A Novel Reaction Promoted by Hydrogen Polyiodides (HI_{2n+1}): Cyclization of 1-(1*H*-3-Indolyl)-4-(methylthio)-2-(*p*-tolylsulfonyl)-1,3-butadienes Accompanied with 1,2-Sulfonyl Migration

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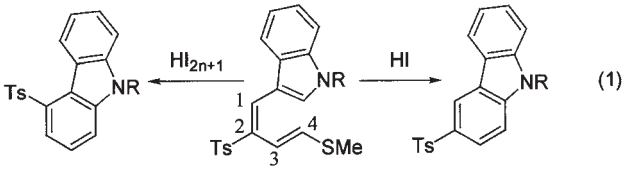
Reaction of 1-(1*H*-3-indolyl)-4-(methylthio)-2-(*p*-tolylsulfonyl)-1,3-butadienes (**1**) with iodine was accompanied with an unusual 1,2-migration of the sulfonyl group to give an abnormal cyclization product (**3**). This 1,2-migration reaction was brought about by the action of hydrogen polyiodides that are produced from excess I_2 and EtSH. It is noteworthy that the reaction of **1** with HI resulted in formation of a normal product (**2**).

Hitherto, hydrogen halides (HX) have been utilized as a proton source in organic synthesis and it is well established for HX to form a complex ($HX{\bullet}nX_2$ or HX_{2n+1}) with halogen molecules (X_2).[1] Especially, hydrogen iodide (HI) complexes more easily with iodine (I_2) to produce a variety of hydrogen polyiodides such as HI_3, HI_5, and so on.[2] We were interested in the difference between HI and hydrogen polyiodide (HI_{2n+1}) in their chemical behavior, but there have been few references.[3] Here, we wish to report that HI_{2n+1} exhibits entirely different chemical reactivity from HI: The reaction of 1-(1*H*-3-indolyl)-4-(methylthio)-2-(*p*-tolylsulfonyl)-1,3-butadienes (**1**) with HI afforded a normal cyclization product (**2**), but the action of HI_{2n+1} on **1** caused an unusual 1,2-migration of the *p*-tolylsulfonyl group to give another cyclization product (**3**) predominantly.



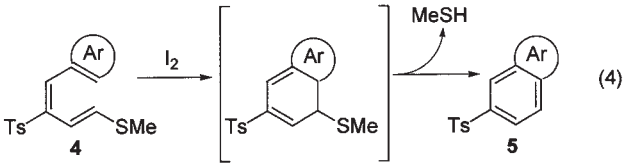
3 **1** **2** (Ts = *p*-TolSO$_2$) (1)

(**a**, R = Me; **b**, R = Ac; **c**, R = H; **d**, R = Ph; **e**, R = *p*-MeO(C_6H_4))

I_2 + RSH ⟶ HI + RSSR (2)

HI + n I_2 ⟷ HI_{2n+1} (3)

Recently, we reported the I_2-promoted cyclization reaction of 1-aryl-4-(methylthio)-2-(*p*-tolylsulfonyl)-1,3-butadienes (**4**) that was followed by elimination of methanethiol to give the corresponding naphthalene derivatives (**5**).[4]

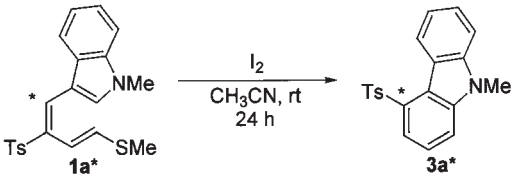


4 **5** (4)

In order to examine the scope and limitation of this reaction, **1** and its regioisomer [**4** (Ar = 1-methyl-1*H*-2-indolyl)] were subjected to the reaction with I_2. Treatment of **4** (Ar = 1-methyl-1*H*-2-indolyl) with I_2 in refluxing acetonitrile gave the normal cyclization product (**5**) as the sole product (97% yield).

To our surprise, 1,2-migration of the *p*-tolylsulfonyl group occurred in the cyclization reaction of **1a** with I_2 to give an abnormal product (**3a**): When **1a** was treated with I_2 (0.6 mol-equiv.) in acetonitrile at room temperature for 24 h, **3a** was produced in 78% yield along with **2a** (11% yield). The structure of **3a** was determined by single-crystal X-ray crystallographic analysis.[5] In order to examine the possibility that the *p*-tolylsulfonyl group migrates via a carbon skeletal rearrangement, we prepared the ^{13}C-labeled **1a*** that has ^{13}C enriched at the 1-position (β to the sulfonyl group). On treatment of the ^{13}C-labeled **1a*** with I_2, the ^{13}C-enriched **3a*** was obtained. Its ^{13}C-NMR spectrum revealed that ^{13}C was enriched at the carbon α to the sulfonyl group. Thus, it was confirmed that **3a** was formed through simple 1,2-migration of the sulfonyl group. It should be noted that the 1,2-migration reaction of a sulfonyl group has been scarcely reported in the literature.[6]

Next, we investigated the factor that brings about the sulfonyl 1,2-migration. As reported in our previous paper, the cyclization reaction of **4** is induced by a proton species such as *p*-toluenesulfonic acid and HI.[4] In the reaction of **1a**, the action of *p*-toluenesulfonic acid or 57% hydroiodic acid resulted in the exclusive formation of **2a**. We generated anhydrous HI and HI_{2n+1} (n = 1, 2, and 3) from I_2 and EtSH that were subjected to the reaction with **1a**. Recently, Chervin and Koreeda reported that the reaction of I_2 with a thiol in $CDCl_3$ or CH_2Cl_2 generates anhydrous HI that is used as a useful reagent for organic synthesis.[7] Therefore, it is likely that, if an excess amount of I_2 is used in the reaction with a thiol, the residual iodine would complex with the generated HI to give a variety of HI_{2n+1}. After a mixture of I_2 (1 mol-equiv.) and EtSH (corresponding amount) was stirred in CH_3CN for 2 h at room temperature, **1a** was added. The results are summarized in Table 1.



1a* **3a*** (5)

When the initial ratio of I_2 : EtSH is 2, HI can be generated[7] and the normal product (**2a**) is predominantly formed. With an increasing ratio of I_2 : EtSH, the ratio of **2a** : **3a** was inverted so that the main product became **3a** as summarized in entries 2–4 of Table 1. Thus, the formation of the abnormal product (**3a**) is attributable to the action of HI_{2n+1} (n = 1, 2, and 3). It is noteworthy that the reaction of **1a** with perchloric acid ($HClO_4$) gave **3a** along with **2a** (entry 5). This seems to imply that protic acids having a bulky anion part cause the transformation of **1a** to **3a**.

Table 1. HI_{2n+1}-promoted reaciton of **1a**

Entry	I_2 : EtSH	Estimated as HI_{2n+1}	Ratio[a]		
			2a		**3a**
1	0.5 : 1	HI	83	:	17
2	1.5 : 1	HI_3	12	:	88
3	2.5 : 1	HI_5	11	:	89
4	3.5 : 1	HI_7	8	:	92
5	—[b]	—	31	:	69

[a]Determined by ^{1}H NMR. [b]$HClO_4$ was used.

The molecular orbital calculation with the PM3 method showed the stable conformation of **1** is distorted around the bond between 2 and 3 carbons (Figure 1).

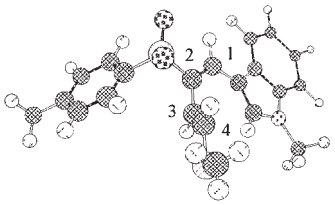
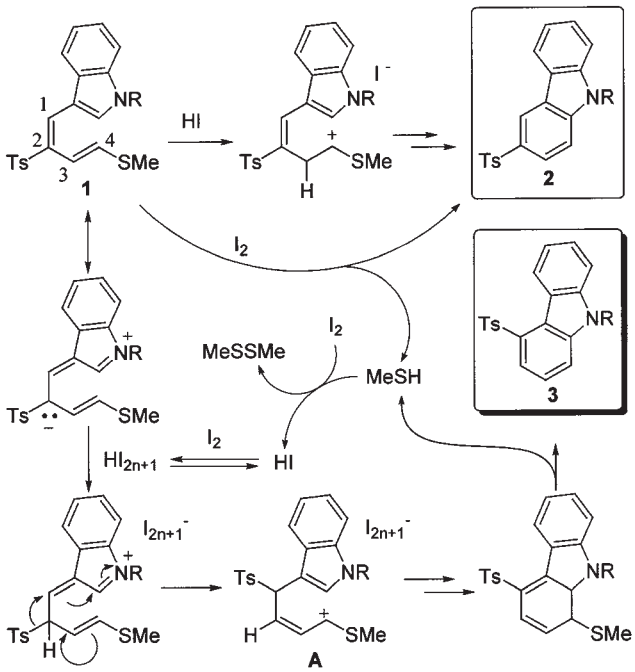


Figure 1. Minimumize structure of **3a** calculated with the PM3.

The normal product (**2**) is thought to result from the attack of I_2 or HI on the 3 carbon as reported previously. In the reaction with I_2, once HI is produced, the remaining I_2 reacts to form HI_{2n+1} that contributes to the formation of the abnormal product (**3**).



Scheme 1.

For the 1,2-migration of a sulfonyl group that is located on an sp^2 carbon, there has been one report:[6a] the 1,2-migration was explained in terms of the attack of a cationic nucleophile on the sp^2 carbon that is converted to an sp^3 carbon, and then the sulfonyl group migrates to the neighboring cationic sp^2 center. If this is applied to the present reaction, a proton attack would occur on the 2-carbon of **1** as shown in Scheme 1. Then, the sulfonyl group migrates to the 1-carbon to produce an intermediary allylic cation (**A**) that is stabilized by the methylthio group. Then, this cation (**A**) is transformed into **3** by intramolecular cyclization followed by removal of the methanethiol moiety. We examined the effect of the substituent at the nitrogen atom of **1** on the product ratio of **2** : **3**. Various derivatives of **1** were treated with I_2 (0.6 mol-equiv.) in CH_3CN for 24 h at room temperature. As a result, an electron-withdrawing acetyl group (**1b**) disturbed the reaction completely. The *N*-phenyl substituent (**1d**) slowed the reaction path leading to the abnormal product (**3d**) to a small extent (72%; **2d** : **3d** = 48 : 52) in comparison with **1a** (89%; **2a** : **3a** = 12 : 88) and **1c** (59%; **2c** : **3c** = 15 : 85). The introduction of a methoxy group on the *N*-phenyl group (**1e**) increased the ratio of **3e** (75%; **2e** : **3e** = 33 : 67). Thus, the formation of **3** is more favorable when a stronger electron-donating group is substituted at the indolyl nitrogen. This is in accordance with the above reaction scheme for the formation of **3**. However, the question why the proton of HI_{2n+1} attacks favorably on the 2-carbon of **1** remains unsolved. A correct answer to this question necessitates further detailed experiments, but it is likely related to the fact that the proton in HI_{2n+1} has a bulky counter anion (I_{2n+1}^-) and, as a result, it becomes more naked, namely, more hard. This is because the anionic 2-carbon is thought to be more hard by the effect of the non-conjugated electron-withdrawing sulfonyl group.

In conclusion, we have found the reaction of 1-(1*H*-3-indolyl)-4-(methylthio)-2-(*p*-tolylsulfonyl)-1,3-butadienes (**1**) accompanied with an unusual 1,2-migration of the sulfonyl group gives an abnormal cyclization product (**3**), that is initiated by the attack of HI_{2n+1} (n = 1, 2, 3). In contrast, HI promoted the formation of the normal product (**2**) from **1**. Since the HI_{2n+1} species can be conveniently prepared by the reaction of excess amount of I_2 with a thiol (EtSH in the present case), the present results promise the HI_{2n+1} species provides a clue to the development of new organic reactions.

Dedicated to celebrate 75th birthday of Professor Emeritus Teruaki Mukaiyama.

References and Notes

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5 Crystal data for **3a**: $C_{20}H_{17}NO_2S$, MW = 335.40, $P\bar{1}$, a = 8.019(3), b = 70.772(3), c = 19.175(4) Å, a = 88.61(2), β = 88.23(2), γ = 81.48(3), V = 1637.1(9) Å^3, Dc = 1.360 Mg/m^3, Z = 4, crystal size = 0.2 × 0.2 × 0.04 mm, λ = 1.5418 Å, μ = 18.473 mm^{-1}, T = 298 K, θ range = 27.12 to 29.89°, Final R = 0.079, wR = 0.074.

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