Pergamon

Tetrahedron 55 (1999) 1977–1988

TETRAHEDRON

A Novel Ring Transformation of 5-Azidothiazoles

Erik Ceulemans, Leonard K. Dyall and Wim Dehaen*

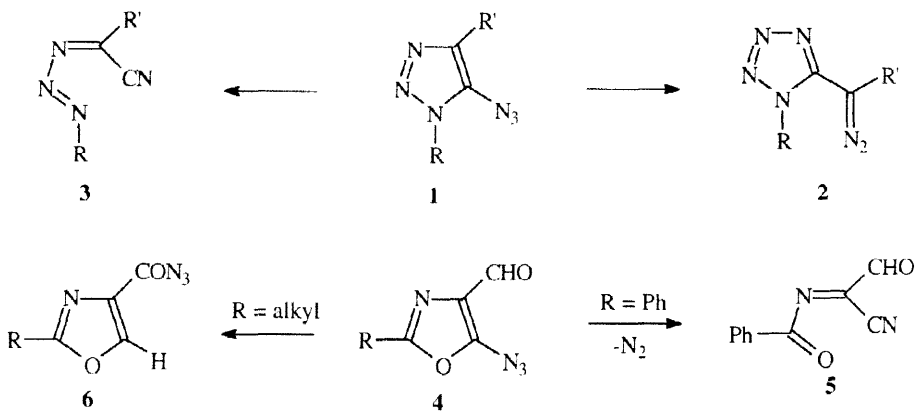
Department of Chemistry, University of Leuven, Celestijnenlaan 200F, B-3001 Heverlee (Leuven)

Received 15 May 1998; accepted 17 December 1998

Abstract: The 4-oxoalkyl- and 4-iminoalkyl-5-azidothiazoles undergo a ring transformation with nitrogen loss at relatively low temperatures to afford 4-cyanooxazoles and 4-cyanoimidazoles, respectively. The mechanism, which is thought to involve a ring opening ring closure process, is discussed. © 1999 Elsevier Science Ltd. All rights reserved.

INTRODUCTION

Heterocyclic compounds have an extraordinary ability to give ring transformations[1]. During many years we have studied the rearrangements of 1,2,3-thiadiazoles and 1,2,3-triazoles[2]. In the case of 5-azido-1,2,3-triazoles **1**, a competition between two different processes can occur[3] : a) a rearrangement with ring opening, followed by 1,5-dipolar electrocyclisation[4] , affording a 5-diazoalkyltetrazole **2** and b) a ring opening to a triazene **3** with nitrogen loss. This last process is general for α-azidoazoles[5] and in a series of articles[6] we have gained insight in the mechanism by studying the kinetics of the thermal decomposition reaction. In the same manner, 5-azido-4-formyloxazoles **4**[7] either undergo ring opening to carbonylimines **5** or rearrange to oxazoles **6** by the Cornforth rearrangement[1]. 2-Alkyl substituents were shown to favor the former pathway and 2-aryl substituents the latter. As a further extension of our ongoing research program on the chemistry and thermal behaviour of heterocyclic azides we have now prepared 5-azidothiazoles and studied their thermal behaviour.



Scheme 1

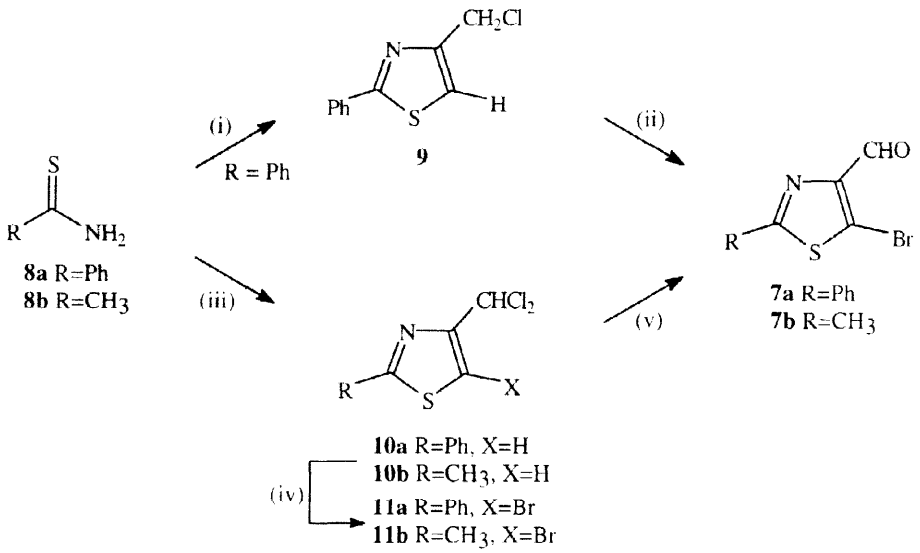
*e-mail: wim.dehaen@chem.kuleuven.ac.be Fax: ++32 16 327990

0040-4020/99/$ - see front matter © 1999 Elsevier Science Ltd. All rights reserved.
PII: S0040-4020(98)01222-8

RESULTS AND DISCUSSION

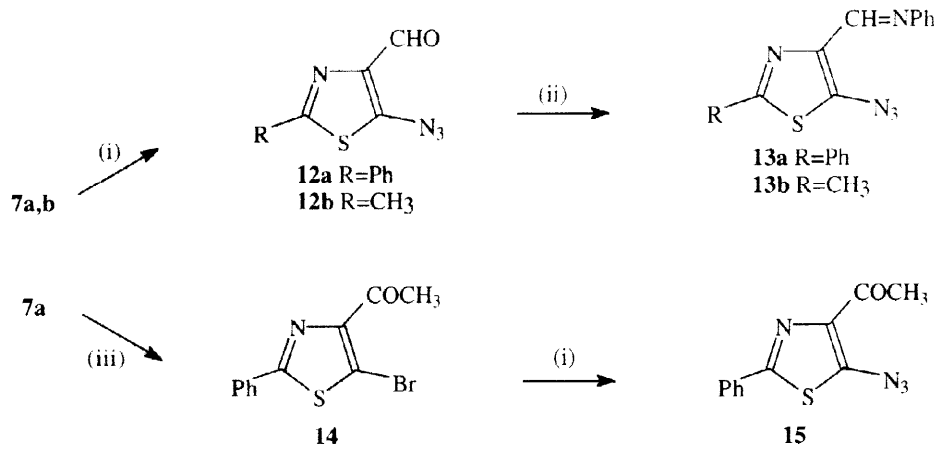
Azide synthesis

The starting materials for the synthesis of the 5-azidothiazoles in this paper are the 5-bromo-4-formylthiazoles **7a,b**. Simiti *et al.* reported a procedure[6] for the preparation of **7a** starting from 1,3-dichloroacetone and thiobenzamide **8a** to give the chloromethylthiazole **9**. This method was rather difficult to reproduce. Alternatively, starting from 1,1,3-trichloroacetone and thioamides **8a,b**. the 4-dichloromethylthiazoles **10a,b** could be obtained. Bromination of **10a,b**, followed by hydrolysis of the resulting **11a,b** gave the aldehydes **7a,b** in good overall yield (**Scheme 2**). Nucleophilic substitution of the chloroaldehydes **7a,b** with azide anion finally gave the 5-azido-4-formylthiazoles **12a,b**. These compounds could be smoothly converted to the corresponding anils **13a,b** by treatment with aniline. The aldehyde **7a** was converted with diazomethane to the 5-acetylthiazole **14** which could be converted in the same manner to the corresponding azide **15** (**Scheme 3**).



(i) 1,3-dichloroacetone , (ii) a) Sommelet reaction, b) bromine/acetic acid ,
(iii) 1,1,3-trichloroacetone, (iv) bromine/acetic acid, (v) calcium carbonate, water, reflux

Scheme 2



(i) sodium azide/dimethylformamide (ii) aniline (iii) diazomethane

Scheme 3

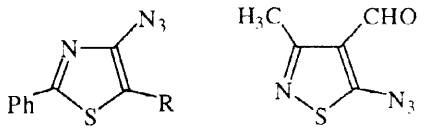
Azide thermolysis: rates and products

The azides **12-13a,b** and **15** decompose readily with evolution of nitrogen upon brief heating at 50°C and even on standing for prolonged time at room temperature. The reactions were cleanly first-order as evident from a kinetic study by FTIR. The rates are summarized in Table 1. A comparison can be made between the azides **12-15a,b** and **15** and the isomeric 4-azidothiazoles **16a-c** we have studied earlier[8]. The latter azides generally decompose at a much slower rate. This fact is in accordance with similar observations[9] by Zanirato *et al.* in the (benzo)thiophene series. The 5-azidoisothiazole[10] **17** has a decomposition rate which is comparable to those of the compounds **12a,b**. This seems to indicate that the location of the nitrogen in the heterocycle does not exert a great influence on the rate of the ring opening.

Table 1: First-Order Rate Constants for Thermal Decomposition of 4-, 5-Azidothiazoles and 5-Azidoisothiazoles in p-Xylene

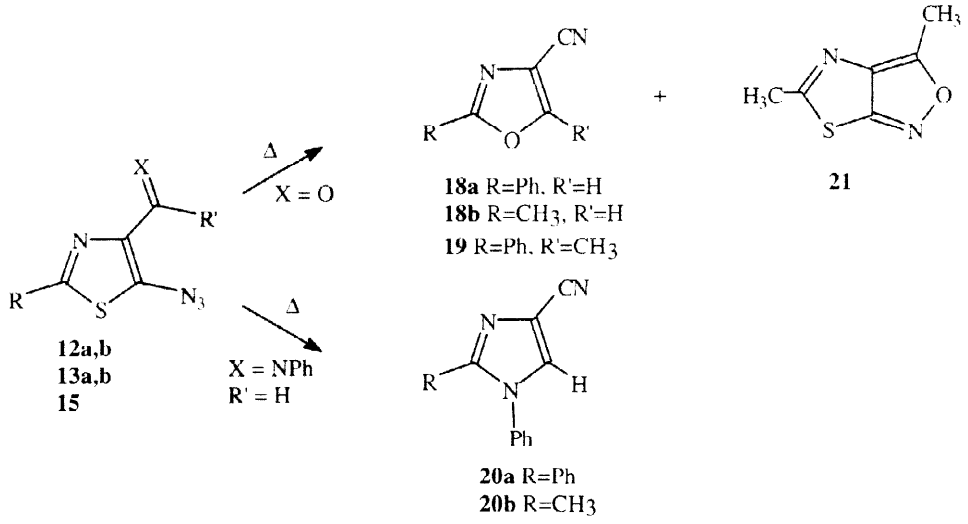
Azide	Temp(°C)	10^5 k_1/s^{-1}
12a	50	10.85
12b	50	6.08
13a	50	64.00
13b	50	35.70
15	50	8.45
16a	50[a]	0.02
16b	50[a]	0.08
16c	50[a]	0.01
17	50[a]	5.95

a.Extrapolation from the literature values, which were obtained at 80°C (division by a factor 27)



16a R = CHO
16b R = CH=NPh
16c R = $COCH_3$

17

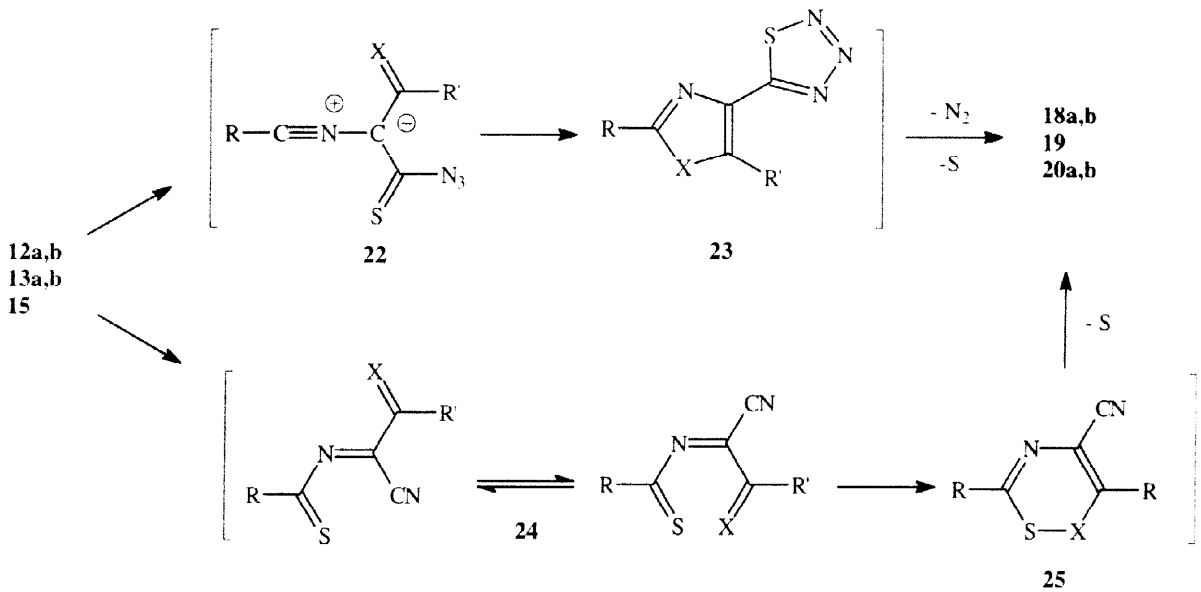


Scheme 4

The thermolysis reactions of the azides **12-13a,b** and **15** were also followed at 50°C by ^{1}H NMR spectroscopy in $CHCl_3$-*d* solution. We observed the formation of 4-cyanooxazoles **18a,b** and **19** (respectively starting from **12a,b** and **15**) and 4-cyanoimidazoles **20a,b** from azides **13a,b**. In the case of azide **15**, the isoxazolothiazole **21** is also formed as a result of intramolecular cyclization of the azide and acetyl functions. The **19:21** ratio was 2:1. The thermolysis products **18-20** were isolated in fair to good yields and fully characterized by NMR, IR and MS spectroscopic techniques. Only a small quantitity of **21** could be obtained from the reaction mixtures starting from **15**. This is due to decomposition during chromatography . From the same chromatography, the expected amount of the 4-cyanooxazole **19** was isolated. The low stability of isoxazolo[5,4-c]thiazoles is not unexpected, as the same was observed for the isomeric isoxazolo[4,5-c]-thiazoles[8,11](**Scheme 4**).

Mechanism

Two different mechanisms can be put forward to explain the products formed in these thermolysis reactions : a) A Cornforth-type rearrangement[1], followed by immediate ring closure of the azidothiocarbonyl group of **22** to a 1,2,3,4-thiatriazole **23**, which then readily extrudes sulfur and nitrogen to form the nitriles **18-20**[12]; b) a ring opening after or at the same time of the loss of nitrogen, giving initially a thiocarbonyl compound **24** which after a *cis/trans* isomerisation can undergo a 1,6-electrocyclisation to give an unstable oxathiazine or thiadiazine **25** which extrudes sulfur to form a heteroaromatic azole **18-20** (**Scheme 5**).



Scheme 5 (X = O or NPh)

We can refute the first mechanism because of the following reasons : a) the initial ring opening to a nitrile ylide **22** is energetically unfavored because of the unstable thiocarbonyl bond formed and in all the Cornforth rearrangements reported[1] a carbonyl bond is formed; b) the decomposition reaction occurs at relatively low temperatures, whereas the Cornforth rearrangement normally takes temperatures of well over 100°C; c) 2-alkyl groups on the thiazole ring stabilize the nitrile ylide formed and hence increase the rate, here the opposite is observed and d) no Cornforth rearrangement starting from a thiazole is known so far in the literature[1]. In fact, in one case a thiazole was formed starting from an oxazole, which is exactly the reverse result that we obtained[13].

Additional support for the second mechanism is provided by the fact that a) the isoelectronic 2-azidothiophenes undergo facile ring-opening, giving thiocarbonyl compounds[14] and 2-nitreno-3-(phenyliminomethyl)thiophenes give 3-cyanopyrroles[15]; b) the driving force for the 1,6-electrocyclization is given by the disappearance of the unstable thiocarbonyl double bond and c) in a similar process, 1,2-dithiins are known to undergo facile ringcontraction to thiophenes[16].

EXPERIMENTAL

General

Remarks regarding safety: Sodium azide is extremely poisonous and organic azides are potentially hazardous. Although we never had any explosions occuring with the heterocyclic azides described in this report, caution is always necessary when handling these compounds. Preparation should be carried out only in a fume cupboard (hood) provided with a powerfull exhaust system. The use of a screen of safety glass is recommended.

Mps were determined using a Reichert Thermovar apparatus. IR spectra of the products were recorded with a Perkin-Elmer 1620 FT spectrometer, using KBr pellets unless otherwise specified. NMR spectra were measured on a Bruker AMX-400 spectrometer, using $CDCl_3$ solutions unless otherwise stated. *J* values are quoted in Hz. Low resolution mass spectra were measured with a Hewlett Packard 5989A spectrometer and high resolution ones with a Kratos MS50 TC machine, both operated at 70eV and in EI mode unless specified otherwise. Chemical ionization (CI) mass spectra used methane as the reagent gas.

Synthesis of 5-azidothiazoles

4-Dichloromethyl-2-phenylthiazole (**10a**). A solution of 1,1',3-trichloropropanone (16g, 0.1mol) and thiobenzamide (18g, 0.13mol) in dry acetone ($80cm^3$) was stirred at room temperature for 24h. The light brown precipitate was filtered off, washed with dry acetone and dried. This compound was dissolved in concentrated sulfuric acid ($15cm^3$) and stirred at room temperature for 1h. The brown solution was poured into ice-water ($100cm^3$) and the precipitated thiazole **10a** was filtered off, washed with water and dried (9.8g, 40%), mp 56°-57°C (from MeOH); ν_{max}/cm^{-1} 3127m, 2969m; δ_H (DMSO-d_6) 7.51-7.57 and 7.95-7.99 (3+2 H, 2m, Ph), 7.60 (1 H, s, $CHCl_2$) and 8.01 (1H, s, H-5); δ_C (DMSO-d_6) 66.6 ($CHCl_2$, $^1J_{CH}$ 178), 119.4 (C-5), 126.4, 129.4, 131.0 and 132.4 (Ph C-2, C-3, C-4 and C-1), 153.7 (C-4) and 168.9 (C-2); m/z 243/245/247 (M^+, 32/23/5%), 208/210 (M^+-Cl, 100/41), 105 (27), 77 (Ph^+, 11) and 45 (HCS^+, 35) (Found: M^+, 242.9697. requires $C_{10}H_7Cl_2NS$ M, 242.9677).

4-Dichloromethyl-2-methylthiazole (**10b**) was prepared in the same way as **10a** starting from thioacetamide (9.8g, 0.13mol). The crude product was purified by column chromatography on silica gel with dichloromethane as the eluent giving white crystals **10b** (3.1g, 17%), mp 80.4°-81.5°C (from MeOH); ν_{max}/cm^{-1} 3112m and 2969s; δ_H 2.73 (3 H, s, Me), 6.81 (1 H, s, $CHCl_2$) and 7.41 (1 H, s, H-5); δ_C 19.2 (Me), 65.9 ($CHCl_2$, $^1J_{CH}$ 179), 117.3 (C-5, $^1J_{CH}$ 189), 153.1 (C-4) and 167.5 (C-2); m/z 181/183/185

($M^{+\cdot}$, 19/13/3%), 146/148 ($M^{+\cdot}$-Cl, 100/51), 105/107 ($M^{+\cdot}$-Cl-MeCN, 46/19), 69 (m/z 105 - HCl, 35) and 45 (HCS^+, 42) (Found: $M^{+\cdot}$, 180.9534. requires $C_5H_5Cl_2NS$ M, 180.9520).

5-Bromo-4-dichloromethyl-2-phenylthiazole (**11a**). To a stirred solution of **10a** (2.74g, 11.3mmol) in acetic acid ($30cm^3$) was added dropwise 1.5 equiv. of bromine (2.7g, 17mmol) at 16°C, while protecting the reaction from light. After stirring at room temperature for 18h, the precipitate **11a** was filtered off and the filtrate was poured into ice-water ($50cm^3$) to give a second crop of **11a** which was filtered off and washed with aqueous Na_2CO_3 (10%, 3x$100cm^3$). Total yield 2.42g, 66%, mp 136.4°-137.2°C (from MeOH); ν_{max}/cm^{-1} 3017s and 2966m; δ_H 6.91 (1 H, s, $CHCl_2$), 7.42-7.50 and 7.88-7.93 (3+2 H, 2m, Ph); δ_C 63.6 ($CHCl_2$, $^1J_{CH}$ 178), 106.1 (C-5), 126.5, 129.1, 131.1 and 132.4 (Ph C-2, C-3, C-4 and C-1), 151.5 (C-4) and 169.4 (C-2); m/z 321/323/325/327 ($M^{+\cdot}$, 25/41/20/4%), 286/288/290 ($M^{+\cdot}$-Cl, 74/100/31), 183/185/187 ($M^{+\cdot}$-Cl-PhCN, 17/22/6), 104/106 ($S{=}C{=}C{=}CHCl^{+\cdot}$, 29/9), 103 ($PhCN^{+\cdot}$, 18), 77 (Ph+) and 69 ($S{=}C{=}C{=}CH^+$, 45) (Found: $M^{+\cdot}$, 320.8787. requires $C_{10}H_6BrCl_2NS$ M, 320.8781).

5-Bromo-4-dichloromethyl-2-methylthiazole (**11b**). To a stirred solution of **10b** (3.25g, 18mmol) in acetic acid ($30cm^3$) was added dropwise 1.5 equiv. of bromine (4.32g, 27mmol). After stirring at room temperature for 15h, the reaction mixture was poured into ice-water ($100cm^3$) and the resulting red oil was extracted with dichloromethane (3x$100cm^3$). The combined extracts were washed with aqueous Na_2CO_3 (10%, 4x$100cm^3$), dried ($MgSO_4$) and evaporated. The crude product was purified by column chromatography on silica gel with dichloromethane as the eluent to give **11b** (2.4g, 51%), mp 79.1°-79.5°C (from MeOH); δ_H 2.73 (3 H, s, Me) and 6.83 (1 H, s, $CHCl_2$); δ_C 19.9 (Me), 63.4 ($CHCl_2$, $^1J_{CH}$ 178), 105.2 (C-5), 15.2 (C-4) and 168.2 (C-2); m/z 259/261/263/265 ($M^{+\cdot}$, 17/28/15/3%), 224/226/228 ($M^{+\cdot}$-Cl, 80/100/43), 183/185/187 ($M^{+\cdot}$-Cl-MeCN, 29/38/12), 104/106 ($S{=}C{=}C{=}CHCl^{+\cdot}$, 28/11) and 69 ($S{=}C{=}C{=}CH^+$, 59) (Found: $M^{+\cdot}$, 258.8625. requires $C_5H_4BrCl_2NS$ M, 258.8625).

5-Bromo-2-phenylthiazole-4-carbaldehyde (**7a**). A suspension of **11a** (500mg, 1.6mmol) and $CaCO_3$ (2.5g, 25mmol) in water ($20cm^3$) was refluxed for 15h under a nitrogen atmosphere. The reaction mixture was extracted with chloroform (3x$100cm^3$) and the combined extracts were dried ($MgSO_4$) and evaporated. The crude product was chromatographed on silica gel with dichloromethane as the eluent to give bromo-aldehyde **7a** (385mg, 86%), mp 93.5°-94.1°C (from EtOH; lit.,[7] 94°-95°C);ν_{max}/cm^{-1} 3046w, 2975m, 2852m, 2803m and 1679s (C=O); δ_H 7.43-7.52 and 7.90-7.95 (3+2 H, 2m, Ph) and 10.1 (1 H, s, CH=O); δ_C 119.2 (C-5, $^3J_{CH}$ 2 Hz), 126.7, 129.2, 131.4 and 132.0 (Ph C-2, C-3, C-4 and C-1), 150.0 (C-4,

$^2J_{CH}$ 26 Hz), 168.9 (C-2) and 183.3 (CHO, $^1J_{CH}$ 184 Hz); m/z 268/270 (M^++H, 19/18%), 267/269 (M^+, 40/44), 188 (M^+-Br, 100), 160 (M^+-Br-CO, 46), 133 (M^+-Br-CHO-CN, 22) and 77 (Ph^+) (Found: M^+, 266.9358. requires $C_{10}H_6BrNOS$ M, 266.9353).

5-Bromo-2-methylthiazole-4-carbaldehyde (**7b**). Compound **11b** (500mg, 1.9mmol) in ethanol (20cm^3) was mixed with an aqueous solution of $NaHCO_3$ (075g in 4cm^3) and the whole was heated at 80°C for 15h under a nitrogen atmosphere. The reaction mixture was then extracted with dichloromethane (3x100cm^3) and the combined extracts were dried ($MgSO_4$) and evaporated to give **7b** (340mg, 86%), mp 71.5°-72°C (from n-hexane); ν_{max}/cm^{-1} 2975m, 2915m, 2856, 2514m and 1679s (C=O); δ_H 2.73 (3 H, s, Me) and 10.0 (1 H, s, CHO); δ_C 19.7 (Me, $^1J_{CH}$ 131), 119.7 (C-5, $^3J_{CH}$ 1.25), 149.2 (C-4, $^2J_{CH}$ 28), 167.4 (C-2, $^2J_{CH}$ 7) and 182.6 (CHO, $^1J_{CH}$ 183 Hz); m/z 205/207 (M^+, 14/15%), 126 (M^+-Br, 100), 98 (M^+-Br-CO, 65); 71 (M^+-Br-CO-CN, 14), 59 ($MeCS^+$, 23) and 57 (94) (Found: M^+, 204.9215. requires C_5H_4BrNOS M, 204.9197).

4-Acetyl-5-bromo-2-phenylthiazole (**14**). This compound was prepared following the literature procedure (yield: 57 %), mp 133°-134°C (from MeOH, lit.,[7] 136°C); ν_{max}/cm^{-1} 3050w, 2926w and 1682s (C=O); δ_H 2.75 (3 H, s, Me) and 7.45-7.50 and 7.85-7.93 (3+2 H, 2m, Ph); δ_C 29.0 (Me), 114.3 (C-5), 126.4, 129.2, 131.0 and 132.4 (Ph C-2, C-3, C-4 and C-1), 149.6 (C-4), 166.9 (C-2) and 193.5 (C=O); m/z 281/283 (M^+, 29/30), 202 (M^+-Br, 100), 160 (M^+-Br-CH_2CO, 53), 159 (M^+-Br-$COCH_3$, 12), 77 (Ph^+, 25), 51 ($C_4H_3^+$, 19) and 43 ($COCH_3^+$, 45) (Found: M^+, 280.9522. requires $C_{11}H_8BrNOS$ M, 280.9510).

5-Azido-2-phenylthiazole-4-carbaldehyde (**12a**). To an ice-cooled solution of **7a** (300mg, 1.12mmol) in DMF (5cm^3) was added 5 equiv. of sodium azide (320mg). After stirring at 0°C for 2h, the reaction mixture was poured into ice-water (50cm^3) and the precipitate was filtered off. A second crop was obtained by extraction of the filtrate with dichloromethane (3x100cm^3), drying ($MgSO_4$) and removal of the solvent. The azide **12a** was purified by column chromatography on silica gel with diethyl ether/n-hexane (1/1) as the eluent (180mg, 70%), mp 85°-86°C (decomposition); ν_{max}/cm^{-1} 2135s (N_3) and 1686s (C=O); δ_H 7.4-7.5 and 7.83-7.9 (5 H, 2m, Ph) and 10.05 (1 H, s, CHO); δ_C 126.5, 129.2, 131.1 and 132.2 (Ph), 141.8 (C-4, d, $^2J_{CH}$ 26 Hz), 148 (C-5, d, $^3J_{CH}$ 4 Hz), 160.0 (C-2, t) and 183.4 (CHO, d, $^1J_{CH}$ 182 Hz); m/z 230 (M^+, 0.4%), 202 (M+.-N_2, 7), 174 (M^+-N_2-CO, 19), 121 ($PhCS^+$, 100) 103 ($PhCN^+$, 10), 77 (Ph^+, 74) and 51 ($C_4H_3^+$, 59) (Found: M^+, 230.0258. requires $C_{10}H_6N_4OS$ M, 230.0262).

5-Azido-2-methylthiazole-4-carbaldehyde (**12b**) was synthesized in the same way as **12a** starting from **7b** (490mg, 2.3mmol) and purified by chromatography on silica gel with diethyl ether/n-hexane (4/1) as the eluent to give **12b** (273mg, 68%), mp 53°-55°C; ν_{max}/cm^{-1} 2966w, 2830m, 2112s (N_3) and 1963s (C=O); δ_H 2.68 (3 H, s Me) and 9.94 (1 H, s, CHO); δ_C 19.7 (Me, $^1J_{CH}$ 120), 140.7 (C-4, $^2J_{CH}$ 25), 148.3 (C-5), 158.6 (C-2, $^2J_{CH}$ 7) and 182.6 (CHO, $^1J_{CH}$ 181); m/z 168 ($M^{+\cdot}$, 3%), 140 (M^+-N_2, 4), 112 (M^+-N_2-CO, 15) and 59/61 ($MeCS^+$, 61/6) (Found: $M^{+\cdot}$, 168.0014. requires $C_5H_4N_4OS$ M, 168.0106).

4-Acetyl-5-azido-2-phenylthiazole (**15**) was prepared as **12a** starting from **14** (200mg, 0.57mmol), but with stirring for 1h at 0°C and further at RT for another 6h. Compound **15** was purified by chromatography on silica gel with dichloromethane as the eluent (120mg, 69%), mp 80°-81°C; ν_{max}/cm^{-1} 3058w, 3016w, 2965w, 2174s/2141m (N_3) and 1681s (C=O); δ_H 2.70 (1 H, s, Me), 7.40-7.55 and 7.80-7.90 (3+2 H, 2m, Ph); δ_C 29.2 (Me, $^1J_{CH}$ 128), 126.2, 129.1, 130.7 and 132.6 (Ph C-2, C-3, C-4 and C-1), 141.5 (C-4, q), 145.5 (C-5, s), 157.9 (C-2, t) and 193.9 (C=O, $^2J_{CH}$ 6 Hz); m/z 244 ($M^{+\cdot}$, 1%), 216 ($M^{+\cdot}$-N_2, 27), 184 ($M^{+\cdot}$-N_2-S, 46), 174 ($M^{+\cdot}$-N_2-CH_2CO, 11), 142 ($M^{+\cdot}$-N_2-S-CH_2CO, 26), 121 ($PhCS^+$, 79), 77 (Ph^+, 37) and 43 (CH_3CO^+, 100) (Found: M+., 244.0408. requires M, 244.0419).

5-Azido-2-phenyl-4(N-phenyliminomethyl)thiazole (**13a**). A solution of the aldehyde **12a** (160mg, 0.069mmol) and aniline (72mg, 0.69mmol) in ethanol (20cm^3) containing a few drops of acetic acid was stirred at 0°C for 1h and left overnight in the refrigerator. The precipitated crystals were collected, washed with aqueous Na_2CO_3 (10%, 50cm^3) and dried ($MgSO_4$) to give the imine **13a** (117mg, 55%), mp 154°-156°C (decomposition); ν_{max}/cm^{-1} 3062w, 2120s (N_3) and 1620m (C=N); δ_H 7.18-7.50 and 7.88-7.95 (8+2 H, 2m, 2 Ph) and 8.57 (1 H, s, CH=N); δ_C 121.1, 126.4, 126.5, 129.0, 129.1, 130.7, 132.8 and 151.6 (2 Ph), 141.5 (C-4), 151.3 (CH=N) and 160.5 (C-2) (C-5 not observed); m/z 306 (M^++H, 0.1%), 277 (M^+-N_2, 10), 245 (4-cyano-1,2-diphenylimidazole), 193 (22), 115 (10), 77 (Ph^+, 17) and 51 ($C_4H_3^+$, 11).

5-Azido-2-methyl-4(N-phenyliminomethyl)thiazole (**13b**) was prepared in the same way as **13a** starting from **12b** (400mg, 2.4mmol). After standing overnight, the solvent was removed and the red oil washed with water (3x50cm^3) and characterized as **13b** (345mg, 59%); $\nu_{max}(CCl_4)/cm^{-1}$ 3065w, 3031w, 2977w and 2132s (N_3); δ_H 2.69 (3 H, s, Me), 7.19-7.30 and 7.31-7.42 (3+2 H, 2m, Ph) and 8.43 (1 H, s, CH=N); δ_C 19.8 (Me, $^1J_{CH}$ 131), 121.0, 126.2 and 128.9 (Ph C-2, C-3 and C-4), 139.9 (C-4, d, $^2J_{CH}$ 13), 141.5 (C-5), 149.9 (CH=N, d, $^1J_{CH}$ 167), 151.4 (Ph C-1), 159.4 (C-2, q, $^2J_{CH}$ 7); m/z 243 ($M^{+\cdot}$, 1%), 215

(M^+-N_2, 20), 201 (M^+-N_2+H, 29), 183 (4-cyano-2-methyl-1-phenylimidazole, 100), 130 (44) and 51 ($C_4H_3^+$, 49).

Products of thermolysis

4-Cyano-2-phenyloxazole **(18a)**. A solution of the azide **12a** (150mg, 0.65mmol) in chloroform (10cm^3) was heated at 50°C for 2 days and the resulting black solution was chromatographed twice on silica gel, first with diethyl ether/n-hexane (1/1) and then with dichloromethane as the eluents to give the oxazole **18a** (50mg, 45%), mp 117°C (decomposition, lit.,[17] 118°-119°C); ν_{max} (CCl_4)/cm^{-1} 3160w, 3068w and 2291m (CN); δ_H 7.45-7.58 and 8.05-8.1 (3+2 H, 2m, Ph) and 8.21 (1 H, s, H-5); δ_C 111.8 (CN), 116.2 (C-4, $^2J_{CH}$ 14), 125.5, 126.9, 129.1 and 131.9 (Ph C-1, C-2, C-3 and C-4), 145.8 (C-5, $^1J_{CH}$ 215) and 163.1 (C-2); m/z 245 (M^+, 96), 244 (M^+-H, 100), 193 (M^+-H-HCCCN, 18), 115 (193-C_6H_6,14), 103 (13), 89 (10), 77 ($C_6H_5^+$, 51), 63 (16), 51 ($C_4H_3^+$, 50) and 39 ($C_3H_3^+$,18) (Found: M^+, 245.0953. requires $C_{16}H_{11}N_3$ M, 245.0953).

4-Cyano-2-methyloxazole **(18b)**[17]. A solution of the azide **12b** (120mg, 0.7mmol) in chlororform (10cm^3) was heated at 50°C for 36h. After evaporating the solvent, the oxazole **18b** was purified by column chromatography on silica gel with diethyl ether/n-hexane (4/1) as the eluent gave an oil (35mg, 46%); 2.53 (1H, s, Me) and 8.07 (1 H, s, H-5);δ_C 13.7 (Me, q, $^1J_{CH}$ 131), 111.8 (CN), 114.9 (C-4, d, $^2J_{CH}$ 14), 146.1 (C-5, d, $^1J_{CH}$ 215) and 163.1 (C-2); m/z 183 (M^+, 88), 182 (M^+-H, 16), 142 (10), 131 (M^+-H-HCCCN, 44), 130 (49), 115 (31), 104 (12), 77 ($C_6H_5^+$, 74), 51 ($C_4H_3^+$, 100) and 39 ($C_3H_3^+$,32) (Found: M^+, 183.0800. requires $C_{11}H_9N_3$ M, 183.0796).

5-Methyl-4-cyano-2-phenyloxazole **(19)**. A solution of the azide **15** (100mg, 0.4mmol) in chloroform (10cm^3) was heated at 50°C for 15h and the crude product was chromatographed on silica gel with dichloromethane as the eluent to give **19** (43mg, 56%), mp 128.1°-129.5°C (from ethanol); (Found: C, 72.14; H, 4.88. $C_{11}H_8N_2O$ requires C, 71.8; H, 4.4); ν_{max}/cm^{-1} 3059w, 2958w and 2237s (CN); δ_H 2.59 (3 H, s, Me) and 7.45-7.52 and 7.98-8.05 (3+2 H, 2m, Ph); δ_C 11.3 (Me, $^1J_{CH}$ 131), 112.4 (C-4, $^3J_{CH}$ 4), 112.6 (CN, $^4J_{CH}$ 1), 125.8, 126.5, 129.0 and 131.4 (Ph C-1, C-2, C-3 and C-4), 158.4 (C-5, $^2J_{CH}$ 7) and 161.2 (C-2); m/z 184 (M^+, 100), 169 (M^+-CH_3), 155 (M^+-CHO), 115 (M^+-CO-CN-CH_3), 77 (Ph^+, 21), 51 ($C_4H_3^+$, 21), 43 ($COCH_3^+$, 30) and 39 ($C_3H_3^+$, 10) (Found: M^+, 184.0633. requires $C_{11}H_8N_2O$ M, 184.0637).

The ^{1}H-and ^{13}C-NMR-spectra from the crude reaction mixture showed also the formation of some bicyclic product **21** (ratio 19:21 was 2:1). We were not able to separate this compound from the mixture. *4-Methyl-2-phenylisoxazole[3,4-d]thiazole* **(21):** δ_H 2.78 (3 H, s, Me) and 7.4-7.55 and 7.93-7.97 (3+2 H, 2m, Ph); δ_C 11.3 (Me), 127.6, 129.1, 131.9 and 133.0 (Ph C-2, C-3, C-4 and C-1), 141.8 (C-3a), 158.2 (C-4, q), 163.9 (C-6a) and 171.2 (C-2).

4-Cyano-1,2-phenylimidazole **(20a)**. A solution of the azide **13a** (100mg, 0.33mmol) in chloroform (10cm^3) was heated at 50°C for 10h and then chromatographed on silica gel with diethyl ether/n-hexane (1/1) as the eluent to give the imidazole **20a** (56mg, 69%), mp 163.6°-164.3°C (from n-hexane); (Found: C, 78.53; H, 4.77. $C_{16}H_{11}N_3$ requires C, 78.3; H, 4.5); ν_{max}/cm^{-1} 3085m, 3024m and 2233m (CN); δ_H 7.2-7.5 (2+2+3+3 H, 4m, 2Ph) and 7.67 (1 H, s, H-5); δ_C 114.4 (C-4, $^2J_{CH}$ 8), 114.6 (CN, $^3J_{CH}$ 1), 125.8, 128.4 (x2), 128.8, 129.4, 129.6, 129.9 and 136.9 (Ph), 130.5 (C-5, $^1J_{CH}$ 197) and 148.4 (C-2); m/z 245 (M^+, 96), 244 (M^+-H, 100), 193 (M^+-H-HCCCN, 18), 142 (M^+-PhCN, 8), 103 ($PhCN^+$, 13) and 77 (Ph^+, 51).

4-Cyano-2-methyl-1-phenylimidazole **(20b)**. A solution of the azide **12b** (300mg, 1.2mmol) in chloroform (10cm^3) was heated at 50°C for 4h and the crude product purified on silica gel with diethyl ether/n-hexane (3/1) as the eluent to give the imidazole **20b** (175mg, 80%), mp 113°C (decomposition, from n-hexane); (Found: C, 72.01; H, 4.97 $C_{11}H_9N_3$ requires C, 72.1; H, 5.0); ν_{max}/cm^{-1} 3110m (H-5), 3052w, 2924w and 2235m (CN); δ_H 2.36 (3 H, s Me), 7.27-7.32 (2 H, m, Ph_{ortho}), 7.52-7.57 (3 H, m, $Ph_{meta+para}$) and 7.56 (1 H, s, H-5); δ_C 13.3 (Me), 112.6 (C-4, $^2J_{CH}$ 7.5), 114.4 (CN), 129.0 (C-5, $^1J_{CH}$ 197), 125.4, 129.5, 129.8 and 135.9 (Ph C-2, C-4, C-3 and C-1) and 147 (C-2); m/z 183 (M^+, 88), 142 (M^+-CH_3-CN, 10), 131 (M^+-H-HCCCN, 44), 104 (M^+-H-C_6H_6, 12), 91 (M^+-HNPh, 15), 77 (Ph^+, 74), 51 ($C_4H_3^+$, 100) and 39 ($C_3H_3^+$, 32).

ACKNOWLEDGEMENTS

Financial support from the University of Leuven, the F.W.O. and the Ministerie voor Wetenschapbeleid is gratefully acknowledged. E.C. thanks the IWT for a predoctoral fellowship.

REFERENCES

1. L'abbé, G. *J. Heterocycl. Chem.*, **1984**, *21*, 627; Vivona, N.; Buscemi, S.; Frenna, V.; Gusmano, G. *Adv. Heterocycl. Chem.*, **1993**, *56*, 49.
2. L'abbé, G. *Bull. Soc. Chim. Belg.*, **1990**, *99*, 281.
3. Smith, P.A.S.; Friar, J.J.; Resemann, W.; Watson, A.C. *J. Org. Chem.*, **1990**, *55*, 3351; L'abbé, G.; Van Stappen, P.; Toppet, S. *Tetrahedron*, **1985**, *41*, 4621; L'abbé, G.; Vandendriessche, A.; Toppet, S. *ibid.*, **1988**, *44*, 3617.
4. Taylor, E.C.; Turchi, I.C. *Chem. Rev.* **1979**, *79*, 181; Huisgen, R. *Angew.Chem. Int. Ed. Engl.*, **1980**, *19*, 947.
5. Dehaen, W.; Becher, J. *Acta Chem. Scand.*, **1993**, *47*, 244; Funicello, M.; Spagnolo, P.; Zanirato, P. *ibid.*, 298.
6. Simiti, I.; Farkas, M. *Bull. Soc. Chim. Fr.*, **1968**, 3862.
7. L'abbé, G.; Ilisiu, A.-M.; Dehaen, W.; Toppet, S. *J. Chem. Soc., Perkin Trans. 1*, **1993**, 2259.
8. Ceulemans, E.; Vercauteren, K.; Dyall, L. K.; Buelens, D.; Dehaen, W. *Tetrahedron*, **1997**, *53*, 9657.
9. Funicello, M.; Spagnolo, P.; Zanirato, P. *J. Chem. Soc., Perkin Trans. 1*, **1990**, 2971, and references cited therein.
10. L'abbé, G.; Dyall, L. K.; Meersman, K.; Dehaen, W. *J. Chem. Research (S)*, **1997**, 226 ; *ibid., (M)* 1631.
11. Athmani, S.; Farhat, M. F.; Iddon, B. *J. Chem. Soc. Perkin Trans. 1*, **1992**, 972.
12. Holm, A. *Adv. Heterocycl. Chem.*, **1976**, *20*, 145.
13. Corrao, S. L.; Macielag, M. J.; Turchi, I. J. *J. Org. Chem.*, **1990**, *55*, 4484.
14. Gronowitz, S.; Spagnolo, P.; Zanirato, P. *J. Org. Chem.*, **1982**, *47*, 317; Zanirato, P.; Spagnolo, P.; Zanardi, G. *J. Chem. Soc., Perkin Trans. 1*, **1983**, 2551.
15. Colburn, V. M.; Iddon, B.; Suschitsky, H.; Gallagher, P. T. *J. Chem. Soc., Chem. Commun.*, **1978**, 453.
16. Bohlmann, F.; Kleine, K.-M. *Chem. Ber.*, **1965**, *98*, 3081; Schroth, W.; Billig, F.; Reinhold, G. *Angew. Chem. Int. Ed. Engl.*, **1967**, *6*, 698.
17. Sycheva, T. P.; Trupp, T; Kh. *J. Gen. Chem. USSR*, **1962**, *32*, 1071.