# A new approach towards the synthesis of sp$^3$ 1,1-diiodoalkanes

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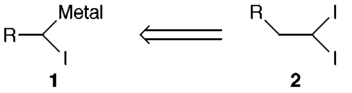
**An easy and straightforward method for the synthesis of *gem*-diiodo derivatives is reported.**

Carbenoids **1**, in which a single carbon atom carries both a metal atom and a leaving group, are valuable reactive molecules and have been used extensively in organic synthesis.[1] They are generally prepared from *gem*-dihaloalkanes by metal–halogen exchange and more specifically from 1,1-diiodoalkanes **2** since they are far more reactive than the corresponding other halogens; in some cases iodides are the only reactive halides[2] [eqn. (1)].



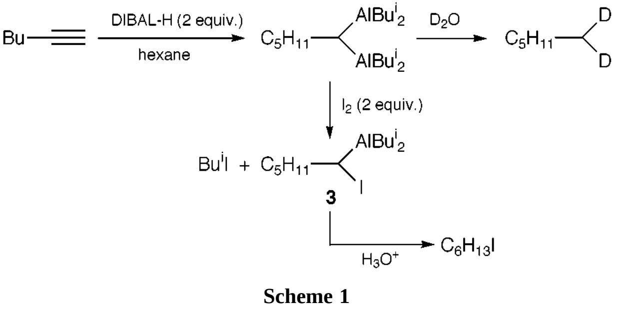
(1)

Unfortunately, they are also more difficult to prepare because of this high C–I bond reactivity. Indeed, few methods have been reported for their preparation[3] and to date, the more versatile approach is based on the alkylation of the diiodomethyllithium or diiodomethylsodium with reactive electrophiles.[4] The major drawback of this strategy is that these reactants are unstable at temperatures above −95 °C, which preclude their preparation on a large scale. So, in the course of our studies on the synthesis and reactivity of carbenoids,[5] we needed a more general approach for the preparation of 1,1-diiodoalkanes allowing access to a large variety of carbon skeletons on multigram scales. For this purpose, we have investigated the iodolysis of 1,1-bis(diisobutylalumino)alkanes,[6] which are readily accessible *via* double hydroalumination of alk-1-ynes.[7] As expected the deuterolysis of 1,1-bis(diisobutylalumino)hexane gave us 1,1-dideuterohexane in good chemical yield (which proved the presence of the 1,1-bisanion) but the addition of 2 equiv. of $I_2$ gave only the 1-iodohexane, as described in Scheme 1.

In order to obtain *gem*-diiodohexane, it was necessary to add more than 6 equiv. of $I_2$ since each isobutyl group on the aluminium atom reacts faster than the carbenoid **3**. To overcome this large excess of iodine, we thought to use a hydroaluminating reagent with nontransferable alkyl groups, such as dichloroaluminium hydride[8] ($HAlCl_2$). This is easily obtained by mixing $AlCl_3$ with $LiAlH_4$[9] as described in eqn. (2).

The LiCl formed during the preparation of $HAlCl_2$ is not troublesome for the following step and no separation was required. The double hydroalumination of various alkynes with $HAlCl_2$ occurs in very high yields ( > 95%) even on a large scale (except entry 3, Table 1). Moreover, the addition of 2 equiv. of $I_2$ at 0 °C leads now to the formation of 1,1-diiodoalkane derivatives as described in Scheme 2 and in Table 1.

$$3\ AlCl_3 + LiAlH_4 \xrightarrow{Et_2O} 4\ AlCl_2H + LiCl \qquad (2)$$



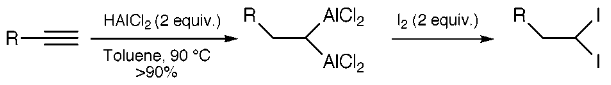
**Scheme 1**

The results reported in Table 1 fulfil our expectations. In the experiments described in the entries 1, 2 and 6 the yields in 1,1-diiodoalkanes are good.

**Table 1** Synthesis of 1,1-diiodoalkanes

| Entries | R | Compounds | Yield (%)[a] |
|---|---|---|---|
| 1 | Hexyl | **4** | 81 |
| 2 | Octyl | **5** | 75 |
| 3 | Bu$^t$ | **6** | 52 |
| 4 | Ph | **7** | 50 |
| 5 | $PhCH_2$ | **8** | 46 |
| 6 | $PhCH_2CH_2$ | **9** | 75 |

[a] Isolated yields after hydrolysis.



**Scheme 2**

For the double hydroalumination of *tert*-butylacetylene (entry 3) the yield is lower since it was difficult to obtain in good yield the corresponding 1,1-bis(dichloroalumino)-3,3-dimethylbutane (the starting material is very volatile). The presence of an electon-withdrawing substituent on the triple bond, as in phenylacetylene (entry 4), increases the acidity of the acetylenic hydrogen and hence leads to increased metalation during the double hydroalumination. Thus, the reaction of phenylacetylene with 2 equiv. of $HAlCl_2$ in toluene gives the expected product but a possible metalation of the triple bond could impair the yield of the bis-alane (entry 4). In a similar way, when the reaction is performed on 3-phenylprop-1-yne (entry 5), the presence of acidic benzylic and propargylic hydrogens decrease the yield. Moreover, the hydrolysis of the reaction mixture is also a crucial step and needs to be done at 0 °C. Indeed, after iodinolysis, 2 equiv. of the strong Lewis acid $IAlCl_2$ are present in the reaction and can affect the chemical yield (see experimental procedure[10]).

In conclusion, we have elaborated a new and straightforward approach for the one-pot synthesis of sp$^3$ 1,1-diiodoalkanes in good yield *via* the synthesis of 1,1-bis(dichloroalumino)alkanes. Low temperature is not required (90 °C for the bismetallic synthesis and 0 °C for the reaction with $I_2$) and the method has been applied to large scale preparations.

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9 The $LiAlH_4$ was used as an ethereal solution which was titrated either by the iodometric method (H. Felkin, *Bull. Soc. Chim. Fr.*, 1951, **18**, 347) or with salicylaldehyde phenylhydrazone as indicator (B. E. Love and E. G. Jones, *J. Org. Chem.*, 1999, **64**, 3755).

10 *Experimental procedure*: To a suspension of $AlCl_3$ (0.66 g, 4.95 mmol, 1.65 equiv.) in 3 ml of pentane and 7.5 ml of $Et_2O$ was added an ethereal solution of $LiAlH_4$ (1.09 M, 1.51 ml, 1.65 mmol, 0.55 equiv.) at room temperature. After stirring for 5 min, the solvents were removed at room temperature under vacuum (20 mmHg) through $CaCl_2$ to give a white suspension of LiCl and $HAlCl_2$ (6.6 mmol, 2.2 equiv.). 6 ml of toluene was then added, followed by dec-1-yne (0.415 g, 3 mmol, 1 equiv.). The reaction mixture was heated at 90 °C for 3 h to give the 1,1-bis(dichloroalumino)decane. After cooling to 0 °C, 20 ml of THF was added and a solution of $I_2$ (1.675 g, 6.6 mmol, 2.2 equiv.) in 20 ml of cold THF was then added. The reaction mixture was allowed to warm to room temperature and stirred for 15 min. The reaction mixture was then transferred into a cold solution (0 °C) of aqueous HCl (1 M, 100 ml). After stirring for 5 min, the aqueous layer was extracted with $Et_2O$, the collected organic phases were washed with aq.$Na_2S_2O_3$ and saturated brine, and then dried over $MgSO_4$. After filtration and evaporation of the solvents, the residue was chromatographed on silica gel.

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