N,*N*′-Carbonyldiimidazole as a reagent of choice for the synthesis of thienyl-substituted pyrrolidine-2,5-diones

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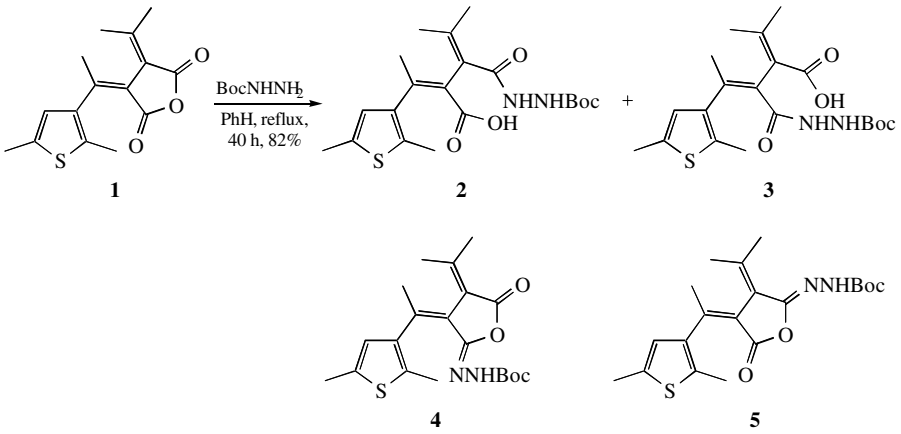
10.1070/MC2003v013n04ABEH001761

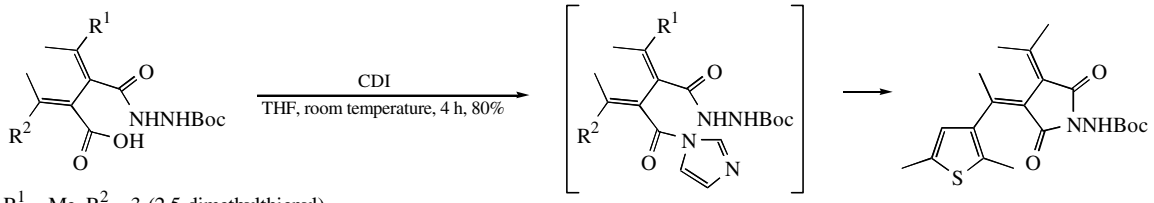
N-tert-Butyloxycarbonylamino-3-[*Z*-α-(2,5-dimethyl-3-thienyl)ethylidene]-4-isopropylidenepyrrolidine-2,5-dione was prepared in 80% yield from the corresponding isomeric hydrazidic acids using *N*,*N*′-carbonyldiimidazole, whereas a number of other cyclisation reagents were ineffective.

Within the framework of our investigation of photochromic thiophene derivatives, we had to prepare *N-tert*-butyloxycarbonylamino-3-[*Z*-α-(2,5-dimethyl-3-thienyl)ethylidene]-4-isopropylidenepyrrolidine-2,5-dione. The reaction of 3-[*Z*-α-(2,5-dimethyl-3-thienyl)ethylidene]-4-isopropylidene-2,5-furanidinedione[1] (fulgide) **1** with *tert*-butyloxycarbonylhydrazine was chosen as the best synthetic pathway. Note that the synthesis of fulgide **1** is multistage; therefore, a simple and efficient method leading from compound **1** to *N-tert*-butyloxycarbonylamino-3-[*Z*-α-(2,5-dimethyl-3-thienyl)ethylidene]-4-isopropylidenepyrrolidine-2,5-dione **8** and its derivatives is of prime interest.

The reaction between **1** and *tert*-butyloxycarbonylhydrazine in refluxing benzene for 40 h led (Scheme 1) to a mixture of isomeric hydrazidic acids **2** and **3** in 82% yield (in a ratio of 3:1, as was determined by HPLC (eluent: acetonitrile–aqueous phosphate buffer, 60:40). However, the preparation of aminoimide **8** from acids **2** and **3** unexpectedly appeared to be a challenge. Whereas the standard cyclisation reagents (*e.g.*, acetyl chloride or trifluoroacetic anhydride) were unsuitable since their application would cause inevitable cleavage of the Boc group, all our attempts to prepare compound **8** from acids **2** and **3** using protocols for the conversion of sensitive amido acids to imides were unsuccessful. The yields of compound **8** were low, or no traces of **8** at all were detected (Table 1). Furthermore, in a number of experiments, isoimides **4** and **5** (identified by their IR and mass spectra†), which are isomeric to **8**, were formed as major products. The attention should be devoted to the fact that attempts to isomerise isoimides **4** and **5** to **8** in accordance with previously described methods[2,3] were fruitless. Thus, even the prolonged (for 100 h) reflux of isoimides **4** and **5** in THF or benzene with triethylammonium acetate or sodium acetate did not cause the expected isomerisation to **8** and only starting compounds **4** and **5** were detected.

It is well known that *N*,*N*′-carbonyldiimidazole (CDI) reacts readily with carboxylic acids to form acylimidazolides, which are potent acylating agents. Thus, CDI can be applied to the cyclisation of amido acids to imides.[6] This property of CDI allowed us to assume that it can promote the required cyclization of **2** and **3** to **8**. Indeed, the reaction of acids **2** and **3** with CDI in THF for 4 h at room temperature afforded **8** in 80%





2 R^1 = Me, R^2 = 3-(2,5-dimethylthienyl)
3 R^1 = 3-(2,5-dimethylthienyl), R^2 = Me

6 R^1 = 3-(2,5-dimethylthienyl), R^2 = Me
7 R^1 = Me, R^2 = 3-(2,5-dimethylthienyl)

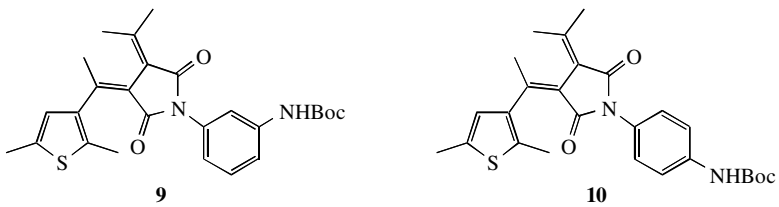


Table 1 Reactions of compounds **2** and **3** with cyclisation reagents.

Reagent	Conditions	Yield of **8** (%)	Notes	Ref.
Thermal dehydration	Heating in DMF or refluxing in *m*-xylene	0	Heavy formation of tar	
$Ti(OPr^i)_4$	THF, room temperature, 24 h	0		4
$ClCO_2Et–Et_3N$	CH_2Cl_2, 0 °C, 1 h	0	Isoimides **4** and **5** as major products	2
Dicyclohexylcarbodiimide (DCC)	CH_2Cl_2, room temperature, 3 h	10	Isoimides **4** and **5** as major products	2, 3
$Me_3SiNHSiMe_3–ZnCl_2$	PhH, reflux, 4 h	26		5
$HC(OMe)_2NMe_2$	THF, room temperature, 48 h	30		
$Ac_2O–Et_3N$	CH_2Cl_2, 0 °C, 3 h	36	40% isoimides	2
N,*N*′-carbonyldiimidazole	THF, room temperature, 4 h	80		6

yield. The five-membered imide ring is formed apparently *via* intermediates **6** and **7**, which undergo the elimination of imidazole thus forming **8**. The structure of **8** was unequivocally confirmed by NMR and IR spectroscopy, mass spectrometry and elemental analysis. In a similar manner, *m*-*tert*-butyloxycarbonylaminophenyl-3-[*Z*-α-(2,5-dimethyl-3-thienyl)ethylidene]-4-isopropylidenepyrrolidine-2,5-dione **9** and *p*-*tert*-butyloxycarbonylaminophenyl-3-[*Z*-α-(2,5-dimethyl-3-thienyl)ethylidene]-4-isopropylidenepyrrolidine-2,5-dione **10** were prepared in 50‡ and 70% yields, respectively.

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Received: 16th April 2003; Com. 03/2087

† Compounds **4**, **5** and **8**–**10** were characterised using spectroscopic methods and elemental analysis.

4 and **5**: MS, *m*/*z*: 390 (M^+). IR (KBr, ν_{max}/cm^{-1}): 1795, 1683.

8: ^{1}H NMR (250 MHz, $CDCl_3$) δ: 1.45 (s, 9H), 1.98 (s, 3H), 2.08 (s, 3H), 2.3 (s, 3H), 2.41 (s, 3H), 2.44 (s, 3H), 6.31 (s, 1H), 6.51 (s, 1H). MS, *m*/*z*: 391 (M + 1), 390 (M^+), 319, 275, 260, 217, 203, 189, 137, 112, 57. IR (KBr, ν_{max}/cm^{-1}): 1764, 1736, 1704, 1252, 1160, 804. Found (%): C, 61.44; H, 6.94; S, 8.04; N, 7.25. Calc. for $C_{20}H_{26}N_2O_4S$ (%): C, 61.52; H, 6.71; S, 8.21; N, 7.17.

9: ^{1}H NMR (250 MHz, $CDCl_3$) δ: 1.49 (s, 9H), 2.02 (s, 3H), 2.12 (s, 3H), 2.33 (s, 3H), 2.39 (s, 3H), 2.47 (s, 3H), 6.48 (s, 1H), 6.54 (s, 1H), 6.97 (d, 1H, *J* 6.8 Hz), 7.24 (d, 1H, *J* 7.57 Hz), 7.30 (t, 1H, *J* 8.33 Hz), 7.41 (s, 1H). IR (KBr, ν_{max}/cm^{-1}): 1756, 1720, 1700. Found (%): C, 67.04; H, 6.55; S, 6.87; N, 6.04. Calc. for $C_{26}H_{30}N_2O_4S$ (%): C, 66.92; H, 6.48; S, 6.87; N, 6.00.

10: ^{1}H NMR (250 MHz, $CDCl_3$) δ: 1.51 (s, 9H), 2.02 (s, 3H), 2.12 (s, 3H), 2.33 (s, 3H), 2.4 (s, 3H), 2.48 (s, 3H), 6.51 (s, 1H), 6.54 (s, 1H), 7.23 (d, 2H, *J* 7.5 Hz), 7.37 (d, 2H, *J* 8.33 Hz). MS, *m*/*z*: 467 (M + 1). IR (KBr, ν_{max}/cm^{-1}): 1756, 1728, 1708. Found (%): C, 66.65; H, 6.54; S, 6.37; N, 6.18. Calc. for $C_{26}H_{30}N_2O_4S$ (%): C, 66.92; H, 6.48; S, 6.87; N, 6.00.

‡ The intermediate amido acid was not isolated, and the yield was calculated for starting compound **2**.