



Bis-(trifluoroacetoxy)iodobenzene - Iodine System: An Efficient and Selective Reagent for Iodination of Thiophene Derivatives

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Abstract - Bis-(trifluoroacetoxy)iodobenzene - iodine system is a good iodinating reagent of thiophene derivatives giving products with iodine atom in α -position on the thiophene ring.

In our previous papers we used iodothiophene derivatives as starting materials in various photochemical reactions.¹ Consequently, we are interested in the development of new synthetic strategies for these starting materials.² In fact, the preparation of some compounds of this class are very tedious: i.e., the preparation of 5-iodothiophene-2-carbaldehyde requires reduction of thiophene-2-carbaldehyde, iodination and re-oxidation of the alcoholic function.³ 5-Iodothiophene-2-carbonitrile can be prepared only starting from the corresponding aldehyde *via* oxime dehydration.⁴ Finally, methyl 5-iodothiophene-2-carboxylate can be obtained from the ester *via* reaction with iodine, iodic acid, acetic acid, water, carbon tetrachloride, and sulphuric acid.⁵ Generally, we have to consider that with electron-withdrawing 2-substituents, substitution occurs on both 4- and 5-position.⁶

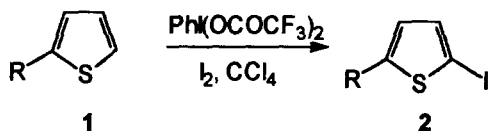
In this context we decided to test the reactivity towards thienyl derivatives of phenyliodosotrifluoroacetate,^{7,8} a reagent not widely used in heterocyclic chemistry.^{9,10} This reagent, in the presence of iodine, gave good yields of the corresponding iodination products rapidly at room temperature. The reaction was rationalised as an electrophilic reaction on an aromatic substrate of trifluoroacetylhypiodide (CF_3COOI), due to the reaction between the reagent and iodine.⁷

In a typical experimental procedure 1.2 mmoles of the substrate (1) were dissolved in carbon tetrachloride (1.5 ml) and treated with iodine (152 mg) and bis-(trifluoroacetoxy)iodobenzene (280 mg). After 2 h, the usual work-up⁷ gave the crude product that was chromatographed on silica gel to give pure 2 (Table 1).

The data collected in Table 1 clearly show that, by using the above reaction conditions, we obtained only the product bearing iodine in the α -position of the thiophene ring. This behaviour is quite general: it occurs using electron releasing groups (Table 1, entry 5), halogen atom (Table 1, entries 2, 3, and 4), and electron withdrawing groups (Table 1, entries 6 - 10).

Furthermore, we observed (GC-MS) the formation of only traces of diiodination products for all the substrates with the exception of 2-nitrothiophene. In this case (Table 1, entry 10) we observed the formation of *ca.* 15% of 2,3-diiodo-5-nitrothiophene.

Table 1



| Entry | R | Yields (%) ^a |
|-------|---------------------------------|-------------------------|
| 1 | H | 83 |
| 2 | Br | 87 |
| 3 | Cl | 85 |
| 4 | I | 87 |
| 5 | CH ₃ | 78 |
| 6 | CHO | 59 |
| 7 | COCH ₃ | 69 |
| 8 | CO ₂ CH ₃ | 78 |
| 9 | CN | 71 |
| 10 | NO ₂ | 50 |

a) All the yields refer to isolated chromatographically pure compounds.

In conclusion, we think that the reagent obtained from bis-(trifluoroacetoxy)iodobenzene and iodine is a useful iodinating reagent in the synthesis of heterocyclic derivatives.

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