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A Direct Preparation of N-Unsubstituted Pyrrole-2,5-dicarboxylates from 2-Azidocarboxylic Esters

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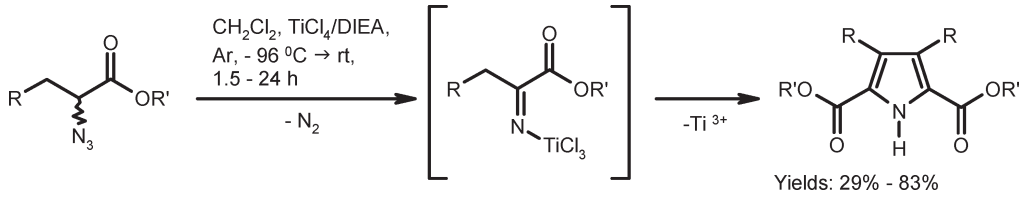
ABSTRACT



A new and easy method for synthesis of symmetric pyrrole-2,5-dicarboxylate derivatives via a simple titanium(IV)-mediated oxidative dimerization of 2-azidocarboxylic esters is described. The process involves a transformation of titanium(IV) enolates into nonisolated 2-iminoesters, which undergo an oxidative coupling and ring closure to give the aromatic pyrrole system. A mechanism, scope and limitations of the new method are discussed.

Pyrrole-2,5-dicarboxylates have many applications in various fields of medicinal and bioorganic chemistry, phytochemistry, and materials science and as building blocks for synthesis of chiral catalysts and natural products. The 3,4-diaryl-substituted pyrrole ring bearing 2,5-dicarboxylates is a structural subunit found in marine natural products ningalin A and storniamide A, which are precursors of cytotoxic antitumor agents.[1] Similarly, the pyrrole-2,5-dicarboxylate core has been indicated in chromopyrrolic acid (CPA), which is the key intermediate of biosynthesis of cytotoxic indolocarbazoles[2] and in some bisindole alkaloids isolated from *Arcyria cinerea* and *Lycogala epidendrum*.[3] Symmetrical 3,4-disubstituted pyrrole-2,5-dicarboxylates have found utility in the preparation of modified porphyrins[4] and as useful precursors of novel chiral ancillary ligands designed for molecular catalysis.[5] Some amide and thioamide derivatives of the 1*H*-pyrrole-2,5-dicarboxylic acid have been synthesized and investigated as a new group of neutral anion receptors because of their complexation properties.[6] In the past decade, a very intensive exploration of pyrrole-2,5-dicarboxylic acid derivatives has been observed in the area of research on self-assembling systems and self-organization processes, development of novel "intelligent" materials with tailor-made properties, and the search for new self-folding molecules.[7]

The growing interest in the applications and efficiency of 1*H*-pyrrole-2,5-dicarboxylate derivatives has led to two main synthetic approaches.[8] Simple, unsubstituted at C-3 and C-4 1-*H*-pyrrole-2,5-dicarboxylates are prepared directly from

(1) Boger, D. L.; Boyce, C. W.; Labroli, M.; Sehon, C. A.; Jin, Q. *J. Am. Chem. Soc.* **1999**, *121*, 54–62.
(2) Howard-Jones, A.; Walsh, C. T. *J. Am. Chem. Soc.* **2007**, *129* (36), 11016–11017.
(3) Kamata, K.; Kiyota, M.; Nade, A.; Nakatani, S.; Yamamoto, Y.; Hayashi, M.; Komiyama, K.; Yamori, T.; Ishibashi, M. *Chem. Pharm. Bull* **2005**, *53* (5), 594–597.
(4) (a) Kaesler, R. W.; LeGoff, E. *J. Org. Chem.* **1982**, *47*, 5243–5246. (b) Whitlock, Jr., H. W.; Hanauer, R. *J. Org. Chem.* **1968**, *33* (5), 2169–2171.
(5) Mazet, C.; Gade, L. H. *Eur. J. Inorg. Chem.* **2003**, 1161–1168.
(6) (a) Zielinski, T.; Jurczak, J. *Tetrahedron* **2005**, *61*, 4081–4089. (b) Dobrzycki, L.; Zielinski, T.; Jurczak, J.; Wozniak, K. *J. Phys. Org. Chem.* **2005**, *18*, 864–869.
(7) (a) Schmuck, C. *Chem. Commun.* **1999**, 843–844. (b) Schmuck, C. *Eur. J. Org. Chem.* **1999**, 2397–2403. (c) Schmuck, C. *J. Org. Chem.* **2000**, *65* (8), 2432–2437. (d) Schmuck, C.; Lex, J. *Eur. J. Org. Chem.* **2001**, 1519–1523. (e) Schmuck, C.; Wienand, W. *J. Am. Chem. Soc.* **2003**, *125* (2), 452–459. (f) Lin, Q.; Geib, S. J.; Hamilton, A. D. *J. Chem. Soc., Perkin Trans. 2* **1998**, 2109–2116.

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