Modified Synthesis of Iododihydropyrrole by Iodine-mediated Cyclization

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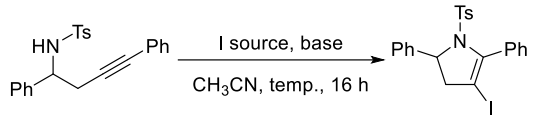
Development of the synthesis of iodine-containing compounds is important under environmentally benign and inexpensive conditions. Ding and co-workers reported that iododihydropyrroles were obtained by the reaction of *N*-tosyl-4-amino-1-butynes with iodine and potassium carbonate in the presence of silver acetate,[1)] which is somewhat expensive. Herein, we will report the simple methods without silver acetate.

We examined the reaction of *N*-tosyl-4-amino-1-butynes without silver acetate (Table 1). Iodine monochloride was not a suitable source of iodine (Entries 1 and 2). The yield was improved with 3 equivalents of iodine under reflux conditions (Entries 3-8). Using lithium carbonate as the base, the yield was significantly improved (Entry 10). Those reaction conditions exceeded the yield of the reported method (69%).[1)]

Table 1

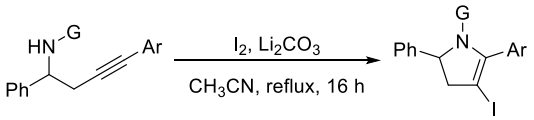


Entry	I source (x equiv.)	Base	Temp.	Yield (%)[a)]
1	ICl (3.0)	$NaHCO_3$	r.t.	trace
2	ICl in aq. HCl (3.0)	$NaHCO_3$	r.t.	0
3	I_2 (3.0)	$NaHCO_3$	r.t.	60[b)]
4	I_2 (3.0)	$NaHCO_3$	50 °C	71
5	I_2 (3.0)	$NaHCO_3$	reflux	72
6	I_2 (1.0)	$NaHCO_3$	refrux	51
7	I_2 (2.0)	$NaHCO_3$	reflux	61
8	I_2 (4.0)	$NaHCO_3$	reflux	49
9	I_2 (3.0)	K_3PO_4	reflux	34
10	I_2 (3.0)	Li_2CO_3	reflux	90
11	I_2 (3.0)	Na_2CO_3	reflux	68
12	I_2 (3.0)	K_2CO_3	reflux	45
13	I_2 (3.0)	CS_2CO_3	reflux	53

a) Determined by the integration of ^{1}H NMR using hydroquinone dimethyl ether as an internal standard. b) Isolated by column chromatography.

We also examined the substituent effect on triple bond (Scheme 1). The excellent yield was obtained in *m*- and *p*-substituents whereas the *o*-substituent gave low yield. Both electron-donating (Me) and electron-withdrawing (CF_3) substituents gave the good yield. But the complex mixture was obtained in the case of Ph substituent on nitrogen atom instead of Ts group. It suggests that the achievement of the iododihydropyrrole formation is strongly influenced by the substituent on nitrogen atom.

Scheme 1



G = Ts, Ar = *o*-MeC_6H_4	11%
G = Ts, Ar = *m*-MeC_6H_4	87%
G = Ts, Ar = *p*-MeC_6H_4	99%
G = Ts, Ar = *p*-$CF_3C_6H_4$	77%
G = Ph, Ar = Ph	0%

1) Ding, C. H.; Dai, L. X.; Hou, X. L. *Tetrahedron* **2005**, *61*, 9586–9593.