# Chromium-Catalyzed Intramolecular Enyne Metathesis

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Intramolecular enyne metathesis is realized using a catalytic amount of Fischer chromium carbene complex. The reactions of the enynes **12**, which possess the same substituents on the alkene as those on the carbene carbon, with 10 mol % Fischer chromium carbene complexes **13** in MeOH proceeded smoothly to give the metathesis products in good to moderate yields.

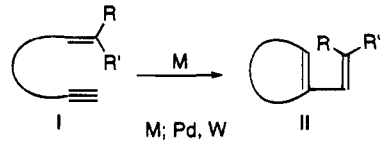
Intramolecular enyne metathesis is quite interesting because the reaction involves formal [2 + 2] cycloaddition followed by ring opening of the resultant cyclobutane. As a result, one alkylidene group of the alkene migrates to the alkyne carbon. This process involves bond fission between alkene carbons and bond formation between the alkene carbon and the alkyne carbon (Scheme 1).

Until recently, two types of intramolecular enyne metathesis using transition metals have been known. One of them is the palladium-catalyzed [2 + 2] cycloaddition of the enyne reported by Trost,[1] and the other is the metal-catalyzed rearrangement of alkene–alkyne using the tungsten carbene complex reported by Katz.[2] In the former case, the reaction of enyne **1** with palladium catalyst (TCPC) in the presence of DMAD gave cyclized product **4** and **5** in good yield. In this case, highly strained cyclobutene **3** was formed from the five-membered metalacycles **2** by reductive elimination. Thus, the reaction seems like the formal [2 + 2] cycloaddition. On the other hand, in the latter case, the alkylidene carbene complex plays an important role and the reaction of alkyne of enyne with carbene complex gives metalacyclobutane **7**. This process was successfully demonstrated by Katz using a molecule with restricted bond rotations and a catalytic amount of the tungsten carbene complex **9** as an initiator. As a result, the (alkylidene)tungsten carbene complex **10**, which is not stabilized by a heteroatom, is formed and it acts as a real catalyst. On the other hand, ruthenium-catalyzed enyne metathesis was recently reported by three groups[3] (Scheme 2).

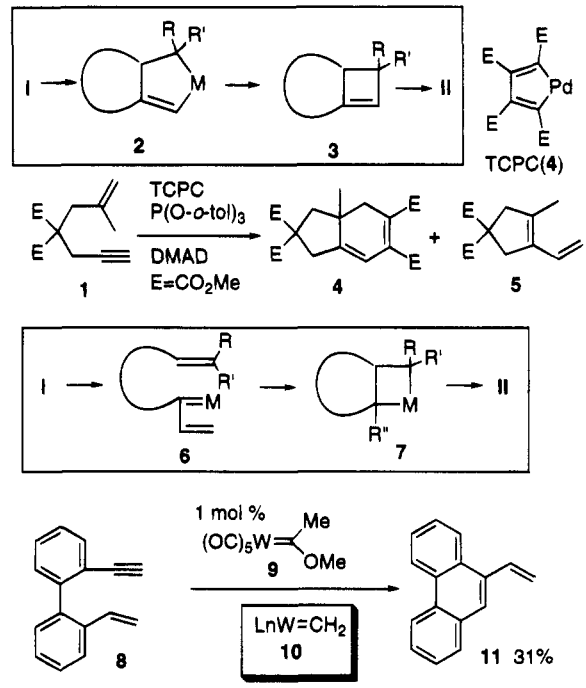
In a previous paper,[4] we reported enyne metathesis using a chromium carbene complex[5] and clarified the reaction course by substituent effects on the alkene. In this reaction, the important intermediate is chromacyclobutane **14** generated from enyne **12** and a chromium carbene complex. If the electron-withdrawing groups are attached on the alkene of enyne **12**, three-membered ring formation is accelerated. And if the electron-donating groups are attached on the alkene, the metathesis reaction is accelerated because the (alkylidene)-chromium carbene complex **15** generated from **14** is stabilized by the substituents, $R^1$ and $R^2$. In the metathesis reaction, if the substituents of the generated carbene **15**, $R^1$ and $R^2$, are R and OEt, initial chromium carbene complex **13** would be regenerated. It means that chromium-catalyzed enyne metathesis would be realized.

In order to make the metathesis reaction proceed using a catalytic amount of the Fischer chromium carbene complex, the same substituents on the alkene

**Scheme 1. Enyne Metathesis**




**Scheme 2**




[⊗] Abstract published in *Advance ACS Abstracts,* September 15, 1995.

(1) (a) Trost, B. M.; Yanai, M.; Hoogsteen, K. *J. Am. Chem. Soc.* **1993**, *115*, 5294. (b) Trost, B. M.; Hashmi, S. K., *Angew. Chem., Int. Ed. Engl.* **1993**, *32*, 1085. (c) For a review, see: Trost, B. M. *Acc. Chem. Res.* **1990**, *23*, 34. Trost, B. M.; Matsubara, S.; Caringi, J. J. *J. Am. Chem. Soc.* **1989**, *111*, 8745. Trost, B. M.; Chan, C.; Ruhter, G. *J. Am. Chem. Soc.* **1987**, *109*, 3486.

(2) (a) Katz, T. J.; Sivavec, T. M. *J. Am. Chem. Soc.* **1985**, *107*, 737. (b) Sivavec, T. M.; Katz, T. J. *Organometallics* **1989**, *8*, 1620.

(3) (a) Chatani, N.; Morimoto, T.; Muto, T.; Murai, S. *J. Am. Chem. Soc.* **1994**, *116*, 6049. (b) Kim, S.-H.; Bowden, N.; Grubbs, R. H. *J. Am. Chem. Soc.* **1994**, *116*, 10801. (c) Kinoshita, A.; Mori, M. *Synlett* **1994**, 1020.

(4) (a) Mori, M.; Watanuki, S. *J. Chem. Soc., Chem. Comm.* **1992**, 1082. (b) Watanuki, S.; Mori, M. *Heterocycles* **1993**, *35*, 679. (c) Preliminary report for this work: Watanuki, S.; Ochifuji, N.; Mori, M. *Organometallics* **1994**, *13*, 4129.

(5) Hoye reported the metathesis reactions by a chromium carbene complex: Hoye, T. R.; Suriano, J. A. *Organometallics* **1992**, *11*, 2044.

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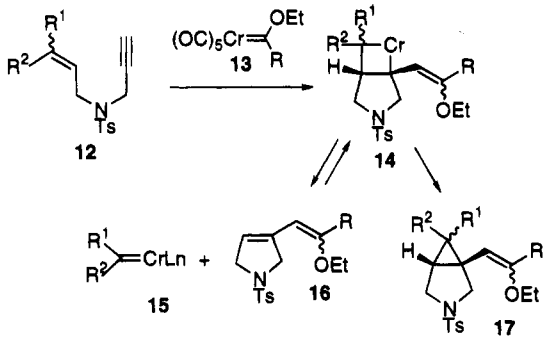
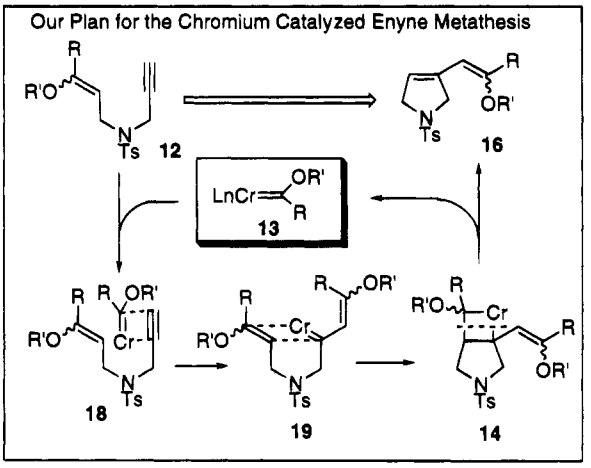
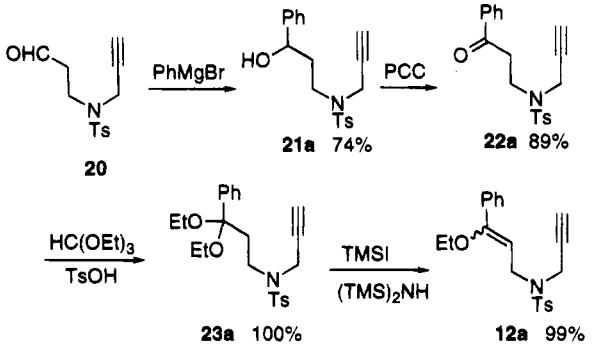
**Scheme 3**




**Scheme 4. Preparation of the Substrate**



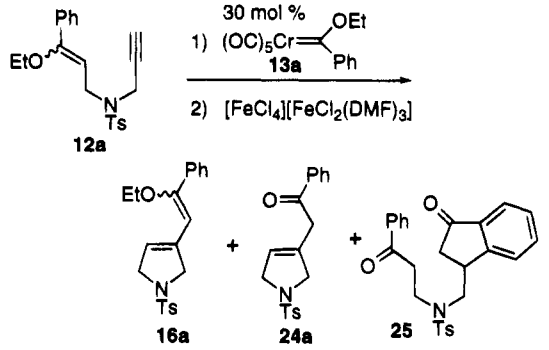

and on the carbene carbon are required. Our plan for the chromium-catalyzed intramolecular enyne metathesis reaction is shown in Scheme 3. If enyne **12** is treated with chromium carbene complex **13**, the chromacyclobutane **14** is produced *via* **18** and **19**. From **14**, initial chromium carbene complex **13** would be regenerated.

**Reaction of Enyne 12a with Fischer Chromium Carbene Complex 13a.** We chose compound **12a** as the starting enyne because the electron-donating group on the alkene would accelerate the metathesis reaction. The starting enyne **12a** was prepared from the aldehyde **20**. Treatment of the aldehyde **20** with PhMgBr followed by PCC oxidation afforded **22a** in high yield. Acetalization with ethyl orthoformate followed by treatment with TMSI in the presence of $(TMS)_2NH$[8] gave enol ether **12a** in quantitative yield (Scheme 4).

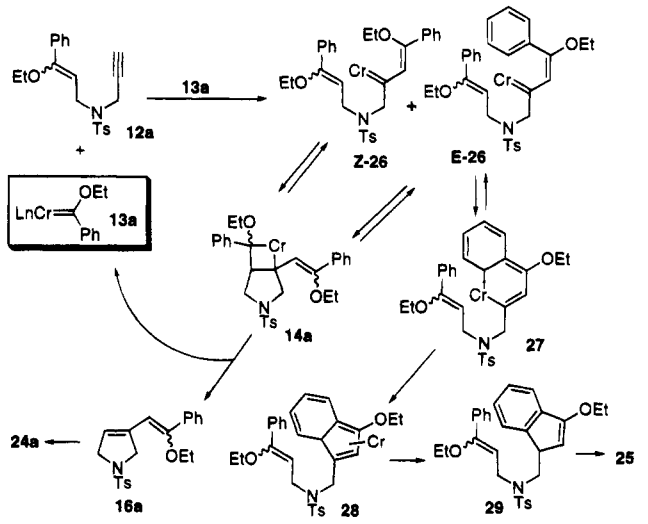
When a $CH_3CN$ solution of enyne **12a** and chromium carbene complex **13a** (30 mol %) was refluxed for 18.5 h followed by treatment with $[FeCl_4][Fe(DMF)_3Cl_2]$,[6] the

(6) Tobinaga, S.; Kotani, E. *J. Am. Chem. Soc.* **1972**, *94*, 309.

**Scheme 5. Reaction of 12a with 13a (30 mol %)**




**Scheme 6. Reaction Course for Enyne Metathesis**




expected metathesis products, **16a** and **24a**, were obtained in 30% yields, along with the indanone **25** in 7% yield. The structures of these compounds were determined by the spectral data. The metathesis products **16a** and **24a** would be formed from ***Z*-26** and ***E*-26**. However, formation of indanone **25** would be derived from the carbene complex ***E*-26** generated from **12a** and **13a** as shown in Scheme 6. It is curious that the only benzannulation product was indanone **25** and not the naphthol. Presumably, the electron-rich enol ether functionality coordinates to chromium as a ligand and this would be expected to retard CO insertion. The chromium-catalyzed enyne metathesis is intercepted by formation of indanone **25** because a stoichiometric amount of the chromium carbene complex is consumed to produce the indanone **25**.[7] The reaction was carried out under various conditions (Table 1). Though the yields of metathesis products **16a** and **24a** using 30 mol % **13a** went up to 30% yield when EtOH, $CH_3CN$, and THF were used as the solvents (runs 1–3), it is not clear whether the catalytic cycle is established or not. Various solvents can be used for this reaction, but the formation of **25** could not be suppressed in each case.

In order to confirm the regeneration of carbene complex **13a**, the reaction of enyne **12a** with the other carbene complex **13b** was tried. When a THF solution of **12a** and chromium carbene complex **13b** (30 mol %) was refluxed for 24 h followed by treatment with $[FeCl_4][Fe(DMF)_3Cl_2]$, the pyrrolidine derivatives **16a**

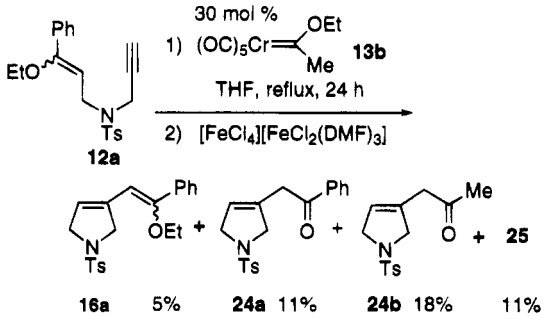
(7) Yamashita, A. *Tetrahedron Lett.* **1986**, *27*, 5915.
(8) Miller, R. D.; McKean, D. R. *Tetrahedron Lett.* **1982**, *23*, 323.

**Table 1. Reaction of Enyne 12a with a Catalytic Amount of 13a[a]**

| run | conditions | yield, % 16a + 24a | 16a | 24a | 25 |
|---|---|---|---|---|---|
| 1 | $CH_3CN$, 70 °C, 18.5 h | 30 | 16 | 14 | 7 |
| 2 | THF, reflux, 17 h | 31 | 9 | 22 | 22 |
| 3 | EtOH, 70 °C, 24 h | 35 | 14 | 21 | 21 |
| 4 | $CH_2Cl_2$, reflux, 24 h | 27 | | 27 | 22 |
| 5 | PhH, 70 °C, 12.5 h | 24 | 5 | 19 | 18 |
| 6 | PhMe, 70 °C, 24 h | 17 | | 17 | 27 |
| 7 | DMF, 70 °C, 24 h | 23 | 23 | | |
| 8 | i-PrOH, 70 °C, 24 h | 25 | 12 | 13 | 20 |
| 9 | acetone, 70 °C, 30 h | 16 | 3 | 13 | 12 |
| 10 | THF, reflux, 24 h[b,c] | 20 | | 20 | 20 |

[a] All reactions were carried out using 30 mol % of **13a**. [b] Additive: $PPh_3$ (39 mol %). [c] **22a** was recovered (30%).

**Scheme 7. Reaction of Enyne 12a with 13b**




and **24a,b** were obtained in 5%, 11%, and 18% yields, respectively, along with **25** in 11% yield. Though metathesis product **24b** was derived by the reaction of **12a** with chromium carbene complex **13b**, compounds **16a** and **24a** were formed by the reaction of **12a** with **13a**. These results indicate that the chromium carbene complex was regenerated in this reaction system (Scheme 7).

**Enyne Metathesis Using a Catalytic Amount of Fischer Chromium Carbene Complex.** For the chromium-catalyzed enyne metathesis, the use of chromium carbene complex **13a** is not suitable because the formation of indanone is accompanied and it requires a stoichiometric amount of chromium carbene complex. Therefore, chromium carbene complex **13b** was used for this reaction. In this case, the enyne **12b** was required. The synthetic procedure of **12b** was same as that of **12a** as shown in Scheme 8. Treatment of acetal **23b** with TMSI in the presence of $(TMS)_2NH$ gave a mixture of the *E*- and *Z*-isomers of **12b**. Separation of ***E*-12b** and ***Z*-12b** was carried out by careful column chromatography on silica gel, and these isomers could be separated in 63% and 5% yields, respectively, along with **30** (17% yield). The stereochemistry of these compounds, ***E*-12b** or ***Z*-12b**, was determined by NOE experiments. Enyne **12c** was prepared in a similar manner.

Refluxing a mixture of enyne ***E*-12b** and 10 mol % chromium carbene complex **13b** in MeOH for 2 h followed by treatment with 10% HCl gave the metathesis product **24b** in 70% yield. Even with the use of 5 mol % chromium catalyst, the desired product **24b** was obtained in 39% yield (Table 2). Addition of $PPh_3$ as the ligand did not affect the yield of the desired product. As the solvent, THF (43%), toluene (50%), benzene (39%), EtOH (39%), and dichloroethane (31%) can be used for this reaction, but use of $CH_3CN$ (4%) or HMPA

**Scheme 8. Preparation of the Substrates**

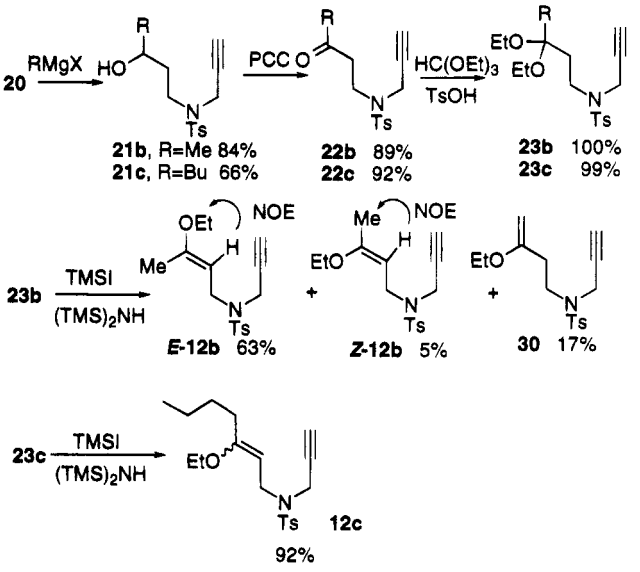



**Table 2. Reaction of *E*-12b with a Catalytic Amount of 13b**

| run | 13b, mol % | additive | yield, % 24b | 22b |
|---|---|---|---|---|
| 1 | 10 | | 70 | |
| 2 | 5 | | 39 | 44 |
| 3 | 5 | $PPh_3$ (5 mol %) | 32 | 58 |

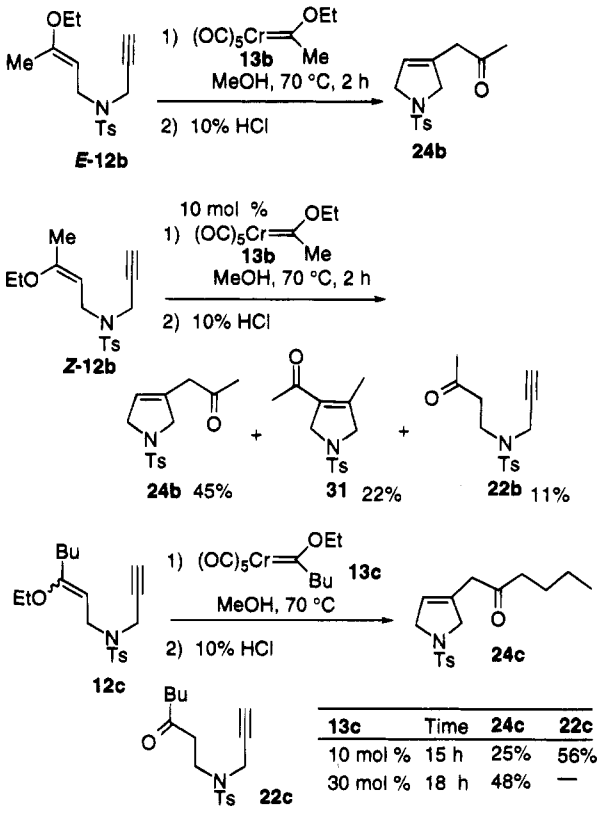
(0%) did not give good results. Treatment of ***Z*-12b** with **13b** (10 mol %) in MeOH in a similar manner afforded the same metathesis product **24b** in 45% yield. In this reaction, a fair amount of **31** (22%) was obtained. Presumably, **31** would be formed by the chromium-promoted oxidative cyclization of ***Z*-12b**. That is, the oxidative cyclization of ***Z*-12b** by the low-valent chromium complex afforded chromacyclopentene **32**, which was converted into **33** by $\beta$-H elimination from the methyl group of **32**. Then, reductive elimination from the chromium hydride complex occurs to give **31**. The reason that **31** was obtained from only the *Z*-isomer of **12b** is not clear yet. Moreover, compound **12c** (*E*/*Z* = 2.7/1) was treated with chromium carbene complex **13c** in MeOH followed by treatment with 10% HCl to give metathesis product **24c** in 25% yield (**22c** was recovered in 56% yield). Use of 30 mol % **13c** for this reaction afforded the desired product **24c** in 48% yield. The chromium-promoted oxidative cyclization product was not produced in this case, though the starting material was a mixture of *E*- and *Z*-isomers [*E*/*Z* = 2.7/1]. Apparently, $\beta$-H elimination from the methylene group did not occur (Schemes 9 and 10).

The important characteristics for this reaction are as follows. The reaction proceeds with a catalytic amount of the Fischer chromium carbene complex. The chromium-catalyzed metathesis of the enyne having the same substituents on the alkene as on the carbene carbon of the chromium carbene complex means that the alkoxy–alkylidene carbon of the alkene formally migrates to the terminal alkyne of the enyne.

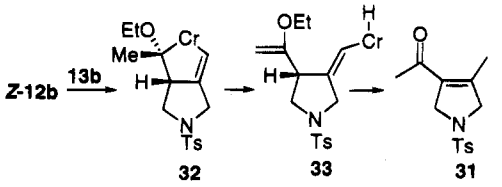
## Experimental Section

All manipulations were performed under an argon atmosphere using standard Schlenk techniques, and all the reaction solutions were degassed through freeze–pump–thaw cycles.

**Scheme 9. Chromium-Catalyzed Metathesis Reaction**




**Scheme 10. Reaction Course for 31**




Solvents were distilled under an argon atmosphere from sodium benzophenone (THF) or $CaH_2$ ($CH_2Cl_2$). All other reagents and solvents were purified when necessary using standard procedures. Column chromatography was performed on silica gel 60 (70–230 mesh, 60 Å), and flash chromatography was performed on silica gel 60 (230–400 mesh, 60 Å) using the indicated solvent. Melting points are uncorrected.

**General Procedure for the Synthesis of 21.** To a THF solution of **20** (1 equiv) was added RMgX (1.5 equiv) at −30 °C, and the solution was stirred at −10 °C for 2.5 h. Solvent was removed. To the residue was added saturated $NH_4Cl$ solution. The aqueous layer was extracted with ethyl acetate. The organic layer was dried over $Na_2SO_4$ and concentrated. The residue was purified by column chromatography on silica gel to give **21**.

**4-Aza-1-phenyl-4-(*p*-tolylsulfonyl)-6-heptyn-1-ol (21a).** The crude product which was prepared from **20** (1.55 g, 5.84 mmol) in THF (14.0 mL) and PhMgBr (21 mmol) in THF (14 mL) was purified by column chromatography on silica gel (ethyl acetate–hexane, 2:5) to give **21a** as a colorless oil (1.48 g, 74%): IR (neat) $\nu$ 3524, 3287, 2119, 1345, 1159 $cm^{-1}$; $^1$H-NMR ($CDCl_3$) $\delta$ 1.82–2.10 (m, 2 H), 2.05 (t, $J$ = 2.4 Hz, 1 H), 2.43 (s, 3 H), 2.70 (d, $J$ = 4.2 Hz, 1 H), 3.22 (dt, $J$ = 14.2, 5.0 Hz, 1 H), 3.58 (dt, $J$ = 14.2, 5.0 Hz, 1 H), 4.04 (dd, $J$ = 2.4, 18.6 Hz, 1 H), 4.30 (dd, $J$ = 2.4, 18.6 Hz, 1 H), 4.88 (dt, $J$ = 4.2, 5.0 Hz, 1 H), 7.20–7.74 (m, 7 H), 7.75 (d, $J$ = 8.3 Hz, 2 H); MS $m/z$ 343 ($M^+$), 324, 222, 188, 155, 91, 68 (base peak). Anal. Calcd for $C_{19}H_{21}NO_3S$: C, 66.45; H, 6.16; N, 4.08. Found: C, 66.18; H, 6.17; N, 3.99.

**5-Aza-5-(*p*-tolylsulfonyl)-7-octyne-2-ol (21b).** The crude product which was prepared from **20** (362 mg, 1.36 mmol) in THF (14.0 mL) and MeMgBr (1.92 mmol) in THF (14 mL) was purified by column chromatography on silica gel (ethyl acetate–hexane, 1:2) to give **21b** as a colorless oil (320 mg, 84%): IR (neat) $\nu$ 3500, 3280, 2110, 1595, 1340, 1160 $cm^{-1}$; $^1$H-NMR ($CDCl_3$) $\delta$ 1.25 (d, $J$ = 6.8 Hz, 3 H), 1.44–1.85 (m, 3 H), 2.05 (t, $J$ = 2.3 Hz, 1 H), 2.44 (s, 3 H), 3.00–3.70 (m, 2 H), 3.80–4.23 (m, 3 H), 7.30 (d, $J$ = 8.3 Hz, 2 H), 7.76 (d, $J$ = 8.3 Hz, 2 H); MS $m/z$ 266, 222, 155, 126 (base peak), 91, 68. Anal. Calcd for $C_{14}H_{19}NO_3S$: C, 59.76; H, 6.81; N, 4.98. Found: C, 59.68; H, 6.78; N, 4.87.

**8-Aza-8-(*p*-tolylsulfonyl)-10-undecyn-5-ol (21c).** The crude product prepared from **20** (1.14 g, 4.30 mmol) in THF (29 mL) to which was added BuMgBr (17.2 mmol) at rt (room temperature) was purified by column chromatography on silica gel (ethyl acetate–hexane, 1:3) to give **21c** as a colorless oil (922 mg, 66%): $^1$H NMR ($CDCl_3$, 270 MHz) $\delta$ 0.91 (t, $J$ = 6.9 Hz, 3 H), 1.23–1.58 (m, 7 H), 1.71–1.83 (m, 1 H), 2.05 (dd, $J$ = 2.5, 2.5 Hz, 1 H), 2.37 (d, $J$ = 4.8 Hz, 1 H), 2.43 (s, 3 H), 3.18 (ddd, $J$ = 4.1, 6.2, 14.4 Hz, 1 H), 3.52 (ddd, $J$ = 6.1, 9.5, 14.4 Hz, 1 H), 3.74–3.83 (m, 1 H), 4.09 (dd, $J$ = 2.5, 18.5 Hz, 1 H), 4.28 (dd, $J$ = 2.5, 18.5 Hz, 1 H), 7.30 (d, $J$ = 8.3 Hz, 2 H), 7.75 (d, $J$ = 8.3 Hz, 2 H); IR (neat) 3532, 3286, 2118, 1598, 1344, 1160 $cm^{-1}$; MS $m/z$ 323, 305, 221, 168, 155, 91. Anal. Calcd for $C_{17}H_{25}NO_3S$: C, 63.12; H, 7.79; N, 4.33. Found: C, 63.03; H, 7.79; N, 4.40.

**General Procedure for the Synthesis of 22.** To a solution of **21** (1 equiv) and MS4A was added PCC (3 equiv) in $CH_2Cl_2$ at 0 °C, and the solution was stirred at rt. Ether was added, the ether solution was chromatographed through a short column of Florisil, and the solution was concentrated. The residue was purified by column chromatography on silica gel to give **22**.

**4-Aza-1-phenyl-4-(p-tolylsulfonyl)-6-heptynone (22a).** The crude product which was prepared from **21a** (355 mg, 1.03 mmol), PCC (668 mg, 3.10 mmol), and MS4A (2.10 g) in $CH_2Cl_2$ (20 mL) was purified by column chromatography on silica gel (ethyl acetate–hexane, 1:3) to give **22a** as a colorless oil (314 mg, 89%): IR (Nujol) $\nu$ 3289, 1674, 1595, 1348, 1161 $cm^{-1}$; $^1$H-NMR ($CDCl_3$) $\delta$ 2.07 (t, $J$ = 2.6 Hz, 1 H), 2.43 (s, 3 H), 3.42 (t, $J$ = 6.9 Hz, 2 H), 3.62 (t, $J$ = 6.9 Hz, 2 H), 4.21 (d, $J$ = 2.6 Hz, 2 H), 7.30 (d, $J$ = 8.4 Hz, 2 H), 7.43–7.52 (m, 2 H), 7.55–7.62 (m, 1 H), 7.75 (d, $J$ = 8.4 Hz, 2 H), 7.92–7.99 (m, 2 H); MS $m/z$ 299, 222, 186 (base peak), 222, 155, 105, 91 (base peak); mp 102 °C. Anal. Calcd for $C_{19}H_{19}NO_3S$: C, 66.84; H, 5.61; N, 4.10. Found: C, 66.96; H, 5.64; N, 4.06.

**5-Aza-5-phenyl-4-(*p*-tolylsulfonyl)-7-octyn-2-one (22b).** The crude product which was prepared from **21b** (95 mg, 0.338 mmol), PCC (218 mg, 1.01 mmol), and MS4A (665 mg) in $CH_2Cl_2$ (6.8 mL) was purified by column chromatography on silica gel (ethyl acetate–hexane, 1:2) to give **22b** as a colorless oil (82.6 mg, 87%): IR (neat) $\nu$ 3260, 2110, 1715, 1595, 1340, 1160 $cm^{-1}$; $^1$H-NMR ($CDCl_3$) $\delta$ 2.04 (t, $J$ = 2.0 Hz, 1 H), 2.20 (s, 3 H), 2.43 (s, 3 H), 2.87 (t, $J$ = 7.0 Hz, 2 H), 3.43 (t, $J$ = 7.0 Hz, 2 H), 4.15 (d, $J$ = 2.0 Hz, 2 H), 7.32 (d, $J$ = 8.2 Hz, 2 H), 7.74 (d, $J$ = 8.2 Hz, 2 H); MS $m/z$ 280 ($M^+$ + 1), 222, 155, 124 (base peak), 91. Anal. Calcd for $C_{14}H_{17}NO_3S$: C, 60.19; H, 6.13; N, 5.01. Found: C, 60.17; H, 6.14; N, 5.00.

**8-Aza-8-(*p*-tolylsulfonyl)-10-undecyn-5-one (22c).** The crude product which was prepared from **21c** (49.8 mg, 0.154 mmol), PCC (98 mg, 0.454 mmol), and MS4A (307 mg) in $CH_2Cl_2$ (3 mL) was purified by column chromatography on silica gel (ethyl acetate–hexane, 1:5) to give **22c** as a colorless oil (45.2 mg, 92%): IR (neat) $\nu$ 3288, 2118, 1712, 1596, 1338, 1160 $cm^{-1}$; $^1$H NMR ($CDCl_3$, 270 MHz) $\delta$ 0.91 (t, $J$ = 7.2 Hz, 3 H), 1.50–1.61 (m, 2 H), 1.23–1.38 (m, 2 H), 2.04 (t, $J$ = 2.4 Hz, 1 H), 2.43 (t, $J$ = 7.5 Hz, 2 H), 2.43 (s, 3 H), 2.83 (t, $J$ = 6.9 Hz, 2 H), 3.43 (t, $J$ = 6.9 Hz, 2 H), 4.14 (d, $J$ = 2.4 Hz, 2 H), 7.30 (d, $J$ = 8.3 Hz, 2 H), 7.73 (d, $J$ = 8.3 Hz, 2 H); MS $m/z$ 321, 222, 166, 155, 91, 57. Anal. Calcd for $C_{17}H_{23}NO_3S$: C, 63.52; H, 7.21; N, 4.36. Found: C, 63.43; H, 7.17; N, 4.37.

**General Procedure for the Synthesis of 23.** To a solution of **22** (1 equiv) and a catalytic amount of *p*-TsOH•$H_2O$ (1.5 mol %) in EtOH was added $HC(OEt)_3$ (3 equiv), and the solution was stirred at rt. To the solution was added saturated $NaHCO_3$ solution, and the aqueous layer was washed with ethyl acetate. The organic layer was washed with brine, dried over $Na_2SO_4$, and concentrated. The residue was purified by chromatography on silica gel to give **23**.

**4-Aza-7,7-diethoxy-7-phenyl-4-(*p*-tolylsulfonyl)heptyne (23a).** The crude product prepared from **22a** (1.15 g, 3.36 mmol), $HC(OEt)_3$ (1.7 mL, 10.1 mmol), and *p*-TsOH•$H_2O$ (10.0 mg) was purified by silica gel column chromatography (ethyl acetate–hexane, 1:9) to give **23a** as a colorless oil (1.39 g, 100%): IR (KBr) $\nu$ 3245, 2116, 1599, 1342, 1161 $cm^{-1}$; $^1H$-NMR ($CDCl_3$) $\delta$ 1.19 (t, $J$ = 7.1 Hz, 6 H), 1.93 (t, $J$ = 3.4 Hz, 1 H), 2.12–2.40 (m, 2 H), 2.39 (s, 3 H), 2.76–3.00 (m, 2 H), 3.31 (dt, $J$ = 2.9, 7.1 Hz, 2 H), 3.45 (dt, $J$ = 2.9, 7.1 Hz, 2 H), 3.98 (d, $J$ = 3.4 Hz, 2 H), 7.22 (d, $J$ = 8.3 Hz, 2 H), 7.20–7.52 (m, 5 H), 7.52 (d, $J$ = 8.3 Hz, 2 H); MS $m/z$ 370, 222, 214, 179 (base peak), 155, 91; mp 102 °C. Anal. Calcd for $C_{23}H_{29}NO_4S$: C, 66.48; H, 7.03; N, 3.37. Found: C, 66.32; H, 7.09; N, 3.27.

**4-Aza-7,7-diethoxy-4-(*p*-tolylsulfonyl)octyne (23b).** The crude product prepared from **22b** (43.5 mg, 0.256 mmol), $HC(OEt)_3$ (0.4 mL, 0.299 mmol), and *p*-TsOH•$H_2O$ (1.5 mg) was purified by silica gel column chromatography (ethyl acetate–hexane, 1:5) in EtOH (1.2 mL) to give **23b** as a colorless oil (54.4 g, 99%): IR (KBr) $\nu$ 3250, 2110, 1595, 1340, 1160 $cm^{-1}$; $^1H$ NMR ($CDCl_3$, 270 MHz) $\delta$ 1.15 (t, $J$ = 7.0 Hz, 6 H), 1.30 (s, 3 H), 1.76–2.05 (m, 2 H), 2.05 (t, $J$ = 2.2 Hz, 1 H), 2.43 (s, 3 H), 3.12–3.40 (m, 2 H), 3.44 (q, $J$ = 7.0 Hz, 4 H), 4.15 (d, $J$ = 2.2 Hz, 2 H), 7.30 (d, $J$ = 8.2 Hz, 2 H), 7.74 (d, $J$ = 8.2 Hz, 2 H); MS $m/z$ 338 ($M^+$ – Me), 308, 222, 155, 152 (base peak), 117, 91. Anal. Calcd for $C_{18}H_{27}NO_4S$: C, 61.16; H, 7.70; N, 3.96. Found: C, 61.05; H, 7.68; N, 3.94.

**4-Aza-7,7-diethoxy-4-(*p*-tolylsulfonyl)undecyne (23c).** The crude product which was prepared from **22c** (32.4 mg, 0.101mmol), $HC(OEt)_3$ (0.84 mL, 0.505mmol), and *p*-TsOH•$H_2O$ (2 mg) in EtOH (0.5 mL) was purified by silica gel column chromatography (ethyl acetate–hexane, 1:5) to give **23a** as a colorless oil (40.3 mg, 100%): IR (neat) $\nu$ 3270, 2118, 1598, 1350, 1162 $cm^{-1}$; $^1H$ NMR ($CDCl_3$, 270 MHz) $\delta$ 0.90 (t, $J$ = 6.6 Hz, 3 H), 1.15 (t, $J$ = 7.1 Hz, 6 H), 1.21–1.35 (m, 4 H), 1.51–1.56 (m, 2 H), 1.91 (ddd, $J$ = 5.0, 5.0, 8.3 Hz, 2 H), 2.07 (t, $J$ = 2.5 Hz, 1 H), 2.42 (s, 3H), 3.18 (ddd, $J$ = 5.0, 5.0, 8.5 Hz, 2 H), 3.41 (q, $J$ = 7.1 Hz, 2 H), 3.42 (q, $J$ = 7.1 Hz, 2 H), 4.16 (d, $J$ = 2.5 Hz, 2 H), 7.29 (d, $J$ = 8.1 Hz, 2 H), 7.73 (d, $J$ = 8.1 Hz, 2 H); MS $m/z$ 349, 337, 221, 194, 155, 91. Anal. Calcd for $C_{21}H_{33}NO_4S$: C, 63.76; H, 8.41; N, 3.54. Found: C, 63.46; H, 8.27; N, 3.61.

**General Procedure for the Synthesis of 12.** To a solution of **23** (1 equiv) and $(TMS)_2NH$ (3 equiv) in $CH_2Cl_2$ was added TMSI (2 equiv), and the solution was stirred at rt overnight. To the solution was added aqueous saturated $NaHCO_3$ solution, and the aqueous layer was extracted with ethyl acetate. The organic layer was washed with brine, dried over $Na_2SO_4$, and concentrated. The residue was purified by chromatography on silica gel to give **12**.

**4-Aza-1-ethoxy-1-phenyl-4-(*p*-tolylsulfonyl)-1-hepten-6yne (12a).** The crude product prepared from **23a** (371 mg, 0.895 mmol), $(TMS)_2NH$ (0.57 mL, 2.68 mmol), and TMSI (0.25 mL, 1.79 mmol) in $CH_2Cl_2$ (5 mL) at rt for 15 h was purified by chromatography on silica gel (ethyl acetate–hexane, 1:10) to give enyne **12a** (328 mg, 99%): $^1H$ NMR ($CDCl_3$, 400 MHz) (mixture of two isomers in a ratio of 2:1) $\delta$ 1.24 and 1.33 (t and t, $J$ = 7.0 and 7.0 Hz, 3 H), 1.74 and 2.05 (t and t, $J$ = 2.2 and 2.2 Hz, 1 H), 2.39 and 2.43 (s and s, 3 H), 3.69 and 3.81 (q and q, $J$ = 7.0 and 7.0 Hz, 2 H), 3.89 and 4.12 (d and d, $J$ = 7.3 and 7.3 Hz, 2 H), 4.05 and 4.15 (d and d, $J$ = 2.2 and 2.2 Hz, 2 H), 4.65 and 5.16 (t and t, $J$ = 7.3 and 7.3 Hz, 1 H), 7.20–7.43 (m, 7 H), 7.76 and 7.78 (d and d, $J$ = 8.4 and 8.4 Hz, 2 H); IR (KBr) 3287, 2120, 1647, 1599, 1348, 1161 $cm^{-1}$; MS $m/z$ 369 ($M^+$), 368, 340, 324, 186 (base peak), 91, 77. Anal. Calcd for $C_{21}H_{23}NO_3S$: C, 68.27; H, 6.27; N, 3.79. Found: C, 68.14; H, 6.26; N, 3.81.

***E*- and *Z*-5-Aza-2-ethoxy-5-(*p*-tolylsulfonyl)-2-octen-7-yne (*E*- and *Z*-12b).** To a solution of **23b** (2.34 mg, 6.62 mmol) and $(TMS)_2NH$ (3.50 mL, 16.6 mmol) in $CH_2Cl_2$ (40 mL) was added TMSI (1.40 mL, 9.84 mmol) under gentle reflux, and the solution was refluxed for 15 min. The crude product was purified by flash chromatography on silica gel (ethyl acetate–hexane, 1:10) to give ***E*-12a** (1.28 g, 63%), ***Z*-12b** (102 mg, 5%), and **30** (345 mg, 17%). ***E*-12b**: $^1H$ NMR ($CDCl_3$, 270 MHz) $\delta$ 1.28 (t, $J$ = 7.0 Hz, 3 H), 1.84 (s, 3 H), 1.99 (t, $J$ = 2.4 Hz, 1 H), 2.44 (s, 3 H), 3.66 (q, $J$ = 7.0 Hz, 2 H), 3.86 (d, $J$ = 7.7 Hz, 2 H), 4.11 (t, $J$ = 2.4 Hz, 2 H), 4.31 (t, $J$ = 7.7 Hz, 1 H), 7.36 (d, $J$ = 8.3 Hz, 2 H), 7.65 (d, $J$ = 8.3 Hz, 2 H); $^{13}C$ NMR ($CDCl_3$, 100 MHz) $\delta$ 158.17, 143.34, 136.28, 129.39, 127.78, 90.55, 77.18, 73.30, 62.33, 44.02, 34.88, 21.53, 16.48, 14.50; IR (neat) 3275, 2118, 1662, 1598, 1346, 1161 $cm^{-1}$; MS $m/z$ 308 ($M^+$ + 1), 222, 155, 152, 91 (base peak). Anal. Calcd for $C_{16}H_{21}NO_3S$: C, 62.51; H, 6.89; N, 4.56; S, 10.43. Found: C, 62.51; H, 6.91; N, 4.51; S, 10.53. ***Z*-12b**: mp 64 °C; $^1H$ NMR ($CDCl_3$, 270 MHz) $\delta$ 1.21 (t, $J$ = 7.1 Hz, 3 H), 1.85 (s, 3 H), 1.99 (t, $J$ = 2.4 Hz, 1 H), 2.43 (s, 3 H), 3.79 (q, $J$ = 7.1 Hz, 2 H), 3.90 (d, $J$ = 6.9 Hz, 2 H), 4.08 (t, $J$ = 2.4 Hz, 2 H), 4.42 (t, $J$ = 6.9 Hz, 1 H), 7.29 (d, $J$ = 8.4 Hz, 2 H), 7.75 (d, $J$ = 8.4 Hz, 2 H); $^{13}C$ NMR ($CDCl_3$, 100 MHz) $\delta$ 155.16, 143.16, 136.56, 129.32, 127.76, 101.54, 77.58, 72.75, 63.20, 41.50, 35.68, 21.53, 17.76, 15.22; IR (neat) 3286, 1670, 1597, 1333, 1164 $cm^{-1}$; MS (EI) $m/z$ 307 ($M^+$), 306 ($M^+$ – 1), 262, 222, 155, 152, 91, 71 (base peak). Anal. Calcd for $C_{16}H_{21}NO_3S$: C, 62.51; H, 6.89; N, 4.56; S, 10.43. Found: C, 62.47; H, 7.07; N, 4.52; S, 10.38. **30**: $^1H$ NMR ($CDCl_3$, 270 MHz) $\delta$ 1.30 (t, $J$ = 7.0 Hz, 3 H), 2.05 (t, $J$ = 2.4 Hz, 1 H), 2.38 (t, $J$ = 7.3 Hz, 2 H), 2.44 (s, 3 H), 3.40 (t, $J$ = 7.3 Hz, 2 H), 3.72 (q, $J$ = 7.0 Hz, 2 H), 3.91 (d, $J$ = 2.0 Hz, 1 H), 3.93 (d, $J$ = 2.0 Hz, 1 H), 4.16 (d, $J$ = 2.4 Hz, 2 H), 7.36 (d, $J$ = 8.3 Hz, 2 H), 7.65 (d, $J$ = 8.3 Hz, 2 H); $^{13}C$ NMR ($CDCl_3$, 100 MHz) 159.67, 143.38, 136.21, 129.44, 127.71, 82.81, 76.92, 73.52, 62.86, 44.48, 36.72, 34.29, 21.54, 14.39; IR (neat) 3278, 2118, 1655, 1598, 1348, 1161 $cm^{-1}$; MS (EI) $m/z$ 307 ($M^+$), 306 ($M^+$ – 1), 262, 222, 155, 152, 124, 91 (base peak). Anal. Calcd for $C_{16}H_{21}NO_3S$: C, 62.51; H, 6.89; N, 4.56; S, 10.43. Found: C, 62.56; H, 6.76; N, 4.66; S, 10.36.

***E*- and *Z*-8-Aza-5-ethoxy-8-(p-tolylsulfonyl)-5-undecen-10-yne (12c).** To a solution of **23c** (838 mg, 2.12 mmol) and $(TMS)_2NH$ (1.12 mL, 5.30 mmol) in $CH_2Cl_2$ (21 mL) was added TMSI (0.45 mL, 3.16 mmol) with heating, and the solution was refluxed for 15 min. The crude product was purified by flash chromatography on silica gel (ethyl acetate–hexane, 1:30) to give **12c** (682 mg, 92%, *E*:*Z* = 2:1): $^1H$ NMR ($CDCl_3$, 270 MHz; mixture of two isomers in a ratio of 2.7:1) $\delta$ 0.89 (t, $J$ = 7.1 Hz, 3 H), 1.22–1.54 (m, 7 H), 2.05 and1.99 (t and t, $J$ = 2.5 and 2.5 Hz, 1 H), 2.16 (t, $J$ = 7.2 Hz, 2 H), 2.44 (s, 3 H), 3.64 (q, $J$ = 7.1 Hz, 2 H), 3.36 and 3.86 (dd and d, $J$ = 8.9, 8.9, and 7.8 Hz, 2 H), 4.11 and 4.17 (d and d, $J$ = 2.5 and 2.5 Hz, 2 H), 4.27 and 4.42 (t and dd, $J$ = 8.9, 8.9, and 7.8 Hz, 1 H), 7.31 (d, $J$ = 8.4 Hz, 2 H), 7.76 (d, $J$ = 8.4 Hz, 2 H); IR (neat) 3276, 2118, 1656, 1598, 1348, 1162 $cm^{-1}$; MS $m/z$ 349 ($M^+$), 304, 222, 194, 155, 91 (base peak). Anal. Calcd for $C_{19}H_{27}NO_3S$: C, 65.29; H, 7.79; N, 4.01; S, 9.17. Found: C, 64.97; H, 7.95; N, 3.99; S, 8.97.

**Typical Procedure for the Chromium-Catalyzed Metathesis Reaction.** To a solution of the enyne ***E*-12b** (50.0 mg, 163 $\mu$mol) in MeOH (1.0 mL) under an argon atmosphere was added dropwise a solution of the carbene complex **13b** (4.3 mg, 0.016 $\mu$mol) in MeOH (0.6 mL) at −78 °C. The solution was heated at 70 °C for 2 h and then quenched with 1.0 mL of 10% HCl. The aqueous layer was extracted with ethyl acetate, and the organic layer was washed with $H_2O$ and then brine, dried over $Na_2SO_4$, and concentrated. The residue was purified by chromatography on silica gel (hexane/ethyl acetate = 2/1) to give **24b** (32.1 mg, 70%): $^1H$ NMR ($CDCl_3$, 270 MHz) $\delta$ 2.21 (s, 3 H), 2.43 (s, 3 H), 3.18 (s, 2 H), 4.02–4.15 (m, 4 H),

5.48 (brs, 1 H), 7.32 (d, $J$ = 8.3 Hz, 2 H), 7.72 (d, $J$ = 8.3 Hz, 2 H); $^{13}$C NMR ($CDCl_3$, 100 MHz) $\delta$ 204.35, 143.49, 134.09, 132.19, 129.75, 127.40, 122.77, 56.38, 54.85, 43.27, 29.68, 21.47; IR (neat) 1717, 1630, 1597, 1341, 1161 cm$^{-1}$; MS (EI) $m/z$ 279 ($M^+$), 236, 155, 91 (base peak), 82; HRMS (EI) ($m/z$) calcd for $C_{14}H_{17}NO_3S$ 279.0929; found 279.0916. Anal. Calcd for $C_{14}H_{17}NO_3S$: C, 60.19; H, 6.13; N, 5.01; S, 11.48. Found: C, 60.33; H, 6.30; N, 4.93; S, 11.44.

**Reaction of 12a with 13a.** According to the typical procedure, an EtOH (1.0 mL) solution of **12a** (35.8 mg, 96.8 mmol) and **13a** (9.5 mg, 0.029 mmol) was warmed at 70 °C for 24 h. After the usual workup, the residue was purified by column chromatography on silica gel (ethyl acetate–hexane, 1:6–1:3) to give **16a** (5.0 mg, 14%), **24a** (6.8 mg, 21%), and **25** (9.0 mg, 21%). **16a**: $^1$H NMR ($C_6D_6$, 270 MHz) (mixture of two isomers in a ratio of 1:1) $\delta$ 1.04 (t, $J$ = 7.3 Hz, 3 H), 1.89 and 1.92 (s and s, 3 H), 3.41 (q, $J$ = 7.3 Hz, 2 H), 3.77–3.83 and 4.01–4.08 (m and m, 2 H), 4.10–4.17 and 4.79–4.85 (m and m, 2 H), 4.92 and 5.11 (brs and brs, 1 H), 5.18 and 5.52 (s and s, 1 H), 6.79 and 6.82 (d and d, $J$ = 8.4 and 8.4 Hz, 2 H), 7.05–7.29 (m, 5 H), 7.71 and 7.90 (d and d, $J$ = 8.4 and 8.4 Hz, 2 H); IR (neat) 2777, 1643, 1596, 1345, 1164 cm$^{-1}$; MS (EI) $m/z$ 369 ($M^+$), 367 ($M^+$ – 2), 339, 234, 214, 186, 168, 105 (base peak). Anal. Calcd for $C_{21}H_{23}NO_3S$: C, 68.27; H, 6.27; N, 3.79; S, 8.68. Found: C, 68.12; H, 6.35; N, 3.67; S, 8.71. **24a**: $^1$H NMR ($CDCl_3$, 270 MHz) $\delta$ 2.41 (s, 3 H), 3.70 (s, 2 H), 4.08–4.12 (m, 4 H), 6.48 (brs, 1 H), 7.30 (d, $J$ = 8.3 Hz, 2 H), 7.45 (dd, $J$ = 7.9, 8.2 Hz, 2 H), 7.50–7.60 (m, 1 H), 7.71 (d, $J$ = 8.3 Hz, 2 H), 7.88 (d, $J$ = 7.9 Hz, 2 H); IR (neat) 1687, 1595, 1340, 1160 cm$^{-1}$; MS (EI) $m/z$ 341 ($M^+$), 236, 186, 155, 105 (bp), 91. Anal. Calcd for $C_{19}H_{19}NO_3S$: C, 66.84; H, 5.61; N, 4.10; S, 9.39. Found: C, 66.75; H, 5.76; N, 3.99; S, 9.03. **25**: $^1$H NMR ($CDCl_3$, 400 MHz) $\delta$ 2.43 (s, 3 H), 2.66 (dd, $J$ = 3.4, 19.5 Hz, 1 H), 2.80 (dd, $J$ = 7.8, 19.5 Hz, 1 H), 3.21 (dt, $J$ = 18.1, 7.3 Hz, 1 H), 3.32 (dt, $J$ = 18.1, 7.3 Hz, 1 H), 3.35 (dd, $J$ = 9.3, 14.2 Hz, 1 H), 3.41 (dd, $J$ = 5.9, 14.2 Hz, 1 H), 3.57 (t, $J$ = 7.3 Hz, 2 H), 3.74–3.82 (m, 1 H), 7.31 (d, $J$ = 8.3 Hz, 2 H), 7.38 (dd, $J$ = 7.8, 7.8 Hz, 1 H), 7.46 (dd, $J$ = 7.5, 8.8 Hz, 2 H), 7.56 (dd, $J$ = 7.8, 7.8 Hz, 1 H), 7.55–7.61 (m, 2 H), 7.69 (d, $J$ = 8.3 Hz, 2 H), 7.75 (d, $J$ = 7.8 Hz, 1 H), 7.87 (d, $J$ = 8.8 Hz, 2 H); IR (KBr) 1712, 1682, 1595, 1340, 1160 cm$^{-1}$; MS (EI) 448 ($M^+$ + 1), 316, 184, 155, 132, 91 (base peak). Anal. Calcd for $C_{26}H_{25}NO_4S$: C, 69.78; H, 5.63; N, 3.13; S, 7.16. Found: C, 69.60; H, 5.74; N, 3.15; S, 7.16.

**Reaction of *Z*-12b with 13b.** According to the typical procedure, a MeOH (1.5 mL) solution of ***Z*-12b** (47.0 mg, 0.153 mmol) and **13b** (4.0 mg, 0.015 mmol) was warmed at 70 °C for 2 h. After the usual workup, the residue was purified by column chromatography on silica gel (ethyl acetate–hexane, 1:2) to give **24b** (19.1 mg, 45%), **31** (9.2 mg, 22%), and **22b** (4.8 mg, 11%). **31**: $^1$H NMR ($CDCl_3$, 270 MHz) $\delta$ 2.02 (s, 3 H), 2.22 (s, 3 H), 2.44 (s, 3 H), 4.17–4.22 (m, 2 H), 4.30–4.38 (m, 2 H), 7.35 (d, $J$ = 8.3 Hz, 2 H), 7.73 (d, $J$ = 8.3 Hz, 2 H); IR (KBr) 1650, 1640, 1595, 1335, 1160 cm$^{-1}$; MS (EI) $m/z$ 279 ($M^+$), 264, 236, 222, 155, 124, 91, 43 (base peak); HRMS (EI) ($m/z$) calcd for $C_{14}H_{17}NO_3S$ 279.0930, found 279.0955.

**Reaction of 12c with 13c.** According to the typical procedure, a MeOH (1.5 mL) solution of **12c** (51.7 mg, 0.148 mmol) and **13b** (5.0 mg, 0.017 mmol) was warmed at 70 °C for 2 h. After the usual workup, the residue was purified by column chromatography on silica gel (ethyl acetate–hexane, 1:5) to give **24c** (12.0 mg, 25%) and **22c** (26.7 mg, 56%). **24c**: $^1$H NMR ($CDCl_3$, 270 MHz) $\delta$ 0.81 (t, $J$ = 7.4 Hz, 3 H), 1.19–1.35 (m, 2 H), 1.44–1.62 (m, 2 H), 2.30 (t, $J$ = 7.4 Hz, 2 H), 2.36 (s, 3 H), 3.13 (s, 2 H), 3.96–4.13 (m, 4 H), 5.44 (brs, 1 H), 7.31 (d, $J$ = 8.3 Hz, 2 H), 7.71 (d, $J$ = 8.3 Hz, 2 H); IR (neat) 1714, 1636, 1598, 1346, 1162 cm$^{-1}$; MS (EI) $m/z$ 321 ($M^+$), 236 (base peak), 166, 155; HRMS (EI) ($m/z$) calcd for $C_{17}H_{23}NO_3S$ 321.1399, found 321.1397; $^{13}$C NMR ($CDCl_3$, 100 MHz) $\delta$ 206.73, 143.47, 134.24, 132.41, 129.79, 127.47, 122.60, 56.49, 54.90, 42.50, 42.36, 25.73, 22.22, 21.53, 13.79.

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