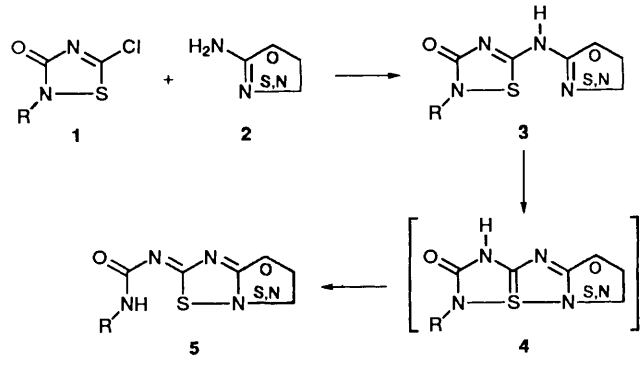
A New Approach to Azapentalenes by an Addition–Rearrangement Sequence: Synthesis of Fused 1,2,4-Thiadiazoles

Gerrit L'abbé,* Johan Buelens and Wim Dehaen
Department of Chemistry, University of Leuven, Celestijnenlaan 200F, 3001 Leuven (Heverlee), Belgium

Carbamoylimino substituted thiazolo[3,2-*b*][1,2,4]thiadiazoles **7** and **8**, [1,3,4]thiadiazolo[3,2-*b*]-[1,2,4]thiadiazole **9**, [1,2,4]thiadiazolo[3,2-*b*]benzoxazole **10**, [1,2,4]thiadiazolo[3,2-*b*]benzothiazole **11** and [1,2,4]thiadiazolo[2,3-*a*]benzimidazole **12** are conveniently prepared from 5-chloro-1,2,4-thiadiazol-3-(2*H*)-one **6** and an appropriate 2-aminoazole by an addition–rearrangement sequence.

A large number of synthetic methods are available for the construction of classical azapentalenes.[1] They most often involve the building of one ring onto an existing five-membered ring. In some rare cases rearrangement occurs during this transformation.[2] Another approach, discussed in this paper, is based on the knowledge that 1,2,4-thiadiazoles having an amidine substituent at the 5-position can rearrange to other 1,2,4-thiadiazoles with a different substitution pattern.[3,4] With this in mind, we surmised that 5-chloro-1,2,4-thiadiazol-3(2*H*)-ones **1** might react with the heterocyclic amidines **2** to give products **5** as a result of rearrangement of the adducts **3** through hypervalent sulphur intermediates **4** (Scheme 1). This concept proved to be correct as shown below.

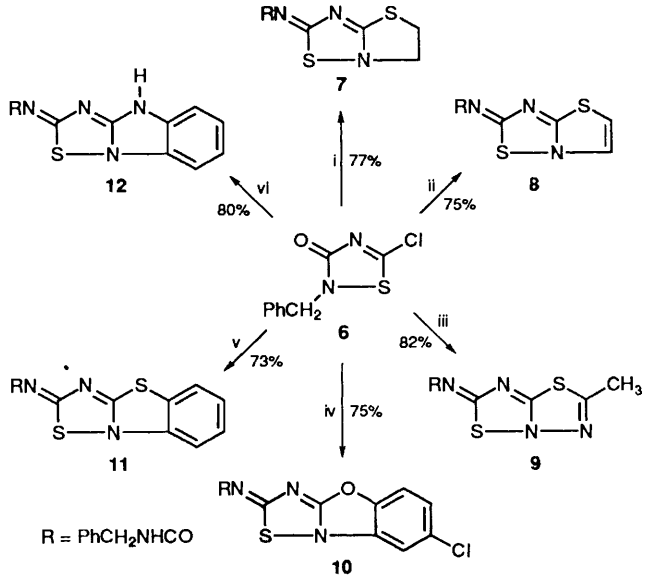


Scheme 1

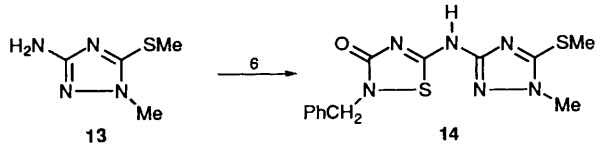
The thiadiazolin-3(2*H*)-one **6** used in this work, was prepared by chlorination of ethoxymethyl isothiocyanate in the presence of benzyl isocyanate following a reported procedure.[5] Reactions of compound **6** were carried out with six aminoazoles and furnished the fused heterocycles **7**–**12** in good yields (Scheme 2).† That rearrangement has occurred during the reactions is evident from the benzyl methylene doublets at δ 4.3–4.4 and the NH triplets at δ 8.2–8.5 in the ^{1}H NMR spectra. Furthermore, the spectra indicated the presence of two conformational isomers in a ratio of 90:10 due to restricted rotation about the amide side-chain.

The wide choice of aminoazoles, coupled with the ease of operation, makes the sequence **1** + **2** ⟶ **5** an excellent method for the synthesis of fused 1,2,4-thiadiazoles. The only limitation resides in the nucleophilicity of the amidine function of the heterocycles **2**. For instance, 5-aminotetrazole did not react with compound **6**, and the aminotriazole **13** furnished a

† All compounds were unambiguously characterized by IR, ^{1}H and ^{13}C NMR and mass spectral results and microanalysis.



Scheme 2 *Reagents:* i, 2-amino-4,5-dihydrothiazole; ii, 2-amino-thiazole; iii, 2-amino-5-methyl-1,3,4-thiadiazole; iv, 2-amino-5-chloro-benzoxazole; v, 2-aminobenzothiazole; vi, 2-aminobenzimidazole



thermostable addition product **14** (m.p. 203 °C, 66%) with a benzyl methylene singlet at δ_H 4.7 in the NMR spectrum.

Experimental

Typical Procedure: 2-Benzylcarbamoylimino-5,6-dihydro-2H-thiazolo[3,2-b][1,2,4]thiadiazole **7**.—A suspension of compound **6** (1 g, 4.4 mmol), 2-amino-4,5-dihydrothiazole (450 mg, 4.4 mmol) and triethylamine (535 mg, 5.3 mmol) in dry ethanol (50 cm^3) was stirred at room temperature for 1 h. After removal of the solvent, the residue was washed successively with water (5 × 50 cm^3), ethanol (2 × 10 cm^3) and diethyl ether (2 × 20 cm^3), and dried *in vacuo* (982 mg, 77%), m.p. 163 °C (from EtOH); ν_{max}(KBr)/cm^{-1} 3310s and 1635s; δ_H($CDCl_3$) 3.8 (t, 5-H), 4.1 (t, 6-H), 4.5 (d, benzyl CH_2), 5.9 (br t, NH), 7.2–7.4 (m, Ph); minor isomer resonates at δ_H 3.82 (t), 4.2 (t), 4.6 (d) and 5.45 (br t, 10%) and disappears at 55 °C; δ_H ([$^2H_6$]-DMSO) 3.95 (t, 5-H), 4.2 (t, 6-H), 4.3 (d, benzyl CH_2, $^3J_{HH}$ 6), 8.3 (t, NH) and 7.1–7.4 (m, Ph); minor isomer resonates at δ_H 4.45 (d);

$\delta_C(CDCl_3)$ 33.3 (C-5, $^1J_{CH}$ 148), 44.8 (C-6, $^1J_{CH}$ 148), 44.9 (benzyl CH_2, $^1J_{CH}$ 140), 127.4, 127.6, 128.6 and 138.5 (Ph C-atoms), 155.9 (C-3a), 163.2 (C=O) and 171.9 (C-2); $\delta_C([^2H_6]$-DMSO) 33.5 (C-5), 43.5 (benzyl CH_2), 45.1 (C-6), 126.5, 127.0, 128.1 and 139.9 (Ph C-atoms), 156.8 (C-3a), 163.0 (C=O) and 170.2 (C-2); *m/z* 292 ($M^{\bullet+}$, 54%), 188 (12), 186 ($M^{\bullet+}$ – $PhCH_2NH$, 100), 160 ($PhCH_2NHCONC^{\bullet+}$, 25), 159 ($M^{\bullet+}$ – $PhCH_2NCO$, 14), 118 (10), 106 ($PhCH_2NH^+$, 12), 104 (10), 103 (11), 102 (12), 101 (15) and 91 ($C_7H_7^+$, 86) (Found: C, 49.1; H, 4.1. $C_{12}H_{12}N_4OS_2$ requires C, 49.30; H, 4.14%).

Note: For the synthesis of **9** (m.p. 239 °C) and **12** (m.p. 230 °C) the reactions were carried out at room temperature for 12 and 24 h respectively, whereas **8** (m.p. 170 °C), **10** (m.p. 182 °C) and **11** (m.p. 206 °C) required heating at 60 °C for 30 h.

Acknowledgements

Financial support from the N.F.W.O. and the Ministerie voor Wetenschapsbeleid is gratefully acknowledged. This work has been accomplished with fellowships from the N.F.W.O. (for W. Dehaen) and the I.W.O.N.L. (for J. Buelens).

References

1 K. H. Pilgram in *Comprehensive Heterocyclic Chemistry*, eds. A. R. Katritzky and C. W. Rees, Pergamon, Oxford, 1984, vol. 6, p. 973.
2 T. Sasaki, E. Ito and I. Shimizu, *J. Org. Chem.*, 1982, **47**, 2757.
3 K. Akiba, T. Kobayashi and S. Arai, *J. Am. Chem. Soc.*, 1979, **101**, 5857; K. Akiba, S. Arai, T. Tsuchiya, Y. Yamamoto and F. Iwasaki, *Angew. Chem. Int. Ed. Engl.*, 1979, **18**, 166.
4 G. L'abbé, E. Albrecht and S. Toppet, *J. Heterocycl. Chem.*, 1991, **28**, 1619; G. L'abbé and E.Albrecht, *J. Heterocycl. Chem.*, 1992, **29**, 451; G. L'abbé, E. Albrecht and S. Toppet, *J. Heterocycl. Chem.*, 1992, **29**, 1317.
5 G. Keilen and K. Undheim, *Acta Chem. Scand., Ser. B*, 1988, **42**, 362.

Paper 3/03378C
Received 11*th June* 1993
Accepted 21*st June* 1993