Studies toward the synthesis of the L-thyroxine hormone.

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Keywords: total synthesis, L-thyroxine, T4 hormone

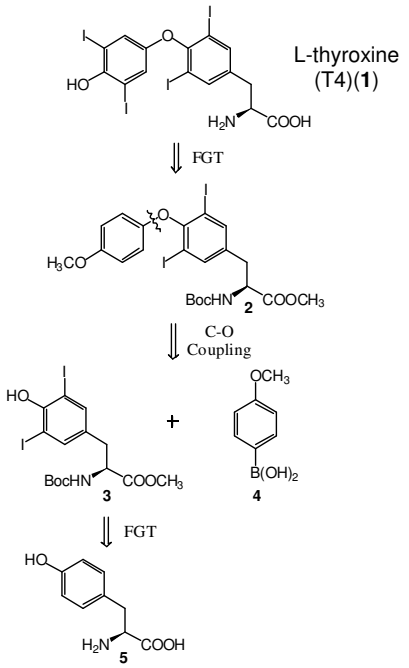
INTRODUCTION

L-Thyroxine (T4) (**1**) is a hormone produced by the thyroid gland. The thyroid gland uses iodine, from exogenous sources, to produce L-thyroxine (**1**), which acts as a precursor of 3,5,3'-triiodothyronine (T3). Individuals with low levels of T4 and T3 can suffer from hypothyroidism. Accordingly, L-thyroxine (**1**) has been indicated for the treatment of this type of endocrine disorder. Although since 1927 the production of the T4 hormone is carried out in laboratory,[1] short synthetic routes involving mild reaction conditions to obtain this important substance are still of considerable interest. In this work we show our preliminary results toward the synthesis of L-thyroxine (**1**) employing a route that will use in two steps an efficient and selective diiodination reaction developed in our research group.[2]

RESULTS AND DISCUSSION

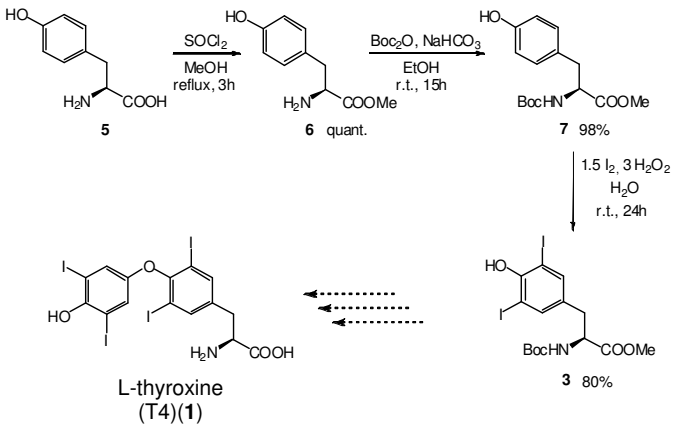
Initially, we present the retrosynthetic analysis for L-thyroxine (**1**) (**Scheme 1**).

Scheme 1. Retrosynthetic analysis for L-thyroxine (**1**).



Reaction of the amino acid L-tyrosine (**5**) with thionyl chloride in methanol led to the formation of the L-tyrosine methyl ester (**6**) in quantitative yield. Next, the ester **6** had its amino group selectively protected with di-*tert*-butyl dicarbonate resulting in the *N*-Boc-L-tyrosine methyl ester (**7**) in an isolated yield of 98%. Afterwards, compound **7** was subjected to the diiodination reaction, which uses iodine and hydrogen peroxide (30%) in water at room temperature for 24 hours, producing the diiodinated intermediate **3** in a good yield of 80% (**Scheme 2**).

Scheme 2. Sequence of reactions toward the synthesis of L-thyroxine (**1**).



CONCLUSION

In this work we present the synthesis of the diiodinated intermediate **3**, obtained by an efficient and selective diiodination reaction developed in our research group, which will be employed in the production of L-thyroxine (T4) (**1**).

ACKNOWLEDGEMENTS

We acknowledge CNPq and FUNDECT for financial support.

REFERENCES

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