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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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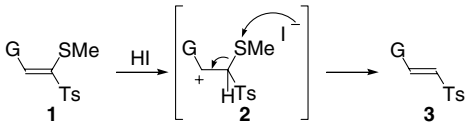
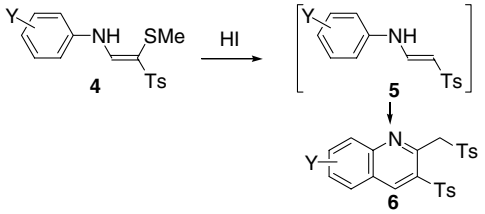
Abstract—The reaction of 2-(arylamino)-1-(methylthio)-1-tosylethenes (**4**) with hydrogen iodide in refluxing toluene gave 3-tosyl-2-(tosylmethyl)quinoline derivatives (**6**) in good yields. In this reaction, hydrogen iodide dose not only reductively removes the methylthio group of **4** to form an 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

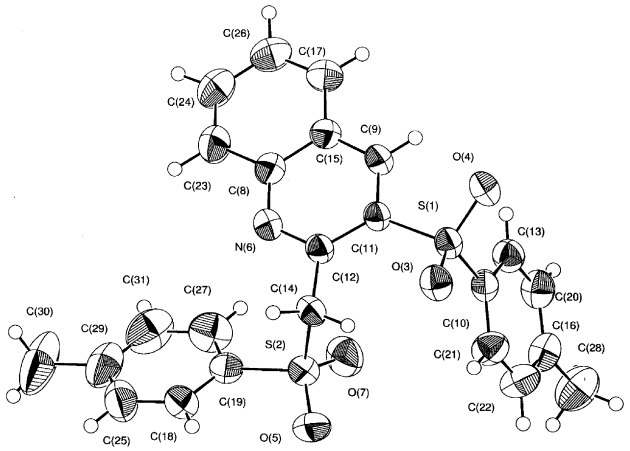
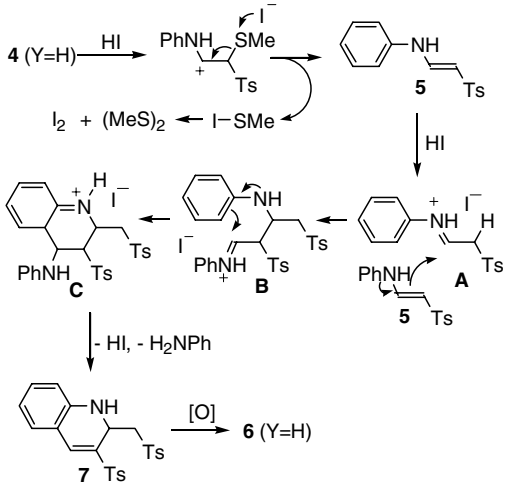


Figure 1. X-ray structure of **6** (Y = H).



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%.