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N-(Pyrid-3-yl)thioureas and Derivatives as Acaricides. I. Synthesis and Biological Properties

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Abstract: In the course of optimization studies around diafenthiuron, the central aromatic nucleus linked directly to the thiourea unit was replaced by a pyridine moiety. A series of *N*-(pyrid-3-yl)thioureas, -isothioureas and -carbodiimides was synthesised and evaluated for acaricidal activity. The synthetic methodology used and the screening results against some spider mites (*Tetranychus* spp. and *Panonychus* ssp.) are discussed.

1 INTRODUCTION

Disubstituted *N*-aryl-*N'*-alkylthioureas possessing insecticidal activity were first described by Enders *et al.*,[1,2] who also synthesised the corresponding isothioureas.[3,4] This initial work led to compounds showing activity against mites and insect pests. Closely following these initial steps, work started by Drábek and Böger showed the importance of a 4-aryloxy substituent on the aromatic ring. This modification led to compounds with much improved biological activity.[5–9] The discovery of the chemical stability and insecticidal potency of certain carbodiimides[10] greatly broadened the scope of the optimisation activities. The synthesis of carbon[11] and nitrogen[12] bridged compounds, followed by the preparation of heterocyclic derivatives linked by an oxygen[13–15] or a sulfur atom[16–18] to the central aromatic nucleus was included in the work. These modifications led to highly active compounds which were intensively evaluated. Further work included the substitution of the central aromatic ring with a variety of systems like isoxazoles,[19,20] pyridines[21] and thiophenes.[22] From this combined effort during the last decade, diafenthiuron (Fig. 1, **1**) was later introduced into the market as an acaricide and insecticide used on a variety of crops against a broad spectrum of pest complexes.[23,24]

The present paper reports the synthesis and biological properties of *N*-(pyrid-3-yl)thioureas, -isothioureas and -carbodiimides as heterocyclic analogues of diafenthiuron and related derivatives. Additionally, some examples where the phenoxy substituent is omitted are discussed.

2 EXPERIMENTAL METHODS

2.1 General Chemistry

The target molecules required a specific synthetic approach, which is shown in Figs 2 and 3. The synthesis of particular phenoxy- and thiophenoxypyridines **4** from the nitro pyridines **3** has been described elsewhere.[25] Reduction thereof led to the amines **5**, which underwent reaction with carbon disulfide under two-phase conditions[26] to give the corresponding isothiocyanates **8**. Compounds **8** were allowed to react with aliphatic amines in toluene to yield the thioureas **9**. Reaction of **9** with 2-chloro-1-methylpyridinium iodide[27] or with methyl iodide in ethanol afforded the corresponding carbodiimides, **10**, or isothioureas, **11**, respectively in excellent yields. Additionally, compounds **3** could be selectively hydrogenated with Raney nickel to give the corresponding 6-chloropyridine-3-amines, **6**, or with palladium on carbon achieving simultaneous reduction of both nitro and chlorine groups to yield compounds **7**. Compound types **6** and **7** were similarly elaborated to the final products **13**, **14** and **15**.

It was known from the previous work on derivatives of diafenthiuron that the carbodiimides were very sensitive to moisture if one of the substituents on the carbodiimide unit was linear. Therefore, all of the

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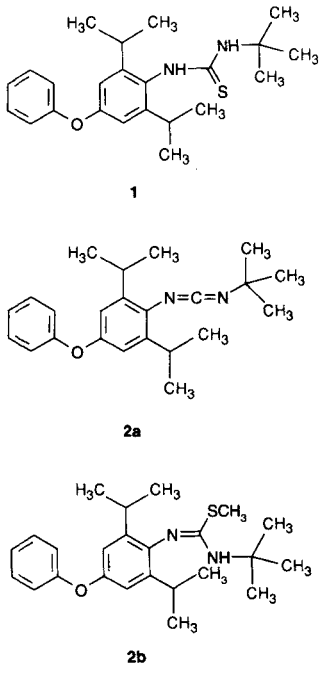
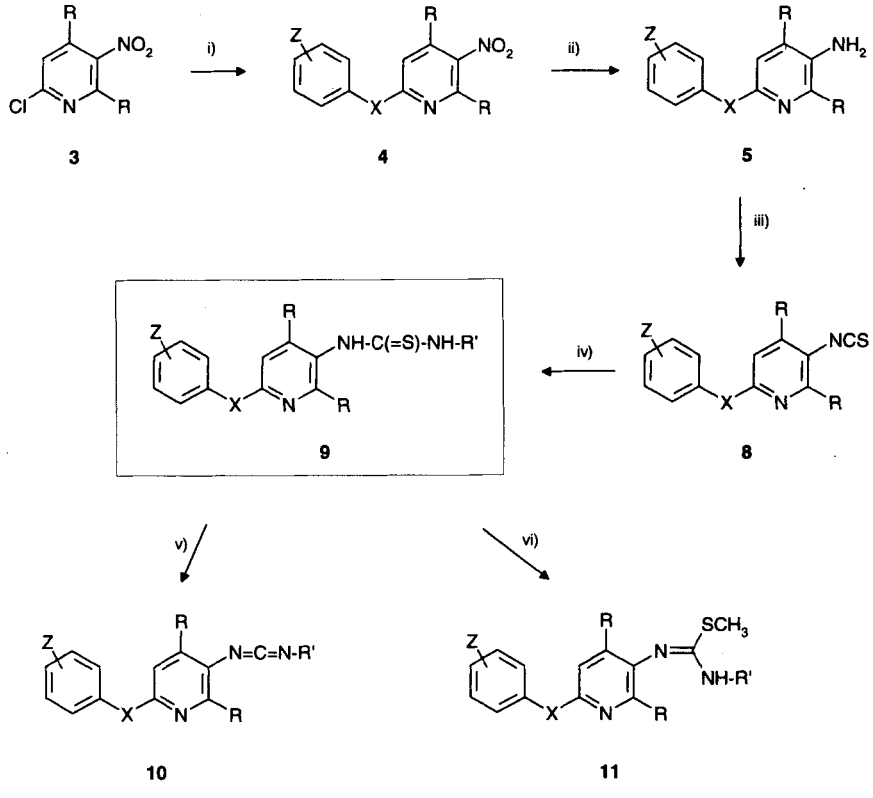


Fig. 1. Structure of diafenthiuron (**1**) and of the corresponding carbodiimide (**2a**) and S-methylisothiourea (**2b**).

prepared derivatives **10** and **14** contain bulky groups on either side of the carbodiimide functionality. This blocking of the reactive moiety produces compounds stable against hydrolysis which could be tested as an aqueous dilution (EC formulation) in most cases.

2.2 Physicochemical characterisation

Melting points (mp) were determined on a Kofler hot-plate apparatus (Fa. Reichert, Vienna). IR spectra were recorded on a Perkin-Elmer-157G spectrometer in carbon tetrachloride, unless otherwise stated; values are given for the main bands in cm^{-1}. [^{1}H]NMR spectra were recorded on a Varian-EM 360-EL (60 MHz) or a Bruker-AC-F250 (250 MHz) spectrometer in deuterochloroform, unless otherwise stated; chemical shifts (δ) are in ppm relative to tetramethylsilane as internal standard and coupling constants (J) are given in Hz. The refractive indices were measured with a Carl-Zeiss refractometer. UV spectra were recorded on a Perkin-Elmer Lambda-5 UV/VIS apparatus, in ethanol; values are given in nm. Elemental analyses were in all cases consistent with the calculated values.



i) subst. phenol or thiophenol, K_2CO_3/DMSO
ii) H_2, Ra-Ni, THF/C_2H_5OH, 30-35°C
iii) 1) CS_2, $(C_2H_5)_3N$/Py, -10°C; 2) DCC
iv) $R'NH_2$, toluene
v) 2-chloro- 1 -methylpyridinium iodide, $(C_2H_5)_3N/CH_3CN$
vi) CH_3I/C_2H_5OH

Fig. 2. Synthesis of the phenoxy and phenylthio substituted 3-pyridylthioureas **9** and carbodiimide and isothiourea derivatives **10** and **11**.

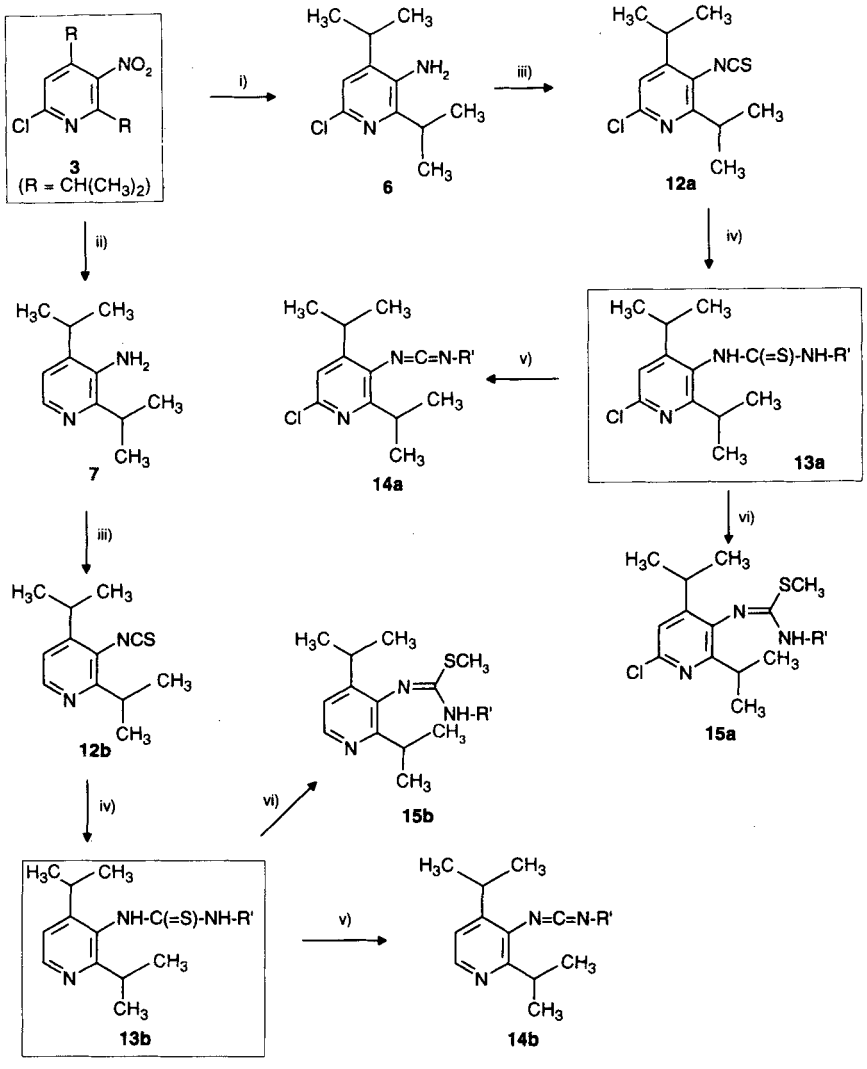


Fig. 3. Synthesis of the thioureas **13** and carbodiimide and isothiourea derivatives **14** and **15**.

2.3 Methods of synthesis

2.3.1 6-Chloro-2,4-diisopropylpyridine-3-amine (Fig. 3; 6)
6-Chloro-2,4-diisopropyl-3-nitropyridine (**3**, R = CH-$(CH_3)_2$,[25] 30·0 g, 0·124 mol) was dissolved in tetrahydrofuran (450 ml) and, after the addition of Raney nickel (30·0 g suspended in ethanol), hydrogenated under a hydrogen pressure of 20 bar at a temperature of 30–35°C. The reaction mixture was filtered over diatomaceous earth and the filtrate concentrated. The residue was purified by flash chromatography[28] (eluent: ethyl acetate + hexane (1 + 4 by volume)) on silica gel yielding **6** (21·1 g, 80%) in the form of a clear crystalline powder, mp 53–56°C. IR: 3500, 3410, 2970, 1620, 1585, 1430; UV($\lambda(\varepsilon)$): 246 (9740), 303 (4840); [^{1}H]NMR (60 MHz): 1·20 and 1·25 (2d, 12H), 2·7–3·2 (m, 2H), 3·65 (br s, 2H), 6·85 (s, 1H).

2.3.2 2,4-Diisopropylpyridine-3-amine (7)
6-Chloro-2,4-diisopropyl-3-nitropyridine (5·0 g, 0·0206 mol) was dissolved in tetrahydrofuran (100 ml) and, after the addition of triethylamine (2·75 g) and 5% palladium/carbon catalyst (7·5 g), hydrogenated under normal pressure at a temperature of 20–25°C. The reaction mixture was filtered over diatomaceous earth and the filtrate concentrated. The residue was purified by flash chromatography (eluent: ethyl acetate + hexane (1 + 3 by volume)) on silica gel yielding **7** (3·0 g, 82%) as a waxlike solid, mp 35–39°C. IR: 3480, 3400, 2970, 1615, 1420; UV($\lambda(\varepsilon)$): 239 (5740), 294 (4020); [^{1}H]NMR (60 MHz): 1·22 and 1·30 (2d, 12H), 2·88 and 3·06 (2 hept, 2H), 3·70 (br s, 2H), 6·82 (d, 1H, J = 5), 7·98 (d, 1H, J = 5).

*2.3.3 6-(4-Chlorophenoxy)-2,4-diisopropylpyridine-3-amine (**5b**)*

6-(4-Chlorophenoxy)2,4-diisopropyl-3-nitropyridine (**4**, R = $CH(CH_3)_2$, X = O, Z = 4-Cl)[25] (26·0 g, 0·0776 mol) was dissolved in tetrahydrofuran (260 ml) and, after the addition of Raney nickel (15·0 g suspended in ethanol), hydrogenated under normal pressure at a temperature of 30–35°C. The reaction mixture was filtered over diatomaceous earth and the filtrate concentrated. The residue was purified by column chromatography (eluent: ethyl acetate + hexane (1 + 3 by volume)) on silica gel yielding **5b** (19·3 g, 82%) in the form of a light-yellow crystalline powder, mp 86–88°C. IR: 3480, 3400, 2970, 1590, 1485, 1410, 1350, 1225, 1090, 975; UV($\lambda(\varepsilon)$): 244 (13940), 306 (5120); [^{1}H]NMR (60 MHz): 1·20 (d, 12H), 2·7–3·2 (m, 2H), 3·50 (br s, 2H), 6·50 (s, 1H), 6·95 and 7·25 (AA'BB'-system, 4H).

*2.3.4 6-(4-Chlorophenoxy)-2,4-diethylpyridine-3-amine (**5o**)*

3,5-Heptanedione was condensed with cyanoacetamide in ethanol[29] to form 4,6-diethyl-2-oxopyridine-3-carbonitrile (77%), mp 188–189°C; this was nitrated by means of fuming nitric acid in acetic anhydride[25,29] to yield 4,6-diethyl-5-nitro-2-oxopyridine-3-carbonitrile (74%), mp 207–208°C (dec.; from toluene), which was hydrolysed and decarboxylated in hot dilute sulfuric acid[30] to yield crude 4,6-diethyl-5-nitro-2-pyridone (93%), mp 163–165°C. Chlorination of the nitropyridone in neat phosphorus pentachloride[25,31] yielded 2-chloro-4,6-diethyl-5-nitropyridine (68% after chromatography), which was condensed directly with *p*-chlorophenol in dimethylsulfoxide in the precence of potassium carbonate[25] at 95°C for 3 h to give, after flash chromatography (ethyl acetate + hexane (1 + 10 by volume)), pure 6-(4-chlorophenoxy)-2,4-diethyl-3-nitropyridine (73%), mp 55–58°C. This was hydrogenated as described in Section 2.3.3. Flash chromatography (eluent: ethyl acetate + hexane (1 + 2 by volume)) of the crude product gave pure **5o** as a viscous oil in 98% yield. IR: 3480, 3400, 2980, 1595, 1485, 1415, 1350, 1230, 1165; UV: 244 (13780), 305 (5380); [^{1}H]NMR (250 MHz): 1·23 and 1·24 (t + t, 6H), 2·48 (q, 2H), 2·68 (q, 2H), 3·50 (br s, 2H), 6·52 (s, 1H), 6·97 and 7·25 AA'BB'-system, 4H).

*2.3.5 6-(4-Chlorophenoxy)-2,4-diisopropylpyrid-3-yl isothiocyanate (**8b**)*

A solution of triethylamine (5·0 g) in pyridine (10 ml) was cooled to −5° to −10°C by means of an ice/salt bath, and carbon disulfide (20 ml) added dropwise. At −10°C, a solution of **5b** (15·0 g, 0·0492 mol) in pyridine (27 ml) was slowly added dropwise. The mixture was stirred at −10°C for 1 h. A solution of *N,N'*-dicyclohexylcarbodiimide (10·0 g) in pyridine (10 ml) was then added. After a further 3 h at −10°C, the mixture was stirred at room temperature for 28 h. The reaction mixture was concentrated by evaporation and hexane added to the residue. The hexane mixture was filtered off and the filtrate concentrated by evaporation, yielding crude **8b** (16·3 g, 100%) as a dark oil, which was used directly for the synthesis of **9b** without further purification. IR: 2090, 1490, 1220.

*2.3.6 N-tert-Butyl-N'-[6-(4-chlorophenoxy)-2,4-diisopropylpyrid-3-yl]thiourea (**9ba**)*

Crude **8b** (8·15 g, *c.* 0·024 mol) was diluted with toluene (30 ml) and *tert*-butylamine (2·00 g, 0·0274) mol) added dropwise. The reaction mixture was then stirred for 2 h at 60°C. The reaction mixture was concentrated and hexane added to the residue. The resulting solid was filtered off and subsequently washed with hexane. **9ba** (9·00 g, 88%) was obtained in the form of colourless crystals, mp 165–167°C. IR (potassium bromide): 3480, 3160, 2980, 1540, 1490, 1400, 1345, 1270, 1220; UV($\lambda(\varepsilon)$): 242 (22 180), 280 (sh); [^{1}H]NMR (60 MHz, hexadeuterodimethylsulfoxide): 1·00 and 1·20 (d + d, 12H), 1·45 (s, 9H), 2·8–3·3 (m, 2H), 5·35 (br s, NH), 6·75 (s, 1H), 7·10 and 7·40 (AA'BB'-system, 4H), 8·40 (s, 1H).

*2.3.7 N-tert-Butyl-N'-[2,4-diisopropyl-6-(4-fluorophenoxy)pyrid-3-yl]carbodiimide (**10ca**)*

A solution of **9ca** (3·0 g, 0·0074 mol) and 2-chloro-1-methylpyridinium iodide (2·2 g) in acetonitrile (20 ml) was treated at room temperature with a solution of triethylamine (1·6 g) in acetonitrile (7 ml). The reaction mixture was then stirred for 1 h at 70°C. After evaporation of the solvent, the residue was taken up in hexane/water. The organic phase was dried over magnesium sulfate and the solvent removed under vacuum. The crude product was purified by column chromatography on silica gel (eluent: ethyl acetate + hexane (1 + 5 by volume)), yielding **10ca** (2·50 g, 92%) as a colourless oil which solidified after a few minutes, mp 56–60°C. IR: 2980, 2140, 1590, 1505, 1395, 1340, 1200; UV($\lambda(\varepsilon)$): 253 (13 740), 290 (sh); [^{1}H]NMR (60 MHz): 1·18 and 1·26 (d + d, 12H), 1·35 (s, 9H), 3·1–3·7 (m, 2H), 6·52 (s, 1H), 6·97 and 7·10 (AA'BB'-system, 4H).

*2.3.8 N-tert-Butyl-N'-[2,4-diisopropyl-6-(4-fluorophenoxy)pyrid-3-yl]-S-methylisothiourea (**11ca**)*

Methyl iodide (2·40 g) was added at room temperature to **9ca** (3·0 g, 0·0074 mol) in ethanol (35 ml) and the mixture heated at 75°C for 5 h. The mixture was then concentrated by evaporation and the residue taken up in methylene chloride and washed twice with dilute sodium hydrogen carbonate solution. The organic layer was dried over magnesium sulfate and the solvent evaporated. The crude product was purified by column chromatography on silica gel (eluent: ethyl acetate + hexane (1 + 5 by volume)). **11ca** (2·70 g, 87%) was obtained in the form of colourless crystalline powder, mp 97–100°C. IR (potassium bromide): 3420, 2970, 1610, 1500, 1430, 1390, 1320, 1190, 970; UV($\lambda(\varepsilon)$): 245 (15 280), 298 (5840); [^{1}H]NMR (60 MHz): 1·05 and 1·15 (d + d,

12H), 1·45 (s, 9H), 2·20 (s, 3H), 2·65–3·25 (m, 2H), 4·15 (br s, 1H), 6·45 (s, 1H), 6·90–7·20 (m, 4H).

2.3.9 General
Further details of yields and physical properties of all compounds synthesized are given as supplementary material in Tables S1, S2 and S3.

2.4 Biological test methods

2.4.1 Activity against the two-spotted spider mite, Tetranychus urticae *Koch*
Young bean plants (*Phaseolus vulgaris* L.) were infested with a mixed population of *T. urticae* and sprayed one day later with an aqueous spray containing 400 mg litre^{-1} of the active ingredient. The plants were then incubated for six days at 25°C and subsequently evaluated. The percentage of the reduction in population (% effect) was ascertained by comparing the number of dead eggs, larvae and adults on the treated plants with those on untreated plants.

2.4.2 Activity against the carmine spider mite, Tetranychus cinnabarinus *Boisd*
Young bean plants were infested with a mixed population of OP-resistant *T. cinnabarinus* and sprayed one day later with an aqueous spray containing 200, 100 or 50 mg litre^{-1} of the active igredient. The plants were then incubated at 25°C and subsequently evaluated after nine days. The mortality rate (% effect) in population was ascertained as in Section 2.4.1.

2.4.3 Persistence against Tetranychus cinnabarinus
Young bean plants were sprayed with an aqueous dispersion containing 200 mg litre^{-1} of the active ingredient and incubated for eight days at 25°C. The plants were then populated with a mixed population of OP-resistant *T. cinnabarinus*, incubated for a further five days and subsequently evaluated. The mortality rate (% effect) in population was ascertained as in Section 2.4.1.

2.4.4 Activity against the European red spider mite, Panonychus ulmi *Koch*
Apple seedlings were populated with adult females of OP- and carbamate-resistant *P. ulmi*. Seven days later the infested plants were sprayed to run-off with an aqueous spray containing 200 mg litre^{-1} of the test compound and incubated for a further two weeks in the greenhouse at 25°C. The percentage of the reduction in population (% effect) was ascertained by comparing the number of dead spider mites on the treated plants with that on untreated plants.

3 RESULTS AND DISCUSSION

3.1 Biological activity

3.1.1 General remarks
The pyridine derivatives **9**, **10**, **11** and **13**–**15** showed a wide activity against insects and mites, especially against chewing insects (e.g. *Spodoptera* ssp., *Heliothis* ssp., *Crocidolomia binotalis* Zell.) and spider mites (e.g. *Tetranychus* ssp.). The most promising activity was found to be the acaricidal one; in this paper only the results of the acaricidal screening will be discussed (Tables 1, 2, 3). For a closer inspection of the acaricidal efficacy of the compounds included in the present study, it is convenient to discuss the thioureas **9** and **13**, the carbodiimides **10** and **14** and the isothioureas **11** and **15** in a separate way. The activity range in the biological tests (hence the accuracy of the data presented in Tables 1, 2 and 3) is quite broad (usually a factor of two) but consistent and similar to the normal variation observed in most biological systems. The screening procedure included a first test against *T. urticae* at 400 mg litre^{-1}; compounds showing good activity in this test checked against *T. cinnabarinus* for persistence and a preliminary activity level (down to 50 mg litre^{-1}) was determined. The best compounds therein were subsequently tested against *P. ulmi*. Within the present study, the results obtained against *T. cinnabarinus* are the most relevant ones.

3.1.2 Acaricidal activity of thioureas 9 and 13
Compounds with small substituents at the 6-position of the pyridine ring (**13a**, **13b**) as well as those bearing a 2,4-dimethyl pattern on the heteroaromatic ring (**9qa**, **9ra**, **9ta**) are mostly inactive (Table 1); good potency is associated with the simultaneous presence of 2,4-diethyl or 2,4-diisopropyl substitution and an aromatic system linked by a heteroatom to the pyridine nucleus. The *tert*-butyl type of substitution (R′ = *tert*-butyl) in the non-aromatic part usually shows much better results than isopropyl substitution. The substitution pattern on the phenoxy part of the molecule can be varied considerably; the presence of acetyl (compound **9ha**), dimethylamino (**9ia**) or acetamido (**9ja**) groups is detrimental to activity. Results with compounds **9da** (2,4-Cl_2) and **9ka** (2-F) suggest that the presence of 2-substitution is also detrimental to the activity against *T. cinnabarinus*. The most active compounds against the same spider mite were **9fa** (4-CH_3O) and **9na** (4-C_6H_5CO), whilst **9bc** (4-Cl), **9fa** (4-CH_3O), **9ga** (4-*t*-C_4H_9) and **9la** (4-CH_3S) were the most persistent.

A common weakness of many thioureas **9** is the lack of ovicidal activity. No correlation was observed for the thioureas **9** with respect to their activity level and persistence against *T. cinnabarinus*. A few tested compounds showed high activity against *P. ulmi*.

TABLE 1
Acaricidal Activity of Thioureas **9** and **13**

Comp.	X	R	Z	R'	Activity against T. urticae[a]			Activity against T. cinnabarinus: Persistence[b]			Activity against T. cinnabarinus: Activity level[c]			Activity against P. ulmi[d]
					Eggs	Larvae	Adults	Eggs	Larvae	Adults	Eggs	Larvae	Adults	
9aa	O	*iso*-C_3H_7	H	*tert*-C_4H_9	++	++	++	·	·	·	−−	100	>200	·
9ab	O	*iso*-C_3H_7	H	*iso*-C_3H_7	−−	++	++	·	·	·	−−	>200	−−	·
9ac	O	*iso*-C_3H_7	H	*cyclo*-C_5H_9	−−	−−	++	·	<40	<40	−−	−−	−−	·
9ba	O	*iso*-C_3H_7	4-Cl	*tert*-C_4H_9	−−	++	++	<40	<40	<40	−−	50	>200	·
9bb	O	*iso*-C_3H_7	4-Cl	*iso*-C_3H_7	−−	++	++	·	<40	<40	−−	>200	−−	·
9bc	O	*iso*-C_3H_7	4-Cl	$C(CH_3)_2C_2H_5$	−−	++	++	·	100	100	−−	50	100	++
9ca	O	*iso*-C_3H_7	4-F	*tert*-C_4H_9	++	++	++	·	50	60	>200	⩽50	⩽50	·
9cb	O	*iso*-C_3H_7	4-F	*iso*-C_3H_7	++	++	++	·	0	10	−−	>200	200	·
9da	O	*iso*-C_3H_7	2,4-Cl_2	*tert*-C_4H_9	++	++	++	·	0	0	−−	>200	>200	·
9db	O	*iso*-C_3H_7	2,4-Cl_2	*iso*-C_3H_7	+	+	+	·	0	30	−−	>200	>200	·
9ea	O	*iso*-C_3H_7	3,4-Cl_2	*tert*-C_4H_9	++	++	++	·	0	0	−−	50	100	·
9eb	O	*iso*-C_3H_7	3,4-Cl_2	*iso*-C_3H_7	−−	++	++	·	0	0	−−	−−	−−	·
9fa	O	*iso*-C_3H_7	4-CH_3O	*tert*-C_4H_9	++	++	++	·	80	98	−−	50	50	++
9fb	O	*iso*-C_3H_7	4-CH_3O	*iso*-C_3H_7	−−	++	++	·	0	0	−−	−−	−−	·
9ga	O	*iso*-C_3H_7	4-*tert*-C_4H_9	*tert*-C_4H_9	++	++	++	·	100	100	−−	100	100	++
9gb	O	*iso*-C_3H_7	4-*tert*-C_4H_9	*iso*-C_3H_7	−−	++	++	·	0	0	−−	−−	−−	·
9ha	O	*iso*-C_3H_7	4-CH_3CO	*tert*-C_4H_9	−−	++	++	·	0	0	−−	−−	−−	·
9hb	O	*iso*-C_3H_7	4-CH_3CO	*iso*-C_3H_7	−−	−−	−−	·	·	·	·	·	·	·
9ia	O	*iso*-C_3H_7	4-$(CH_3)_2N$	*tert*-C_4H_9	++	++	++	·	0	0	−−	>200	>200	·
9ja	O	*iso*-C_3H_7	4-CH_3CONH	*tert*-C_4H_9	−−	−−	−−	·	·	·	·	·	·	·
9ka	O	*iso*-C_3H_7	2-F	*tert*-C_4H_9	++	++	++	·	0	0	−−	>200	>200	·
9la	O	*iso*-C_3H_7	4-CH_3S	*tert*-C_4H_9	++	++	++	100	70	98	−−	50	100	+
9ma	O	*iso*-C_3H_7	4-CH_3	*tert*-C_4H_9	++	++	++	70	70	80	−−	50	100	++
9na	O	*iso*-C_3H_7	4-C_6H_5CO	*tert*-C_4H_9	+	++	++	·	40	60	−−	⩽50	⩽50	·
9oa	O	C_2H_5	4-Cl	*tert*-C_4H_9	+	++	++	<40	<40	<40	−−	50	200	·
9pa	O	C_2H_5	4-F	*tert*-C_4H_9	++	++	++	<40	<40	<40	−−	50	200	·
9qa	O	CH_3	H	*tert*-C_4H_9	−−	−−	−−	·	·	·	·	·	·	·
9ra	O	CH_3	4-Cl	*tert*-C_4H_9	−−	−−	++	·	·	·	−−	−−	−−	·
9sa	S	*iso*-C_3H_7	H	*tert*-C_4H_9	++	++	++	·	0	0	>200	50	100	·
9ta	S	CH_3	H	*tert*-C_4H_9	−−	−−	−−	·	·	·	·	·	·	·
13aa	Cl	*iso*-C_3H_7	−−	*tert*-C_4H_9	−−	−−	++	<40	<40	<40	−−	−−	−−	·
13ab	Cl	*iso*-C_3H_7	−−	*iso*-C_3H_7	−−	−−	−−	·	·	·	·	·	·	·
13ba	H	*iso*-C_3H_7	−−	*tert*-C_4H_9	−−	+	+	<40	<40	<40	−−	−−	−−	·
13bb	H	*iso*-C_3H_7	−−	*iso*-C_3H_7	−−	−−	−−	·	·	·	·	·	·	·
1					++	++	++	<40	100	100	⩽50	50	⩽50	++

[a] Test 2.4.1. ++: 100%–80% mortality at 400 mg litre^{-1}; +: 70%–30%; −−: inactive or slightly active.
[b] Test 2.4.3. %-Mortality at 200 mg litre^{-1} after 8 days; ·: not tested/not evaluated.
[c] Test 2.4.2. Lowest rate (mg litre^{-1}) showing 80%–100% mortality after 9 days; −−: inactive; ·: not tested.
[d] Test 2.4.4. ++: Very good against all stages (100%–80% mortality), +: active (<80%), ·: not tested.

Several of the compounds **9** were as active as diafenthiuron.

*3.1.3 Acaricidal activity of carbodiimides **10** and **14***

Good levels of biological activity are usually associated with the same subsitution patterns as described for the thioureas (Table 2). Similarly, there is no good correlation between persistence and activity level against *T. cinnabarinus*, and good ovicidal activity is also lacking. *Para*-substitution on the phenoxy part of the molecules of the same substituents as were effective in compound **9**, leads to good biological activity against *T. cinnabarinus*, but surprisingly, compounds **10ha** (4-acetyl) and **10ia** (4-dimethylamino) are also highly active, although their thiourea counterparts show little or no activity. On the other hand, carbodiimides containing a 2-substituent show weak or no activity at all (**10da**, **10ka**).

In general, the carbodiimides **10** show more interesting activity against *T. cinnabarinus* than the corresponding thioureas **9** (compare Tables 1 and 2), and, in terms of activity against this pest, are comparable to compound **2a**. Against *P. ulmi*, however, the activities of compounds **10** are clearly inferior to that of compound **2a**.

TABLE 2
Acaricidal Activity of Carbodiimides **10** and **14**

Comp.	X	R	Z	R'	*Activity against* T. urticae[a]			*Activity against* T. cinnabarinus						*Activity against* P. ulmi[d]
								Persistence[b]			*Activity level*[c]			
					Eggs	*Larvae*	*Adults*	*Eggs*	*Larvae*	*Adults*	*Eggs*	*Larvae*	*Adults*	
10aa	O	*iso*-C_3H_7	H	*tert*-C_4H_9		Phytotoxicity		·	·	·	·	·	·	·
10ab	O	*iso*-C_3H_7	H	*iso*-C_3H_7		Phytotoxicity		·	·	·	·	·	·	·
10ac	O	*iso*-C_3H_7	H	*cyclo*-C_5H_9	++	++	++	·	50	95	−−	50	100	·
10ba	O	*iso*-C_3H_7	4-Cl	*tert*-C_4H_9	++	++	++	·	0	50	>200	50	100	·
10bb	O	*iso*-C_3H_7	4-Cl	*iso*-C_3H_7	++	++	++	·	·	·	−−	50	−−	·
10bc	O	*iso*-C_3H_7	4-Cl	$C(CH_3)_2C_2H_5$	++	++	++	·	0	90	>200	50	50	·
10ca	O	*iso*-C_3H_7	4-F	*tert*-C_4H_9	++	++	++	·	0	0	−−	>200	>200	·
10cb	O	*iso*-C_3H_7	4-F	*iso*-C_3H_7	−−	−−	−−	·	·	·	·	·	·	·
10da	O	*iso*-C_3H_7	2,4-Cl_2	*tert*-C_4H_9	++	++	++	·	0	0	−−	>200	>200	·
10db	O	*iso*-C_3H_7	2,4-Cl_2	*iso*-C_3H_7	++	++	++	·	0	0	−−	>200	100	·
10ea	O	*iso*-C_3H_7	3,4-Cl_2	*tert*-C_4H_9	++	++	++	·	10	0	>200	100	100	·
10eb	O	*iso*-C_3H_7	3,4-Cl_2	*iso*-C_3H_7	++	++	++	·	0	0	>200	200	200	·
10fa	O	*iso*-C_3H_7	4-CH_3O	*tert*-C_4H_9	++	++	++	·	50	50	−−	50	50	·
10fb	O	*iso*-C_3H_7	4-CH_3O	*iso*-C_3H_7	++	++	++	·	0	0	−−	50	200	·
10ga	O	*iso*-C_3H_7	4-*tert*-C_4H_9	*tert*-C_4H_9	++	++	++	·	30	30	−−	⩽50	100	·
10gb	O	*iso*-C_3H_7	4-*tert*-C_4H_9	*iso*-C_3H_7	++	++	++	·	0	0	−−	200	200	·
10ha	O	*iso*-C_3H_7	4-CH_3CO	*tert*-C_4H_9	++	++	++	·	90	100	−−	50	50	+
10hb	O	*iso*-C_3H_7	4-CH_3CO	*iso*-C_3H_7	++	++	++	·	0	0	−−	>200	>200	·
10ia	O	*iso*-C_3H_7	4-$(CH_3)_2N$	*tert*-C_4H_9	++	++	++	<40	<40	<40	−−	50	50	·
10ja	O	*iso*-C_3H_7	4-CH_3CONH	*tert*-C_4H_9	−−	++	++	·	30	30	−−	−−	−−	·
10ka	O	*iso*-C_3H_7	2-F	*tert*-C_4H_9	−−	−−	−−	·	·	·	·	·	·	·
10la	O	*iso*-C_3H_7	4-CH_3S	*tert*-C_4H_9	++	++	++	70	10	10	−−	⩽50	⩽50	·
10ma	O	*iso*-C_3H_7	4-CH_3	*tert*-C_4H_9	++	++	++	<40	<40	<40	−−	50	100	·
10na	O	*iso*-C_3H_7	4-C_6H_5CO	*tert*-C_4H_9	++	++	++	·	70	95	−−	⩽50	⩽50	+
10oa	O	C_2H_5	4-Cl	*tert*-C_4H_9	−−	+	+	<40	<40	<40	−−	−−	−−	·
10pa	O	C_2H_5	4-F	*tert*-C_4H_9		Phytotoxicity		·	·	·	·	·	·	·
10qa	O	CH_3	H	*tert*-C_4H_9	−−	−−	−−	·	·	·	·	·	·	·
10ra	O	CH_3	4-Cl	*tert*-C_4H_9	−−	−−	−−	·	·	·	·	·	·	·
10sa	S	*iso*-C_3H_7	H	*tert*-C_4H_9	++	++	++	<40	<40	<40	200	⩽50	⩽50	·
10ta	S	CH_3	H	*tert*-C_4H_9	−−	−−	++	·	·	·	−−	>200	>200	·
14aa	Cl	*iso*-C_3H_7	−−	*tert*-C_4H_9	−−	++	++	<40	<40	<40	−−	−−	−−	·
14ab	Cl	*iso*-C_3H_7	−−	*iso*-C_3H_7	−−	++	++	<40	<40	<40	−−	−−	−−	·
14ba	H	*iso*-C_3H_7	−−	*tert*-C_4H_9	−−	−−	+	0	0	0	−−	>200	>200	·
14bb	H	*iso*-C_3H_7	−−	*iso*-C_3H_7	−−	+	+	<40	<40	<40	−−	−−	−−	·
2a					++	++	++	⩽40	20	75	50	⩽50	⩽50	++

[a] Test 2.4.1. ++: 100%–80% mortality at 400 mg litre^{-1}; +: 70%–30%; −−: inactive or slightly active.
[b] Test 2.4.3. %-Mortality at 200 mg litre^{-1} after 8 days; ·: not tested/not evaluated.
[c] Test 2.4.2. Lowest rate (mg litre^{-1}) showing 80%–100% mortality after 9 days; −−: inactive; ·: not tested.
[d] Test 2.4.4. ++: very good against all stages (100%–80% mortality), +: active (<80%), ·: not tested.

3.1.4 Acaricidal activity of isothioureas 11 and 15
In this series a much lower level of activity can be observed (Table 3). Only a few compounds reached an acceptable activity level and persistence, but were still clearly inferior to compound **2b**. The isothioureas were, therefore, not further investigated.

3.2 Discussion

The present work concentrates on the replacement of the central aromatic nucleus of diafenthiuron by a pyridine ring, taking advantage of the structure–activity relationships for the thiourea (or carbodiimide) moiety already developed in the series of compounds containing a central aromatic nucleus. The following general conclusions can be drawn from data available in Tables 1, 2 and 3:

(a) Compounds of the types **9** and **10** show a very interesting level of activity in the acaricidal tests, a few of them reaching the activity of diafenthiuron and its relatives. The isothioureas **11** are, comparatively, much weaker (Table 3) and deviate, therefore, from the known behaviour of the isothioureas in the series of compounds with a central benzene ring.

TABLE 3
Acaricidal Activity of Isothioureas **11** and **15**

					Activity against T. urticae[a]			*Activity against* T. cinnabarinus					
								Persistence[b]			*Activity level*[c]		
Comp.	*X*	*R*	*Z*	*R'*	*Eggs*	*Larvae*	*Adults*	*Eggs*	*Larvae*	*Adults*	*Eggs*	*Larvae*	*Adults*
11aa	O	*iso*-C_3H_7	H	*tert*-C_4H_9	−−	+	++	·	·	·	·	·	·
11ab	O	*iso*-C_3H_7	H	*iso*-C_3H_7	−−	++	++	·	·	·	−−	>200	>200
11ac	O	*iso*-C_3H_7	H	cyclo-C_5H_9	−−	−−	−−	·	·	·	·	·	·
11ba	O	*iso*-C_3H_7	4-Cl	*tert*-C_4H_9	−−	−−	−−	·	·	·	·	·	·
11bb	O	*iso*-C_3H_7	4-Cl	*iso*-C_3H_7	−−	−−	−−	·	·	·	·	·	·
11bc	O	*iso*-C_3H_7	4-Cl	$C(CH_3)_2C_2H_5$	−−	−−	++	·	·	·	−−	−−	−−
11ca	O	*iso*-C_3H_7	4-F	*tert*-C_4H_9	+	++	++	·	0	0	−−	>200	>200
11cb	O	*iso*-C_3H_7	4-F	*iso*-C_3H_7	++	++	++	·	0	0	−−	200	200
11da	O	*iso*-C_3H_7	2,4-Cl_2	*tert*-C_4H_9	−−	−−	−−	·	·	·	·	·	·
11db	O	*iso*-C_3H_7	2,4-Cl_2	*iso*-C_3H_7	−−	++	++	<40	<40	<40	−−	−−	−−
11ea	O	*iso*-C_3H_7	3.4-Cl_2	*tert*-C_4H_9	−−	−−	−−	·	·	·	·	·	·
11eb	O	*iso*-C_3H_7	3,4-Cl_2	*iso*-C_3H_7	+	++	++	·	20	20	−−	200	>200
11fa	O	*iso*-C_3H_7	4-CH_3O	*tert*-C_4H_9	+	++	++	·	60	60	−−	100	200
11fb	O	*iso*-C_3H_7	4-CH_3O	*iso*-C_3H_7	−−	−−	−−	·	·	·	·	·	·
11ga	O	*iso*-C_3H_7	4-*tert*-C_4H_9	*tert*-C_4H_9	−−	−−	++	·	0	0	−−	−−	−−
11gb	O	*iso*-C_3H_7	4-*tert*-C_4H_9	*iso*-C_3H_7	−−	−−	++	·	0	0	−−	−−	−−
11ha	O	*iso*-C_3H_7	4-CH_3CO	*tert*-C_4H_9	−−	−−	−−	·	·	·	·	·	·
11hb	O	*iso*-C_3H_7	4-CH_2CO	*iso*-C_3H_7	−−	−−	−−	·	·	·	·	·	·
11ia	O	*iso*-C_3H_7	4-$(CH_3)_2N$	*tert*-C_4H_9	−−	++	++	<40	<40	<40	−−	−−	−−
11ja	O	*iso*-C_3H_7	4-CH_3CONH	*tert*-C_4H_9	−−	−−	−−	·	·	·	·	·	·
11ka	O	*iso*-C_3H_7	2-F	*tert*-C_4H_9	+	++	++	·	0	50	−−	−−	−−
11la	O	*iso*-C_3H_7	4-CH_3S	*tert*-C_4H_9	++	++	++	70	0	40	−−	200	−−
11ma	O	*iso*-C_3H_7	4-CH_3	*tert*-C_4H_9	−−	−−	−−	·	·	·	·	·	·
11na	O	*iso*-C_3H_7	4-C_6H_5CO	*tert*-C_4H_9	+	++	++	<40	<40	<40	−−	>200	>200
11oa	O	C_2H_5	4-Cl	*tert*-C_4H_9	−−	++	++	<40	<40	<40	−−	−−	−−
11pa	O	C_2H_5	4-F	*tert*-C_4H_9	+	++	++	<40	<40	<40	−−	−−	−−
11ra	O	CH_3	4-Cl	*tert*-C_4H_9	−−	−−	−−	·	·	·	·	·	·
11sa	S	*iso*-C_3H_7	H	*tert*-C_4H_9	+	++	++	<40	<40	<40	−−	−−	−−
15aa	Cl	*iso*-C_3H_7	−−	*tert*-C_4H_9	−−	−−	−−	·	·	·	·	·	·
15ab	Cl	*iso*-C_3H_7	−−	*iso*-C_3H_7	−−	−−	−−	·	·	·	·	·	·
15ba	H	*iso*-C_3H_7	−−	*tert*-C_4H_9	−−	+	+	<40	<40	<40	−−	−−	−−
15bb	H	*iso*-C_3H_7	−−	*iso*-C_3H_7	−−	−−	−−	·	·	·	·	·	·
2b					++	++	++	<40	100	100	>200	100	⩽50

[a] Test 2.4.1. + +: 100%–80% mortality at 400 mg litre^{-1}; +: 70%–30%; −−: inactive or slightly active.
[b] Test 2.4.3. %-Mortality at 200 mg litre^{-1} after 8 days; ·: not tested/not evaluated.
[c] Test 2.4.2. Lowest rate (mg litre^{-1}) showing 80%–100% mortality after 9 days; −−: inactive; ·: not tested.

(b) Good persistence is shown only by very few compounds (mostly thioureas **9**).

(c) The substitution pattern must contain, in all derivatives, sterically demanding groups at both sides of the thiourea/carbodiimide unit. Simultaneously, a phenoxy (or phenylthio) group at position 6 of the pyridine ring is needed in order to reach a useful level of activity. This observation supports the conclusions drawn from the exhaustive studies already performed in the series of compounds with a central benzene ring.[24]

(d) The role of the substituents at the phenoxy group (Z) is at the moment poorly understood. Small changes to the substituents in the phenoxy ring can lead to large differences in the biological behaviour of the corresponding molecules.

(e) There is apparently no good correlation between the best thioureas, **9**, and the best carbodiimides, **10**, in respect of their activity level and persistence against *T. cinnabarinus*. Both facts are probably closely related to (d).

The general differences observed between the pyridine derivatives and the analogues of diafenthiuron are then mostly unfavourable for the pyridines and can be summarised as follows:

(i) lack of persistence;
(ii) lack of correlation between good active compounds **9** and **10**.

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REFERENCES

1. Enders, E., Stendel, W. & Hammann, I. (Bayer AG), German Pat. Appl. 2,639,748 (1978); *CA* **89**: 6132d.
2. Enders, E., Hammann, I. & Stendel, W. (Bayer AG), German Pat. Appl. 2,801,376 (1979): *CA* **91**: 174906u.
3. Enders, E., Stendel, W., Hammann, I. & Behrenz, W. (Bayer AG), German Pat. Appl. 2,730,620 (1979): *CA* **90**: 151852p.
4. Enders. E., Stendel, W., Hammann I. & Behrenz, W. (Bayer AG), German Pat. Appl. 2,801,318 (1979); *CA* **92**: 75962y.
5. Drábek, J. & Böger, M. (Ciba-Geigy AG), German Pat. Appl. 3,034,905 (1981).
6. Drábek, J. (Ciba-Geigy AG), European Pat. Appl. 145,662 (1985); *CA* **104**: 88320d.
7. Ehrenfreund, J. (Ciba-Geigy AG), European Pat. Appl. 282,452 (1988); *CA* **110**: 172897d.
8. Böger, M., Drábek, J. & Ehrenfreund, J. (Ciba-Geigy AG), European Pat. Appl. 296,120 (1988); *CA* **110**: 192459r.
9. Ehrenfreund, J. & Drábek, J. (Ciba-Geigy AG), European Pat. Appl. 481,921 (1992); *CA* **117**: 111278a.
10. Böger, M. & Drábek, J. (Ciba-Geigy AG), European Pat. Appl. 175,649 (1986); *CA* **108**: 94206v.
11. Ehrenfreund, J. (Ciba-Geigy AG), European Pat. Appl. 304,025 (1989); *CA* **111**: 39019y.
12. Böger, M., Drábek, J. & Ehrenfreund, J. (Ciba-Geigy AG), European Pat. Appl. 304,402 (1989); *CA* **111**: 96866w.
13. Böger, M. & Drábek, J. (Ciba-Geigy AG), European Pat. Appl. 239,535 (1987); *CA* **108**: 70646n.
14. Böger, M., Drábek, J., Ehrenfreund, J. & Kristiansen, O. (Ciba-Geigy AG), European Pat. Appl. 256,985 (1988); *CA* **109**: 73462f.
15. Ehrenfreund, J., Böger, M., Kristiansen, O., Drábek, J. & Kristinsson, H. (Ciba-Geigy AG), European Pat. Appl. 262,087 (1988); *CA* **109**: 6507m.
16. Böger, M., Drábek, J. & Ehrenfreund, J. (Ciba-Geigy AG), European Pat. Appl. 298,915 (1989); *CA* **110**: 231444d.
17. Ehrenfreund, J., Böger, M. & Drábek, J. (Ciba-Geigy AG), European Pat. Appl. 302,014 (1989): *CA* **110**: 231295f.
18. Böger, M., Drábek, J. & Ehrenfreund, J. (Ciba-Geigy AG), German Pat. Appl. 3,801,395 (1988); *CA* **109**: 170052.
19. Pascual, A., Herstellung von substituierten 2-Aminooxazole-4-carbonitrilen. *Helv. Chim. Acta*, **72** (1989) 556.
20. Pascual, A., Transformations in the isoxazole series: Synthesis of substituted 2-aminothiazoles. *Helv. Chim. Acta*, **74** (1991) 531.
21. Pascual, A. (Ciba-Geigy AG), European Pat. Appl. 407,346 (1991); *CA* **114**: 247150y.
22. Pascual, A. (Ciba-Geigy AG), European Pat. Appl. 423,072 (1991); *CA* **115**: 71384g.
23. Streibert, H. P., Drábek, J. & Rindlisbacher, A., CGA 106630—A new type of acaricide/insecticide for the control of the sucking pest complex in cotton and other crops. *Brighton Crop Prot. Conf.—Pests Dis.*, **1** (1988) 25.
24. Drábek, J., Böger, M., Ehrenfreund, J., Stamm, E., Steinemann, A., Alder, A. & Burckhardt, U., New thioureas as insecticides. In *Recent Advances in Chemical Insect Control, II*. RSC, Spec. Publ. **79**, 1990, pp. 170–83.
25. Pascual, A., Nucleophilic displacement reactions on sterically hindered chloro-pyridines: Some optimisation studies. *Bull. Soc. Chim. Belg.*, **101** (1992) 297.
26. Jochims, J. Ch., Über eine neue Synthese aromatischer Isothiocyanate. *Chem. Ber.*, **101** (1968) 1746.
27. Shibanuma, T., Shiono, M. & Mukaiyama, T., A convenient method for the preparation of carbodiimides using 2-chloropyridinium salt. *Chem. Lett.*, (1977) 575.
28. Still, W. C., Kahn, M. & Mitra, A., Rapid chromatographic technique for preparative separations with moderate resolution. *J. Org. Chem.*, **43** (1978) 2923.
29. Wibaut, J. P., Uhlenbroek, J. H., Kooyman, E. C. & Kettenes, D. K., Note on the preparation of 3-hydroxy-5-hydroxymethyl-2,4-dimethyl-pyridine (4-desoxyadermine). *Rec. Trav. Chim. Pays-Bas.*, **79** (1960) 481.
30. Loth, H. & Hempel, B., Untersuchungen zum Mechanismus der Oxydation von Hydroxy-pyridonen und Synthese einiger Hydroxy-methyl-pyridone. *Arch. Pharmaz.*, **305** (1972) 724.
31. Mariella, R. P., Callahan, J. J. & Jibril, A. O., Some novel color reactions of some pyridine derivatives. *J. Org. Chem.*, **20** (1955) 1721.

SUPPLEMENTARY MATERIAL

TABLE S1
Pyrid-3-ylamines **5** and isothiocyanates **8** and **12**

Comp.	*X*	*R*	*Z*	*Yield*[a]	*Mp* (°C)	*Phys. data for corresponding compound* **8**
5a	O	*iso*-C_3H_7	H	76	52–54	Oil; IR(CCl_4): 2120, 2090, 1590, 1360, 1210
5b	O	*iso*-C_3H_7	4-Cl	82	86–88	Oil; IR(CCl_4): 2090, 1490, 1220
5c	O	*iso*-C_3H_7	4-F	91	50–52	Oil; IR(CCl_4): 2120, 2080, 1505, 1200
5d	O	*iso*-C_3H_7	2,4-Cl_2	92	Viscous oil	Oil; IR(CCl_4): 2120, 2090, 1600, 1475
5e	O	*iso*-C_3H_7	3,4-Cl_2	90	Viscous oil	Oil; IR(CCl_4): 2120, 2090, 1585, 1470
5f	O	*iso*-C_3H_7	4-CH_3O	95	Viscous oil	Oil; IR(CCl_4): 2120, 2090, 1505, 1205
5g	O	*iso*-C_3H_7	4-*tert*-C_4H_9	80	Viscous oil	Oil; IR(CCl_4): 2120, 2090, 1510, 1220
5h	O	*iso*-C_3H_7	4-CH_3CO	94	Viscous oil	Oil; IR(CCl_4): 2120, 2080, 1690, 1590, 1225
5i	O	*iso*-C_3H_7	4-$(CH_3)_2N$	77	99–103	Mp 49–61

(*continued*)

TABLE S1 (*cont.*)

Comp.	*X*	*R*	*Z*	*Yield*[a]	*Mp* (°C)	*Phys. data for corresponding compound* ***8***
5j	O	*iso*-C_3H_7	4-CH_3CONH	94	120–121	Mp 122–132
5k	O	*iso*-C_3H_7	2-F	91	Viscous oil	Oil; IR(CCl_4): 2120, 2090, 1500, 1265
5l	O	*iso*-C_3H_7	4-CH_3S	68	Viscous oil	Oil; IR(CCl_4): 2110, 2090, 1590, 1490, 1215
5m	O	*iso*-C_3H_7	4-CH_3	57	Viscous oil	Mp 64–67
5n	O	*iso*-C_3H_7	4-C_6H_5CO	52	Wax	Mp 106–107
5o	O	C_2H_5	4-Cl	98	Viscous oil	Oil; IR(CCl_4): 2080, 1590, 1485, 1215
5p	O	C_2H_5	4-F	98	Viscous oil	Oil; IR(CCl_4): 2080, 1590, 1500, 1195
5q	O	CH_3	H	90	81–85	Oil; IR(CCl_4): 2090, 1345, 1215
5r	O	CH_3	4-Cl	75	93–94	Oil; IR(CCl_4): 2080, 1490, 1345, 1220
5s	S	*iso*-C_3H_7	H	79	Viscous oil	Oil; IR(CCl_4): 2120, 2090, 1570, 935
5t	S	CH_3	H	82	114–116	Wax; IR(CCl_4): 2120, 2080, 1445, 935
Comp.						*Phys. data for corresponding compound* ***12***
12a						Mp 56–74
12b						Oil; [1H]NMR (60 MHz, $CDCl_3$): 6·95 and 8·30 (d + d, J = 5)

[a] In %; all compounds showed a satisfactory elemental analysis (within ±0·4%).

TABLE S2
Pyrid-3-ylthioureas **9** and **13**

Comp.	*X*	*R*	*Z*	*R'*	*Yield* (%)	*Mp* (°C)	*Isolation*[a]
9aa	O	*iso*C_3H_7	H	*tert*-C_4H_9	89	142–146	b
9ab	O	*iso*-C_3H_7	H	*iso*-C_3H_7	69	162–165	b
9ac	O	*iso*-C_3H_7	H	*cyclo*-C_5H_9	87	172–178	b
9ba	O	*iso*-C_3H_7	4-Cl	*tert*-C_4H_9	88	165–167	a
9bb	O	*iso*-C_3H_7	4-Cl	*iso*-C_3H_7	88	156–158	a
9bc	O	*iso*-C_3H_7	4-Cl	$C(CH_3)_2C_2H_5$	78	153–155	a
9ca	O	*iso*-C_3H_7	4-F	*tert*-C_4H_9	89	156–158	b
9cb	O	*iso*-C_3H_7	4-F	*iso*-C_3H_7	90	157–160	b
9da	O	*iso*-C_3H_7	2,4-Cl_2	*tert*-C_4H_9	67	114–116	b
9db	O	*iso*-C_3H_7	2,4-Cl_2	*iso*-C_3H_7	76	160–162	b
9ea	O	*iso*-C_3H_7	3,4-Cl_2	*tert*-C_4H_9	96	149–150	b
9eb	O	*iso*-C_3H_7	3,4-Cl_2	*iso*-C_3H_7	78	127–128	b
9fa	O	*iso*-C_3H_7	4-CH_3O	*tert*-C_4H_9	86	169–173	b
9fb	O	*iso*-C_3H_7	4-CH_3O	*iso*-C_3H_7	98	179–184	a
9ga	O	*iso*-C_3H_7	4-*tert*-C_4H_9	*tert*-C_4H_9	81	143–145	b
9gb	O	*iso*-C_3H_7	4-*tert*-C_4H_9	*iso*-C_3H_7	79	163–165	b
9ha	O	*iso*-C_3H_7	4-CH_3CO	*tert*-C_4H_9	87	131–133	b
9hb	O	*iso*-C_3H_7	4-CH_3CO	*iso*-C_3H_7	87	151–154	b
9ia	O	*iso*-C_3H_7	4-$(CH_3)_2N$	*tert*-C_4H_9	91	154–156	a
9ja	O	*iso*-C_3H_7	4-CH_3CONH	*tert*-C_4H_9	83	190–192	c
9ka	O	*iso*-C_3H_7	2-F	*tert*-C_4H_9	86	136–139	a
9la	O	*iso*-C_3H_7	4-CH_3S	*tert*-C_4H_9	80	156–157	a
9ma	O	*iso*-C_3H_7	4-CH_3	*tert*-C_4H_9	57	160–162	a
9na	O	*iso*-C_3H_7	4-C_6H_5CO	*tert*-C_4H_9	85	159–160	a
9oa	O	C_2H_5	4-Cl	*tert*-C_4H_9	96	137–140	a
9pa	O	C_2H_5	4-F	*tert*-C_4H_9	93	132–134	a
9qa	O	CH_3	H	*tert*-C_4H_9	77	162–163	d
9ra	O	CH_3	4-Cl	*tert*-C_4H_9	63	130–132	b
9sa	S	*iso*-C_3H_7	H	*tert*-C_4H_9	79	152–154	d
9ta	S	CH_2	H	*tert*-C_4H_9	90	144–146	c

TABLE S2 (*cont.*)

Comp.	*X*	*R*	*Z*	*R'*	*Yield* (%)	*Mp* (°C)	*Isolation*[a]
13aa				*tert*-C_4H_9	82	144–145	c
13ab				*iso*-C_3H_7	82	214	d + c
13ba				*tert*-C_4H_9	73	132–134	a
13bb				*iso*-C_3H_7	87	155–157	b

[a] a. Crude product washed with hexane; b. as a, followed by flash-chromatography; c. as a, followed by recrystallisation from cyclohexane or toluene; d. the solid formed during the reaction was filtered off and rinsed with hexane.

TABLE S3
Carbodiimides **10** and **14** and Isothioureas **11** and **15**

Comp.	*Yield* (%)	*Phys. data*	*Comp.*	*Yield* (%)	*Mp* (°C)
10aa	92	$n_D^{27} = 1.5470$	**11aa**	85	119–122
10ab	78	$n_D^{25} = 1.5485$	**11ab**	85	80–82
10ac	86	$n_D^{23} = 1.5605$	**11ac**	81	80–83
10ba	98	mp 46–55°C	**11ba**	89	95–100
10bb	97	$n_D^{23} = 1.5575$	**11bb**	98	90–95
10bc	90	$n_D^{22} = 1.5515$	**11bc**	71	91–93
10ca	92	mp 56–60°C	**11ca**	87	97–100
10cb	95	$n_D^{24} = 1.5439$	**11cb**	87	87–90
10da	92	$n_D^{23} = 1.5525$	**11da**	82	97–99
10db	84	$n_D^{23} = 1.5595$	**11db**	86	73–76
10ea	92	mp 62–65°C	**11ea**	90	121–123
10eb	82	$n_D^{24} = 1.5645$	**11eb**	82	80–82
10fa	96	mp 37–45°C	**11fa**	82	78–81
10fb	85	$n_D^{22} = 1.5520$	**11fb**	80	107–109
10ga	97	mp 60–63°C	**11ga**	85	110–112
10gb	98	$n_D^{23} = 1.5445$	**11gb**	77	80–83
10ha	87	mp 46–51°C	**11ha**	84	128–130
10hb	81	$n_D^{25} = 1.5610$	**11hb**	71	115–118
10ia	89	$n_D^{23} = 1.5629$	**11ia**	80	104–106
10ja	84	mp 152–154°C	**11ja**	89	155–158
10ka	91	$n_D^{25} = 1.5379$	**11ka**	90	95–97
10la	67	$n_D^{24} = 1.5721$	**11la**	71	95–96
10ma	61	mp 46–47°C	**11ma**	75	94–96
10na	79	mp 105–108°C	**11na**	68	41–42
10oa	93	$n_D^{21} = 1.5676$	**11oa**	90	90–93
10pa	95	$n_D^{21} = 1.5504$	**11pa**	91	94–97
10qa	97	$n_D^{25} = 1.5668$			
10ra	94	mp 59–61°C	**11ra**	98	118–120
10sa	89	$n_D^{25} = 1.6078$	**11sa**	85	76–80
10ta	82	$n_D^{23} = 1.5774$			
14aa	89	$n_D^{23} = 1.5310$	**15aa**	88	89–92
14ab	92	$n_D^{23} = 1.5363$	**15ab**	92	89–91
14ba	88	$n_D^{24} = 1.5173$	**15ba**	80	69–71
14bb	84	$n_D^{24} = 1.5230$	**15bb**	82	118–120