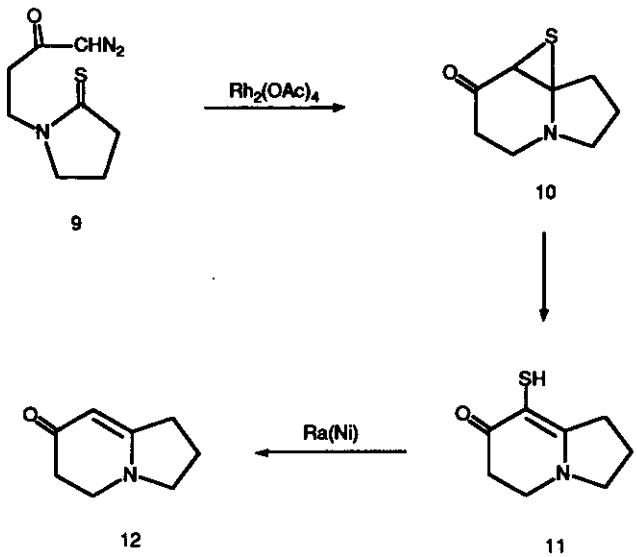

route to oxapolycyclic ring systems which involves the tandem cyclization-cycloaddition reaction of a rhodium carbenoid intermediate.[16] In an effort to increase the versatility of the method, we became interested in examining hetero π-systems other than carbonyl groups.[17] The formation and dipolar trapping of thiocarbonyl ylides *via* the interaction of carbenes or carbenoids derived from diazo compounds with thiocarbonyl compounds has not been investigated to the same extent[18-21] as the corresponding carbonyl ylide system.[22] In this paper we describe our studies in this area which make use of several different classes of diazothiocarbonyls as precursors for the thiocarbonyl ylide dipole.

## Results and Discussion

The potential for ylide formation by reaction of a thioamide with an electron-deficient carbene was first exploited by Potts and co-workers[23] for the preparation of the mesoionic anhydro-4-hydroxythiazolium hydroxide (thioisomünchnone)[24,25] ring. Recent interest in this system may be attributed to (1) its ease of preparation from simple thioamides,[26,27] (2) the interesting physical properties it possesses, and (3) the propensity for its thiocarbonyl ylide dipole to undergo 1,3-dipolar cycloaddition with a wide range of dipolarophiles to produce complex heterocyclic ring systems.[28,29] A mixture of 3*H*-quinazoline-4-thione (**5**) and α-(tosylhydrazone)phenylacetyl chloride (**6**) in the presence of triethylamine gave diazothioamide (**7**).[23] This compound afforded the aromatic mesoionic system (**8**) in 86% yield upon treatment with rhodium(II) acetate. This intramolecular carbenoid-type cyclization provides an efficient synthesis of

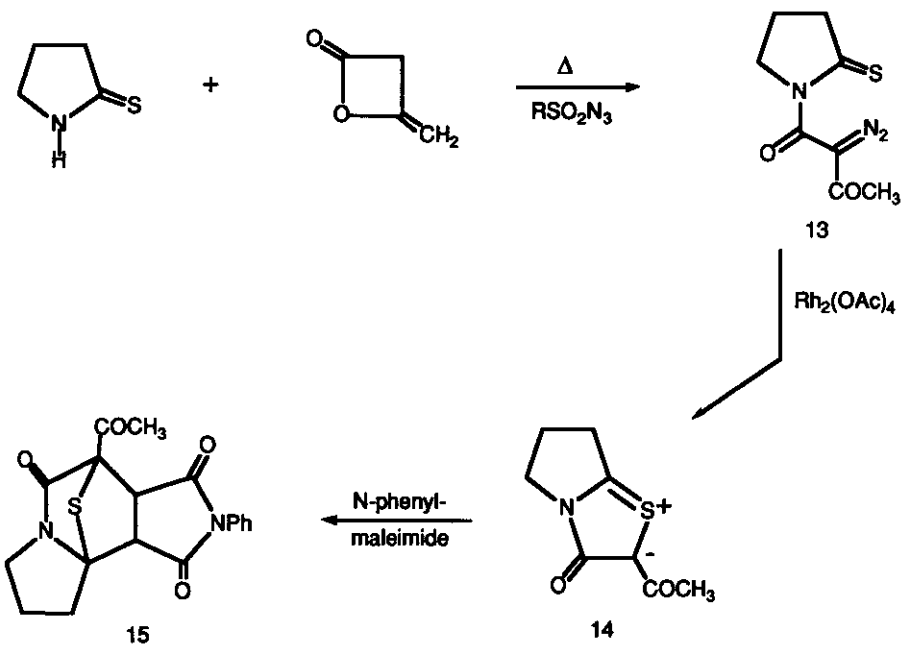



the mesoionic thiazolium hydroxide dipole. Thioisomünchnones such as **8** contain a thiocarbonyl ylide dipole within their framework and therefore should be willing participants in 1,3-dipolar cycloaddition.[30] In contrast to the abundant literature dealing with the addition of rhodium carbenoid intermediates onto the oxygen atom of an amido group,[31-34] little was known about the interaction of the metal carbenoid with a thioamide when we started our work in this area. Two questions of immediate concern were (1), whether the thioamide functionality would cyclize more or less efficiently than the amido group to give the 1,3-dipole, and (2), would the resulting thioisomünchnone undergo dipolar cycloaddition with typical dipolarophiles. Thiocarbonyl ylides are known to cyclize to give episulfides which readily extrude a sulfur atom to produce olefins.[35] This reaction pathway is reminiscent of the Eschenmoser sulfide-contraction reaction using thiolactam substrates.[36] In fact, Danishefsky and co-workers have applied this reaction to the synthesis of a variety of novel heterocyclic natural products.[2] One interesting example involves the annulation of diazomethyl vinyl ketone with a variety of secondary thiolactams to give heterocycles such as **9**.[37] This diazo thioamide afforded **12** upon treatment with rhodium(II) acetate in refluxing benzene followed by Raney nickel desulfurization. The intermediate involved in the conversion of **9** to **12** prior to treatment with Raney nickel was identified as ene thiol (**11**). In this case, the initially formed thiocarbonyl ylide intermediate cyclized to episulfide (**10**) which underwent subsequent isomerization to produce **11**.




9 10 11 12

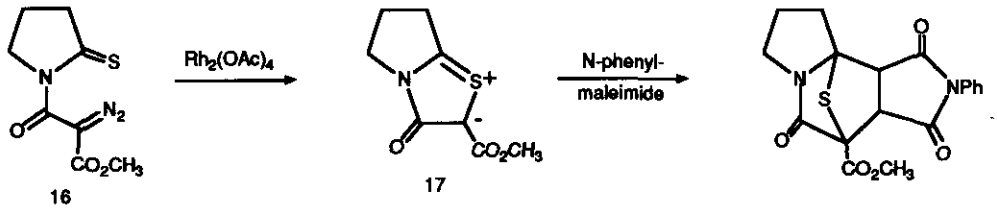
Cyclic diazothioimide (**13**) was easily prepared from 2-thiopyrrolidinone by reaction with diketene followed by diazo transfer using 1-ethyl-2-chloropyridinium tetrafluoroborate and sodium azide[38] to give *N*-(2-diazo-1,3-dioxobutyl)-2-thiopyrrolidinone (**13**). A sample of **13** was allowed to react with rhodium(II) acetate in benzene at 80°C and the initially formed rhodium carbenoid cyclized onto the adjacent thioamide group to produce thioisomünchnone (**14**) in 78% yield as an isolable compound ($^1$H-nmr




13 14 15

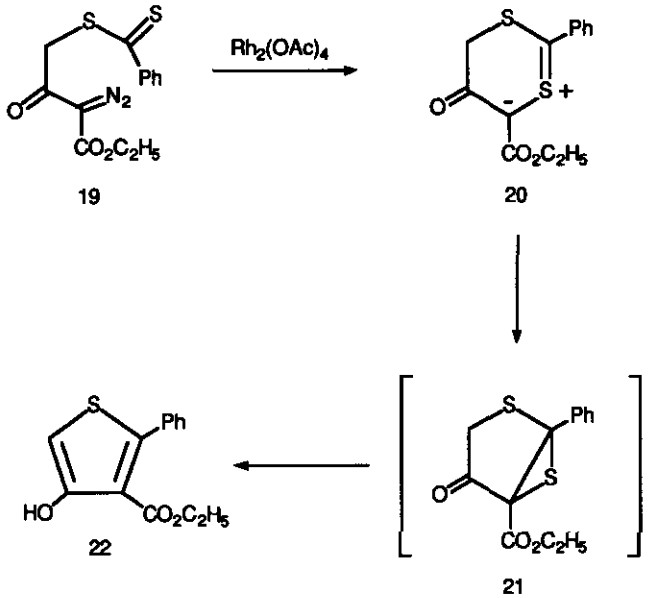
($CDCl_3$, 300 MHz) δ 2.45 (s, 3H), 2.66 (quin., 2H, J=7.6 Hz), 3.28 (t, 2H, J=7.6Hz) and 4.09 (t, 2H, J=7.6 Hz); $^{13}$C-nmr ($CDCl_3$, 75 MHz) δ 24.5, 26.1, 31.3, 47.5, 105.4, 158.1, 170.8, and 189.2). Heating **14** with *N*-phenylmaleimide gave cycloadduct (**15**) in 82% isolated yield. No signs of any product(s) derived from a rearranged episulfide intermediate could be detected in the crude reaction mixture.

A closely related system that we also examined involved the rhodium(II) catalyzed reaction of diazothioamide (**16**) with *N*-phenylmaleimide. In this case cycloadduct (**18**) was isolated as the major product in 75% yield. The facility with which the cycloaddition occurs is undoubtedly related to the stability of the aromatic mesoionic dipole (**17**). Ring closure to an episulfide would not only destroy the aromatic character of the dipole but would also lead to a highly strained ring.




16 17 18

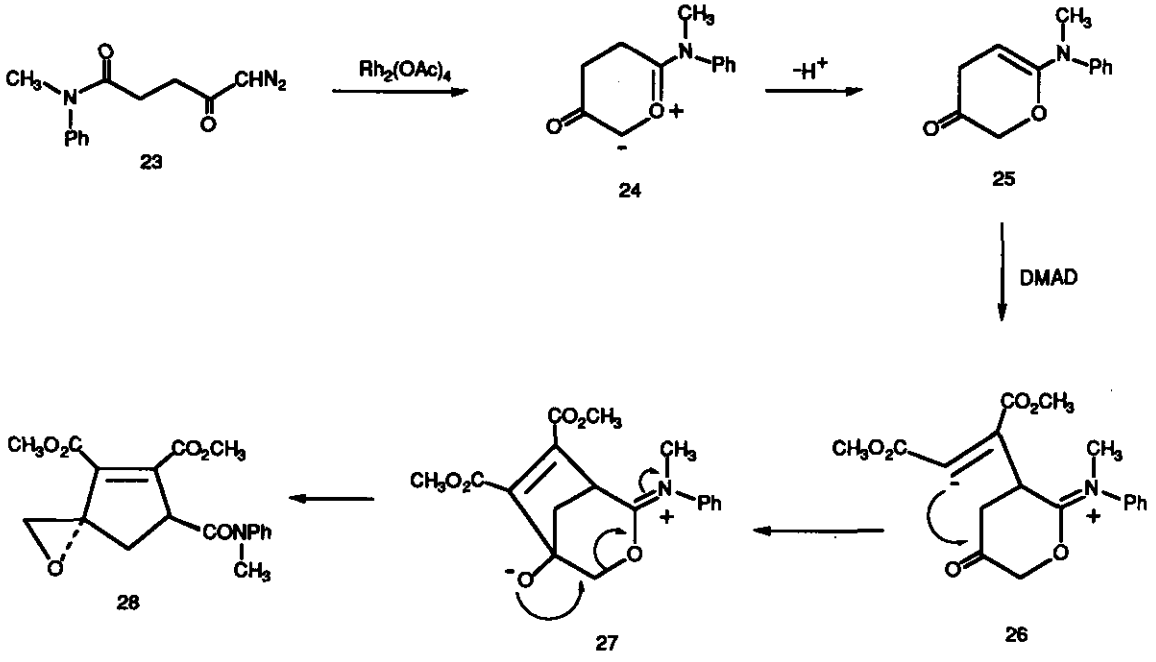
Another system we investigated involved the rhodium(II) catalyzed reaction of diazodithioester (**19**) in the presence of various dipolarophiles. In this case the resulting dipole is no longer part of a mesoionic system and thus might be expected to undergo competitive cyclization to an episulfide intermediate. Indeed, the major product isolated (80%) in all cases corresponded to hydroxythiophene (**22**). No detectable




19 20 21 22

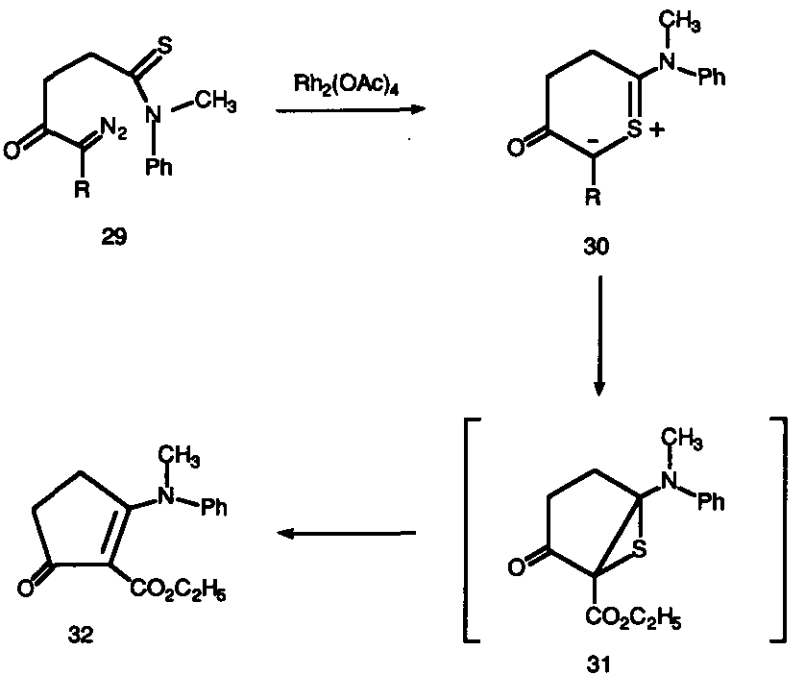
quantities of any cycloadduct could be found in the crude reaction mixture. Apparently, the initially formed thiocarbonyl ylide (**20**) prefers to collapse to episulfide (**21**) which rapidly loses sulfur to give **22** rather than undergo dipolar cycloaddition.[39]

In an earlier report[40] we described the rhodium(II) catalyzed behavior of α-diazo keto amide (**23**). The initial reaction involved generation of the expected carbonyl ylide dipole (**24**) by intramolecular cyclization of the keto carbenoid onto the oxygen atom of the amide group. The highly stabilized dipole does not readily undergo 1,3-dipolar cycloaddition but rather loses a proton to produce the cyclic ketene *N,O*-acetal (**25**). This material reacted with the activated π-bond of the dipolarophile (i.e., DMAD) to produce zwitterion (**26**). The anionic portion of **26** underwent addition to the adjacent carbonyl group affording **27** which was converted to cycloadduct (**28**).



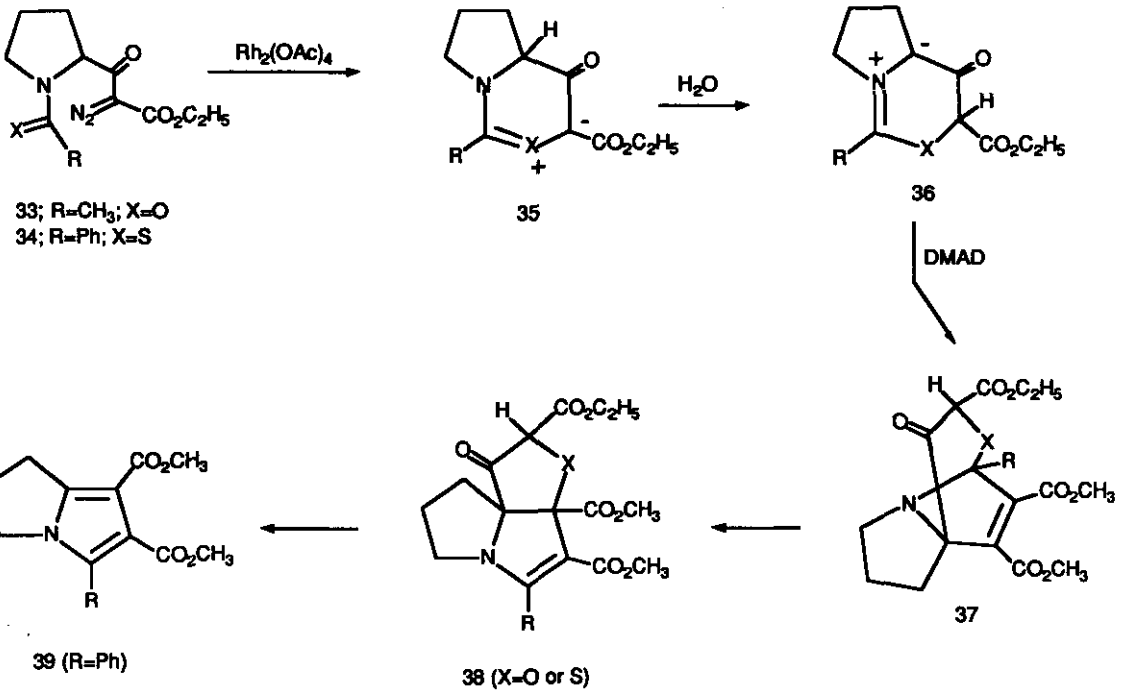

23 24 25 26 27 28

As part of our studies dealing with the rhodium(II) catalyzed behavior of diazo thioamides, we attempted to carry out an analogous reaction with the closely related thioamide (**29**). However, under identical experimental conditions to that used with **23**, the corresponding thioamide (**29**) produced the cyclic vinylogous amide (**32**) in 90% isolated yield. Both systems require formation of the respective carbonyl (**24**) and thiocarbonyl ylides (**30**). The two systems diverge at this point. Whereas carbonyl ylide (**24**) undergoes proton loss to give **25**, the closely related dipole (**30**) cyclizes to produce a transient




episulfide (**31**) which subsequently eliminates sulfur to give **32**.[41] The thermal ring closure of thiocarbonyl ylides to episulfides generally proceeds in a conrotatory fashion as a consequence of orbital symmetry factors.[9] The cyclization of **30** to **31** (and then on to **32**) however, involves a disrotatory closure. More than likely the weaker C-S bonds and thermodynamic stability of **32** combine to lower the activation energy of the ring closure even though this represents a formal violation of the Woodward-Hoffman rules for electrocyclization.[9]

Recently, a new method for azomethine ylide formation was developed in our laboratory which involves a cascade of dipoles.[42] This novel process was uncovered during an examination of the reaction of *N*-acetyl-2-(1-diazoacetyl)pyrrolidine (**33**) with DMAD in the presence of rhodium(II) acetate. In an effort to extend this reaction to other dipoles, we studied the rhodium(II) catalyzed behavior of the closely related thioamide derivative (**34**). Treatment of **34** with rhodium(II) acetate at 80°C in the presence of DMAD afforded pyrrole (**39**) as the major product in 62% yield after column chromatography. By analogy with **33**, we believe that the reaction proceeds *via* dipole (**35**) which is converted to azomethine ylide (**36**) by a small amount of water present in the solvent. Dipolar cycloaddition with DMAD provides cycloadduct (**37**) which readily undergoes a 1,3-thio shift to generate **38**. This material is ultimately converted to **39** upon chromatographic workup.[43]




In conclusion, we have demonstrated that cyclic thiocarbonyl ylides can be generated from several thiocarbonyl compounds. The resulting products depend on the nature of the functional groups which flank the π-bond as well as the ring size of the cyclic dipole. We are continuing to explore the scope and mechanistic details of thiocarbonyl ylides and will report additional findings at a later date.

## EXPERIMENTAL SECTION

Melting points are uncorrected. Mass spectra were determined at an ionizing voltage of 70 eV. Unless otherwise noted, all reactions were performed in oven dried glassware under an atmosphere of extra dry nitrogen. Solutions were evaporated under reduced pressure with a rotatory evaporator and the residue was chromatographed on a silica gel column using an ethyl acetate-hexane mixture as the eluent unless specified otherwise.

**Preparation and Rhodium(II) Catalyzed Reaction of N-(2-Diazo-1,3-dioxobutyl)-2-thiopyrrolidinone (13).** To a solution containing 3.0 g (35.3 mmol) of 2-pyrrolidinone in 50 ml of toluene was added 8.55 g (21.2 mmol) of Lawesson's reagent[44] and the resulting suspension was heated at reflux for 5 h. The solution cooled to room temperature and the solvent was removed under reduced pressure. The resulting residue was subjected to flash silica gel chromatography using a 50% hexane-ethyl acetate mixture as the eluent to give 2.35 g (66%) of 2-thiopyrrolidinone[45] as a colorless solid; mp 110-111°C;

ir ($CDCl_3$) 3280, 3150, 3000, 1665, 1440, and 1240 $cm^{-1}$; $^1H$-nmr ($CDCl_3$, 300 MHz) δ 2.08 (quin., 2H, J=7.6 Hz), 2.79 (t, 2H, J=7.6 Hz), 3.55 (t, 2H, J=7.6 Hz), and 9.26 (s, 1H); $^{13}C$-nmr ($CDCl_3$, 75 MHz) δ 22.5, 43.2, 49.5, and 205.0.

To a solution containing 0.50 g (4.95 mmol) of the above thiolactam in 80 ml of dry THF at -78°C under a nitrogen atmosphere was added 3.25 ml of a 1.6 M n-BuLi solution and the mixture was stirred for 60 min at this temperature. A sample containing 0.42 ml (5.40 mmol) of diketene was added to the solution and the resulting mixture was allowed to warm to room temperature and then poured into 50 ml of an aqueous saturated ammonium chloride solution. The aqueous phase was separated and extracted with ether. The combined organic phase was dried over anhydrous magnesium sulfate, filtered, and the solvent was removed under reduced pressure. The residue was subjected to flash silica gel chromatography using a 35% ethyl acetate in hexane mixture as the eluent to give 0.49 g (54%) of N-(1,3-dioxobutyl)-2-thiopyrrolidinone as a yellow oil; ir (neat) 2975, 2901, 1723, 1694, 1617, 1387, 1335, 1256, and 1122 $cm^{-1}$; $^1H$-nmr ($CDCl_3$, 300 MHz) δ 1.99 (quin., 2H, J=7.4 Hz), 2.19 (s, 3H), 3.09 (t, 2H, J=7.4 Hz), and 4.11 (t, 2H, J=7.4 Hz); $^{13}C$-nmr ($CDCl_3$, 75 MHz) δ 19.1, 30.1, 49.9, 53.1, 53.6, 168.0, 200.4, and 209.1.

A solution containing 0.82 g (3.57 mmol) of 1-ethyl-2-chloropyrridinium tetrafluoroborate in 20 ml of a 70% aqueous methanol solution was treated with 0.23 g (3.57 mmol) of sodium azide at -25°C.[38] After stirring for 10 min, a solution containing 0.55 g (2.97 mmol) of *N*-(1,3-dioxobutyl)-2-thiopyrrolidinone in 3 ml of 70% aqueous methanol and 0.29 g (3.57 mmol) of sodium acetate was added in that order. The resulting solution was stirred for 18 h at -25°C and was then allowed to warm to room temperature. The solvent was removed under reduced pressure and the residue was taken up in 20 ml of water and extracted with ether. The combined organic phase was dried over anhydrous magnesium sulfate, filtered, and the solvent was removed under reduced pressure. The resulting residue was subjected to flash silica gel chromotography using a 45% ethyl acetate in hexane solution as the eluent to give 0.13 g (21%) of *N*-(2-diazo-1,3-dioxobutyl)-2-thiopyrrolidinone (**13**) as a yellow solid; mp 83-84°C; ir (neat) 2984, 2907, 2139, 1653, 1396, and 1335 $cm^{-1}$; $^1H$-nmr ($CDCl_3$, 300 MHz) δ 2.12 (quin., 2H, J=7.4 Hz), 2.48 (s, 3H), 3.06 (t, 2H, J=7.4 Hz), and 4.08 (t, 2H, J=7.4 Hz); $^{13}C$-nmr ($CDCl_3$, 75 MHz) δ 20.3, 28.5, 47.5, 53.7, 83.2, 162.5, 189.2, and 206.2.

A solution containing 67.5 mg (0.32 mmol) of the above diazo compound and 83 mg (0.48 mmol) of *N*-phenylmaleimide in 5 ml of xylene was treated with a catalytic amount of rhodium(II) acetate and the solution was heated at reflux for 1 h. The mixture was cooled to room temperature and the solvent was

removed under reduced pressure. The resulting residue was subjected to flash silica gel chromatography using a 50% ethyl acetate in hexane mixture as the eluent to give 72 mg (63%) of 4-acetyl-4,9a-epithio-2,3a,4,7,8,9,9a,9b-octahydro-2-phenyl-1,3,5-trioxo-1*H*-pyrrolo[3,4-*g*]indolizine (**15**) as a white crystalline solid; mp 212-213°C; ir (neat) 3080, 2995, 2915, 1721, 1510, 1396, and 1205 $cm^{-1}$; $^1$H-nmr ($CDCl_3$, 300 MHz) δ 2.21-2.35 (m, 2H), 2.42 (dt, 1H, J=14.2 and 5.9 Hz), 2.67 (s, 3H), 2.67-2.78 (m, 1H), 3.27 (dt, 1H, J=11.1 and 7.5 Hz), 3.57-3.62 (m, 1H), 3.64 (d, 1H, J=6.9 Hz), 4.12 (d, 6.9 Hz), 7.09-7.24 (m, 2H), and 7.39-7.48 (m, 3H); $^{13}$C-nmr (DMSO-$d_6$, 75 MHz) δ 26.1, 28.3, 28.5, 42.9, 49.9, 57.2, 81.7, 81.9, 126.9, 129.2, 129.4, 132.0, 170.3, 173.4, 173.7 and 199.8; Anal. Calcd for $C_{18}H_{16}N_2O_4S$: C, 60.66; H, 4.53; N, 7.87; S, 8.98. Found: C, 60.58; H, 4.57; N, 7.80; S, 8.94.

The rhodium(II) catalyzed reaction of **13** was also carried out in the absence of a dipolarophile. A solution containing 89 mg (0.42 mmol) of **13** in 5 ml of dry benzene was treated with a catalytic amount of rhodium(II) acetate and heated at reflux for 2 h. The solution was cooled to room temperature and the solvent was removed under reduced pressure to give 60 mg (78%) of thioisomünchnone (**14**) as an oily, black solid; $^1$H-nmr ($CDCl_3$, 300 MHz) δ 2.45 (s, 3H), 2.66 (quin., 2H, J=7.6 Hz), 3.28 (t, 2H, J=7.6 Hz), and 4.09 (t, 2H, J=7.6 Hz); $^{13}$C-nmr ($CDCl_3$, 75 MHz) δ 24.5, 26.1, 31.3, 47.5, 105.4, 158.1, 170.8, and 189.2. To a solution containing 40 mg (0.22 mmol) of thioisomünchnone **14** in 5 ml of xylene under a nitrogen gas atmosphere was added 57 mg (0.33 mmol) of *N*-phenylmaleimide and the mixture was heated at reflux for 2 h. The solution was cooled to room temperature and the solvent was removed under reduced pressure. The resulting residue was subjected to flash silica gel chromatography to give 64 mg (82%) of 4-acetyl-4,9a-epithio-2,3a,4,7,8,9,9a,9b-octohydro-2-phenyl-1,3,5-trioxo-1*H*-pyrrolo[3,4-*g*]indolizine (**15**).

**Preparation and Rhodium(II) Catalyzed Reaction of 1-(2-Diazomethylformylaceto)-2-thiopyrridinone (16).** To a solution containing 500 mg (5.0 mmol) of 2-thiopyrrolidinone[45] and 750 mg (5.0 mmol) of methyl(chloroformyl) acetate in 20 ml of anhydrous THF at 0°C was slowly added 600 mg (6.0 mmol) of triethylamine. The mixture was stirred for 12 h and was allowed to warm to room temperature and stirred overnight. The solution was quenched with a $NH_4Cl$ solution, extracted with ether, dried over anhydrous $Na_2SO_4$, and concentrated under reduced pressure. Purification of the residue by flash silica gel chromatography afforded 155 mg (37%) of 1-methylformylaceto-2-thiopyrrolidinone as a pale yellow oil; ir (neat) 1750, 1710, 1480, 1360, 1280, 940, and 700 $cm^{-1}$; $^1$H-nmr ($CDCl_3$, 90 MHz) δ 2.08 (q, 2H, J=9 Hz), 3.20 (t, 2H, J=9 Hz), 3.70 (s, 3H), 4.20 (t, 2H, J=9 Hz), and 4.32 (s, 2H).

To a room temperature solution containing 140 mg (0.7 mmol) of the above β-keto ester and 90 mg (0.75

mmol) of mesyl azide in 1.2 ml of dry dichloromethane was added 188 mg (1.9 mmol) of triethylamine. Stirring was continued for 3 h followed by concentration of the mixture under reduced pressure. Purification by flash silica gel chromatography afforded 62 mg (37%) of 1-(2-diazomethylformylaceto)-2-thiopyrrolidinone (**16**) as a yellow oil; ir (neat) 2140, 1740, 1710, 1400, 1260, 1160, 770 and 730 $cm^{-1}$; $^1$H-nmr ($CDCl_3$, 90 MHz) δ 2.15 (q, 2H, J=7 Hz), 3.08 (t, 2H, J=7 Hz), 3.82 (s, 3H), and 4.06 (t, 2H, J=7 Hz).

A solution containing 50 mg (0.23 mmol) of **16** and 192 mg of *N*-phenylmaleimide (0.7 mmol) in 3 ml of benzene in the presence of 5 mg of rhodium(II) acetate was immersed in a 100°C oil bath and maintained at this temperature for 30 min. The mixture was cooled, filtered and concentrated under reduced pressure. Purification of the residue by flash silica gel chromatography afforded 36 mg (44%) of methyl-4,9a-epithio-2,3,3a,4,5,9b-hexahydro-1,3,5-trioxo-2-phenyl-1-*H*-pyrrolo[3,4-*g*]indolizine-4-carboxylate (**18**) as a white solid; mp 218-219°C; ir ($CHCl_3$) 1760, 1720, 1505, 1470, 1270, 1200, and 700 $cm^{-1}$; $^1$H-nmr ($CDCl_3$, 300 MHz) δ 2.25-2.32 (m, 2H), 2.42 (dt, 1H, J=14.7 and 5.6 Hz), 2.72 (dt, 1H, J=14.7 and 5.6 Hz), 3.26 (dt, 1H, J=11.1 and 7.5 Hz), 3.58 (d, 1H, J=6.8 Hz), 3.58-3.66 (m, 1H), 3.92 (s, 3H), 4.13 (d, 1H, J=6.8 Hz), and 7.22-7.48 (m, 5H); Anal. Calcd for $C_{18}H_{16}N_2SO_5$: C, 58.05; H, 4.33; N, 7.53. Found: C, 57.93; H, 4.21; N, 7.38.

**Preparation and Rhodium(II) Catalyzed Reaction of Ethyl 2-Diazo-3-oxo-4-thiobenzoylthiobutanoate (19).** To a solution containing 1.0 g (4.71 mmol) of thiobenzoylthioacetic acid in 75 ml of THF was added 0.92 g (5.65 mmol) of *N,N'*-carbonyldiimidazole and the mixture was stirred for 16 h at room temperature. Treatment of this solution with 7.07 mmol of the magnesium chelate of ethyl hydrogen malonate dianion[46] at 0°C led to the formation of a gummy precipitate. The reaction mixture was warmed to 25°C and stirred for 16 h. At the end of this time, the mixture was poured into 100 ml of an ice cold 1.0 M $H_3PO_4$ solution. The resultant mixture was extracted with ethyl acetate, dried over $Na_2SO_4$ and concentrated under reduced pressure. The crude keto ester was dissolved in 10 ml of benzene. To this solution was added 0.57 g (4.71 mmol) of mesyl azide and 1.3 ml (9.42 mmol) of triethylamine and the reaction was stirred for 12 h at room temperature. The crude product mixture was concentrated under reduced pressure to leave behind a red oil which was chromatographed on silica gel to give 0.95 g (65%) of ethyl 2-diazo-3-oxo-4-thiobenzoylthiobutanoate (**19**) as an orange solid; mp 96-97°C; ir (neat) 2147, 1692, 1644, 1389, 1274 and 1201 $cm^{-1}$; $^1$H- nmr ($CDCl_3$, 90 MHz) δ 1.35 (t, 3H, J=7 Hz), 4.38 (q, 2H, J=7 Hz), 4.82 (s, 2H), 7.45 (m, 3H), and 8.10 (m, 2H).

To a stirred solution containing 0.55 g (1.78 mmol) of **19** in 20 ml of benzene was added 10 mg of

rhodium(II) octanoate. The reaction was heated at reflux for 2 h. The mixture was concentrated under reduced pressure and the resultant red oil was chromatographed on silica gel to give 0.35 g (80%) of ethyl 2-phenyl-4-hydroxythiophene-3-carboxylate (**22**)[47] as an orange solid; mp 60-61°C; ir ($CHCl_3$) 1666, 1566, 1431 and 1154 $cm^{-1}$; $^1$H-nmr ($CDCl_3$, 90 MHz) δ 1.05 (t, 3H, J= 7 Hz) 4.24 (q, 2H, J=7 Hz), 6.37 (s, 1H), 7.41 (m, 5H), and 9.32 (s, 1H); $^{13}$C-nmr ($CDCl_3$, 75 MHz) δ 13.5, 61.0, 98.9, 115.1, 127.5, 127.6, 128.6, 129.7, 134.2, 150.3, 156.1, and 166.1; Anal. Calcd for $C_{13}H_{12}O_3S$: C, 62.89; H, 4.88. Found: C, 62.74; H, 4.63.

**Preparation and Rhodium(II) Catalyzed Reaction of Ethyl 2-Diazo-6-(*N*-methyl-*N*-phenyl)amino-3-oxo-6-thioxohexanoate (29).** To a solution containing 10.5 g (50 mmol) of *N*-methyl-*N*-phenylsuccinimic acid[48] in 100 ml of methanol at -20°C was slowly added 4 ml of thionyl chloride over a 15 min time span. The reaction mixture was allowed to warm to room temperature and was stirred at 25°C for 1 h. Removal of the solvent under reduced pressure and chromatography of the crude residue on silica gel afforded 9.1 g (82%) of a colorless oil whose structure was assigned as methyl *N*-methyl-*N*-phenylsuccinimate; $^1$H-nmr (90 MHz, $CDCl_3$) δ 2.25-2.65 (m, 4H), 3.30 (s, 3H), 3.69 (s, 3H), and 7.23-7.60 (m, 5H).

A solution containing 9.1 g (41 mmol) of the above amide and 8.1 g (42 mmol) of Lawesson's reagent[44] in 100 ml of THF was stirred at room temperature for 3 h and at 60°C for an additional 1 h. Removal of the solvent under reduced pressure and chromatography of the residue on silica gel gave 7.5 g of a white solid (79%) whose structure was assigned as methyl 4-(N-methyl-N-phenyl)amino-4-thioxobutanoate; mp 67-68°C; $^1$H-nmr (300 MHz, $CDCl_3$) δ 2.64 (t, 2H, J=6.9 Hz), 2.86 (t, 2H, J=6.9 Hz), 3.63 (s, 3H), 3.74 (s, 3H), 7.21 (d, 2H, J=7.5 Hz), and 7.40-7.52 (m, 3H), $^{13}$C-nmr (75 MHz, $CDCl_3$) δ 32.9, 36.6, 45.2, 51.0, 125.0, 127.0, 129.5, 144.8, 172.5, and 202.9.

Saponification of 7.5 g of the above compound with 1.0 equiv. of sodium hydroxide in a 1:1 mixture (100 ml) of 1.0 N NaOH and methanol afforded an almost quantitative yield (7.2 g) of 4-(*N*-methyl-*N*-phenyl)-amino-4-thioxobutanoic acid as a white solid; mp 135-136°C, $^1$H-nmr (90 MHz, $CDCl_3$) δ 2.62 (t, 2H, J=6.3 Hz), 2.91 (t, 2H, J=6.3 Hz), 3.77 (s, 3H), 7.20-7.58 (m, 5H), and 10.20 (bs, 1H). A solution containing 6.7 g (30 mmol) of this acid in 100 ml of THF was treated with 4.86 g (35 mmol) of *N,N'*-carbonyldiimidazole. The yellowish solution darkened in color over several min and was allowed to stir at room temperature overnight. The resulting mixture was added to a freshly prepared magnesium (II) ethyl malonate dianion solution[46] in 50 ml of THF and the combined mixture was allowed to stir at room temperature for 4 h. The solution was quenched with 120 ml of an ice cold 1.0 M phosphoric acid solution. This was followed by

extraction with ethyl acetate, drying over anhydrous $Na_2SO_4$, removal of the solvent and recrystallization of the residue from an ether-hexane mixture to give 5.0 g (54%) of ethyl 6-(*N*-methyl-*N*-phenyl)amino-3-oxo-6-thioxohexanoate as a white solid; mp 49-50°C; nmr (90 MHz, $CDCl_3$) δ 1.27 (t, 3H, J=6.6 Hz), 2.63 (t, 2H, J=6.4 Hz), 3.13 (t, 2H, J=6.4 Hz), 3.54 (s, 2H), 3.77 (s, 3H), 4.18 (q, 2H, J=6.6 Hz), and 7.20-7.62 (m, 5H).

A solution containing 4.5 g (15 mmol) of this material in 50 ml of acetonitrile was treated with 3.3 g (27 mmol) of methanesulfonyl azide and 2.5 ml of triethylamine for 12 h. The reaction mixture was washed with a 10% sodium hydroxide solution and the aqueous phase was extracted with ethyl acetate. The combined organic layer was dried over sodium sulfate and concentrated under reduced pressure. The crude residue was chromatographed on a silica gel column to give 4.1 g (86%) of diazothioamide (**29**) as a yellow solid; mp 93-94°C; ir (KBr) 2130, 1705, 1640, 1490, 1450, 1230, 780, and 701 $cm^{-1}$; $^1H$-nmr (300 MHz, $CDCl_3$) δ 1.33 (t, 3H, J=7.1 Hz), 2.68 (t, 2H, J=6.4 Hz), 3.40 (t, 2H, J=6.4 Hz), 3.73 (s, 3H), 4.30 (q, 2H, J=7.1 Hz), 7.27 (d, 2H, J=7.5 Hz), 7.39 (t, 1H, J=7.5 Hz), and 7.47 (t, 2H, J=7.5 Hz); $^{13}C$-nmr (75 MHz, $CDCl_3$) δ 13.7, 36.0, 39.1, 45.2, 60.7, 125.1, 127.7, 129.4, 144.9, 160.7, 190.7, and 203.3. Anal. Calcd for $C_{15}H_{17}N_3O_3S$: C, 56.41; H, 5.36; N, 13.16; S, 10.04. Found: C, 56.34; H, 5.37; N, 13.11; S, 9.99.

Treatment of 320 mg (1.1 mmol) of compound (**29**) with a catalytic amount of rhodium(II) acetate dimer at 60°C in 10 ml of benzene, either in the presence or absence of a dipolarophile, gave rise to a clear oil in 90% yield whose structure was assigned as 2-carboethoxy-3-(*N*-methyl-*N*-phenyl)amino-2-cyclopentenone (**32**); ir (neat) 1720, 1663, 1561, 1492, 1405, 1034 and 700 $cm^{-1}$; $^1H$-nmr (300 MHz, $CDCl_3$) δ 1.18 (t, 3H, J=7.0 Hz), 2.41-2.46 (m, 2H), 2.57 (m, 2H), 3.45 (s, 3H), 3.93 (m, 2H) and 7.21-7.47 (m, 5H); $^{13}C$-nmr (75 MHz, $CDCl_3$) δ 13.5, 27.9, 33.0, 42.4, 60.0, 108.0, 125.1, 127.2, 129.1, 144.8, 164.6, 173.3, and 199.0, Anal. Calcd for $C_{15}H_{17}NO_3$: C, 69.47; H, 6.61, N, 5.40. Found: C, 69.28; H, 6.52; N, 5.23.

**Preparation and Rhodium(II) Catalyzed Reaction of Ethyl 2-Diazo-3-oxo-3-(1-thiobenzoylpyrrolidin-2-yl)propionate (34).** A solution containing 12.0 ml (104 mmol) of benzoyl chloride in 75 ml of ether was added dropwise to a stirred solution of 10.0 g (86.9 mmol) of L-proline , 10.0 g of sodium carbonate, 100 ml of a 10 N sodium hydroxide solution, and 100 ml of water at 5°C. The reaction was allowed to warm to room temperature, and stirred for an additional 1.5 h. The resultant precipitate was filtered and the filtrate was extracted with ether and the aqueous layer was acidified to pH 2 with concentrated HCl. The acidic mixture was extracted with ethyl acetate, dried over $Na_2SO_4$, and

concentrated under reduced pressure to give an opaque oil that was redissolved in 200 ml of ethanol. To this solution was added 200 mg of *p*-toluenesulfonic acid and the mixture was heated at reflux for 8 h. The reaction mixture was concentrated under reduced pressure and the residue was partitioned between a saturated $NaHCO_3$ solution and ethyl acetate. The organic layer was dried over $Na_2SO_4$ and concentrated under reduced pressure to give a thick clear oil which was dissolved in 400 ml of THF. To this solution was added 17.6 g (43.5 mmol) of Lawesson's reagent[44] and the mixture was stirred at 25°C for 16 h. The solution was concentrated under reduced pressure and chromatographed on silica gel to give 19.7 g (86%) of *N*-thiobenzoylproline ethyl ester as a light yellow crystalline solid; mp 86-87°C; ir ($CHCl_3$) 1738, 1445, 1264, 1194 and 1024 $cm^{-1}$; $^1$H-nmr ($CDCl_3$, 90 MHz) δ 1.25 (t, 3H, J=7 Hz), 1.80-2.45 (m, 4H), 3.63 (m, 2H), 4.28 (q, 2H, J=7 Hz), 5.15 (m, 1H), and 7.36 (m, 5H).

To a stirred solution containing 2.5 g (9.50 mmol) of the above material in 25 ml of acetone was added 100 ml of 1N NaOH solution. The reaction was stirred at 25°C for 4 h, then the excess acetone was removed under reduced pressure and the remaining aqueous solution was made acidic (pH 2) with conc. HCl. The resultant mixture was extracted with $CH_2Cl_2$ and concentrated under reduced pressure to give the crude carboxylic acid. To a solution of the crude acid in 100 ml of THF was added 1.5 g (9.50 mmol) of *N,N*-carbonyldiimidazole and the mixture was stirred for 16 h at room temperature. Treatment of this solution with 14.3 mmol of the magnesium chelate of ethyl hydrogen malonate dianion[46] at 0°C led to the formation of a gummy precipitate. The reaction mixture was warmed to 25°C and stirred for 16 h. At the end of this time, the mixture was poured into 200 ml of an ice cold 1.0 N $H_3PO_4$ solution. The mixture was extracted with ethyl acetate, dried over $Na_2SO_4$ and concentrated under reduced pressure to give the crude ketoester which was dissolved in 20 ml of benzene. To this solution was added 1.2 g (9.5 mmol) of mesyl azide and 2.6 ml (19.0 mmol) of triethylamine and the solution was stirred for 12 h at room temperature. The crude product mixture was concentrated to a dark yellow oil and chromatographed on silica gel to give 1.6 g (52% yield) of ethyl 2-diazo-3-oxo-3-(1-thiobenzoylpyrrolidin-2-yl) propionate (**34**) as a thick yellow oil; ir (neat) 2125, 1710, 1665, 1450, 1305 and 1225 $cm^{-1}$; $^1$H-nmr ($CDCl_3$, 90 MHz) δ 1.25 (t, 3H, J=7 Hz), 1.80-2.35 (m, 4H), 3.52 (m, 2H), 4.21 (q, 2H, J=7 Hz), 6.05 (m, 1H), and 7.25 (m, 5H).

To a stirred solution containing 300 mg (0.905 mmol) of **34** and 0.17 ml (1.36 mmol) of DMAD in 5 ml of benzene was added 10 mg of rhodium(II) octanoate. The reaction mixture was heated at reflux for 3 h, concentrated under reduced pressure and the residue was chromatographed on silica gel to give 202 mg (62%) of dimethyl 2,3-dihydro-5-phenyl-1*H*-pyrrolizine-6,7-dicarboxylate (**39**)[49] as a crystalline solid; mp

155-156°C; ir ($CHCl_3$) 1716, 1441, 1223 and 1098 $cm^{-1}$; $^1H$-nmr ($CDCl_3$, 90 MHz) δ 2.52 (m, 2H), 3.15 (t, 2H, J=7 Hz), 3.75 (s, 3H), 3.81 (s, 3H), 3.95 (t, 2H, J=7 Hz), and 7.37 (m, 5H); Anal. Calcd for $C_{17}H_{17}NO_4$ : C, 68.21; H, 5.73, N, 4.68. Found: C, 68.20; H, 5.72; N, 4.65.

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†*Dedicated with respect and admiration to Professor Edward C. Taylor, one of the leading pioneers in the area of heterocyclic chemistry, on the occasion of his 70th birthday.*

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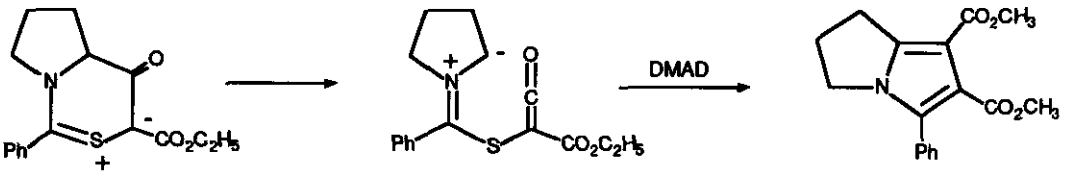
43. The mechanism proposed is based solely on analogy to the results obtained with amide (**12**).[42] An alternative possibility would involve ring opening of **35** to give azomethine ylide (**40**) which then undergoes cycloaddition with DMAD and aromatization with elimination of the side chain.

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