CROATICA CHEMICA ACTA CCACAA **65** (4) 847–849 (1992)

ISSN 0011-1643
UDC 547
CCA—2033

Preliminary Communication

Synthesis of New Heteropolycyclic Bis-Carboxamide: 3,5-Dichloro-*N,N'*(*p*-Chlorophenyl)dithieno [3,2-b:2',3'-d]Furan-2,6-Carboxamide

Grace M. Karminski-Zamola, Miroslav Malešević, Miroslav Bajić and Gordan Golja*

Department of Organic Chemistry, Faculty of Chemical Engineering and Technology, University of Zagreb, 41000 Zagreb, Croatia

Received September 21, 1992

New heteropolycyclic bis-carboxamide **5** was synthesized in multistep synthesis starting from furylacrylic acid (**1**). This type of compounds are now being examined as potential anti-AIDS agent. The most important stage in the multistep synthesis is the preparation of intermediate 3,5-dichloro-dithieno[3,2-b:2',3'-d]furan-2,6-dicarbonyl chloride (**4**).

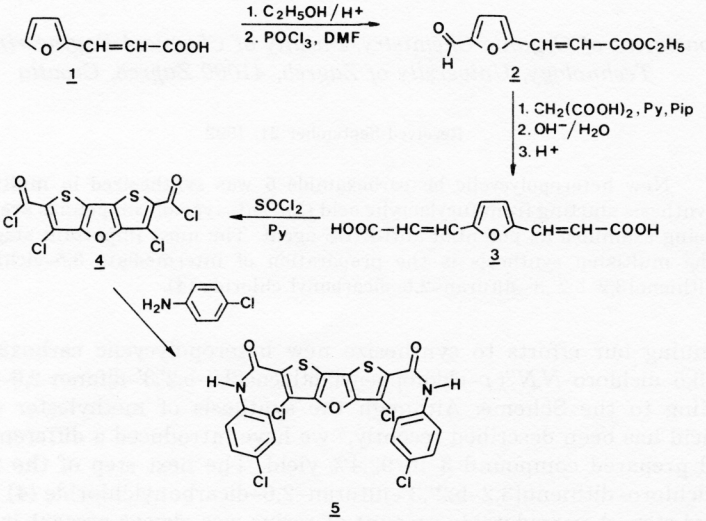
Continuing our efforts to synthesize new heteropolycyclic carboxamides,[1–4] we prepared 3,5-dichloro-*N,N''*(*p*-chlorophenyl)dithieno[3,2-b:2',3'-d]furan-2,6-dicarboxamide (**5**) according to the Scheme. Although the synthesis of methylester of 2,5-furandiacrylic acid has been described recently,[5] we have introduced a different way of synthesis and prepared compound **3** in 92.4% yield. The next step of the reaction of **3** into 3,5-dichloro-dithieno[3,2-b:2',3'-d]furan-2,6-dicarbonylchloride (**4**) was the most complicated step. A considerable amount of resins was always present in the reaction mixture. The best results were obtained when the reaction time was about 30 hours. This step is also the most important one because it is the first example of the synthesis of one dithieno[3,2-b:2',3'-d]furan derivative.

After conversion in ethyl ester, furylacrylic acid (**1**) (34 g, 0.175 mole) was formylated with $POCl_3$ in the presence of DMF by Vilsmeier-Haack method[4] into ethyl 3-(5-formyl-2-furyl)acrylate (**2**) (21 g, 62.03%), m.p. 81 °C; IR(cm^{-1}): 1710(COOEt), 1675(CHO), 1635(C=C); ^1H NMR($CDCl_3$, δ/ppm): 9.84 (s,1H,CHO), 7.67(d,1H, J = 17.7 Hz, H-ethylenic), 7.29 (d,1H, $J_{3,4}$ = 3.3 Hz, H-4 furanic), 6.98(d,1H, $J_{3,4}$ = 3.3 Hz, H-3 furanic), 6.60(d,1H, J = 17.7 Hz, H-ethylenic), 4.26(q,2H, J = 7.8 Hz, CH_2), 1.33(t,3H, J = 7.8 Hz, CH_3).

* To whom correspondence should be addressed.

2 (30.25 g, 0.156 mole) was condensed with malonic acid in pyridine and, in the presence of a few drops of piperidine, into mono-ethyl ester of 2,5–furan–diacrylic acid; m.p. 169 °C; IR(cm^{-1}): 1705(COOEt), 1650(COOH), 1630(C=C); ^{1}H NMR($CDCl_3$, δ/ppm): 7.41(d,2H, J = 15.82 Hz),H–3,H–3', ethylenic), 6.68(s,2H,H–3,H–4 furanic), 6.44(d,1H, J = 15.82 Hz, H–2 ethylenic), 6.41(d,1H, J = 15.82 Hz, H–2' ethylenic), 4.26(q,2H, J = 7.32 Hz, CH_2), 1.33(t,3H, J = 7.8 Hz, CH_3). This compound was hydrolized into 2,5–-furandiacrylic acid (**3**) (27.7 g, 92.45%), m.p. > 320 °C; IR(cm^{-1}): 1670(COOH), 1640(C=C); ^{1}H NMR($CDCl_3$, δ/ppm): 12.36(s,2H,COOH), 7.37(d,2H, J = 17.7 Hz, H-ethylenic), 6.98(s,2H, furanic), 6.37(d,2H, J = 17.7 Hz, H-ethylenic).

Compound **3** (5 g, 0.024 mole) reacted with $SOCl_2$ in the presence of pyridine.[6] Dichloride **4** (0.585 g, 11.3%) was obtained as brown crystals, m.p. 191 °C; IR(cm^{-1}): 1750(COCl). Dichloride **4** (0.4 g, 0.01 mole) reacted with *p*-chloroaniline (2.55 g, 0.02 mole) in benzene and dicarboxamide **5** (0.27 g, 44%) was obtained, m.p. 262 °C; IR(cm^1): 3400(NH), 1670(CONH); ^{1}H NMR(DMSO–d_6, δ/ppm): 10.37(s,2H,NH), 7.76(d,4H, J =11.5 Hz, H-arom.), 7.41(d,4H, J = 11.5 Hz, arom.).



Scheme

REFERENCES

1. M. Orlić-Nuber, M. G. Karminski-Zamola, L. Fišer-Jakić, and K. Jakopčić, *Bull. Soc. Chim.* (Beograd) **48** (1983) 415.
2. L. Fišer-Jakić and M. G. Karminski-Zamola, *Croat. Chem. Acta* **59** (1986) 891.
3. M. G. Karminski-Zamola and M. Bajić, *Synth. Comm.* **19** (1989) 1325.
4. M. G. Karminski-Zamola, D. Pavličić, M. Bajić, and N. Blažević, *Heterocycles* **32** (1991) 2323.
5. G. T. Crips and A. I. O'Donoghue, *Synth. Comm.* **19** (1989) 1745.
6. W. B. Wright, Jr. and H. J. Brabander, *J. Heterocycl. Chem.* **8** (1971) 711.

SAŽETAK

Sinteza novog heteropolicikličkog bis-karboksamida: 3,5–diklor– *N,N'(p*–klorfenil)ditieno[3,2–b:2',3'–*d*]furan–2,6–karboksamid

Grace M. Karminski-Zamola, Miroslav Malešević, Miroslav Bajić i Gordan Golja

Sintetiziran je novi heteropoliciklički bis-karboksamid **5** višestupnjevitom sintezom, počevši od furilakrilne kiseline (**1**). U najnovije vrijeme taj se tip spojeva istražuje kao potencijalni anti-AIDS agens. Najvažniji stupanj u opisanoj sintezi jest priprava intermedijara; 3,5–diklor–ditieno[3,2–b:2',3'–d]furan–2,6–dikarbonil–klorida (**4**).