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A novel reaction of 2-(arylamino)-1-(methylthio)-1-tosylethenes with hydrogen iodide leading to quinoline derivatives

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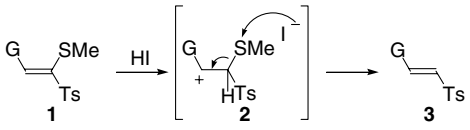
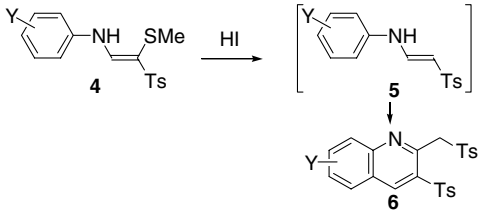
Abstract—The reaction of 2-(arylamino)-1-(methylthio)-1-tosylethenes (**4**) with hydrogen iodide in refluxing toluene gave 3-tosyl-2-(tosylmethyl)quinoline derivatives (**6**) in good yields. In this reaction, hydrogen iodide dose not only reductively removes the methylthio group of **4** to form an intermediary 1-(arylamino)-2-tosylethene (**5**), but also serves as a protic catalyst for the subsequent dimeric cyclization of **5** to lead to the quinoline derivatives (**6**).

Ketene dithioacetal *S*,*S*-dioxides (**1**),[1] easily prepared from (methylthio)methyl *p*-tolyl sulfone[2,3] and various aldehydes, show unique reactivities that can be utilized in various organic syntheses.[1,2,4] The ketene dithioacetal *S*,*S*-dioxide functionality has a good acceptability for radicals[5–7] and hydride ion.[8] Furthermore, an electron can be transferred to this functionality either electrochemically[9] or from Mg metal.[10] In these cases, the carbon–sulfonyl bond of **1** (G = Ar) was reductively cleaved to give 1-aryl-2-(methylthio)ethenes. To the best of our knowledge, no reductive removal of the methylthio group of **1** has appeared in the literature. In this context, we initiated our investigation to reductively eliminate the methylthio group of **1** with hydrogen iodide, which is well known to have reducing ability.[11] A plausible mechanism is depicted in Eq. 1 that is analogous to the mechanism described for the dehalogenation of α-halo carbonyl compounds with hydrogen iodide.[12]



(1)

We treated **1** (G = *p*-tol) with hydrogen iodide in refluxing toluene, but a trace amount (~2%) of 1-tolyl-2-tosylethene was obtained along with a large amount (~98%) of the starting material. Hence, we designed compound (**1**) bearing an amino group as the G group, which would stabilize an intermediary cation (**2**) so as to promote the addition of the proton to the C–C double bond. With this expectation in mind, we carried out the reaction of 2-anilino-1-(methylthio)-1-tosylethene (**4**; Y = H) with hydrogen iodide. To our surprise, the formation of 3-tosyl-2-(tosylmethyl)quinoline (**6**; Y = H) was observed as shown in Eq. 2. This intriguing reaction seems to be via the anticipated reduction product (**5**). Herein we report a novel reaction of **4** with hydrogen iodide to produce quinoline derivatives (**6**) in good yield.



(2)

The starting materials (**4**)[13] were prepared by the condensation reaction of anilines with 2-(methylthio)-2-tosylethanal.[6c] At first, we examined the reaction of **4** (Y = H) with hydrogen iodide. To a solution of **1** (Y = H) in dry toluene was added a 55% aqueous solution of hydrogen iodide (1.0 equiv), and the resulting mixture was stirred at room temperature, but no reaction occurred. As the reaction temperature became higher, the reaction proceeded faster as summarized in Table 1. The reaction in refluxing toluene completed within 2 h

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Table 1. The reaction of **4** (Y = H) with hydrogen iodide

Entry	HI (equiv)	Conditions	Yield (%) of **6** (Y = H)
1	1.0	Toluene, rt, >4 h	0[a]
2	1.1	Toluene, 75 °C, 24 h	66
3	1.1	CH_3CN, 75 °C, 24 h	55[b]
4	1.1	Toluene, reflux, 2 h	77
5	0.5	Toluene, reflux, 11 h	73[c]
6	2.2	Toluene, reflux, 3 h	56

[a] No reaction.
[b] Starting material was recovered in 14%.
[c] Starting material was recovered in 7%.

to give **6** (Y = H) in a 77% yield.[14] From its spectral data (^{1}H NMR, ^{13}C NMR, IR and EA), we assigned the structure (**6**; Y = H) to this product. Finally, it was confirmed by single-crystal X-ray crystallographic analysis (Fig. 1).[15]

As shown in Table 1, the reaction in toluene was somewhat faster than that in acetonitrile (entry 2 vs 3). The amount of hydrogen iodide affected the yield of **6** (Y = H) slightly: the presence of a small excess of hydrogen iodide gave the best result as summarized in entries 4–6. Interestingly, the present reaction is characteristic of hydrogen iodide. In the reaction of **4** (Y = H) with various protic acids such as perchloric acid, *p*-toulenesulfonic acid, acetic acid, trifluoroacetic acid, hydrochloric acid and hydrobromic acid, no quinoline derivative **6** (Y = H) was obtained except for the reaction with hydrobromic acid, which gave **6** (Y = H) in a 10% yield even after the reaction time was prolonged to 29 h.

Next, the compounds (**4**) having various substituents at the phenyl group were subjected to the reaction with hydrogen iodide in refluxing toluene. The results are given in Table 2, showing that both of the electron-donating substituents (OMe and Me) and the electron-withdrawing substituent (COOMe) are tolerated in the present reaction to give the corresponding **6** in from moderate to high yields. It is noteworthy that the methoxy group remained unchanged in the reaction of **4** (Y = *p*-OMe). This is because the present reaction conditions using 1.1 equiv of hydrogen iodide are too mild to cleave the O–Me bond.[16]

For the formation of the quinoline derivative (**6**; Y = H) starting from **4** (Y = H), we suppose the reaction pathway in Scheme 1, which proceeds by way of the intermediary 1-anilino-2-tosylethene (**5**). The intermediate (**5**) is given by the action of hydrogen iodide on **4** (Y = H). This reduction is accompanied by the formation of methanesulfenyl iodide which is subsequently converted to iodine and dimethyl disulfide. Hydrogen iodide promotes the dimerization of **5**: hydrogen iodide adds to **5** to produce the cationic intermediate (**B**) which undergoes the ring-closure reaction. The elimination of a proton and aniline forms a dihydroquinoline intermediate (**7**). The subsequent oxidative aromatization of **7** produces the quinoline derivative (**6**; Y = H). It is likely that

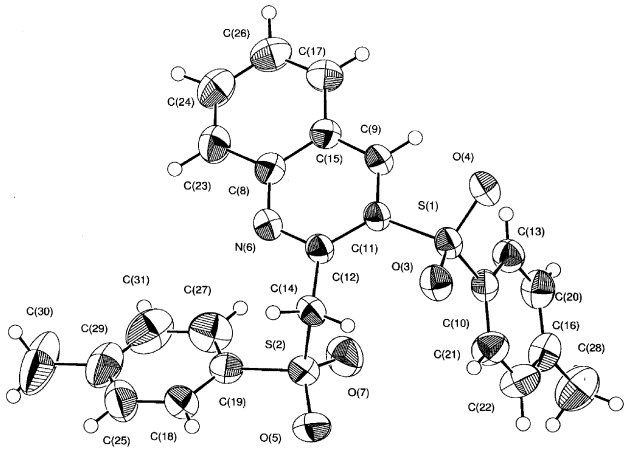
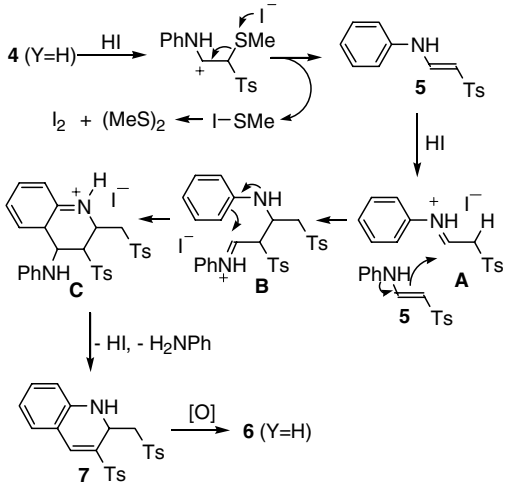


Figure 1. X-ray structure of **6** (Y = H).



Scheme 1. Representation of a plausible reaction mechanism.

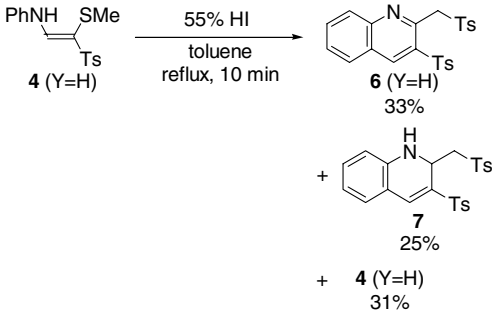
Table 2. The reaction of various substituted **4**

Entry	Compound	Time (h)	Product	Yield (%)
1	**4** (Y = *p*-OMe)	1	**6** (Y = 6-OMe)	68
2	**4** (Y = *p*-Me)	1.5	**6** (Y = 6-Me)	85
3	**4** (Y = *o*-Me)	2	**6** (Y = 8-Me)	84
4	**4** (Y = *m*-Me)	2	**6** (Y = 5- and 7-Me)	87[a]
5	**4** (Y = *p*-Br)	15	**6** (Y = 6-Br)	40[b]
6	**4** (Y = *p*-COOMe)	5	**6** (Y = 6-COOMe)	60

[a] Ratio of **6** (Y = 5-Me) and **6** (Y = 7-Me) was 9:1 determined by ^{1}H NMR analysis.
[b] Compound **6** (Y = H) was obtained in 12%.

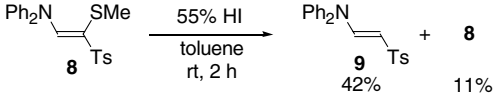
the final oxidation is achieved by iodine. Iodine can be produced by hydrogen iodide and air.

It is crucial to the proposed mechanism that the initially formed **5** easily dimerizes by the aid of hydrogen iodide. When the reaction was stopped at the initial stage (10 min), we isolated the supposed intermediate **7** (25% yield) along with **6** (Y = H) (33% yield) as summarized in Eq. 3. This result suggested that intermediate **5** can be smoothly converted to **7**. The structure of **7** was deduced from its physical properties and its easy derivation into **6** (Y = H) in the presence of hydrogen iodide under aerobic conditions.



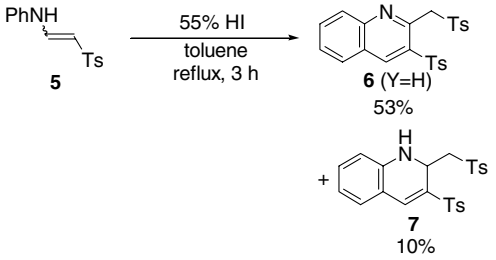
(3)

If the aniline group of **5** is replaced by a bulky amino group, the dimerization would be retarded. In fact, 2-diphenylamino-1-tosylethene (**9**) was obtained by the reaction of 1-(methylthio)-2-diphenylamino-1-tosylethene (**8**) with hydrogen iodide (Eq. 4).



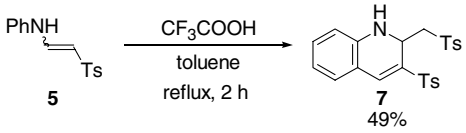
(4)

Furthermore, we prepared the proposed intermediate (**5**) from aniline and tosylacetylene according to the literature.[17] Surprisingly, this compound was too reactive to be isolated in a pure form by column chromatography on silica gel. Therefore, it was subjected to the reaction with hydrogen iodide without any purification. By the reaction of crude **5** with hydrogen iodide in refluxing toluene, **6** (Y = H) and **7** were formed in 53% and 10% yields, respectively (Eq. 5).[18]



(5)

As shown in the mechanism of Scheme 1, the transformation of **5** to **7** would be induced by the action of proton. This means that, for this transformation, hydrogen iodide is not always necessary. Indeed, we obtained **7** in a 49% yield when trifluoroacetic acid was employed instead of hydrogen iodide (Eq. 6). Thus, the mechanism of Scheme 1 was shown to be plausible for the present transformation of **5** into **7**.



(6)

Thus, we have found that the reaction of 2-(arylamino)-1-(methylthio)-1-tosylethenes (**4**) with hydrogen iodide resulted in the formation of 3-tosyl-2-(tosylmethyl)quinoline derivatives (**6**). Now we are investigating the application of this intriguing quinoline ring formation to the compounds having other electron-withdrawing groups instead of the sulfonyl group of **4** or **5**.

Acknowledgement

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Supplementary data

Supplementary data associated with this article can be found, in the online version, at doi:10.1016/j.tetlet.2006.12.054.

References and notes

1. (a) Ogura, K.; Yahata, N.; Hashizume, K.; Tsuyama, K.; Takahashi, K.; Iida, H. *Chem. Lett.* **1983**, 767; (b) Ogura, K.; Iihama, T.; Kiuchi, S.; Kajiki, T.; Koshikawa, O.; Takahashi, K.; Iida, H. *J. Org. Chem.* **1986**, *51*, 700; (c) Ogura, K.; Yahata, N.; Fujimori, T.; Fujita, M. *Tetrahedron Lett.* **1990**, *31*, 4621.
2. Ogura, K. *Rev. Heteroatom Chem.* **1991**, *5*, 85.
3. (a) Ogura, K.; Yahata, N.; Takahashi, K.; Iida, H. *Tetrahedron Lett.* **1983**, *24*, 5761; (b) Ogura, K.; Ohtsuki, K.; Nakamura, M.; Yahata, N.; Takahashi, K.; Iida, H. *Tetrahedron Lett.* **1985**, *26*, 2455; (c) Ogura, K.; Yahata, N.; Minoguchi, M.; Ohtsuki, K.; Takahashi, K.; Iida, H. *J. Org. Chem.* **1986**, *51*, 508; (d) Ogura, K.; Tsuruda, T.; Takahashi, K.; Iida, H. *Tetrahedron Lett.* **1986**, *27*, 3665; (e) Ogura, K.; Uchida, T.; Tsuruda, T.; Takahashi, K. *Tetrahedron Lett.* **1987**, *28*, 5703.
4. (a) Hewkin, C. T.; Jackson, R. F. W.; Clegg, W. *J. Chem. Soc., Perkin Trans. 1* **1991**, 3091; (b) Ogura, K.; Takahashi, S.; Kawamoto, Y.; Suzuki, M.; Fujita, M.; Suzuki, Y.; Sugiyama, Y. *Tetrahedron Lett.* **1993**, *34*, 2649; (c) Fox, J. M.; Morris, C. M.; Smyth, G. D.; Whitham, G. H. *J. Chem. Soc., Perkin Trans. 1* **1994**, 731; (d) Sugiyama, Y.; Suzuki, Y.; Mitamura, S.; Kawamoto, Y.; Fujita, M.; Ogura, K. *Bull. Chem. Soc. Jpn.* **1994**, *67*, 3346; (e) Ogura, K.; Miokawa, M.; Fujita, M.; Ashidaka, H.; Mito, A. *Nonlinear Optics* **1995**, *13*, 253; (f) Craig, D.; Meadows, J. D.; Pécheux, M. *Tetrahedron Lett.* **1998**, *39*, 147; (g) Ogura, K.; Yanai, H.; Miokawa, M.; Akazome, M. *Tetrahedron Lett.* **1999**, *40*, 8887; (h) Gallos, J. K.; Dellios, C. C. *J. Heterocycl. Chem.* **2001**, *38*, 579; (i) Matsumoto, S.; Ishii, M.; Kimura, K.; Ogura, K. *Bull. Chem. Soc. Jpn.* **2004**, *77*, 1897.
5. (a) Ogura, K.; Sumitani, N.; Kayano, A.; Iguchi, H.; Fujita, M. *Chem. Lett.* **1992**, 1487; (b) Ogura, K.; Kayano, A.; Fujino, T.; Sumitani, N.; Fujita, M. *Tetrahedron Lett.* **1993**, *34*, 8313; (c) González-Cameno, A. M.; Mella, M.; Fagnoni, M.; Albini, A. *J. Org. Chem.* **2000**, *65*, 297.

6. (a) Ogura, K.; Yanagisawa, A.; Fujino, T.; Takahashi, K. *Tetrahedron Lett.* **1988**, *29*, 5387; (b) Ogura, K.; Kayano, A.; Sumitani, N.; Akazome, M.; Fujita, M. *J. Org. Chem.* **1995**, *60*, 1106; (c) Kayano, A.; Yajima, Y.; Akazome, M.; Fujita, M.; Ogura, K. *Bull. Chem. Soc. Jpn.* **1995**, *68*, 3599; (d) Kayano, A.; Akazome, M.; Fujita, M.; Ogura, K. *Tetrahedron* **1997**, *53*, 12101; (e) Ogura, K.; Arai, T.; Kayano, A.; Akazome, M. *Tetrahedron Lett.* **1999**, *40*, 2537.
7. Ogura, K.; Arai, T.; Kayano, A.; Akazome, M. *Tetrahedron Lett.* **1998**, *39*, 9051.
8. Ogura, K.; Ohtsuki, K.; Takahashi, K.; Iida, H. *Chem. Lett.* **1986**, 1597.
9. Kunugi, A.; Ikeda, T.; Hirai, T.; Abe, K. *Electrochim. Acta* **1988**, *33*, 905.
10. Nishiguchi, I.; Matsumoto, T.; Kuwahara, T.; Kyoda, M.; Maekawa, H. *Chem. Lett.* **2002**, 478.
11. Breton, G. W.; Kropp, P. J. In *Encyclopedia of Reagents for Organic Synthesis*; Paquette, L. A., Ed.; John Wiley & Sons: Chichester, 1995; Vol. 4, pp 2728–2731; In recent reports as a reducing reagent: (a) Hicks, L. D.; Han, J. K.; Fry, A. J. *Tetrahedron Lett.* **2000**, *41*, 7818; (b) Davies, I. W.; Taylor, M.; Hughes, D.; Reider, P. J. *Org. Lett.* **2000**, *2*, 3385; (c) Gordon, P. E.; Fry, A. J. *Tetrahedron Lett.* **2001**, *42*, 831; (d) Kumar, J. S. D.; Ho, M. M.; Toyokuni, T. *Tetrahedron Lett.* **2001**, *42*, 5601; (e) Kamal, A.; Reddy, P. S. M. M.; Reddy, D. R. *Tetrahedron Lett.* **2002**, *43*, 6629.
12. Gemal, A. L.; Luche, J. L. *Tetrahedron Lett.* **1980**, *21*, 3195.
13. Ferdinand, G.; Schank, K. *Synthesis* **1976**, 406.
14. *General procedure for the reaction of* **4** *with hydrogen iodide*: To a solution of **4** (Y = H) (0.1601 g, 0.501 mmol) in dry toluene (5 mL) was added a 55% aqueous solution of hydrogen iodide (0.1276 g, 0.549 mmol), and the resulting mixture was refluxed for 2 h under nitrogen atmosphere. After the addition of saturated aqueous $Na_2S_2O_3$ (5 mL) and water (1 mL), the mixture was extracted with ethyl acetate (10 mL × 3). The extracts were combined, dried with $MgSO_4$, evaporated, and subjected to silica gel column chromatography (hexane–ethyl acetate = 1.5:1) to give 3-tosyl-2-(tosylmethyl)quinoline (**6**; Y = H) (0.0877 g, 0.194 mmol; 77% yield) as a pale brown solid. Recrystallization from hexane and ethyl acetate gave a pale brown plate crystals: mp 206.5–207.5 °C; ^{1}H NMR (300 MHz, $CDCl_3$): δ 2.43 (s, 3H), 2.45 (s, 3H), 5.23 (s, 2H), 7.28 (d, 2H, J = 8.7 Hz), 7.36 (d, 2H, J = 8.7 Hz), 7.67 (dt, 1H, J = 1.6, 7.1 Hz), 7.69 (d, 2H, J = 8.4 Hz), 7.85 (dt, 1H, J = 1.5, 8.5 Hz), 7.89 (d, 3H, J = 8.4 Hz), 7.96 (d, 1H, J = 8.1 Hz), 8.97 (s, 1H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 21.54, 21.56, 61.0, 126.0, 128.2, 128.7, 128.96, 128.98, 129.1, 129.5, 130.3, 133.1, 135.0, 137.2, 137.6, 140.4, 144.7, 145.2, 146.3, 148.5; IR (KBr) 3081, 3005, 2922, 1597, 1487, 1379, 1319, 1304, 1290, 1157, 1086, 820, 752, 671, 631, 559 cm^{-1}. Anal. Calcd for $C_{24}H_{21}NO_4S_2$: C, 63.84; H, 4.69; N, 3.10. Found: C, 63.75; H, 4.79; N, 3.07.
15. *Crystal data for* **6** *(Y = H)*: $C_{24}H_{21}NO_4S_2$, MW = 451.563, triclinic, space group $P\bar{1}$ (No. 2), Cu K$_\alpha$, $F(000)$ = 472, μ = 2.45 mm^{-1}, a = 10.006(4) Å, b = 10.950(4) Å, c = 11.696(4) Å, α = 100.45(4)°, β = 102.15(3)°, γ = 113.10(3)°, V = 1101.6(7) Å^3, Z = 2, D_{calcd} = 1.361 Mg/m^3, 3549 observed reflections [$I > 3\sigma I$)], parameters 364, $R1$ = 0.038, $wR2$ = 0.082. CCDC 628832.
16. Bhatt, M. V.; Kulkarni, S. U. *Synthesis* **1983**, 249.
17. Truce, W. E.; Brady, D. G. *J. Org. Chem.* **1966**, *31*, 3543.
18. *Reaction of* **5**[16] *with hydrogen iodide*: To a solution of tosylacetylene[19] (0.1035 g, 0.574 mmol) in EtOH (6 mL) was dropwise added a solution of aniline (0.0532 g, 0.571 mmol) in EtOH (4 mL) over a period of 10 min at room temperature. The resulting mixture was stirred for 20 h at that temperature, and concentrated in vacuo. The obtained solid was dissolved in toluene (3 mL), and a 55% aqueous solution of hydrogen iodide (0.0792 g, 0.571 mmol) was added to that solution. The resulting mixture was refluxed for 3 h under nitrogen atmosphere. After the addition of saturated aqueous $Na_2S_2O_3$ (5 mL) and water (1 mL), the mixture was extracted with chloroform (10 mL × 3). The extracts were combined, dried with Na_2SO_4, evaporated, and subjected to silica gel column chromatography (hexane–ethyl acetate = 2:1) to give **6** (Y = H) (0.0362 g, 0.0802 mmol; 53% yield) and 3-tolyl-2-(tosylmethyl)-1,2-dihydroquinoline (**7**) (0.0070 g, 0.0154 mmol; 10% yield). Further purification of **7** by precipitation from hexane and chloroform gave a pale yellow cotton-like solid: mp 205.8–206.3 °C; ^{1}H NMR (300 MHz, $CDCl_3$): δ 2.43 (s, 3H), 2.52 (s, 3H), 3.43 (dd, 1H, J = 1.4, 14.2 Hz), 3.61 (dd, 1H, J = 9.9, 14.2 Hz), 4.56 (ddd, 1H, J = 1.5, 2.1, 9.9 Hz), 5.19 (d, 1H, J = 1.8 Hz), 6.62 (d, 1H, J = 8.1 Hz), 6.77 (dt, 1H, J = 1.0, 7.4 Hz), 7.14 (d, 1H, J = 7.7 Hz), 7.20 (dt, 1H, J = 1.5, 7.4 Hz), 7.25 (d, 2H, J = 8.1 Hz), 7.43 (d, 2H, J = 8.0 Hz), 7.48 (d, 2H, J = 8.4 Hz), 7.55 (s, 1H), 7.79 (d, 2H, J = 8.4 Hz); ^{13}C NMR (75 MHz, $CDCl_3$): δ 21.5, 21.6, 46.6, 57.8, 115.3, 117.4, 119.6, 128.1, 128.2, 128.8, 130.0, 130.2, 133.2, 135.7 (2C), 135.8, 135.9, 142.5, 144.9, 145.2; IR (KBr) 3440 (br), 3082, 2972, 2912, 1595, 1493, 1456, 1406, 1309, 1286, 1244, 1180, 1161, 1130, 1090, 914, 895, 812, 687, 579, 519 cm^{-1}. Anal. Calcd for $C_{24}H_{23}NO_4S_2$: C, 63.55; H, 5.11; N, 3.09; O, 14.11; S, 14.14. Found C, 63.59; H, 5.12; N, 3.09.
19. Waykole, L.; Paquette, L. A. *Org. Synth.* **1987**, *67*, 149.