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Enaminones via Ruthenium-Catalyzed Coupling of Thioamides and α-Diazocarbonyl Compounds

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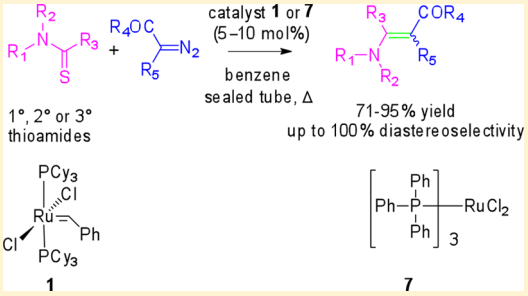
Supporting Information

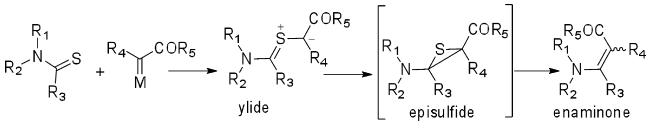
ABSTRACT: Enaminones can be prepared via the $Rh_2(OAc)_4$-catalyzed coupling of α-diazocarbonyl compounds with thioamides. However, rhodium is the most expensive and least abundant among the dominant precious metals used for catalysis. Furthermore, a very limited substrate scope is known for the intermolecular rhodium catalyzed coupling reaction. Therefore, there is a need to find a more economical catalyst substitute with a broad substrate scope. In this paper, we describe the use of Ru(II) catalysts for the synthesis of enaminones. The reaction can be performed efficiently with the Grubbs first-generation catalyst or $[(Ph)_3P]_3RuCl_2$ in a sealed tube. Both catalysts are much less expensive than $Rh_2(OAc)_4$. Secondary and tertiary thioamides, when reacted with α-diazodiesters, α-diazoketoesters, α-diazodiketones, and α-diazomonoketones give enaminones. Primary thioamides give thiazole derivatives when reacted with α-diazomonoketones. However, with other diazo compounds, primary thioamides also give enaminones. All enaminones are obtained in good yields and with good diastereoselectivity. Accordingly, the method described in this paper is an efficient and economical alternative to the $Rh_2(OAc)_4$-catalyzed coupling process.



INTRODUCTION

We investigated whether the synthesis of enaminones is possible by a mild, economical, and selective Ru(II)-catalyzed coupling reaction between thioamides and α-diazocarbonyl compounds. Enaminone compounds possess great potential as synthetic intermediates due to the existence of three electrophilic and two nucleophilic sites present within the enaminone functional group.[1] Enaminones also show the ability to participate in pericyclic and radical reactions.[2] As a result, pharmaceutical development and natural product syntheses utilize the enaminone functional group.[3] Common methods for the preparation of enaminones include the following: the condensation of amines with dicarbonyl compounds,[4] the reaction of lactams or lactims with active methylene compounds and other nucleophiles,[5,6] the conjugate addition of amine derivatives to α,β-unsaturated compounds, addition reactions on nitriles, the cleavage of heterocycles, addition reactions of alkynes and an amine, rearrangement of cyclobutanones, intramolecular aza-Wittig reactions, Friedel–Crafts and Vilsmeier reactions of enecarbamates, acylation of enaminones,[3,7−9] the Eschenmoser coupling reaction,[10−12] and the metal-catalyzed coupling of thioamides with α-diazocarbonyl compounds.[13,14] Recently, Bolm and Priebbenow reported the coupling of amides with α-silyl α-diazoacetates,[15] and Huang and co-workers reported the formation of enaminones via a tertiary amide-based Knovenagel-type reaction.[16] The synthesis of cyclic enaminones has also been achieved via the reaction of donor–acceptor cyclopropanes and amines.[17,18]

Scheme 1. Enaminones via Coupling of Metal Carbenes and Thioamides



A diazo compound converts into a metal carbene in the metal-catalyzed coupling of thioamides with α-diazocarbonyl compounds. The metal carbene reacts with a thioamide, generating an ylide which, through an episulfide intermediate, leads to the formation of an enaminone (Scheme 1).[14,19]

Traditionally, the transformation utilizes $Rh_2(OAc)_4$ for intramolecular coupling reactions.[13,14,20] In this case it amounts

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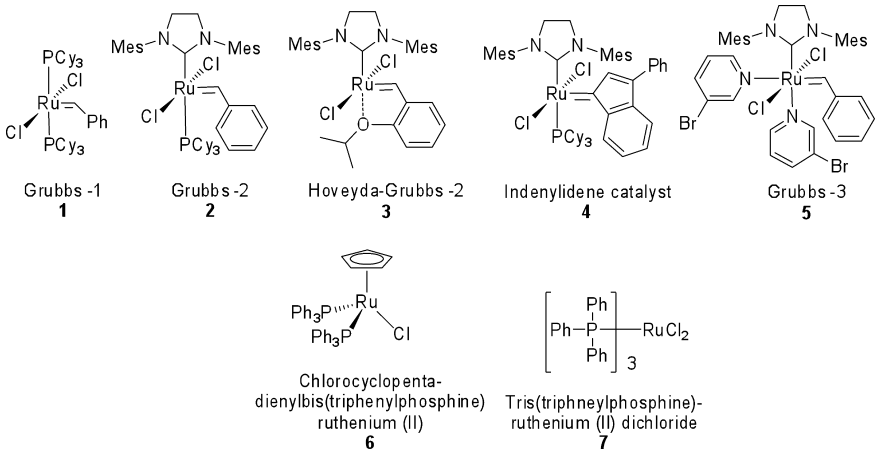


Figure 1. Catalysts screened in the present study.

to the aza-Robinson annulation reaction[21] and synthesizes heterocyclic products.[13] Even with this early success, the rhodium-catalyzed reaction is not a common method for the synthesis of enaminones. Danishefsky and co-workers reported the only example for the intermolecular rhodium-catalyzed coupling reaction.[19] One reason for the lack of intermolecular reaction examples is the homocoupling of diazo compounds.[22] Other side reactions, such as the cyclopropanation reaction, also occur.[23] Rhodium is also the most expensive and least abundant among the dominant precious metals used for catalysis.[24,25] Due to these reasons, chemists have not reported the use of diazodiketones, or the use of primary and secondary thioamides, in the rhodium-catalyzed reaction.

We recently reported our preliminary findings on the use of ruthenium in the coupling of thioamides with α-diazocarbonyl compounds, which have broadened the scope of this transformation.[26] Still, the yields were low and the reaction required harsh conditions. In this paper we address these issues, describe the screening of seven different ruthenium catalysts, and discuss the scope and limitations of the ruthenium-catalyzed coupling of thioamides and α-diazocarbonyl compounds.

RESULTS AND DISCUSSION

Figure 1 shows the catalysts that were screened. All of them are commercially available, and they can be divided into two different types, Grubbs-type catalysts (**1**–**5**) and Ru(II) triphenylphosphine complexes (**6**, **7**). Both types of catalysts have been used in the generation of ruthenacarbenes by their reaction with α-diazocarbonyl compounds.[27,28]

The two types of catalysts generate ruthenacarbenes by two different mechanisms (Scheme 2).[27,28] Therefore, the catalyst selection in Figure 1 provides the opportunity to observe the reactivity of catalysts that act by distinct mechanisms. It also allows for the comparison of different catalysts within each type.

Thioamide **8** and diazomalonate **9** were reacted with catalysts **1**–**7** (Table 1) in a sealed tube. This particular reaction was selected because **8** contains a stereocenter and an additional functional group, thus providing a reasonable test for the suitability of reaction conditions to other functional groups and stereocenters. Additionally, the same reaction was used in our previous studies for screening purposes.[26] Benzene was used as the solvent, as we discovered that it is the best solvent for the transformation.[26] We first determined the lowest temperature at which the conversion of **8** into **10** was observable within 26 h. This was done by checking TLCs of the reaction every 1 h at room temperature and 50, 70, and 90 °C. Once the lowest

Scheme 2. Proposed Mechanisms for the Generation of Ruthenacarbenes

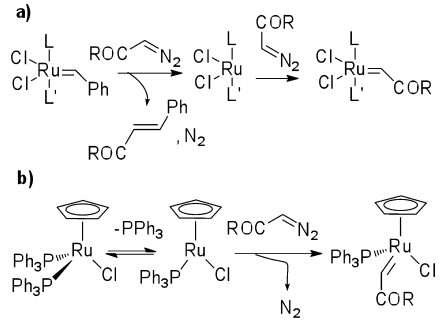
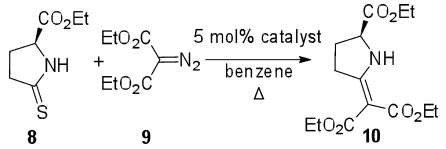


Table 1. Catalyst Screening for the Ruthenium-Catalyzed Synthesis of Enaminones



entry	catalyst	temp (°C)[a]	time (h)	yield (%)
1	**1**	70	9	80[b]
2	**1**	70	26	(10)[c]
3	**2**	70	26	71[b]
4	**2**	70	26	(19)[c]
5	**3**	70	9	71[b]
6	**3**	70	9	(12)[c]
7	**4**	90	9	77[b]
8	**4**	90	26	(26)[c]
9	**5**	70	26	(49)[d]
10	**6**	70	10	82[b]
11	**6**	70	26	(48)[c]
12	**7**	90	4	79[b]
13	**7**	90	26	(64)[c]

[a]Reactions were conducted in a pressure vessel. The temperature indicates the temperature of the oil bath. In each reaction 1.3 equiv of **9** was used. [b]Isolated yield with 5 mol % catalyst loading. [c]Percent conversion of **8** into **10** by ^{1}H NMR with 1 mol % catalyst loading. [d]Percent conversion of **8** into **10** by ^{1}H NMR with 5 mol % catalyst loading.

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temperature for the conversion was found, the reaction mixture was stirred at that temperature until the reaction was complete or for 26 h. The maximum time of 26 h and maximum temperature of 90 °C were chosen because we wanted to find conditions better than those in our preliminary report.[26] Except for **5**, all other catalysts provided 100% conversion of thioamide **8** into enaminone **10**. Attempts to lower the catalyst loading in an appreciable amount (5 mol % to 1 mol %) resulted in an incomplete reaction (entries 2, 4, 6, 8, 11, and 13). Among the Grubbs type catalysts (**1**–**5**), catalyst **1** provided the product in minimal time (entry 1), while between the Ru(II) triphenylphosphine complexes (**6**, **7**), catalyst **7** yielded the product in the least amount of time (entry 12). Catalysts **1** and **7** were selected for further reactions.

In addition to **9**, the diazo compounds that were used in this study are shown in Figure 2. They can generate ruthenacarbenes that can be classified into acceptor/acceptor and acceptor substituted carbenoids as per Davies' definition. The reactivity profiles of these carbenoids are different from each other. Within the acceptor/acceptor class the carbenoids from diketones are usually more reactive than those from diesters.[29]

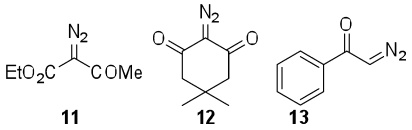
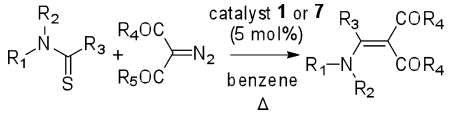


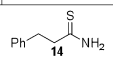
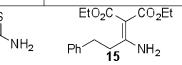
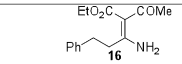
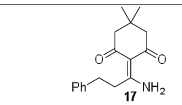
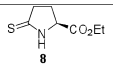
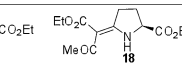
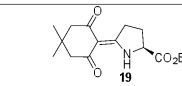
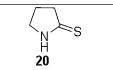
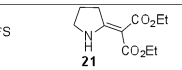
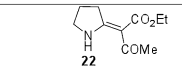
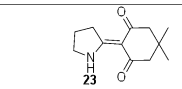
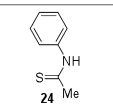
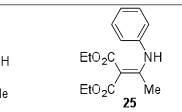
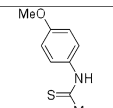
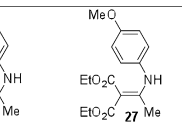
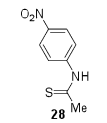
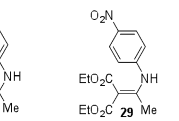
Figure 2. Additional diazo compounds evaluated in the present study.

Table 2 showcases the substrate scope of the coupling reaction of primary and secondary thioamides with α-diazodicarbonyl compounds. Both primary (entries 1–3) and secondary thioamides (entries 4–11) provided enaminones in excellent yields. Both cyclically (entries 4–8) and acyclically positioned (entries 9–11) thioamides were viable substrates. The reaction was successful in coupling diazodiesters (Table 2, entries 1, 6, and 9–11, and Table 1, entries 1 and 12), diazoketoesters (Table 2, entries 2, 4, and 7), and diazodiketones (Table 2, entries 3, 5, and 8) with thioamides. Both cyclic (Table 2, entries 3, 5, and 8) and acyclic (Table 2, entries 1, 2, 4, 6, 7, and 9–11) diazo compounds were able to participate in the reaction. Only single diastereomers were obtained when unsymmetrical diazo compounds were used (Table 2, entries 2, 4 and 7). Such selectivity has been observed before, and it is attributed to the hydrogen bonding between the N–H and the ketone oxygen.[30−32] The ^{1}H spectral data indicated the hydrogen bonding between the N–H and the ketone oxygen. Hydrogen bonding lowers the energy of the product. The *E* stereochemistry was assigned by comparing the ^{1}H values of these compounds with literature reports.[30−33] In the ^{1}H NMR spectrum, the signal of the N–H protons of **16**, **18**, and **22** appear at a higher chemical shift in comparison with the N–H protons of **15**, **10**, and **21**, respectively. These comparisons indicate the existence of intramolecular hydrogen bonding between the NH and the ketonic C=O groups.[31,33]

Coupling of the tertiary thioamide **30** (Scheme 3) proved to be more challenging than the coupling of primary and secondary thioamides (Table 2). Catalyst **1**, which previously provided 100% conversion of thioamides into enaminones on heating the reaction mixtures at 70 °C (Table 1, entry 1, and Table 2, entry 6), changed only 28% of **30** into **31**. Heating to 90 °C afforded slightly better results, but further heating reduced the formation of **31**. Thinking that the low conversion into enaminone is due to the greater steric hindrance of **30**, we attempted the use of catalysts **3** and **4** in the transformation. Catalysts **3** and **4** are more efficient catalysts than **1** in the olefin metathesis reaction of sterically challenging substrates;[34] however, these catalysts, in addition to **6** and **7**, failed to provide high conversion.

Table 2. Coupling of Primary and Secondary Thioamides with α-Diazodicarbonyl Compounds[b]



entry	thioamide	product	Temperature / time / yield using catalyst **1**	Temperature / time / yield using catalyst **7**
1	 **14**	 **15**	(90 °C, 12 h, 85%)	(90 °C, 10 h, 84%)
2	**14**	 **16**	(70 °C, 8 h, 83%)	(90 °C, 6 h, 84%)
3	**14**	 **17**	(90 °C, 7 h, 74%)	(90 °C, 5 h, 76%)
4	 **8**	 **18**	(90 °C, 20 h, 87%)[a]	(90 °C, 14 h, 84%)[a]
5	**8**	 **19**	(90 °C, 22 h, 93%)[a]	(90 °C, 16 h, 89%)[a]
6	 **20**	 **21**	(70 °C, 22 h, 86%)	(90 °C, 6 h, 87%)
7	**20**	 **22**	(70 °C, 22 h, 78%)	(90 °C, 5 h, 71%)
8	**20**	 **23**	(90 °C, 12 h, 89%)[a]	(90 °C, 12 h, 86%)[a]
9	 **24**	 **25**	(90 °C, 6 h, 89%)	(90 °C, 4 h, 92%)
10	 **26**	 **27**	(90 °C, 4 h, 83%)	(90 °C, 3 h, 81%)
11	 **28**	 **29**	(90 °C, 18 h, 78%)	(90 °C, 16 h, 81%)

[a]Two equivalents of diazo compounds was used. [b]Reactions were conducted in a pressure vessel. The temperature indicates the temperature of the oil bath.

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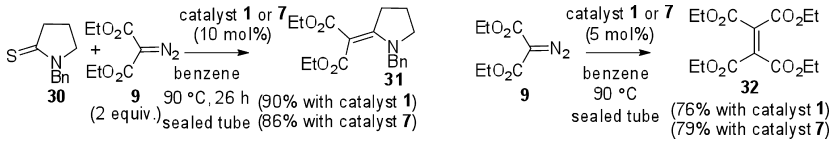
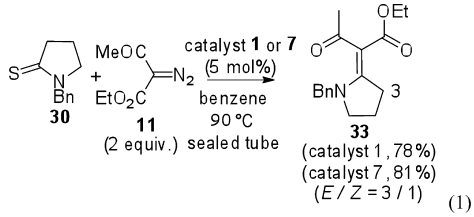
Scheme 3. Synthesis of 31 and the Competing Dimerization of 9



It was suspected that the difficulty in the conversion of **30** into **31** could be due to the competing dimerization reaction of **9**. Indeed, **9** dimerizes completely in the absence of thioamides when it is reacted under the reaction conditions (Scheme 3). Dimerization reactions of diazocarbonyl compounds are known with Ru(II) catalysts.[27,28] Competing dimerization also explains the need for 2 equiv of diazo compounds (**12**) with the secondary thioamides (**8** and **20**) (entries 4, 5, and 8, Table 2). Compound **8** has greater steric hindrance than other secondary thioamides discussed here, and compounds **11** and **12** generate more reactive ruthenacarbenes than does **9**. Therefore, **11** and **12** dimerize more quickly, requiring 2 equiv of **11** and **12** when reacted with thioamide **8**.[29]

With this information in hand, the amount of **9** was increased to allow for the formation of unwanted product **32**. Still, the reaction did not go to completion. After some experimentation, it was found that 10 mol % of the catalyst is necessary for the complete conversion of **30** into **31** (Scheme 3).

Next, **30** was reacted with **11** (eq 1). In these cases, only 5 mol % of catalysts was needed to get the complete conversion

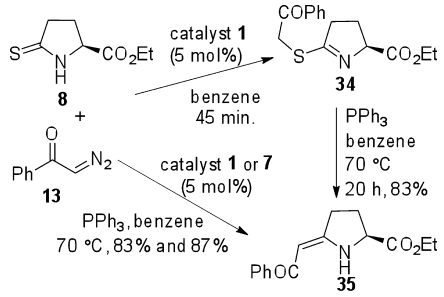


(1)

of **30** into **33**. The need for a lesser amount of catalysts is probably due to the greater reactivity of keto ruthenacarbenes relative to that of ester ruthenacarbenes.[29] The stereochemistry of the major diastereomer of **33** was tentatively assigned as *E*. Similar enaminoketoesters are known to preferentially exist as *E* products.[32,35] Simple molecular modeling calculations (Chem-Bio3D Ultra 12.0 with MM2 parameters)[36] suggested that the *E* diastereomer was 4.7 kcal/mol more stable than the *Z* isomer. The *Z* isomer suffers from $A^{1,3}$ type strain caused by the steric interactions between the C-3 hydrogen atoms and the methyl ketone hydrogen atoms (eq 1).

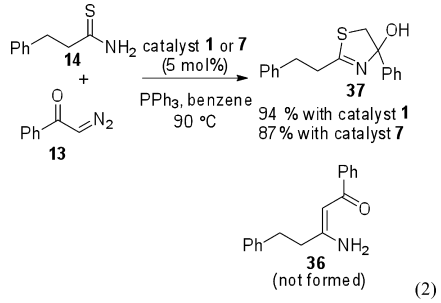
The reaction of diazoacetophenone (**13**) with thioamides required optimization (Scheme 4). Reaction conditions that were previously successful for the reaction of secondary thioamides (Table 2) gave mainly thioether **34**, and less than 40% of enaminone **35** was formed. It was observed that the formation of **34** was complete even at room temperature within 45 min in the presence of catalyst **1**. Formation of **34** also occurs in the Eschenmoser reaction. In the Eschenmoser reaction, the use of PPh_3 as a thiophile can convert **34** into enaminone **35**.[32,35] Indeed, when PPh_3 was added to the reaction mixture after the formation of the thioether **34** and the mixture heated to 70 °C for 20 h, an 83% yield of **35** was obtained. Later, a more convenient protocol was adopted where all reagents, including PPh_3, were added together and heated for 20 h to give a comparable yield of **35**. It was necessary to

Scheme 4. Synthesis of 35 with the Help of Triphenylphosphine



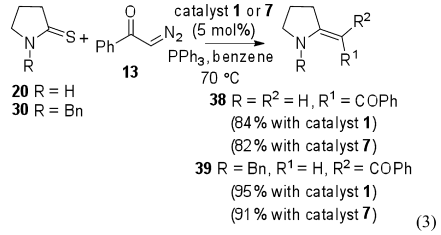
add an excess of PPh_3, as only 60% conversion of **34** into **35** was observed after 26 h with 1 equiv of PPh_3. The excess PPh_3 could be recovered during column chromatography.

Enaminone **35** was obtained as a single diastereomer. The stereochemistry was assigned as *Z* by NOE measurements and by comparison of the spectroscopic data of **35** with the literature values.[37] Under these reaction conditions, the reaction of the primary thioamide **14** to produce **36** did not succeed and instead **37** was obtained in excellent yield (eq 2).



(2)

The reaction of the secondary thioamide **20** produced **38** in excellent yield in just 1.5 h (eq 3). Compound **38** was obtained



(3)

as a single isomer. The stereochemistry was assigned as *Z* by the NOE measurements and by comparison of its spectroscopic data with the literature values.[38,39] As with **16**, **18**, and **22** (Table 2), the stereochemistry of **35** and **38** can be explained as being a consequence of the greater stability of the *Z* isomer. The hydrogen bonding between the N–H and the ketone oxygen makes the *Z* isomer more stable.[38]

Triphenylphosphine was not necessary with tertiary thioamides, and **39** could be obtained as a single *E* diastereomer in

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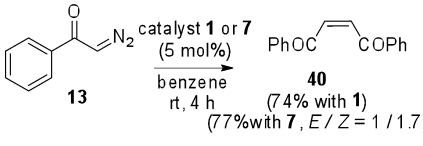
excellent yield (eq 3). However, the reaction required an excess of **13**. This is because **13** undergoes the competing dimerization reaction. In the absence of any thioamide, **13** gave olefin **40** in a diastereoselective manner (eq 4).[40] Such *Z*



(4)

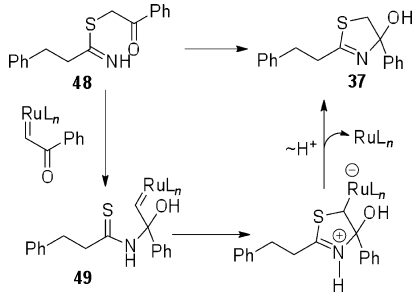
stereoselectivity has been observed previously with Ru(II) catalysts.[27,28] With catalyst **1**, only the *Z* product could be isolated, while with catalyst **7**, the *E* product **40** was also obtained in 25% yield. The stereochemistry of enaminone **39** was assigned as *E* by the NOE measurements and by comparison of its ^{1}H NMR data with literature values.[41] Simple molecular modeling calculations (ChemBio3D with MM2 parameters)[36] suggested that the *E* diastereomer was 9.7 kcal/mol more stable than the *Z* isomer and that the *Z* isomer possesses the $A^{1,3}$ strain caused by the interactions between the benzylic hydrogen atoms and the carbonyl oxygen.

On the basis of these results and our previous studies,[26] the mechanism given in Scheme 5 is proposed. Ruthenacarbene **41**, generated by the action of ruthenium complexes on diazo compounds,[27,28] is attacked by the nucleophilic thioamide to give the ruthenium complex associated thiocarbonyl ylide **42** and the free ylide **43**. Ylide **42** dissociates, regenerating the catalyst **44**, while **43** cyclizes, giving episulfide **45**, which collapses to give the enaminone.[14,19] Since we have isolated thioethers **47** (for example **34**), a shortcut path from **42** to **45** is unlikely.

The proposed mechanism explains why the reaction was slowest with Grubbs-3 (**5**; entry 9, Table 1), which is known to have the fastest initiation rate in comparison with all of the Grubbs-type catalysts shown in Figure 1.[34,42] Unlike the case for the olefin metathesis reaction,[43] the formation of the active catalyst (**44** = **46**) from catalyst **1** does not require dissociation of one L-type ligand from the precatalyst.[27]

Formation of cyclic product **37** could also be explained by the proposed mechanism (Scheme 6). Once thioether **48** is formed, the imine nitrogen could attack the carbonyl carbon,

Scheme 6. Possible Pathways for the Formation of Thiazole Derivatives

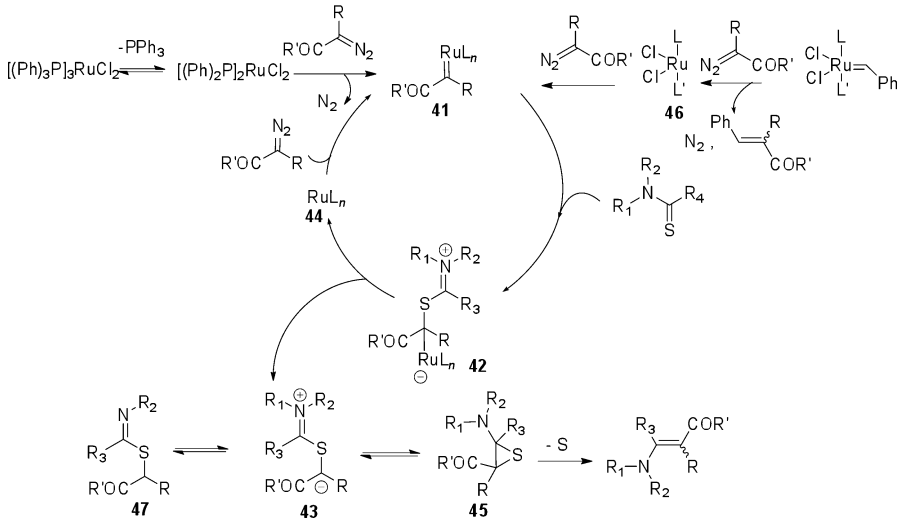


giving the product **37**. However, it cannot be ruled out that the nitrogen first adds to the carbonyl carbon to give **49** and the sulfur atom attacks the ruthenacarbene later. Mechanistic studies are underway to test the validity of the proposed mechanism (Scheme 5).

CONCLUSIONS

In summary, the screening of seven Ru(II) catalysts in the coupling of thioamides with α-diazocarbonyl compounds has been disclosed. Two different types of commercially available Ru(II) catalysts coupled primary, secondary, and tertiary thioamides with α-diazocarbonyl compounds to give enaminones. The method efficiently coupled secondary and tertiary thioamides with α-diazodiesters, α-diazoketoesters, α-diazodiketones, and α-diazomonoketones to provide the corresponding enaminones. Primary thioamides could be coupled with α-diazodiesters, α-diazodiketones, and α-diazoketoesters to furnish enaminones, while their reaction with α-diazomonoketones gave thiazole derivatives. Presently, efforts are underway to study the scope of the thiazole derivative transformation. The approach provided enaminones with good diastereoselectivity, and it is an economical alternative to the rhodium-catalyzed reaction. The reaction was performed under milder conditions and gave better yields in comparison to those in our preliminary report.[26] The reaction could be conducted by catalyst **7**, which is 41% more economical than catalyst **1**, which was communicated in our preliminary report.[26] Ylides have been suggested in the proposed mechanism, which could have

Scheme 5. Proposed Mechanisms for the Formation of Enaminones



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great potential in sulfur ylide chemistry.[13,44,45] Their ability to perform cycloaddition reactions in one pot will be explored in the future. We are also evaluating the possibility of copper as a more economical catalyst for the coupling reaction.

EXPERIMENTAL SECTION

General Methods. NMR spectra were obtained with a 400 MHz spectrometer: ^{1}H NMR (400 MHz) and ^{13}C (100 MHz). Chemical shifts are referenced with the residual solvent peak ($CDCl_3$: 7.26 ppm for ^{1}H NMR and 77.16 ppm for ^{13}C NMR). Accurate mass spectra were obtained in a positive ion electrospray mode using an orbitrap analyzer. Petroleum ether refers to fractions that distill between 30−60 °C. Column chromatography refers to flash chromatography performed using Sorbent silica gel 60 Å (40−63 μm). Benzene and acetonitrile were dried by distillation from calcium hydride onto 4 Å molecular sieves. The molecular sieves were activated by conventional microwave heating until red (1:30−2:30 min). Catalysts **1**−**3** and **5**−**7** were purchased from Aldrich, and catalyst **4** was purchased from STREM Chemicals. Catalysts **1**, **3**, and **7** were 97% pure, catalyst **4** was 95% pure, and the rest of the catalysts were 100% pure according to the vendor's web site.[46] All of the ruthenium-catalyzed reactions were conducted under an argon atmosphere. Compounds **8**,[47] **12**,[26] **14**,[26] **20**,[26] and **30**[32] were prepared by literature methods, and ^{1}H and ^{13}C NMR was used to confirm their identity and purity.

Diethyl Diazomalonate (9). A solution of diethyl malonate (645 mg, 4.03 mmol) in dry CH_3CN (11 mL) was added to a stirred solution of *p*-toluenesulfonyl azide[26] (806 mg, 4.09 mmol) in dry CH_3CN (8 mL) at 0 °C. DBU (98%, 0.93 mL, 6.06 mmol) was added *dropwise*, and the solution was warmed to room temperature overnight. The reaction mixture was concentrated and purified by column chromatography using a short column (25% petroleum ether in CH_2Cl_2). It gave pure **9** (612 mg, 3.29 mmol, 82%) as a viscous yellow liquid. The ^{1}H and ^{13}C NMR chemical shift values match the data reported in the literature.[26]

Ethyl 2-Diazo-3-oxobutanoate (11). A solution of ethyl acetoacetate (345 mg, 2.64 mmol) in dry CH_3CN (10 mL) was added to a stirred solution of *p*-toluenesulfonyl azide[26] (626 mg, 3.17 mmol) in dry CH_3CN (2 mL). DBU (98%, 0.60 mL, 4.02 mmol) was added *dropwise* at 0 °C, and the reaction mixture was warmed to room temperature overnight. The reaction mixture was concentrated and purified by column chromatography (10% acetone in pentane). It gave pure **11** (338 mg, 2.16 mmol, 82%) as a viscous yellow liquid. The ^{1}H and ^{13}C NMR chemical shift values match the data reported in the literature.[26]

α-Diazoacetophenone (13). α-Bromoacetophenone (200 mg, 1.00 mmol) and *N,N′*-ditosylhydrazine (681 mg, 2.00 mmol, 2 equiv) were dissolved in 5 mL of dry THF. The flask was kept in an ice bath, and DBU (0.75 mL, 5.00 mmol, 5 equiv) was added *dropwise*. After 20 min the reaction mixture was concentrated and purified by column chromatography (20% EtOAc in petroleum ether) to give pure **13** (139 mg, 0.95 mmol, 95%) as a yellow solid. R_f = 0.36 (4:1 petroleum ether:EtOAc). The ^{1}H and ^{13}C NMR chemical shift values match the data reported in the literature.[48]

General Experimental Procedure for the Synthesis of Thioamides. A solution of amide in CH_2Cl_2 (0.50 M) was added to a suspension of Lawesson's reagent (0.5 equiv, 0.25 M) in CH_2Cl_2 and stirred at room temperature for the specified period of time. The reaction mixture was concentrated and purified by column chromatography.

*N-Phenylethanethioamide (**24**).*[49] Following the general procedure for the synthesis of thioamides, *N*-phenylacetamide (200 mg, 1.48 mmol) was converted into crude *N*-phenylethanethioamide by stirring for 4 h at room temperature. The reaction mixture was chromatographed (CH_2Cl_2) to give **24** (207 mg, 1.37 mmol, 93%) as a mixture of rotamers in a ratio of 1:2 (pale yellow solid): R_f = 0.43 (in CH_2Cl_2); mp 74−76 °C; IR (neat) ν_{max}/cm^{-1} 3193, 3017, 2971, 1596, 1495, 1369, 1219, 1149, 1071, 994, 764, 708; ^{1}H NMR ($CDCl_3$) δ (major) 9.00 (s, br, 1H), 7.66−7.64 (m, 2H), 7.44−7.33 (m, 2H), 7.28−7.24 (m, 1H), 2.71 (s, 3H), (minor) 9.91 (s, br, 1H), 7.44−7.33 (m, 3H), 7.17−7.15 (m, 2H), 2.50 (s, 3H); ^{13}C NMR ($CDCl_3$) δ (major) 200.6, 138.7, 129.7, 127.1, 124.0, 36.1, (minor) 204.6, 138.1, 129.0, 128.0, 125.2, 30.1; HRMS (ESI$^+$) *m*/*z* (M + H)$^+$ calcd for $C_8H_{10}NS$ 152.0528, found 152.0511.

*N-(4-Methoxyphenyl)ethanethioamide (**26**).*[49] Following the general procedure for the synthesis of thioamides, *N*-(4-methoxyphenyl)acetamide (200 mg, 1.18 mmol) was converted into crude **26** by stirring for 2 h at room temperature. Crude **26** was concentrated and purified by column chromatography (20% ethyl acetate in petroleum ether) to give **26** (off-white solid) as a mixture of rotamers in a ratio of 1:1.15 (210 mg, 1.16 mmol, 98%): R_f = 0.53 (3:2 petroleum ether:EtOAc); mp 116−118 °C; IR (neat) ν_{max}/cm^{-1} 3496, 2092, 1640, 574; ^{1}H NMR ($CDCl_3$) δ (major) 8.77 (s, br, 1H), 7.52−7.49 (m, 2H), 6.93−6.90 (m, 2H), 3.83 (s, 3H), 2.72 (s, 3H), (minor) 9.57 (s, br, 1H), 7.11−7.08 (m, 2H), 6.93−6.90 (m, 2H), 3.81 (s, 3H), 2.45 (s, 3H); ^{13}C NMR ($CDCl_3$) δ (major) 200.6, 158.4, 131.1, 126.0, 114.8, 55.7, 35.8, (minor) 205.1, 159.2, 131.7, 126.9, 114.2, 55.6, 29.9; HRMS (ESI$^+$) *m*/*z* (M + H)$^+$ calcd for $C_9H_{12}NOS$ 182.0634, found 182.0629.

*N-(4-Nitrophenyl)ethanethioamide (**28**).*[50] The reaction was set up according to the general procedure for the synthesis of thioamides, with the exception that dry toluene (7 mL) was used as the solvent. The reaction was refluxed for 1 h in order to convert *N*-(4-nitrophenyl)acetamide (200 mg, 1.13 mmol) into crude **28**. Crude **28** was concentrated and purified by column chromatography (40% ethyl acetate in petroleum ether) to give pure **28** as a yellow solid (198 mg, 1.01 mmol, 89%): R_f = 0.41 (3:2 petroleum ether:EtOAc); mp 173−175 °C; IR (neat) ν_{max}/cm^{-1} 3425, 1644, 1511, 1344, 1148, 1102; ^{1}H NMR ($CDCl_3$ + DMSO-d_6 (14%)) δ 11.06 (s, br, 1H), 8.21−8.09 (m, 4H), 2.68 (s, 3H); ^{13}C NMR ($CDCl_3$ + DMSO-d_6 (14%)) δ 201.8, 145.3, 144.4, 124.3, 122.6, 36.4; HRMS (ESI$^+$) *m*/*z* (M + H)$^+$ calcd for $C_8H_9N_2O_2S$ 197.0379, found 197.0380.

General Procedure A: Coupling of Primary and Secondary Thioamides with α-Diazodicarbonyl Compounds. A solution of thioamide (114 μmol) in dry benzene (0.5 mL) was placed in a vial containing the α-diazodicarbonyl compound (1.3 equiv). The well-mixed solution was transferred to a vial containing the ruthenium catalyst **1** or **7** (5 mol %). After it was mixed, the reaction mixture was transferred to a pressure vessel. The vials were washed twice with 0.25 mL of dry benzene by using the above transfer protocol to ensure the complete transfer of materials. The vessel was sealed, and the reaction mixture was heated to 70 or 90 °C in an oil bath for the specified period of time (Table 1). The crude product was purified by column chromatography.

*(S)-5-(Bis(ethoxycarbonyl)methylidene)pyrrolidine-2-carboxylic Acid Ethyl Ester (**10**). With Catalyst **1**.* Following general procedure A, **8** (20.0 mg, 116 μmol) was converted to crude **10** by heating the reaction mixture to 70 °C for 9 h. Column chromatography (CH_2Cl_2, then 10% ethyl acetate in CH_2Cl_2) of the crude **10** gave pure **10** as a viscous yellow liquid (27.6 mg, 92.3 μmol, 80%).

*With Catalyst **7**.* Following general procedure A, **8** (20.0 mg, 116 μmol) was converted to crude **10** by heating the reaction mixture to 90 °C for 4 h. Column chromatography (CH_2Cl_2, then 10% ethyl acetate in petroleum ether) of crude **10** gave pure **10** as a viscous yellow liquid (27.4 mg, 91.5 μmol, 79%). The ^{1}H and ^{13}C NMR chemical shift values and the $[\alpha]_D$ value match the data reported in the literature.[26]

*Diethyl 2-(1-Amino-3-phenylpropylidene)malonate (**15**). With Catalyst **1**.* Following general procedure A, **14** (20.0 mg, 121 μmol) was converted to crude **15** by heating the reaction mixture to 90 °C for 12 h. Column chromatography (CH_2Cl_2, then 5% ethyl acetate in CH_2Cl_2) of crude **15** gave pure **15** as a yellow oil (30.0 mg, 103 μmol, 85%).

*With Catalyst **7**.* Following general procedure A, **14** (20.0 mg, 121 μmol) was converted to crude **15** by heating the reaction mixture to 90 °C for 10 h. Column chromatography (CH_2Cl_2, then 5% ethyl acetate in CH_2Cl_2) of crude **15** gave pure **15** as a yellow oil (29.5 mg, 101 μmol, 84%). The ^{1}H and ^{13}C NMR chemical shift values match the data reported in the literature.[26]

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*(E)-Ethyl 2-Acetyl-3-amino-5-phenylpent-2-enoate (**16**).*[32] *With Catalyst **1**.* Following general procedure A, **14** (15.0 mg, 90.7 μmol) was converted to crude **16** by heating the reaction mixture to 70 °C for 8 h. Column chromatography (10% petroleum ether in CH_2Cl_2) of crude **16** provided pure **16** (19.7 mg, 75.4 μmol, 83%) as a single diastereomer (viscous brown liquid).

*With Catalyst **7**.* Following general procedure A, **14** (15.0 mg, 90.7 μmol) was converted to crude **16** by heating the reaction mixture to 90 °C for 6 h. Column chromatography (10% petroleum ether in CH_2Cl_2) of crude **16** provided pure **16** (20.2 mg, 77.3 μmol, 85%) as a single diastereomer (viscous brown liquid): R_f = 0.54 (CH_2Cl_2); IR (neat) ν_{max}/cm^{-1} 3423, 2925, 1714, 1650, 1532, 1454, 1373, 1312, 1264, 1092; ^1H NMR ($CDCl_3$) δ 11.06 (s, broad, 1H), 7.31−7.17 (m, 5H), 5.37 (s, broad, 1H), 4.27−4.20 (m, 2H), 2.91 (t, J = 7.6 Hz, 2H), 2.75 (t, J = 7.6 Hz, 2H), 2.28 (s, 3H), 1.31 (t, J = 7.2 Hz, 3H); ^{13}C NMR ($CDCl_3$) δ 197.5, 169.7, 169.0, 140.2, 128.8, 128.5, 126.7, 103.4, 60.5, 38.1, 34.8, 30.3, 14.4; HRMS (ESI^+) m/z $(M + H)^+$ calcd for $C_{15}H_{20}NO_3$ 262.1438, found 262.1447.

*2-(1-Amino-3-phenylpropylidene)-5,5-dimethylcyclohexane-1,3-dione (**17**). With Catalyst **1**.* Following general procedure A, **14** (15.0 mg, 90.7 μmol) was converted to crude **17** by heating the reaction mixture to 90 °C for 7 h. Column chromatography (20% ethyl acetate in petroleum ether) of crude **17** provided pure **17** as a pale white solid (18.3 mg, 67.4 μmol, 74%).

*With Catalyst **7**.* Following general procedure A, **14** (15.0 mg, 90.7 μmol) was converted to crude **17** by heating the reaction mixture to 90 °C for 5 h. Column chromatography (20% petroleum ether in CH_2Cl_2) of crude **17** provided pure **17** as a pale white solid (18.6 mg, 68.5 μmol, 76%). The ^1H NMR chemical shift values of compound **17** prepared by catalyst **1** match those for the compound prepared by catalyst **7**: R_f = 0.44 (3:2 petroleum ether:EtOAc); mp 189−191 °C; IR (neat) ν_{max}/cm^{-1} 3357, 3261, 2925, 1574, 1528, 1453, 1302, 1160, 1097; ^1H NMR ($CDCl_3$) δ 7.78−7.76 (m, 1H), 7.27−7.22 (m, 4H), 6.33 (s, broad, 1H), 5.01 (s, broad, 1H), 3.14 (t, J = 7.6 Hz, 2H), 2.89 (t, J = 7.6 Hz, 2H), 2.39 (s, 4H), 1.02 (s, 6H); ^{13}C NMR ($CDCl_3$) δ 200.6, 196.9, 176.2, 140.4, 129.8, 128.7, 128.6, 126.6, 126.5, 107.1, 53.6, 52.6, 39.9, 34.2, 30.1, 28.3, 21.6; HRMS (ESI^+) m/z $(M + H)^+$ calcd for $C_{17}H_{22}NO_2$ 272.1645, found 272.1639.

*(S,E)-Ethyl 5-(1-ethoxy-1,3-dioxobutan-2-ylidene)pyrrolidine-2-carboxylate (**18**).*[31,51] *With Catalyst **1**.* General procedure A was followed in this experiment, with the exception that 1 equiv of **11** was added at the beginning and an additional 1 equiv was added after 8 h of heating to 90 °C. Thioamide **8** (15.0 mg, 86.6 μmol) was converted to crude **18** by heating to 90 °C for 20 h total. Column chromatography (20% ethyl acetate in petroleum ether) of crude **18** provided pure **18** (20.3 mg, 75.4 μmol, 87%) as a yellow viscous liquid.

*With Catalyst **7**.* General procedure A was followed in this experiment, with the exception that 1 equiv of **11** was added at the beginning and an additional 1 equiv was added after 8 h of heating to 90 °C. Thioamide **8** (15.0 mg, 86.6 μmol) was converted to crude **18** by heating to 90 °C for 14 h total. Column chromatography (20% ethyl acetate in petroleum ether) of crude **18** provided pure **18** (19.8 mg, 72.7 μmol, 84%) as a yellow viscous liquid: R_f = 0.31 (4:1 petroleum ether:EtOAc); $[\alpha]_D^{24}$ = −23.6° (c 0.02, $CHCl_3$); IR (neat) ν_{max}/cm^{-1} 3437, 2966, 2909, 1747, 1696, 1603, 1532, 1194, 1055; ^1H NMR ($CDCl_3$) δ 11.91 (s, br 1H), 4.49 (dd, J = 5.6, 9.2 Hz, 1H), 4.27−4.14 (m, 4H), 3.27−3.12 (m, 2H), 2.42 (s, 3H), 2.37−2.29 (m, 1H), 2.20−2.12 (m, 1H), 1.33−1.27 (m, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 198.2, 173.8, 170.8, 168.5, 99.7, 61.9, 61.4, 59.7, 34.3, 31.0, 25.3, 14.4, 14.1; HRMS (ESI^+) m/z $(M + H)^+$ calcd for $C_{13}H_{20}NO_5$ 270.1336, found 270.1327.

*(S)-Ethyl 5-(4,4-Dimethyl-2,6-dioxocyclohexylidene)pyrrolidine-2-carboxylate (**19**). With Catalyst **1**.* General procedure A was followed in this experiment, with the exception that 1 equiv of **12** was added at the beginning and an additional 1 equiv was added after 10 h of heating to 90 °C. Thioamide **8** (15.0 mg, 86.5 μmol) was converted to crude **19** by heating to 90 °C for 22 h total. Column chromatography (20% ethyl acetate in petroleum ether) of crude **19** provided pure **19** as a white solid (22.6 mg, 80.9 μmol, 93%).

*With Catalyst **7**.* General procedure A was followed in this experiment, with the exception that 1 equiv of **12** was added at the beginning and an additional 1 equiv was added after 8 h of heating to 90 °C. Thioamide **8** (15.0 mg, 86.5 μmol) was converted to crude **19** by heating to 90 °C for 16 h total. Column chromatography (20% ethyl acetate in petroleum ether) of crude **19** provided pure **19** as a white solid (21.4 mg, 76.6 μmol, 89%). The ^1H NMR chemical shift values of compound **19** prepared by catalyst **1** match those for the compound prepared by catalyst **7**: R_f = 0.21 (4:1 petroleum ether:EtOAc); mp 197−198 °C; $[\alpha]_D^{24}$ = −37.2° (c 0.03, $CHCl_3$); IR (neat) ν_{max}/cm^{-1} 3211, 2957, 1742, 1649, 1588, 1545, 1444, 1202, 1037; ^1H NMR ($CDCl_3$) δ 12.01 (s, br, 1H), 4.52 (dd, J = 6.0, 9.6 Hz, 1H), 4.23 (q, J = 7.2 Hz, 2H), 3.50−3.33 (m, 2H), 2.45−2.36 (m, 1H), 2.40 (s, 2H), 2.33 (s, 2H), 2.24−2.15 (m, 1H), 1.29 (t, J = 7.2 Hz, 3H), 1.04 (s, 3H), 1.02 (s, 3H); ^{13}C NMR ($CDCl_3$) δ 199.1, 196.6, 176.0, 170.5, 106.0, 62.2, 61.4, 52.7, 51.9, 34.8, 30.6, 28.7, 28.4, 25.2, 14.2; HRMS (ESI^+) m/z $(M + H)^+$ calcd for $C_{15}H_{22}NO_4$ 280.1543, found 280.1535.

*Diethyl 2-(Pyrrolidin-2-ylidene)malonate (**21**). With Catalyst **1**.* Following general procedure A, **20** (15.0 mg, 148 μmol) was converted to crude **21** by heating to 70 °C for 22 h. Column chromatography (25% ethyl acetate in petroleum ether) of crude **21** gave pure **21** as a yellow viscous liquid (28.9 mg, 127 μmol, 86%).

*With Catalyst **7**.* Following general procedure A, **20** (15.0 mg, 148 μmol) was converted to crude **21** by heating to 90 °C for 6 h. Column chromatography (25% ethyl acetate in petroleum ether) of crude **21** gave pure **21** a yellow viscous liquid (29.3 mg, 129 μmol, 87%). The ^1H and ^{13}C NMR chemical shift values match the data reported in the literature.[26]

*(E)-Ethyl 3-Oxo-2-(pyrrolidin-2-ylidene)butanoate (**22**)..*[30,33] *With Catalyst **1**.* Following general procedure A, **20** (20.0 mg, 198 μmol) was converted to crude **22** by heating to 70 °C for 22 h. Column chromatography (40% ethyl acetate in petroleum ether) of the crude **22** gave pure **22** (30.3 mg, 154 μmol, 78%) as a brown solid.

*With Catalyst **7**.* Following general procedure A, **20** (20.0 mg, 198 μmol) was converted to crude **22** by heating to 90 °C for 5 h. Column chromatography (40% ethyl acetate in petroleum ether) of crude **22** gave pure **22** (27.8 mg, 141 μmol, 71%) as a brown solid. The ^1H and ^{13}C NMR chemical shift values match the data reported in the literature.[33]

*5,5-Dimethyl-2-(pyrrolidin-2-ylidene)cyclohexane-1,3-dione (**23**). With Catalyst **1**.* General procedure A was followed in this experiment, with the exception that 0.5 equiv of **12** was added after 8 h of heating to 90 °C. Thioamide **20** (15.0 mg, 148 μmol) was converted to crude **23** by heating to 90 °C for 12 h. Column chromatography (20% ethyl acetate in petroleum ether) of crude **23** gave pure **23** (27.2 mg, 131 μmol, 89%) as a white solid.

*With Catalyst **7**.* General procedure A was followed in this experiment, with the exception that 0.5 equiv of **12** was added after 8 h of heating to 90 °C. Thioamide **20** (20.0 mg, 198 μmol) was converted to crude **23** by heating to 90 °C for 12 h. Column chromatography (20% ethyl acetate in petroleum ether) of crude **23** gave pure **23** (35.3 mg, 170.3 μmol, 86%) as a white solid. The ^1H and ^{13}C NMR chemical shift values match the data reported in the literature.[26]

*Diethyl 2-(1-(Phenylamino)ethylidene)malonate (**25**).*[52] *With Catalyst **1**.* Following general procedure A, **24** (15.0 mg, 86.5 μmol) was converted to crude **25** by heating to 90 °C for 6 h. Column chromatography (10% ethyl acetate in petroleum ether) of crude **25** gave **25** (24.5 mg, 88.3 μmol, 89%) as a mixture of rotamers in a ratio of 1:2.9 (yellow viscous liquid).

*With Catalyst **7**.* Following general procedure A, **24** (15.0 mg, 86.5 μmol) was converted to crude **25** by heating to 90 °C for 4 h. Column chromatography (10% ethyl acetate in petroleum ether) of crude **25** gave **25** (25.2 mg, 90.8 μmol, 92%) as a mixture of rotamers in a ratio of 1:2.9 (yellow viscous liquid): R_f = 0.47 (3:2 petroleum ether:EtOAc); IR (neat) ν_{max}/cm^{-1} 3350, 2981, 2925, 1714, 1651, 1593, 1501, 1434, 1367, 1244, 1072, 1023, 797, 743, 698; ^1H NMR ($CDCl_3$) δ 11.24 (s, br, 1H), 7.26−7.23 (m, 2H), 7.38−7.34 (m, 1H), 7.10−7.08 (m, 2H), 4.26−4.19 (m, 4H), 3.36 (s, 3H (minor)), 2.08 (s,

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3H), 1.33−1.26 (m, 6H); ^{13}C NMR ($CDCl_3$) δ 168.9, 166.8, 161.7, 138.2, 129.4, 126.5, 126.0, 113.7 (minor), 94.7, 61.7 (minor), 60.8, 60.7 (minor), 59.9, 18.0, 14.5, 14.3; HRMS (ESI$^+$) m/z (M + H)$^+$ calcd for $C_{15}H_{20}NO_4$ 278.1387, found 278.1381.

*Diethyl 2-(1-((4-Methoxyphenyl)amino)ethylidene)malonate (**27**). With Catalyst **1**.* Following general procedure A, **26** (15.0 mg, 82.7 μmol) was converted to crude **27** by heating to 90 °C for 4 h. Column chromatography (20% ethyl acetate in petroleum ether) of crude **27** gave pure **27** as a yellow liquid (21.1 mg, 68.6 μmol, 83%).

*With Catalyst **7**.* Following general procedure A, **26** (15.0 mg, 82.7 μmol) was converted to crude **27** by heating to 90 °C for 3 h. Column chromatography (20% ethyl acetate in petroleum ether) of crude **27** gave pure **27** as a yellow liquid (20.6 mg, 67.0 μmol, 81%) as a mixture of rotamers. The ^{1}H NMR chemical shift values of compound **27** prepared by catalyst **1** match those for the compound prepared by catalyst **7**: R_f = 0.64 (3:2 petroleum ether:EtOAc); IR (neat) ν_{max}/cm^{-1} 2981, 1712, 1651, 1578, 1594, 1514, 1443, 1245, 1074, 1033; ^{1}H NMR ($CDCl_3$) δ 11.08 (s, broad, 1H), 7.02 (d, J = 9.0 Hz, 2H), 6.77 (d, J = 9.0 Hz, 2H), 4.26−4.18 (m, 4H), 3.80 (s, 3H), 2.01 (s, 3H), 1.31−1.28 (m, 6H); ^{13}C NMR ($CDCl_3$) δ 168.96, 168.93, 162.6, 158.3, 131.0, 127.6, 114.5, 93.9, 62.7 (minor), 61.7 (minor), 60.7, 59.8, 55.6, 17.9, 14.49, 14.46 (minor), 14.3, 13.9 (minor); HRMS (ESI$^+$) m/z (M + H)$^+$ calcd for $C_{16}H_{22}NO_5$ 308.1493, found 308.1492.

*Diethyl 2-(1-((4-Nitrophenyl)amino)ethylidene)malonate (**29**). With Catalyst **1**.* Following general procedure A, **28** (15.0 mg, 76.4 μmol) was converted to crude **29** by heating to 90 °C for 18 h. Column chromatography (20% ethyl acetate in petroleum ether) of crude **29** gave **29** (19.2 mg, 59.6 μmol, 78%) as a mixture of rotamers in a ratio of 1:1.2 (brown liquid).

*With Catalyst **7**.* Following general procedure A, **28** (15.0 mg, 76.4 μmol) was converted to crude **29** by heating to 90 °C for 16 h. Column chromatography (20% ethyl acetate in petroleum ether) of crude **29** gave **29** (19.9 mg, 61.7 μmol, 81%) as a mixture of rotamers in a ratio of 1:2 (brown liquid). The ^{1}H NMR chemical shift values of compound **29** prepared by catalyst **1** match those for the compound prepared by catalyst **7**: R_f = 0.53 (3:2 petroleum ether:EtOAc); IR (neat) ν_{max}/cm^{-1} 3383, 2984, 2925, 2848, 1738, 1600, 1506, 1478, 1371, 1323, 1230, 1159, 1112, 1021, 838, 753; ^{1}H NMR ($CDCl_3$) δ 11.45 (s, broad, 1H), 8.23−8.18 (m, 2H), 7.19−7.15 (m, 2H), 4.30−4.23 (m, 4H), 2.22 (s, 3H), 2.20 (s, 3H, minor), 1.34−1.27 (m, 6H); ^{13}C NMR ($CDCl_3$) δ 168.4, 167.7, 158.0, 144.5, 125.1, 123.4, 99.2, 62.5 (minor), 61.0, 60.4, 18.1, 14.2, 14.1, 13.8 (minor); HRMS (ESI$^+$) m/z (M + H)$^+$ calcd for $C_{15}H_{19}N_2O_6$ 323.1238, found 323.1237.

General Procedure B: Coupling of 30 with α-Diazodicarbonyl Compounds. A solution of **30** (114 μmol) in dry benzene (0.1 mL) was placed in a vial containing the α-diazocarbonyl compound (1 equiv). The well-mixed solution was transferred to a vial containing the ruthenium catalyst **1** or **7** (10 mol %). The contents were mixed, and the reaction mixture was transferred to a pressure vessel. The vials were washed twice with 0.25 mL of dry benzene by using the above transfer protocol to ensure the complete transfer of materials. The vessel was sealed, and the reaction mixture was heated to 90 °C in an oil bath. After 8 h at a given temperature another 1 equiv of the α-diazocarbonyl compound was dissolved in 0.2 mL of dry benzene and added to the pressure vessel. The vial containing the α-diazocarbonyl compound was washed twice with 0.1 mL of dry benzene, and the contents were transferred to the pressure vessel. Heating was continued for the specified period of time (eqs 2 and 3). The crude product was purified by column chromatography.

*Diethyl 2-(1-Benzylpyrrolidin-2-ylidene)malonate (**31**). With Catalyst **1**.* Following general procedure B, **30** (15.0 mg, 78.4 μmol) was converted to crude **31** by heating to 90 °C for 26 h. Column chromatography (20% then 30% ethyl acetate in petroleum ether) of crude **31** provided pure **31** as a yellow viscous liquid (22.3 mg, 70.3 μmol, 90%).

*With Catalyst **7**.* Following general procedure B, **30** (15.0 mg, 78.4 μmol) was converted to crude **31** by heating to 90 °C for 26 h. Column chromatography (20% then 30% ethyl acetate in petroleum ether) of crude **31** provided pure **31** as a yellow viscous liquid (21.4 mg, 67.4 μmol, 86%). The ^{1}H and ^{13}C NMR chemical shift values match the data reported in the literature.[32]

*Ethyl 2-(1-Benzylpyrrolidin-2-ylidene)-3-oxobutanoate (**33**). With Catalyst **1**.* Following general procedure B, with the exception that 5 mol % of the catalyst was used, **30** (15.0 mg, 78.4 μmol) was converted to crude **33** by heating to 90 °C for 24 h. Column chromatography (40% ethyl acetate in petroleum ether) of crude **33** provided **33** as an inseparable mixture of diastereomers (yellow viscous liquid) (17.6 mg, 61.2 μmol, 78%, E:Z = 3:1).

*With Catalyst **7**.* Following general procedure B, with the exception that 5 mol % of the catalyst was used, **30** (15.0 mg, 78.4 μmol) was converted to crude **33** by heating to 90 °C for 22 h. Column chromatography (40% ethyl acetate in petroleum ether) of crude **33** provided **33** as an inseparable mixture of diastereomers (yellow viscous liquid) (18.2 mg, 63.3 μmol, 81%, E:Z = 3:1). The ^{1}H NMR chemical shift values of compound **33** prepared by catalyst **1** match those for the compound prepared by catalyst **7**: R_f = 0.36 (petroleum ether:EtOAc 4:1); IR (neat) ν_{max}/cm^{-1} 2924, 2852, 1736, 1595, 1454, 1379, 1136, 1081; ^{1}H NMR ($CDCl_3$) δ 7.34−7.24 (m, 4H), 7.11−7.07 (m, 1H), 4.93 (s, broad, 2H, major), 4.67 (s, broad, 2H, minor), 4.13−4.07 (m, 2H), 3.46−3.40 (m, 4H major and 2H minor), 2.86−2.82 (m, 2H, minor), 2.31 (s, 3H, minor), 2.02−1.95 (m, 2H), 2.00 (s, 3H, major), 1.25−1.20 (m, 3H); ^{13}C NMR ($CDCl_3$) δ 197.6 (minor), 196.3, 169.5, 168.6, 137.0, 136.4 (minor), 128.8, 128.6 (minor), 127.8 (minor), 127.4, 126.7, 105.2, 60.1, 55.8, 55.3 (minor), 53.3, 37.7, 37.4 (minor), 29.8 (minor), 28.7, 21.2, 20.3 (minor), 14.6, 14.24 (minor); HRMS (ESI$^+$) m/z (M + H)$^+$ calcd for $C_{17}H_{22}NO_3$ 288.1594, found 288.1570.

General Procedure C: Coupling of Thioamides with 13. A solution of thioamide (114 μmol) in dry benzene (0.5 mL) was placed in a vial containing **13** (1.3 equiv). The well-mixed solution was transferred to a vial containing the ruthenium catalyst **1** or **7** (5 mol %). After it was mixed, the reaction mixture was transferred to a pressure vessel and 4.3 equiv of triphenylphosphine was added. The vials were washed twice with 0.25 mL of dry benzene by using the above transfer protocol to ensure the complete transfer of materials. The vessel was sealed, and the reaction mixture was heated to 70 or 90 °C in an oil bath for the specified period of time. The crude product was purified by column chromatography.

*(S)-Ethyl 5-((2-Oxo-2-phenylethyl)thio)-3,4-dihydro-2H-pyrrole-2-carboxylate (**34**). With Catalyst **1**.* Following general procedure C, with the exception that no PPh_3 was added, **8** (15 mg, 86.6 μmol) was converted to crude **34** by stirring at room temperature for 45 min. Column chromatography (25% ethyl acetate in petroleum ether) of crude **34** gave pure **34** as a yellow viscous liquid (21.2 mg, 72.8 μmol, 84%). The ^{1}H and ^{13}C NMR chemical shift values match the data reported in the literature.[32] $[\alpha]_D^{25}$ = −19.3° (c 0.015, $CHCl_3$).

*(S,Z)-Ethyl 5-(2-Oxo-2-phenylethylidene)pyrrolidine-2-carboxylate (**35**). With Catalyst **1**.* Following general procedure C, **8** (20 mg, 115.4 μmol) was converted to crude **35** by heating to 70 °C for 20 h. Column chromatography (25% ethyl acetate in petroleum ether) of crude **35** gave pure **35** (24.9 mg, 96.0 μmol, 83%) as a yellow viscous liquid.

*With Catalyst **7**.* Following general procedure C, **8** (15 mg, 86.5 μmol) was converted to crude **35** by heating to 70 °C for 20 h. Column chromatography (25% ethyl acetate in petroleum ether) of crude **35** gave pure **35** (19.5 mg, 75.2 μmol, 87%) as a yellow viscous liquid. The stereochemistry of **35** was determined by the NOE measurements. The ^{1}H and ^{13}C NMR chemical shift values match the data reported in literature.[37] $[\alpha]_D^{23}$ = −18.4° (c 0.01, $CHCl_3$).

*2-Phenethyl-4-phenyl-4,5-dihydrothiazol-4-ol (**37**). With Catalyst **1**.* Following general procedure C, **14** (15 mg, 90.7 μmol) was converted to crude **37** by heating to 90 °C for 15 h. Column chromatography (25% ethyl acetate in petroleum ether) of crude **37** gave pure **37** as a brown viscous liquid (24.2 mg, 85.4 μmol, 94%).

*With Catalyst **7**.* Following general procedure C, **14** (15 mg, 90.7 μmol) was converted to crude **37** by heating to 90 °C for 11 h. Column chromatography (25% ethyl acetate in petroleum ether) of crude **37** gave pure **37** as a brown viscous liquid (22.4 mg, 79.0 μmol, 87%). The ^{1}H NMR chemical shift values of compound **37** prepared

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by catalyst **1** match those for the compound prepared by catalyst **7**: R_f = 0.23 (4:1 petroleum ether:EtOAc); IR (neat) ν_{max}/cm^{-1} 3349, 2920, 2850, 1675, 1604, 1496, 1448, 746; ^1H NMR ($CDCl_3$) δ 7.34−7.25 (m, 10H), 4.38 (s, br, 1H), 3.62 (d, J = 12.0 Hz, 1H), 3.38 (d, J = 12.0 Hz, 1H), 3.07−2.97 (m, 2H), 2.93−2.80 (m, 2H); ^{13}C NMR ($CDCl_3$) δ 175.3, 144.6, 140.2, 128.7, 128.6, 128.4, 128.1, 126.5, 125.0, 107.8, 46.7, 36.0, 33.7; HRMS (ESI^+) m/z $(M + H)^+$ calcd for $C_{17}H_{18}NOS$ 284.1103, found 284.1075.

*(Z)-1-Phenyl-2-(pyrrolidin-2-ylidene)ethanone (**38**). With Catalyst **1**.* Following general procedure C, **20** (15 mg, 148 μmol) was converted to crude **38** by heating to 70 °C for 1.5 h. Column chromatography (20% ethyl acetate in petroleum ether) of crude **38** gave pure **38** (23.2 mg, 124 μmol, 84%) as a white solid.

*With Catalyst **7**.* Following general procedure C, **20** (15 mg, 148 μmol) was converted to crude **38** by heating to 70 °C for 1.5 h. Column chromatography (20% ethyl acetate in petroleum ether) of crude **38** gave pure **38** (22.6 mg, 121 μmol, 82%) as a white solid. The ^1H and ^{13}C NMR chemical shift values match the data reported in the literature.[38,39]

*(E)-2-(1-Benzylpyrrolidin-2-ylidene)-1-phenylethanone (**39**).*[41] *With Catalyst **1**.* General procedure C was followed in this experiment, with the exception that **13** (5.00 mg, 34.0 μmol every 1 h, total 25.0 mg, 171 μmol) was added gradually. Thioamide **30** (15.0 mg, 78.4 μmol) was converted to crude **39** by heating to 70 °C for 6 h. Column chromatography (25% ethyl acetate in petroleum ether) of crude **39** gave pure **39** (20.6 mg, 74.2 μmol, 95%) as a brown liquid.

*With Catalyst **7**.* General procedure C was followed in this experiment, with the exception that **13** (0.44 μmol every 1 h, total 25.0 mg, 171 μmol) was added gradually. Thioamide **30** (15 mg, 78.4 μmol) was converted to crude **39** by heating to 70 °C for 7 h. Column chromatography (25% ethyl acetate in petroleum ether) of crude **39** gave pure **39** (19.8 mg, 71.3 μmol, 91%) as a brown liquid: R_f = 0.29 (petroleum ether:EtOAc 3:2); IR (neat) ν_{max}/cm^{-1} 3059, 2923, 2854, 1725, 1624, 1577, 1540, 1479, 1453, 1299, 1065, 701; ^1H NMR ($CDCl_3$) δ 7.83−7.80 (m, 2H), 7.40−7.31 (m, 5H), 7.25−7.23 (m, 3H), 5.90 (s, 1H), 4.53 (s, 2H), 3.51−3.43 (m, 4H), 2.06 (p, J = 7.6 Hz, 2H); ^{13}C NMR ($CDCl_3$) δ 188.2, 167.7, 142.1, 135.7, 130.5, 129.6, 128.1, 127.9, 127.4, 127.3, 87.0, 52.8, 50.5, 34.0, 21.1; HRMS (ESI^+) m/z $(M + H)^+$ calcd for $C_{19}H_{20}NO$ 278.1539, found 278.1510.

General Procedure D: Dimerization of α-Diazocarbonyl Compounds. A solution of the α-diazocarbonyl compound (107 μmol) in dry benzene (0.5 mL) was added to a vial containing the ruthenium catalyst **1** or **7** (5 mol %). The contents were mixed, and the reaction mixture was transferred to a pressure vessel. The vials were washed twice with 0.25 mL of dry benzene by using the above transfer protocol to ensure the complete transfer of materials. The vessel was sealed, and the reaction mixture was stirred at a specified temperature and time in order to get the crude product. The crude alkene was purified by column chromatography.

*Tetraethyl Ethene-1,1,2,2-tetracarboxylate (**32**).*[53] *With Catalyst **1**.* Following general procedure D, **9** (20.0 mg, 107 μmol) was converted to crude **32** by heating to 90 °C for 24 h. Column chromatography (CH_2Cl_2) of crude **32** provided pure **32** as a yellow liquid (25.8 mg, 81.6 μmol, 76%).

*With Catalyst **7**.* Following general procedure D, **9** (20.0 mg, 107 μmol) was converted to **32** by heating to 90 °C for 20 h. Column chromatography (CH_2Cl_2) of crude **32** provided pure **32** as a yellow liquid (26.9 mg, 85.0 μmol, 79%): R_f = 0.26 (CH_2Cl_2: petroleum ether 3:1); IR (neat) ν_{max}/cm^{-1} 2923, 2853, 1736, 1650, 1465, 1370, 1245, 1096, 1043, 860, 792, 720; ^1H NMR ($CDCl_3$) δ: 4.32 (q, J = 7.0 Hz, 8H), 1.31 (t, J = 7.0 Hz, 12H); ^{13}C NMR ($CDCl_3$) δ 162.5, 135.5, 62.7, 14.0; HRMS (ESI^+) m/z $(M + H)^+$ calcd for $C_{14}H_{21}O_8$ 317.1231, found 317.1226.

*1,4-Diphenylbut-2-ene-1,4-dione (**40**).*[40] *With Catalyst **1**.* Following general procedure D, **25** (15.0 mg, 103 μmol) was converted to crude **40** by stirring at room temperature for 40 min. Column chromatography (20% ethyl acetate in petroleum ether) of the crude provided pure **40** (18.0 mg, 76.2 μmol, 74%, yellow solid) as a single Z diastereomer.

*With Catalyst **7**.* Following general procedure D, **25** (20.0 mg, 137 μmol) was converted to crude **40** by stirring at room temperature for 40 min. Column chromatography (20% ethyl acetate in petroleum ether) of the crude gave (*Z*)-**40** (16.7 mg, 70.7 μmol, 52%, yellow solid) and (*E*)-**40** (8.2 mg, 34.7 μmol, 25%, yellow solid).

(2*Z*)-1,4-diphenylbut-2-ene-1,4-dione: R_f = 0.35 (petroleum ether:-EtOAc 4:1); mp 138−140 °C; IR (neat) ν_{max}/cm^{-1} 2921, 2843, 1664, 1597, 1448, 1395, 1230, 1005, 709; ^1H NMR ($CDCl_3$) δ 7.95−7.94 (m, 2H), 7.93−7.92 (m, 2H), 7.58−7.54 (m, 2H), 7.47−7.43 (m, 4H), 7.16 (s, 2H); ^{13}C NMR ($CDCl_3$) δ 192.5, 136.2, 135.7, 133.7, 128.9, 128.8 ; HRMS (ESI^+) m/z $(M + H)^+$ calcd for $C_{16}H_{13}O_2$ 237.0910, found 237.0913.

(2*E*)-1,4-diphenylbut-2-ene-1,4-dione: R_f = 0.39 (petroleum ether:-EtOAc 4:1); mp 104−106 °C; IR (neat) ν_{max}/cm^{-1} 2924, 2853, 1665, 1596, 1449, 1378, 1230, 1005, 687; ^1H NMR ($CDCl_3$) δ 8.09−8.08 (m, 2H), 8.064−8.056 (m, 2H), 8.02 (s, 2H), 7.66−7.62 (m, 2H), 7.56−7.52 (m, 4H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 189.9, 136.9, 135.1, 133.9, 128.9; HRMS (ESI^+) m/z $(M + H)^+$ calcd for $C_{16}H_{13}O_2$ 237.0910, found 237.0890.

■ ASSOCIATED CONTENT

Supporting Information

Figures giving ^1H and ^{13}C NMR spectra of all compounds described in the Experimental Section, ^1H NMR spectra for enaminones prepared by catalysts **1** and **7**, 1D NOESY (DPFGSE NOE) spectra of compounds **35**, **38**, and **39** and the 2D NOESY spectrum of **39**. This material is available free of charge via the Internet at http://pubs.acs.org.

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Notes

The authors declare no competing financial interest.

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