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Chemistry of polyhalogenated nitrobutadienes, 8: Nitropolychlorobutadienes—Precursors for insecticidal neonicotinoids

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ABSTRACT

Nitropolychlorobutadienes are valuable precursors for highly functionalized acyclic or (hetero)cyclic compounds. In this 8th part of our synthetically oriented series we focus on the application of these versatile starting materials in the synthesis of analogs of the heterocyclic insecticides imidacloprid™ and thiacloprid™, and the acyclic counterpart clothianidin™. In addition to the main synthetic part, leading to imidazolidines or oxazolidines, further promising types of compounds derived by subsequent chemical modifications, are introduced. Most of the new compounds show high insecticidal activity.

1. Introduction

The readily accessible 2-nitroperchloro-1,3-butadiene (**10**)[1a] is one of the most prominent members of the relatively new class of organic compounds, called polyhalogenated nitrobutadienes. The well-defined chemical reactivity of **10** runs contrary, on one hand to the superior reactivity of nitrobutadienes,[2] and on the other hand to the slow conversion rates of the rather stable hexachlorobutadiene. The latter requires harsh conditions and oftentimes leads only to product mixtures.[3]

Thus, being attacked by an appropriate nucleophile, **10** initially reacts at the terminal C-1 carbon atom to yield the product of a nucleophilic vinylic substitution process. Under more rigid conditions a subsequent substitution of the chlorine atom on C-3 is possible.

In the past five years we published the syntheses of a wide range of different acyclic as well as (hetero)cyclic compounds employing this versatile starting material.[4] Aside from synthetic and mechanistic aspects, these kinds of highly substituted organic compounds attracted our interest, owing to their biological activity. Even if chlorinated structures already suffer from lowered biological degradation processes, an additional nitro group enforces the physiological activity.[5]

Moreover, most of the compounds presented in this paper are more or less closely related to known insecticides like imidacloprid, thiacloprid, or clothianidin. All these are commercially available insecticides, essentially similar to the natural (*S*)-(−)-nicotine, and therefore named neonicotinoids (Fig. 1). The synthesis of the most famous member imidacloprid, that is, (2*E*)-1-[(6-chloropyridin-3-yl)methyl]-*N*-nitroimidazolidin-2-imine), from *N*-(6-chloropyridin-3-yl)methylethylenediamine and 1,1-bis(methylsulfanyl)-2-nitroethene) was primarily published by Kagabu et al. in 1992.[6]

Unlike other crop protection compounds, the neonicotinoids selectively bind to the nicotinic acetylcholine receptor (nAChR) of insects, thus inhibiting the regular neuro-transmitting process. This mode of action is based on the structural similarity of these compounds to the regular substrate, at least with respect to three significant aspects: the presence of an electrophilic moiety, especially a pyridine–nitrogen, and an additional H-bond acceptor, both located in a distance of about 0.59 nm.[7] This allows for the strong interaction of the neonicotinoids with the nAChR according to the lock-and-key principle. Interestingly, the selectivity for the nAChR of insects is mainly caused by the particular chemical substructure

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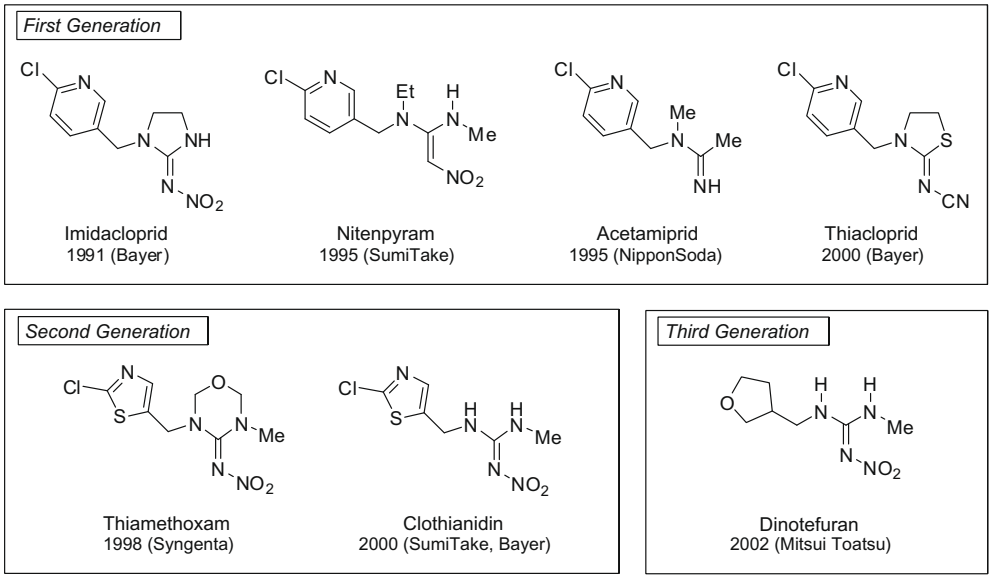


Figure 1. Neonicotinoids—Insecticides similar to natural nicotine.

of the proton acceptor, which is preferably a nitro-substituted imino or methylene group, or otherwise an *N*-cyanoimine.[8a]

Based on the 3-pyridyl residue within the natural insecticide nicotine, Bayer CropScience in 1984 developed an insecticidal compound bearing a 6-chloropyridin-3-yl methyl group attached to its imidazolidine backbone via methylene-spacer (CPM substituent). Therein, on the one hand, the chlorine atom caused a significant increase of the insecticidal activity, on the other hand the application properties of this compound were additionally tuned by introduction of a nitroimino group in 2-position of the saturated bis(hetero) ring. Thus, as a result of all synthetic efforts, due to increased activity, reduced photolability, and satisfactory systemic properties in plants, combined with at least complete degradability, imidacloprid became the most successful insecticide worldwide. The possible field of application comprises crop protection and related processes, such as termite control and garden professional care. In addition, imidacloprid acts as a cat and dog parasiticide.[8b]

A sulfur-containing cyanoimino analog of the above mentioned imidacloprid was introduced also by Bayer CropScience in 2000. Aside from the known CPM functionality it consists of a thiazolidine ring and therefore was named thiacloprid. It shows improved stability, an extremely low vapor pressure and appropriate ecobiological properties. A recent example of commercially available neonicotinoids, structurally associated with our compounds discussed herein, is the open-chain *N*-nitroguanidine clothianidin. It was developed by Takeda Chemical Industries Ltd in 2002. In this novel insecticide the chloropyridinyl moiety was replaced by a 2-chlorothiazole group (attached to the well established methylene bridge via the hetero ring's 5-position). It is quite stable to hydrolysis, especially shows a good absorption to soil and rapid distribution in the plant.[8c]

In general, structural characteristics as well as distinct effectiveness and therefore high market potential of such neonicotinoids enforces the quest for promising analogs obtained by various chemical syntheses both in our group and elsewhere. For example, de Meijere and co-workers developed interesting spirocyclopropanated analogs of these chloronicotinyl insecticides (CNI™).[9] Furthermore, very recently, a pro-drug concept with delayed release of the active agent in vivo was published by Kagabu's group applying a masking group instead of the free proton in 3-position of the imidazolidine ring within imidacloprid.[10]

Our own efforts primarily focus on the application of nitropolychloroalkenes, especially butadienes, as versatile starting material for such neonicotinoids. As a consequence, we focus on the rare class of cyclic or acyclic nitromethylene derivatives, a substructure that was established in the early 2-nitromethylidene-1,3-thiazinane insecticide called nithiazine (Shell, 1978) and later on in the acyclic (*E*)-*N*-[(6-chloropyridin-3-yl)methyl]-*N*-ethyl-*N*′-methyl-2-nitroethene-1,1-diamine, that is, the nitenpyram of SumiTake, 1995 (Fig. 1).

2. Materials and methods

2.1. General methods

All chemicals were purchased from Sigma–Aldrich or Merck and were used as supplied. Melting points were measured on a Büchi 520 apparatus and were uncorrected. ^{1}H and ^{13}C NMR spectra were obtained on a BRUKER Avance with 400 MHz proton frequency. ^{1}H NMR spectra in $CDCl_3$ were referenced to TMS at 0.0 ppm, whereas ^{13}C NMR spectra refer to the solvent signal center at 77.0 ppm. In case of DMSO-d_6, the solvent residual peak were set to 2.50 ppm (^{1}H) and 39.7 ppm (^{13}C). IR spectra were obtained on a BRUKER 'Vector 22' FT IR as film between NaCl plates or as KBr pellet. EI mass spectra were recorded on a Hewlett Packard—System 'MS 5989B' with direct inlet. ESI mass spectra were obtained on a Hewlett Packard 'MS LC/MSD Series 1100'. All masses of chlorine containing molecules or fragments refer to the isotope ^{35}Cl. High-resolution mass spectra were measured with a Varian MAT 311 A spectrometer with pre-selected molecular ion peak matching at $R \gg 10{,}000$ to be within ±2 ppm of the exact masses. TLC was carried out on Merck-plates coated with Silica Gel (60 F 254). Silica Gel 60 was also used for column chromatography.

2.2. Experimental data

2.2.1. *N*,*N*′-Bis[(2-chloro-1,3-thiazol-5-yl)methyl]ethane-1,2-diamine (6)

A solution of 0.30 g (5.0 mmol) ethane-1,2-diamine in 5 mL of acetonitrile was added dropwise to a solution of 1.68 g (10.0 mmol) 2-chloro-5-(chloromethyl)-1,3-thiazole in 5 mL of the same solvent within 10 min. After stirring for 6 h at room temperature, 1.38 g (10.0 mmol) potassium carbonate were added and the mixture was stirred for additional 2 d. Subsequently, the

solvent was removed and to the resulting residue a portion of 100 mL water was added. Extraction with chloroform (3 × 70 mL), washing of the organic phase with water and drying over calcium chloride, after evaporation of the solvents afforded 2.26 g (70%) of diamine **6**; mp 27–29 °C. ^{1}H NMR ($CDCl_3$) δ = 7.35 (t, J = 1.0 Hz, 2H, CH), 3.93 (d, J = 1.0 Hz, 4H, $C_{quat.}CH_2$), 2.75 (s, 4H, NHCH_2), 1.80 (br s, 2H, NH). ^{13}C NMR ($CDCl_3$) δ = 150.9 (CCl), 141.5 (CS), 137.9 (CH), 48.1 (CH_2), 45.8 ($C_{quat.}CH_2$). IR (KBr): 3306, 2825, 1652, 1537, 1422, 1347, 1046, 849, 744, 592 cm^{-1}. MS: m/z (%) 322 [M$^+$] (3), 287 [M$^+$−Cl] (3), 161 (38), 132 [chlorothiazolylmethyl] (100).

2.2.2. *N*-[(6-Chloropyridin-3-yl)methyl]-*N*′-[(2-chloro-1,3-thiazol-5-yl)methyl]ethane-1,2-diamine (7)

The diamine **7** was prepared analogously to bisthiazole **6** in 70% yield as a highly viscous oil, starting from 2-chloro-5-(chloromethyl)-1,3-thiazole, 2-chloro-5-(chloromethyl)pyridine, and ethane-1,2-diamine. ^{1}H NMR ($CDCl_3$) δ = 8.32 (dd, J = 2.5, 0.8 Hz, 1H, H_{py}-2), 7.66 (dd, J = 8.2, 2.5 Hz, 1H, H_{py}-4), 7.34 (t, J = 1.0 Hz, 1H, CH), 7.29 (dd, J = 8.2, 0.8 Hz, 1H, H_{py}-5), 3.93 (d, J = 1.0 Hz, 2H, $SC_{quat.}CH_2$), 3.78 (s, 2H, $C_{py,quat.}CH_2$), 2.75 (br s, 4H, NHCH_2), 2.02 (br s, 2H, NH). ^{13}C NMR ($CDCl_3$) δ 150.9 (SCCl), 149.9 (NCCl), 149.1 (N=CH), 141.6 (CS), 138.6 (CH), 137.9 (CH), 134.6, 123.9 (CH), 50.2 (CH_2), 48.4 (CH_2), 48.2 (CH_2), 45.8 (CH_2). IR (KBr): 3301, 2826, 1663, 1586, 1536, 1458, 1386, 1047, 819, 740, 593 cm^{-1}. MS: m/z (%) 316 [M$^+$] (8), 281 [M$^+$−Cl] (3), 155 (77), 126 [chloropyridylmethyl] (100).

2.2.3. *N*,*N*′-Bis[(2-chloro-1,3-thiazol-5-yl)methyl]cyclohexane-1,2-diamine (8)

Compound **8** was synthesized in analogy to **6** from 2-chloro-5-(chloromethyl)-1,3-thiazole and a *cis*/*trans* mixture of cyclohexane-1,2-diamine in 42% yield; mp 79–80 °C. ^{1}H NMR ($CDCl_3$) δ = 7.34 (s, 2H, CH), 3.91 (d, J = 14.4 Hz, 2H, CH_2N), 3.79 (d, J = 14.4 Hz, 2H, CH_2N), 2.72 (m, 2H, CHN), 1.70 (br s, 2H, NH), 1.61 (m, 4H), 1.36 (m, 4H). ^{13}C NMR ($CDCl_3$) δ = 151.0 (CCl), 142.5 (CS), 137.6 (CH), 55.8 (CH), 43.4 ($C_{quat.}CH_2$), 27.6 (CHCH_2), 22.0 (CH_2). IR (KBr): 3319, 2918, 2850, 1662, 1419, 1112, 1051, 1046, 839, 732, 584 cm^{-1}. MS: m/z (%) 376 [M$^+$] (6), 341 [M$^+$−Cl] (28), 244 (53), 132 [chlorothiazolylmethyl] (100).

2.2.4. *N*,*N*′-Bis[(6-chloropyridin-3-yl)methyl]benzene-1,2-diamine (9)

Diamine **9** was obtained in analogy to diamine **6** from 2-chloro-5-(chloromethyl)pyridine and benzene-1,2-diamine in 57% yield, mp 146–147 °C. ^{1}H NMR (DMSO-d_6) δ = 8.44 (dd, J = 2.6, 0.8 Hz, 2 × 1H, H_{py}-2), 7.84 (dd, J = 8.1, 2.6 Hz, 2 × 1H, H_{py}-4), 7.47 (dd, J = 8.1, 0.8 Hz, 2 × 1H, H_{py}-5), 6.45 (m, 4H, Ph), 5.31 (t, J = 4.3 Hz, 2H, NH), 4.34 (d, J = 4.3 Hz, 4H, CH_2). ^{13}C NMR (DMSO-d_6) δ = 149.3 (CH), 148.8 (CCl), 139.2 (CH), 135.7 ($C_{quat.}$), 135.5 ($C_{quat.}$), 124.1 (CH), 117.9 (CH, Ph), 110.6 (CH, Ph), 44.0 (CH_2). IR (KBr): 3363, 2855, 1586, 1528, 1454, 1384, 1268, 1104, 1026, 815, 738, 588 cm^{-1}. MS: m/z (%) 358 [M$^+$] (30), 232 [M$^+$−chloropyridylmethyl] (100), 126 [chloropyridylmethyl] (42).

2.2.5. 2-Chloro-5-{[(2*E*)-2-(2,3,3-trichloro-1-nitroprop-2-en-1-ylidene)imidazolidin-1-yl]methyl}pyridine (13)

Compound **13** was prepared from nitrodiene **10** and diamine **1** according to the literature[11] in 47% yield.

2.2.6. 2-Chloro-5-{[(2*E*)-2-(2,3,3-trichloro-1-nitroprop-2-en-1-ylidene)imidazolidin-1-yl]methyl}-1,3-thiazole (14)

To a solution of 7.42 g (38.7 mmol) *N*-[(2-chloro-1,3-thiazol-5-yl)methyl]ethane-1,2-diamine (**2**) in 30 mL methanol was added a solution of 5.00 g (18.4 mmol) 1,1,2,4,4-pentachloro-3-nitrobuta-1,3-diene (**10**) in 5 mL methanol at −40 °C within 10 min. Subsequently, the resulting mixture was kept at −40 °C for 1 h and at room temperature for additional 5 h. Then the precipitate was filtered off, washed with water (3 × 40 mL), methanol (1 × 10 mL), and diethyl ether (2 × 20 mL). Drying in vacuo yielded 4.88 g (68%) of **14**, mp 153–154 °C. ^{1}H NMR (DMSO-d_6) δ = 9.39 (br s, 1H, NH), 7.66 (s, 1H, CH), 4.65 (s, 2H, CH_2), 3.72 (s, 4H, NCH_2CH_2N). ^{13}C NMR (DMSO-d_6) δ = 159.3 (NCN), 150.7 (SCCl), 140.5 (CHN), 135.9 ($SC_{quat.}$), 125.6, 125.1 (CCl=CCl_2), 103.2 (CNO_2), 49.8 ($CH_2C_{quat.}$), 45.5 (NCH_2), 42.6 ($NHCH_2$). IR (KBr): 3241, 1589, 1563, 1537, 1429, 1321, 1137, 1045, 949, 842, 717, 640 cm^{-1}. MS: m/z (%) 388 [M$^+$] (3), 353 [M$^+$−Cl] (4), 132 [chlorothiazolylmethyl] (100).

2.2.7. 2-Chloro-5-{[(2*E*)-3-methyl-2-(2,3,3-trichloro-1-nitroprop-2-en-1-ylidene)imidazolidin-1-yl]methyl}pyridine (15)

Compound **15** was achieved from nitrodiene **10** and diamine **3** in analogy to the preparation of **14**. The reaction time was 1 h at −40 °C and additional 24 h at room temperature, yield 48%, mp 155–157 °C. ^{1}H NMR (DMSO-d_6) δ = 8.32 (d, J = 2.5 Hz, 1H, CH), 7.76 (dd, J = 2.5, 8.3 Hz, 1H, CH), 7.56 (d, J = 8.3 Hz, 1H, CH), 4.48 (s, 2H, $C_{quat.}CH_2$), 3.90 (m, 4H, 2 CH_2), 2.92 (s, 3H, Me). ^{13}C NMR (DMSO-d_6) δ = 162.2 (NCN), 150.0 NCCl), 148.6 (NCH), 138.7 (CH), 130.5 ($C_{quat.}CH_2$), 126.1 (CCl), 124.5 (CH), 120.1 (CCl_2), 98.3 (CNO_2), 50.2 (CH_2), 49.1 (CH_2), 47.7 (CH_2), 35.3 (Me). IR (KBr): 3052, 1590, 1524, 1461, 1397, 1313, 1142, 1108, 924, 820, 713, 655 cm^{-1}. MS: m/z (%) 396 [M$^+$] (4), 361 [M$^+$−Cl] (19), 126 [chloropyridylmethyl] (100).

2.2.8. 5,5′-{[2-(2,3,3-Trichloro-1-nitroprop-2-en-1-ylidene)imidazolidine-1,3-diyl]dimethanediyl}bis(2-chloro-1,3-thiazole) (16)

Preparation analogously to **14** starting from **10** and **6**, 60% yield, mp 174–175 °C. ^{1}H NMR (DMSO-d_6) δ = 7.69 (s, 2H, CH), 4.65 (s, 4H, $C_{quat.}CH_2$), 3.82 (s, 4H, NCH_2CH_2N). ^{13}C NMR (DMSO-d_6) δ 161.6 (NCN), 151.8 (SCCl), 141.9 (CHN), 133.7 ($SC_{quat.}$), 125.8, 122.0 (CCl=CCl_2), 97.9 (CNO_2), 47.2 ($CH_2C_{quat.}$), 45.2 ($2CH_2$). IR (KBr): 3092, 1575, 1535, 1415, 1309, 1143, 1047, 914, 825, 716, 593 cm^{-1}. MS: m/z (%) 519 [M$^+$] (2), 484 [M$^+$−Cl] (4), 132 [chlorothiazolylmethyl] (100).

2.2.9. 2-Chloro-5-{[(2*E*)-3-[(2-chloro-1,3-thiazol-5-yl)methyl]-2-(2,3,3-trichloro-1-nitroprop-2-en-1-ylidene)imidazolidin-1-yl]methyl}pyridine (17)

Compound **17** prepared as described for compound **14** applying nitrodiene **10** and diamine **7**. Yield 70%, mp 175–176 °C. ^{1}H NMR (DMSO-d_6) δ = 8.35 (d, J = 2.3 Hz, 1H, CH), 7.78 (dd, J = 8.3, 2.3 Hz, 1H, CH), 7.71 (s, 1H, CH), 7.57 (d, J = 8.3 Hz, 1H, CH), 4.65 (s, 2H, CH_2), 4.54 (s, 2H, CH_2), 3.85 (s, 4H, 2 CH_2). ^{13}C NMR (DMSO-d_6) δ = 162.4 (NCN), 151.9 (SCCl), 148.6 ($N_{py}CH$), 142.2 ($N_{thia}CH$), 138.8 (CH), 133.8 ($SC_{quat.}$), 130.0, 125.8 (=CCl), 124.5 (CH), 121.8 (CCl_2), 98.0 (CNO_2), 49.4 (CH_2), 48.1 (CH_2), 47.4 (CH_2), 45.3 (CH_2). IR (KBr): 2902, 1558, 1533, 1461, 1353, 1326, 1138, 1057, 997, 913, 822, 785, 715, 594 cm^{-1}. MS: m/z (%) 513 [M$^+$] (3), 478 [M$^+$−Cl] (5), 132 [chlorothiazolylmethyl] (98), 126 [chloropyridylmethyl] (100).

2.2.10. 2-Chloro-5-{[(2*E*)-2-(2,3,3-trichloro-1-nitroprop-2-en-1-ylidene)-1,3-oxazolidin-3-yl]methyl}pyridine (18)

Compound **18** was obtained in analogy to **14** applying 1 equiv of nitrodiene **10** and 3 equiv of aminoethanol **4** with 45% yield, mp 156–158 °C. ^{1}H NMR (DMSO-d_6) δ = 8.38 (d, J = 2.3 Hz, 1H, CH), 7.74 (dd, J = 8.2, 2.3 Hz, 1H, CH), 7.39 (d, J = 8.2 Hz, 1H, CH), 4.81 (s, 2H, OCH_2), 4.63 (s, 2H, CH_2), 3.87 (s, 2H, CH_2). ^{13}C NMR ($CDCl_3$) δ = 164.2 (NCN), 150.0 (NCCl), 149.5 (CH), 139.5 (CH), 130.0, 125.1 (=CCl), 124.4 (CH), 124.2 (CCl_2), 104.7 (CNO_2), 68.8 (OCH_2), 51.5 (CH_2), 49.8 (CH_2). IR (KBr): 3091, 3052, 1611, 1434, 1309, 1127, 1027, 957, 922, 833, 800, 716, 648 cm^{-1}. MS: m/z (%) 383 [M$^+$] (2), 478 [M$^+$−Cl] (3), 126 [chloropyridylmethyl] (100).

2.2.11. 2-Chloro-5-({(2*Z*)-2-[chloro(nitro)methylidene]imidazolidin-1-yl}methyl)pyridine (19)

Compound **19** was prepared from nitroethylene **12** and diamine **1** in accordance with the synthesis of **14**. Yield 36%, mp 133–135 °C. ^{1}H NMR (DMSO-d_6) δ = 9.43 (br s , 1H, NH), 8.38 (s, 1H, CH), 7.82 (d, J = 8.1 Hz, 1H, CH), 7.53 (d, J = 8.1 Hz, 1H, CH), 4.83 (s, 2H, $C_{quat.}CH_2$), 3.73 (br s, 4H, 2 CH_2). ^{13}C NMR (DMSO-d_6) δ = 158.8 (NCN), 149.5 (NCCl), 148.8 (NCH), 138.7 (CH), 132.2 ($C_{quat.}CH_2$), 124.4 (CH), 98.2 (CNO_2), 51.2 (CH_2), 49.9 (CH_2), 42.5 (CH_2). IR (KBr): 3275, 1566, 1532, 1460, 1363, 1303, 1105, 1027, 952, 835, 734, 590 cm^{-1}. MS: m/z (%) 288 [M^+] (6), 242 [M^+-NO_2] (5), 206 [M^+-NO_2-HCl] (20), 126 [chloropyridylmethyl] (32).

2.2.12. 2-Chloro-5-({(2*Z*)-2-[chloro(nitro)methylidene]imidazolidin-1-yl}methyl)-1,3-thiazole (20)

The thiazole **20** was synthesized in analogy to **14** from nitroethylene **12** and diamine **2**. Yield 32%, mp 132–134 °C. ^{1}H NMR (DMSO-d_6) δ = 9.37 (br s , 1H, NH), 7.71 (s, 1H, CH), 4.91 (s, 2H, $C_{quat.}CH_2$), 3.73 (m, 4H, 2CH_2). ^{13}C NMR (DMSO-d_6) δ = 158.4 (NCN), 151.3 (SCCl), 141.3 (CH), 136.1 ($SC_{quat.}$), 98.2 (CNO_2), 50.5 (CH_2), 45.9 (CH_2), 42.4 (CH_2). IR (KBr): 3263, 3100, 2894, 1554, 1521, 1421, 1332, 1300, 1190, 1053, 959, 876, 737, 665 cm^{-1}. MS: m/z (%) 294 [M^+] (12), 248 [M^+-NO_2] (5), 212 [M^+-NO_2-HCl] (17), 132 [chlorothiazolylmethyl] (100).

2.2.13. 2-Chloro-5-{[(2*E*)-2-(nitromethylidene)imidazolidin-1-yl]methyl}pyridine (21)

A solution containing 0.15 g (1.2 mmol) hydroiodic acid in 2 mL of acetone was added dropwise to a solution of 0.29 g (1.0 mmol) imidazolidine **19** in 5 mL acetone at 0 °C. The reaction mixture then was stirred for 3 h at 0 °C and 1 d at room temperature. After removal of acetone in vacuo, 20 mL of cold water and 2 mL of a 30% sodium dithionite solution was added. Subsequent to one additional hour with stirring, the mixture was extracted with chloroform (4 × 20 mL). The combined organic layers were washed with water and dried over calcium chloride. Finally, purification by column chromatography yielded 0.12 g (50%) of nitroethylene **21**, mp 165–166 °C. NMR, mass spectral, and IR data were in accordance with the literature.[11,12c]

2.2.14. 1,3-Bis[(2-chloro-1,3-thiazol-5-yl)methyl]-2-(2,3,3-trichloro-1-nitroprop-2-en-1-ylidene)octa-hydro-1*H*-benzimidazole (22)

Preparation analogously to imidazolidine **14** starting from nitrodiene **10** and diamine **8**. Yield 37%, mp 191–192 °C. ^{1}H NMR (DMSO-d_6) δ = 7.74 (s, 1H, CH), 4.77 (d, J = 16.5 Hz, 2H, $C_{quat.}CH_2$), 4.63 (d, J = 16.5 Hz, 2H, NCH_2), 4.08 (s, 2H, NCH), 1.74 (m, 4H, CH_2), 1.33 (br s, 4H, CH_2). ^{13}C NMR (DMSO-d_6) δ = 158.6 (NCN), 151.6 (SCCl), 141.7 (CHN), 134.4 ($SC_{quat.}$), 125.6, 122.3 ($CCl{=}CCl_2$), 97.7 (CNO_2), 57.5 (CH), 42.1 (NCH_2), 23.4 (CH_2), 19.2 (CH_2). IR (KBr): 3104, 2945, 2863, 1666, 1536, 1488, 1418, 1323, 1126, 1049, 935, 828, 593 cm^{-1}. ESI-MS: m/z (%) 596 [M+Na]$^+$ (12).

2.2.15. 1,3-Bis[(6-chloropyridin-3-yl)methyl]-2-(2,3,3-trichloro-1-nitroprop-2-en-1-ylidene)-2,3-dihydro-1*H*-benzimidazole (23)

Preparation analogously to imidazolidine **14** starting from nitrodiene **10** and *o*-phenylenediamine derivative **9**. Yield 75%, mp 202–204 °C. ^{1}H NMR (DMSO-d_6) δ = 8.31 (dd, J = 2.2, 0.6 Hz, 2H, NCH), 7.78 (m, 2H, Ph), 7.62 (m, 4H), 7.52 (dd, J = 8.3, 0.6 Hz, 2H), 5.60 (s, 4H, CH_2). ^{13}C NMR (DMSO-d_6) δ = 150.0 (NCCl), 149.0 (NCN), 148.3 (CH), 138.2 (CH), 131.7, 129.3, 126.7 (CH), 125.5 (CCl), 124.4 (CH), 121.9 (CCl_2), 113.3 (CH), 96.8 (CNO_2), 47.3 (CH_2). IR (KBr): 3034, 1571, 1513, 1466, 1384, 1308, 1187, 1096, 1021, 863, 762 cm^{-1}. ESI-MS: m/z (%) 578 [M+Na]$^+$ (14).

2.2.16. 2-[(2*Z*)-3-Chloro-1,3-dinitroprop-2-en-1-ylidene]-1,3-bis[(6-chloropyridin-3-yl)methyl]-2,3-dihydro-1*H*-benzimidazole (24)

The dinitro compound **24** was obtained from diamine **9** (1.7 equiv) and butadiene **11** in 68% yield as described for imidazolidine **14**. Reaction time: 1 h at −40 °C, then 2 d at room temperature. Mp 144–146 °C. ^{1}H NMR ($CDCl_3$) δ = 9.34 (s, 1H, $CHCNO_2$), 8.46 (d, J = 2.2 Hz, 2H, NCH), 7.60 (m, 4H, Ph), 7.62 (m, 4H), 7.56 (dd, J = 8.3, 2.2 Hz, 2H), 7.31 (d, J = 8.3 Hz, 2H), 5.57 (d, J = 17.0 Hz, 2H, NCH_2), 5.43 (d, J = 17.0 Hz, 2H, NCH_2). ^{13}C NMR ($CDCl_3$) δ = 152.7 (NCCl), 148.9 (CHN), 147.1 (NCN), 138.4 (CH), 130.8, 129.2 ($CHCNO_2$), 128.1 (CH), 127.0, 125.2 (CH), 118.6 ($CClNO_2$), 113.4 (CH), 100.2 (CNO_2), 47.6 (CH_2). IR (KBr): 3049, 1572, 1473, 1345, 1193, 1099, 997, 919, 729 cm^{-1}. ESI-MS: m/z (%) 555 [M+Na]$^+$ (12).

2.2.17. 2-Chloro-5-({(2*E*)-2-[(2*Z*)-3-chloro-1,3-dinitroprop-2-en-1-ylidene]imidazolidin-1-yl}methyl)-1,3-thiazole (25)

The dinitro compound **25** was obtained from diamine **2** and dinitrobutadiene **11** in 85% yield as described for azole **14**. Mp 150–152 °C. ^{1}H NMR (DMSO-d_6) δ = 10.6 (br s 1H, NH), 8.99 (s, 1H, $CHCNO_2$), 7.68 (s, 1H, NCH), 4.76 (s, 2H, $C_{quat.}CH_2$), 3.94 (s, 4H, CH_2). ^{13}C NMR (DMSO-d_6) δ = 160.4 (NCN), 151.2 (N=CCl), 142.6 (NCH), 134.0, 129.5 ($CHCNO_2$), 117.4 ($CClNO_2$), 104.9 (CNO_2), 48.0 (CH_2), 42.8 (CH_2), 42.3 (CH_2). IR (KBr): 3099, 1709, 1594, 1530, 1489, 1418, 1206, 1111, 1011, 904, 803, 724, 438 cm^{-1}. ESI-MS: m/z (%) 388 [M+Na]$^+$ (11).

2.2.18. 5,5′-({2-[(2*Z*)-3-Chloro-1,3-dinitroprop-2-en-1-ylidene]-imidazolidine-1,3-diyl}dimethanediyl)bis(2-chloro-1,3-thiazole) (26)

The dinitro compound **26** was obtained from the symmetrical diamine **6** and diene **11** in 45% yield as described for azole **14**. Mp 161–162 °C. ^{1}H NMR (DMSO-d_6) δ = 9.04 (s, 1H, $CHCNO_2$), 7.66 (s, 2H, NCH), 4.86 (d, J = 15.8 Hz, 2H, $C_{quat.}CH_2$), 4.76 (d, J = 15.8 Hz, 2H, $C_{quat.}CH_2$), 3.97 (s, 4H, CH_2). ^{13}C NMR (DMSO-d_6) δ = 160.2 (NCN), 151.9 (N=CCl), 142.7 (NCH), 133.4, 129.6 ($CHCNO_2$), 116.9 ($CClNO_2$), 102.4 (CNO_2), 46.8 (CH_2), 42.8 (CH_2). IR (KBr): 3054, 1583, 1465, 1409, 1343, 1175, 1047, 1008, 966, 799, 594 cm^{-1}. ESI-MS: m/z (%) 519 [M+Na]$^+$ (14).

2.2.19. 2-Chloro-5-({(2*Z*)-2-[(2*Z*)-3-chloro-1,3-dinitroprop-2-en-1-ylidene]-3-methylimidazolidin-1-yl}methyl)pyridine (27)

The dinitro compound **27** was obtained from amine **3** and dinitrodiene **11** in 70% yield as described for imidazole **14**. Mp 186–188 °C. ^{1}H NMR (DMSO-d_6) δ = 9.03 (s, 1H, $CHCNO_2$), 8.33 (d, J = 2.0 Hz, 1H, NCH), 7.77 (dd, J = 8.2, 2.0 Hz, 1H), 7.58 (d, J = 8.2 Hz, 1H), 4.61 (d, J = 15.3 Hz, 1H, $C_{quat.}CH_2$), 4.48 (d, J = 15.3 Hz, 1H, $C_{quat.}CH_2$), 3.96 (m, 4H, 2CH_2), 2.96 (s, 3H, Me). ^{13}C NMR (DMSO-d_6) δ = 160.7 (NCN), 150.3 (N=CCl), 150.1 (CHN), 140.1 (CH), 129.6, 129.2 ($CHCNO_2$), 124.5 (CH), 116.6($CClNO_2$), 103.2 (CNO_2), 49.3 (CH_2), 47.4 (CH_2), 46.9 (CH_2), 33.9 (CH_3). IR (KBr): 3052, 1608, 1578, 1468, 1390, 1351, 1188, 1014, 976, 801, 449 cm^{-1}. ESI-MS: m/z (%) 396 [M+Na]$^+$ (86).

2.2.20. (2*E*)-2-[(2*Z*)-3-Chloro-1,3-dinitroprop-2-en-1-ylidene]-1-[(6-chloropyridin-3-yl)methyl]hexahydro-pyrimidine (28)

The dinitro compound **28** was obtained from diaminopropane **5** and diene **11** in 25% yield as described for azole **14**, mp 136–138 °C. ^{1}H NMR (DMSO-d_6) δ = 10.2 (br s, 1H, NH), 9.01 (s, 1H, $CHCNO_2$), 8.34 (s, 1H, NCH), 7.76 (d, J = 8.3 Hz, 1H), 7.55 (d, J = 8.3 Hz, 1H), 4.62 (m, 2H, $C_{quat.}CH_2$), 3.50 (m, 4H, 2 CH_2), 1.98 (m, 2H, CCH_2C). ^{13}C NMR (DMSO-d_6) δ = 155.6 (NCN), 150.3 (CHN), 150.1 (N=CCl), 140.3 (CH), 130.0, 129.0 ($CHCNO_2$), 124.6 (CH), 116.4 ($CClNO_2$), 109.4 (CNO_2), 54.2 (CH_2), 46.2 (CH_2), 45.3 (CH_2), 38.8 (CH_3). IR (KBr): 3052, 2955, 1628, 1571, 1462, 1351, 1175, 1043, 982, 797, 732, 633 cm^{-1}. ESI-MS: m/z (%) 396 [M+Na]$^+$ (44).

2.2.21. 4-[(3*E*)-1,1-Dichloro-3-{1-[(6-chloropyridin-3-yl)methyl] imidazolidin-2-ylidene}-3-nitroprop-1-en-2-yl]morpholine (29)

A solution of 3.84 g (10.0 mmol) of imidazolidine **13** and 4.35 g (50.0 mmol) of morpholine in 70 mL of methanol was stirred at 50–55 °C for 2 h. After cooling down to 5 °C, the mixture was diluted with 200 mL of water, then neutralized dropwise with concd hydrochloric acid. The viscous organic product that precipitated was collected, dissolved in 10 mL of methanol, and stored at −18 °C for one night. The obtained solid then was filtered off, washed with water (3 × 20 mL) and diethyl ether (2 × 10 mL) and dried in vacuo. Yield 60%, mp 92–94 °C. ^{1}H NMR (DMSO-d_6) δ = 9.48 (br s, 1H, NH), 8.37 (d, J = 2.2 Hz, 1H, NCH), 7.80 (dd, J = 8.2, 2.2 Hz, 1H, CH), 7.55 (d, J = 8.2 Hz, 1H, CH), 4.44 (br s, 2H, $C_{quat.}CH_2$), 3.70 (s, 4H, $2CH_2$), 3.58 (s, 4H, OCH_2), 3.06 (s, 4H, NCH_2). ^{13}C NMR (DMSO-d_6) δ = 160.2 (NCN), 149.7 (NCCl), 148.9 (CH), 141.1, 138.8 (CH), 131.3, 124.4 (CH), 103.7, 103.3, 66.5 (OCH_2), 50.1 (CH_2), 49.9 (CH_2), 48.6 (CH_2), 42.1 (CH_2). IR (KBr): 3421, 3281, 2970, 2842, 1559, 1519, 1459, 1326, 1113, 921, 804, 726, 630 cm^{-1}. HR-ESIMS: m/z $[M+H]^+$ calcd for $C_{16}H_{19}Cl_3N_5O_3$: 434.05480; found: 434.05474.

2.2.22. 5-({(2*E*)-2-[2-(Aziridin-1-yl)-3,3-dichloro-1-nitroprop-2-en-1-ylidene]imidazolidin-1-yl}methyl)-2-chloropyridine (30)

Chloropyridine **30** was obtained from aziridine and imidazolidine **13** in analogy to compound **29** in 60% yield after column chromatography on silica gel (eluent: ethyl acetate). Mp 130–131 °C. ^{1}H NMR ($CDCl_3$) δ = 9.60 (br s, 1H, NH), 8.31 (dd, J = 2.5, 0.7 Hz, 1H, NCH), 7.60 (dd, J = 8.2, 2.5 Hz, 1H, CH), 7.37 (dd, J = 8.2, 0.7 Hz, 1H, CH), 5.14 (d, J = 16.4 Hz, 1H, $C_{quat.}CH_2$), 4.50 (d, J = 16.4 Hz, 1H, $C_{quat.}CH_2$), 3.83 (m, 3H, CH_2), 3.53 (m, 1H, CH_2), 2.37 (m, 2H, CH_2), 2.13 (m, 2H, CH_2). ^{13}C NMR ($CDCl_3$) δ = 159.2 (NCN), 151.1 (NCCl), 148.4 (CH), 139.3, 137.6 (CH), 130.2, 124.4 (CH), 114.3 (CCl_2), 105.8 (CNO_2), 50.3 (CH_2), 48.7 (CH_2), 41.7 (CH_2), 29.9 (CH_2NCH_2). IR (KBr): 3331, 2999, 2971, 1720, 1564, 1523, 1445, 1333, 1122, 1026, 952, 818, 730, 587 cm^{-1}. ESI-MS: m/z (%) 390 $[M+H]^+$ (81).

2.2.23. (3*Z*)-1,1-Dichloro-*N*-[(6-chloropyridin-3-yl)methyl]-3-{3-[(6-chloropyridin-3-yl)methyl]-1,3-oxazolidin-2-ylidene}-*N*-methyl-3-nitroprop-1-en-2-amine (31)

The bis(chloropyridinyl) derivative **31** was obtained from amine **18** in analogy to compound **29** and was pure after initial precipitation, 80% yield, mp 57–58 °C. ^{1}H NMR ($CDCl_3$) δ = 8.38 (d, J = 2.4 Hz, 1H, NCH), 8.33 (d, J = 2.4 Hz, 1H, NCH), 7.71 (m, 2H, CH), 7.35 (d, J = 8.3 Hz, 1H, CH), 7.27 (d, J = 8.3 Hz, 1H, CH), 4.80 (m, 2H, OCH_2), 4.55 (m, 2H, CH_2), 4.13 (s, 2H, CH_2), 3.88 (m, 2H, CH_2), 2.70 (s, 3H, CH_3). ^{13}C NMR ($CDCl_3$) δ = 166.1 (NCN), 152.3 (NCCl), 149.9 (NCCl), 149.6 (CH), 149.1 (CH), 140.6, 139.2 (CH), 138.6 (CH), 133.9, 128.1, 124.9 (CH), 123.9 (CH), 110.2 (CCl_2), 106.3 (CNO_2), 66.9 (OCH_2), 55.6 (CH_2), 50.3 (CH_2), 49.5 (CH_2), 40.2 (CH_3). IR (KBr): 2896, 1587, 1566, 1460, 1304, 1261, 1103, 1024, 913, 816, 633 cm^{-1}. ESI-MS: m/z (%) 504 $[M+H]^+$ (8).

2.2.24. 2-Chloro-5-({(2*E*)-2-[3,3-dichloro-2-(methylsulfanyl)-1-nitroprop-2-en-1-ylidene]imidazolidin-1-yl}methyl)pyridine (32)

A solution of 380 mg (1.0 mmol) imidazolidine **13** and 77 mg (1.1 mmol) of sodium methanethiolate in 3 mL of methanol was stirred for 1 h at room temperature and additional 3 h at 40 °C. Subsequently, 30 mL of water were added at 5 °C and the mixture then was neutralized dropwise with concd hydrochloric acid. The resulting precipitate was filtered off and washed with water (3 × 20 mL). Finally, drying in vacuo yielded 320 mg (80%) of sulfide **32**, mp 84–86 °C. ^{1}H NMR (DMSO-d_6) δ = 9.56 (br s, 1H, NH), 8.32 (d, J = 2.3 Hz, 1H, NCH), 7.74 (dd, J = 8.2, 2.3 Hz, 1H, CH), 7.53 (d, J = 8.2 Hz, 1H, CH), 4.54 (br s, 2H, $C_{quat.}CH_2$), 3.74 (br s, 4H, CH_2), 2.20 (s, 3H, CH_3). ^{13}C NMR (DMSO-d_6) δ = 159.9 (NCN), 149.5 (NCCl), 147.9 (CH), 137.9 (CH), 132.5, 131.6, 124.3 (CH), 114.3 (CCl_2), 102.4 (CNO_2), 50.8 (CH_2), 48.9 (CH_2), 42.5 (CH_2), 14.2 (CH_3). IR (KBr): 3314, 2894, 1578, 1550, 1522, 1461, 1297, 1187, 1126, 1041, 954, 842, 721 cm^{-1}. ESI-MS: m/z (%) 395 $[M+H]^+$ (80).

2.2.25. Methyl {[(3*E*)-1,1-dichloro-3-{1-[(6-chloropyridin-3-yl) methyl]imidazolidin-2-ylidene}-3-nitroprop-1-en-2-yl]sulfanyl} acetate (33)

The heterocycle **33** was obtained from methyl 2-mercaptoacetate and imidazolidine **13** in analogy to compound **32** in 50% yield, mp 99–100 °C. ^{1}H NMR ($CDCl_3$) δ = 9.66 (br s, 1H, NH), 8.38 (dd, J = 2.5, 0.5 Hz, 1H, NCH), 7.71 (dd, J = 8.4, 2.5 Hz, 1H, CH), 7.39 (dd, J = 8.4, 0.5 Hz, 1H, CH), 4.97 (d, J = 16.1 Hz, 1H, $C_{quat.}CH_2$), 4.47 (d, J = 16.1 Hz, 1H, $C_{quat.}CH_2$), 3.80 (m, 2H, SCH_2), 3.71 (s, 3H, CH_3), 3.58 (m, 4H, CH_2). ^{13}C NMR ($CDCl_3$) δ 170.4 (CO), 159.7 (NCN), 151.4 (NCCl), 148.7 (CH), 138.1 (CH), 129.8, 128.4, 124.6 (CH), 119.5 (CCl_2), 104.5 (CNO_2), 52.9 (OMe), 50.4 (CH_2), 49.1 (CH_2), 41.7 (CH_2), 33.6 (SCH_2). IR (KBr): 3323, 2903, 1732, 1574, 1547, 1512, 1433, 1294, 1122, 1026, 930, 833, 632 cm^{-1}. MS: m/z (%) 452 $[M^+]$ (2), 417 $[M^+-Cl]$ (2), 126 [chloropyridylmethyl] (100).

2.2.26. 5,5′-[(2-{3,3-Dichloro-2-[(4-methylphenyl)sulfanyl]-1-nitroprop-2-en-1-ylidene}imidazolidine-1,3-diyl)dimethanediyl]bis(2-chloro-1,3-thiazole) (34)

Imidazolidine **34** was synthesized from 4-methylbenzenethiol and azole **16** as described for compound **32** in 70% yield, mp 108–110 °C. ^{1}H NMR (DMSO-d_6) δ = 7.62 (s, 2H, NCH), 7.27 (d, J = 8.3 Hz, 2H, Ph), 7.20 (d, J = 8.3 Hz, 2H, Ph), 4.07 (s, 4H, $C_{quat.}CH_2$), 3.64 (s, 4H, CH_2), 2.27 (s, 3H, CH_3). ^{13}C NMR (DMSO-d_6) δ = 161.8 (NCN), 152.1 (NCCl), 142.3 (CH), 138.2, 133.4, 131.0 (CH, Ph), 130.4 (CH, Ph), 129.3, 128.6, 122.4 (CCl_2), 100.1 (CNO_2), 46.7 (CH_2), 44.1 (CH_2), 20.8 (CH_3). IR (KBr): 3442, 2920, 1563, 1524, 1415, 1387, 1302, 1127, 1047, 913, 847, 594 cm^{-1}. ESI-MS: m/z (%) 608 $[M+H]^+$ (78).

2.2.27. (3*E*)-1,1-Dichloro-3-{1-[(6-chloropyridin-3-yl)methyl] imidazolidin-2-ylidene}-3-nitropropan-2-one (35)

The nitropropanone **35** was prepared according to the literature.[11] All spectroscopic data were found as expected.

2.2.28. (3*E*)-1,1-Dichloro-3-{1-[(2-chloro-1,3-thiazol-5-yl)methyl] imidazolidin-2-ylidene}-3-nitropropan-2-one (36)

The nitropropan-2-one **36** was obtained from imidazolidine **14** in an analogous manner as described for compound **35** in 58% yield. Mp 148–149 °C. ^{1}H NMR (DMSO-d_6) δ = 10.30 (br s, 1H, NH), 7.65 (s, 1H, NCH), 7.49 (s, 1H, $CHCl_2$), 4.64 (s, 2H, $C_{quat.}CH_2$), 3.87 (s, 4H, CH_2). ^{13}C NMR (DMSO-d_6) δ = 175.4 (CO), 161.9 (NCN), 152.1 (NCCl), 142.5 (CH), 134.1, 107.6 (CNO_2), 69.6 ($CHCl_2$), 42.8 (CH_2), 42.2 (CH_2). IR (KBr): 3262, 1610, 1577, 1457, 1415, 1313, 1284, 1055, 1022, 827, 767, 677 cm^{-1}. MS: m/z (%) 370 $[M^+]$ (3), 132 [chlorothiazolylmethyl] (100).

2.2.29. (3*E*)-1,1-Dichloro-3-{1-[(6-chloropyridin-3-yl)methyl] imidazolidin-2-ylidene}-1,3-dinitropropan-2-one (37)

At −10 °C were added 0.77 g (2.0 mmol) imidazolidine **13** to 10 mL of fuming nitric acid within 5 min. The reaction mixture then was stirred for 1 h at 0 °C and additional 4 h at room temperature. After pouring onto 100 mL of ice-water, the resulting precipitate was filtered off and washed with water (3 × 20 mL). The crude product was dissolved in 50 mL of chloroform and dried over anhydrous calcium chloride. After removal of the solvent, subsequent column chromatography with an appropriate chloroform/acetone gradient, and drying in vacuo 0.25 g (30%) of dinitropropanone **37** were obtained. Mp 109–111 °C. ^{1}H NMR

(DMSO-d_6) δ = 10.61 (br s, 1H, NH), 8.33 (d, J = 1.8 Hz, 1H, NCH), 7.74 (dd, J = 8.2, 1.8 Hz, 1H, CH), 7.58 (d, J = 8.2 Hz, 1H, CH), 4.45 (s, 2H, $C_{quat.}CH_2$), 3.92 (s, 4H, 2 CH_2). ^{13}C NMR (DMSO-d_6) δ = 167.4 (CO), 161.5 (NCN), 150.4 (NCCl), 149.9 (CH), 139.8 (CH), 129.6, 124.7 (CH), 109.6 (=CNO_2), 105.3 (CCl_2NO_2), 48.0 (CH_2), 46.6 (CH_2), 43.0 (CH_2). IR (KBr): 3052, 2892, 1623, 1583, 1450, 1346, 1323, 1148, 1032, 906, 804, 657, 488 cm^{-1}. HR-ESIMS: m/z [M+H]$^+$ calcd for $C_{12}H_{11}Cl_3N_5O_5$: 409.98203; found: 409.98234.

2.2.30. (3*Z*)-1,1-Dichloro-3-{1-[(6-chloropyridin-3-yl)methyl]-3-[(2-chloro-1,3-thiazol-5-yl)methyl]imidazolidin-2-ylidene}-1,3-dinitropropan-2-one (38)

Preparation analogously to dinitropropanone **37** starting from imidazolidine **17** and concd nitric acid. Yield 45%, mp 174–175 °C. ^{1}H NMR ($CDCl_3$) δ = 8.35 (s, 1H, NCH), 7.64 (d, J = 7.7 Hz, 1H, CH), 7.54 (s, 1H, $SC_{quat.}CH$), 7.40 (d, J = 7.7 Hz, 1H, CH), 4.72 (s, 2H, CH_2), 4.55 (s, 2H, CH_2), 3.96 (s, 4H, 2 CH_2). ^{13}C NMR ($CDCl_3$) δ 168.9 (CO), 162.2 (NCN), 154.8 (SCCl), 152.4 (NCCl), 149.8 (CH), 142.7 (CH), 139.5 (CH), 131.2, 127.0, 125.2 (CH), 108.7 (=CNO_2), 103.3 (CCl_2NO_2), 48.6 (CH_2), 46.5 (CH_2), 46.2 (CH_2), 43.7 (CH_2). IR (KBr): 2939, 1586, 1567, 1452, 1332, 1296, 1143, 1046, 900, 802, 769, 649, 489 cm^{-1}. HR-ESIMS: m/z [M+H]$^+$ calcd for $C_{16}H_{13}Cl_4N_6O_5S$: 540.94168; found: 540.94164.

2.2.31. 1-{1,3-Bis[(6-chloropyridin-3-yl)methyl]-1,3-dihydro-2*H*-benzimidazol-2-ylidene}-3,3-dichloro-1-nitropropan-2-one (39)

A suspension of 0.56 g (1.0 mmol) of benzimidazolidine **23** in a mixture of 10 mL dimethylsulfoxide and 1 mL of water was stirred at 100–105 °C for 3 h. Cooling down to room temperature and mixing up with ice-water (100 mL) afforded a precipitate that was filtered off, then washed with water (3 × 20 mL) and diethyl ether (2 × 10 mL). After drying in vacuo, 0.43 g of *mono*-nitro compound **39** was obtained (80% yield), mp 192–194 °C. ^{1}H NMR (DMSO-d_6) δ = 8.40 (s, 2H, NCH), 7.97 (m, 2H), 7.69 (s, 2H), 7.65 (s, 2H), 7.53 (s, 2H), 7.49 (s, 1H, $CHCl_2$), 5.68 (s, 4H, CH_2). ^{13}C NMR (DMSO-d_6) δ = 176.9 (CO), 150.5 (NCCl), 149.4 (CH), 147.8 (NCN), 139.3 (CH), 130.8, 129.6, 127.5 (CH), 124.7 (CH), 114.3 (CH), 106.0 (CNO_2), 69.9 ($CHCl_2$), 46.3 (CH_2). IR (KBr) : 3049, 1609, 1589, 1527, 1470, 1319, 1108, 1025, 945, 815, 730, 631 cm^{-1}. ESI-MS: m/z (%) 560 [M+Na]$^+$ (7).

2.2.32. 3-{1,3-Bis[(6-chloropyridin-3-yl)methyl]-1,3-dihydro-2*H*-benzimidazol-2-ylidene}-1,1-dichloro-1,3-dinitropropan-2-one (40)

Synthesis in analogy to benzimidazoline **37** starting from compound **23** and concd nitric acid. Yield 50%, mp 196–198 °C. ^{1}H NMR ($CDCl_3$) δ = 8.44 (d, J = 2.3 Hz, 2H, NCH), 7.60 (m, 4H, CH), 7.55 (dd, J = 8.4, 2.3 Hz, 2H, CH), 7.30 (d, J = 8.4 Hz, 2H, CH), 5.53 (s, 4H, CH_2). ^{13}C NMR ($CDCl_3$) δ 169.9 (CO), 152.2 (NCN), 148.7 (CH), 147.3 (NCCl), 138.2 (CH), 130.8, 127.8 (CH), 127.4 (CH), 125.0 (CH), 113.6 (CH), 108.8 (=CNO_2), 103.3 (CCl_2NO_2), 47.3 (CH_2). IR (KBr): 3049, 1622, 1578, 1505, 1464, 1337, 1105, 1024, 909, 837, 751, 650, 565, 490 cm^{-1}. HR-ESIMS: m/z [M+H]$^+$ calcd for $C_{22}H_{15}Cl_4N_6O_5$: 582.98525; found: 582.98530.

3. Results and discussion

The condensation reaction of the commercially available 2-chloro-5-chloromethylpyridine or 2-chloro-5-(chloromethyl)-1,3-thiazole with 1,2-diaminoethane, *N*-methyl-1,2-diaminoethane, 2-aminoethanol, or 1,3-diaminopropane, respectively, in each case leads to the formation of bifunctional nucleophiles **1–5**,[12] which are suitable for hetero ring formation with nitro-substituted polychlorobuta-1,3-dienes (Fig. 2).

As in the above mentioned potpourri of known bisnucleophiles a bis(chlorothiazolyl) and a mixed chloropyridyl/chlorothiazolyl derivative both are missing, we synthesized compound **6** and **7**, each in 70% yield upon treatment of ethylenediamine with the corresponding chloromethylated hetero ring. Furthermore, structurally and electronically we varied the C_2-backbone, from ethane to the more rigid cyclohexane and finally to an aromatic ring. The subsequent reaction of each of these bisnucleophiles with 2 equiv of 2-chloro-5-(chloromethyl)-1,3-thiazole in case of diaminocyclohexane, or with 2-chloro-5-chloromethylpyridine in case of *o*-phenylendiamine, gave the complex bisnucleophiles **8** and **9** in 42% and 57%, respectively (Scheme 1).

3.1. Synthesis of imidacloprid analogs

The chloronitroalkenes **10**–**12**[1] allowed for a twofold vinylic substitution (addition–elimination pathway) of the chlorine atoms in the dichloromethylene group, and in the case of nitroethylene **12** the one adjacent to the nitro group (Fig. 3).

As expected, applying the pentachlorobutadiene **10** as the electrophilic substrate for the bifunctional nucleophiles **1**–**3**, **6**, **7**, and **4**, the imidazolidines **13**–**17** and the oxazolidine **18**, respectively, were obtained with up to 70% yield (Scheme 2).

Due to distinct intramolecular hydrogen bonding of the N–H, the neonicotinoids **13** and **14** were found as their *E*-isomers. However, an unambiguous assignment of the configuration in the allylidene derivatives **15–18** must await X-ray analyses. Nevertheless, the above mentioned compounds with a free NH proton also occur as single isomers. Interestingly, the N-substituted derivatives **15–17** as well as the oxazolidine **18** receive an additional stabilization caused by mesomeric structures, that is, the corresponding nitronic acids (Fig. 4).

As assumed above, the reaction of nitroethylene **12** with 2-chloro-5-(chloromethyl)pyridine or 2-chloro-5-(chloromethyl)thiazole is less selective than the corresponding conversion of the perhalogenated nitrobutadiene **10**. Therefore, the imidazolidines **19**,**20** were prepared in only 36% and 32% yield, but interestingly, pure *Z*-isomers were found. Furthermore, with the chloropyridylmethyl-substituted imidazolidine **19** in hand we tried to selectively remove the chlorine atom within the chloro(nitro)methylidene group. Due to the unusual electron distribution there, selective

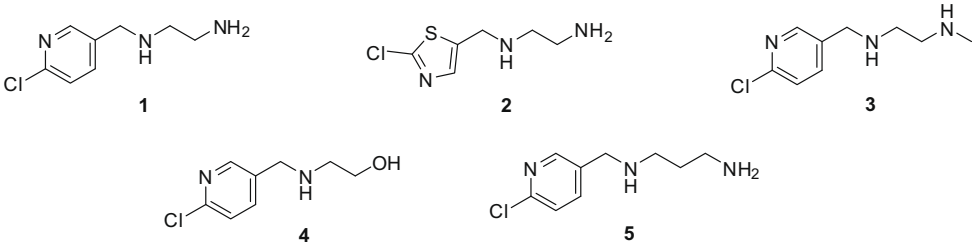
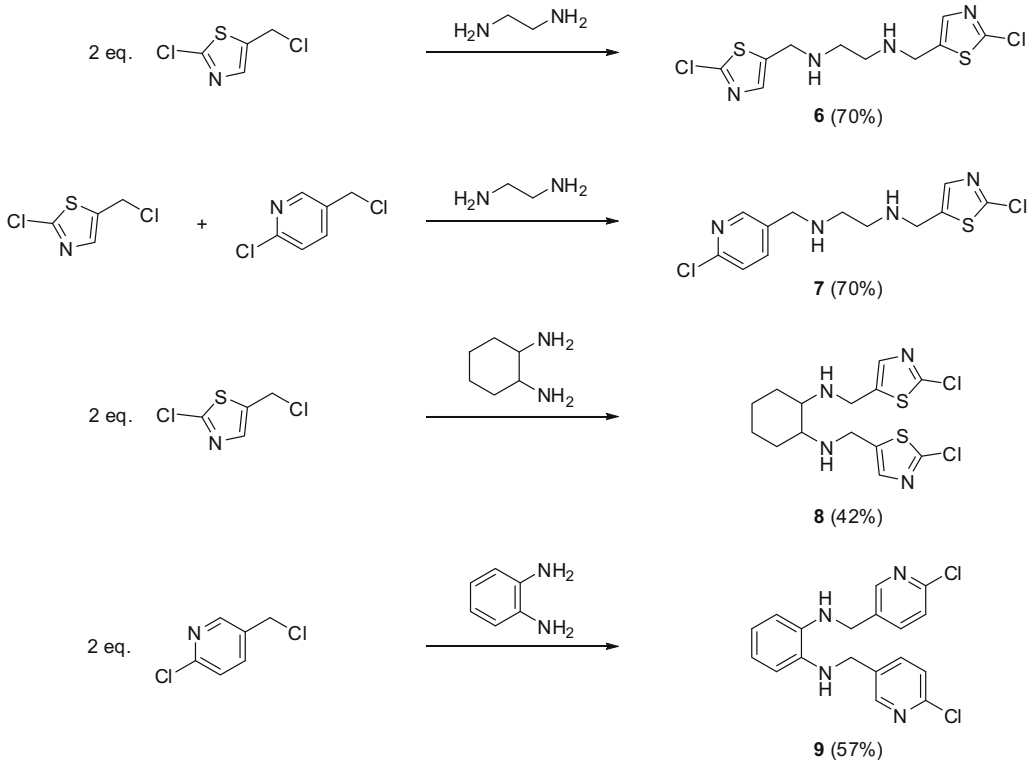


Figure 2. Known bifunctional nucleophiles **1**–**5**, suitable for the conversion of nitro-substituted polychlorobuta-1,3-dienes.



Scheme 1. Synthesis of novel diamines **6**–**9**.

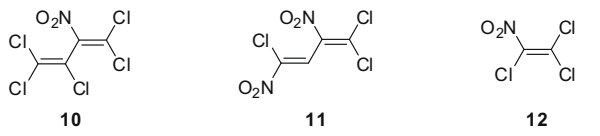


Figure 3. Nitropolychloroalkenes as versatile starting material for insecticidal compounds.

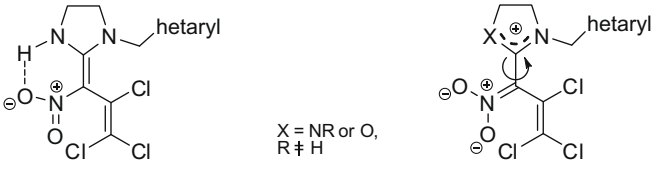
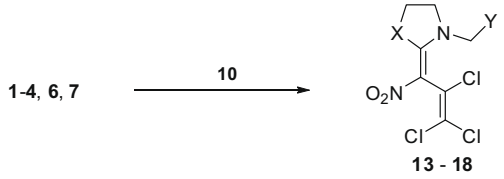


Figure 4. Stabilizing effects in different imidacloprid analogs.



13	(X = NH,	Y = 6-chloropyridin-3-yl, 47%)
14	(X = NH,	Y = 2-chlorothiazol-5-yl, 68%)
15	(X = NMe,	Y = 6-chloropyridin-3-yl, 48%)
16	(X = N-[(2-chlorothiazol-5-yl)methyl],	Y = 2-chlorothiazol-5-yl, 60%)
17	(X = N-[(6-chloropyridin-3-yl)methyl],	Y = 2-chlorothiazol-5-yl, 70%)
18	(X = O,	Y = 6-chloropyridin-3-yl, 45%)

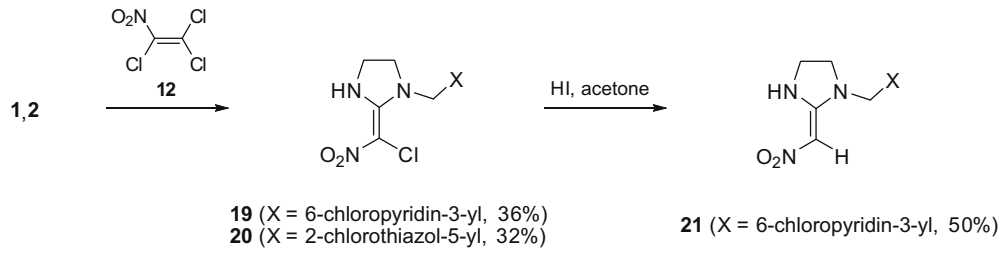
Scheme 2. Synthesis of neonicotinoids similar to imidacloprid.

reduction is quite a challenge, although some similar examples are given in the literature.[13] In our case, applying hydroiodic acid in acetone at 0–5 °C afforded the nitromethylidene group, hence compound **21**, in 50% yield (Scheme 3).

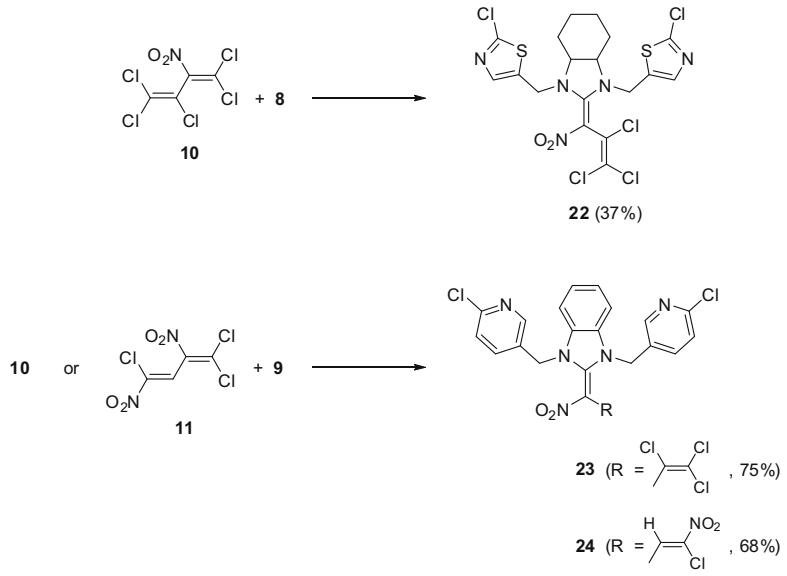
In this context it is worthy to note, that the latter described synthetic pathway can serve as a substitute for the classical reduction of (*E*)-1,1-dichloro-3-(1-((6-chloropyridin-3-yl)methyl)imidazolidin-2-ylidene)-3-nitropropan-2-one by means of sodium borohydride that also leads to **21** as we reported recently.[11] Fortunately, this imidazolidine **21**, as expected for such a structural member of the neonicotinoids, indeed shows remarkable insecticidal activity.[14]

Moreover, the reaction of *N*,*N*′-bis[(2-chloro-1,3-thiazol-5-yl)methyl]cyclohexane-1,2-diamine (**8**) with the perchlorinated nitrobuta-1,3-diene **10** produces the partially symmetric octahydrobenzimidazole **22** in only 37% yield. But, the similar reaction of **10** and additionally of dinitrodiene **11** with the less reactive aromatic diamine **9** gives in good yields (75% and 68%) the 2,3-dihydro-1*H*-benzimidazoles **23** and **24**, respectively (Scheme 4).

Subsequently, a variety of allylidene-substituted neonicotinoids were synthesized from dinitrodiene **11** and the bifunctional nucleophiles mentioned above. Thus, with the *mono*-substituted ethylene-1,2-diamines **2**,**3**,**6** or with *N*-[(6-chloropyridin-3-yl)methyl]propane-1,3-diamine (**5**) under mild conditions the 3-chloro-1,3-dinitroallylidene functionalized imidazolidines **25–27** and the hexahydropyrimidine **28** were achieved. It is well documented that also such hexahydropyrimidines exhibit remarkable insecticidal activity.[12e,15]



Scheme 3. Formation of heterocycles and subsequent protodechlorination of the chloro(nitro)methylidene moiety.



Scheme 4. Synthesis of octahydro- and dihydrobenzimidazoles.

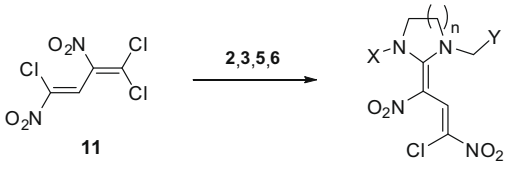
Regrettably, dinitro derivative **28** was isolated in only moderate yield; however, the imidazolidines **25–27** were obtained with up to 85% yield (Scheme 5).

3.2. Subsequent chemistry of novel imidacloprid analogs

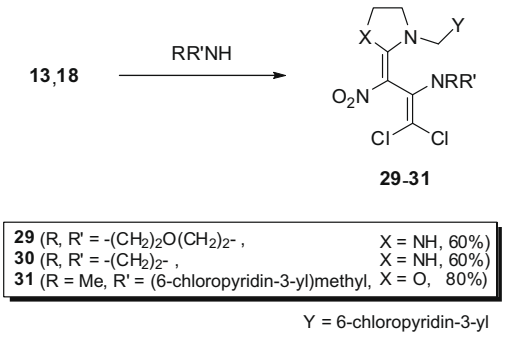
3.2.1. Substitution reactions with *N*- and *S*-nucleophiles

Even though the initial products of the hetero-ring formation that was discussed above are structurally and physiologically interesting neonicotinoids, the introduced trichlorovinyl group provides an opportunity for further synthetic transformations. Even though both types of chloro positions should in principle be able to react, the geminal as well as the CCl group, in our case, the inner chloro substituent within the allylidene group served as the leaving group on nucleophilic attack. In this manner, the reaction of a morpholine nitrogen or an aziridine in the case of **13** as the substrate, or otherwise the choice of (chloropyridinylmethyl)methylamine in case of **18** as the allylidene compound led to the amino-substituted imidacloprid analogs **29–31** in good yields (Scheme 6). No side products were found, that is, the terminal dichloro moiety was left unchanged. Expectedly, due to a less activation of this trichlorovinyl group by the nitro substituent, compared to its effect on a α-nitrodichlorovinyl group, more vigorous conditions (i.e., refluxing methanol) were required. The formation of such dichlorovinylamines is quite rare in literature.[4b,16]

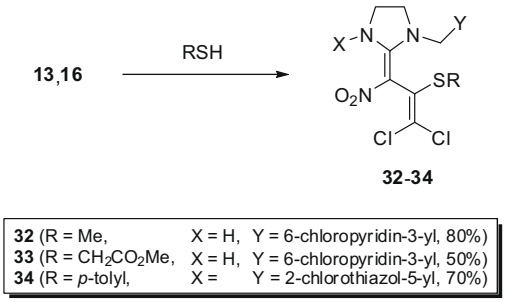
Analogously, applying thiols instead of amines, the dichlorovinyl sulfides **32–34** are accessible in comparable chemical yields. Similar transformations of more simple trichlorovinyl derivatives



Scheme 5. Reaction of dinitrodiene **11** with bifunctional nucleophiles.



Scheme 6. Neonicotinoids with amino-substituted allylidene moiety.



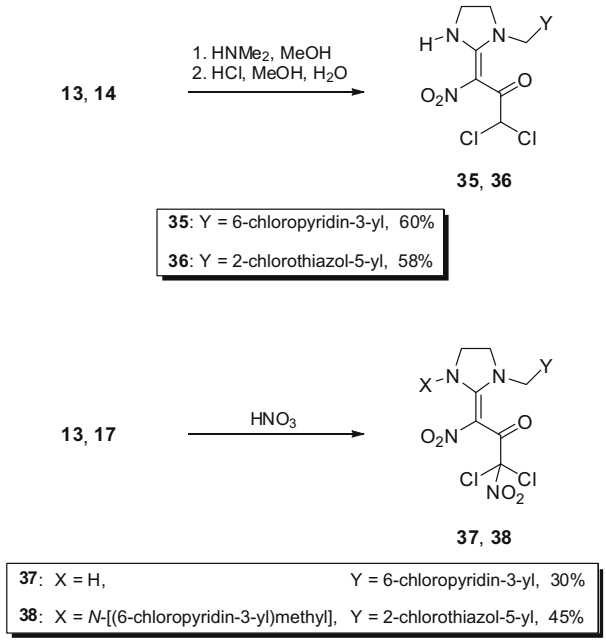
Scheme 7. Neonicotinoids with terminal dichloromethylene sulfanyl group.

to the corresponding dichlorovinyl sulfides have been published (Scheme 7).[17]

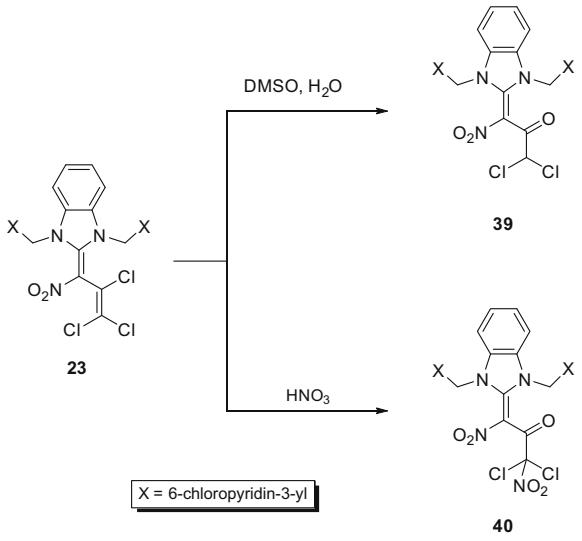
3.2.2. Formation of dichloromethylcarboxy and dichloro(nitro) methylcarboxy units

To introduce a completely different and also widely applicable functional group, we subjected the trichlorovinyl compounds **13** and **14** to a methanolic solution of dimethylamine (fourfold excess). As the amine attacked the tertiary CCl-position of this moiety, enamines were formed as intermediates. These, upon reaction with hydrochloric acid then gave the corresponding enols. Subsequently, tautomerization led to the dichloromethylketones **35** and **36** with 60% and 58% yield, respectively. The structure of the latter compounds had been confirmed by an X-ray analysis as published before.[11]

The additional reaction of imidazolidine **13** with fuming nitric acid at room temperature gave the 1,3-dinitropropan-2-one **37**. We assume, that initially in this process the trichlorovinylic group within **13** analogously to the formation of **35** and **36** is hydrolyzed to the dichloromethylcarbonyl fragment. Then, nitration takes place to yield the nitrodichloromethyl unit. Due to these harsh conditions a low yield (30%) is obtained, with water soluble, acidic C_1- and C_2-fragments as evidenced during work-up. Similar transformations of a trihalovinylic group to nitrodihalomethylcarbonyl fragment are rare in literature. The few cases which are described



Scheme 8. Formation of imidazolidine-based, highly substituted ketones.



Scheme 9. Ketone synthesis from benzo-annelated neonicotinoids.

comprise quite unselective chemical reactions.[18] Nevertheless, applying nitric acid to imidazolidine **17** we obtained the 1,3-dinitropropan-2-one **38** in 45% yield (Scheme 8).

In the case of the benzimidazoline **23**, the described ketone formation was effective by means of aqueous dimethylsulfoxide at 100 °C. Thus, the dichloromethylcarboxy compound **39** was obtained in 80% yield. The same benzo-annelated substrate afforded the interesting dinitropropanone **40** with 50% yield upon treatment with nitric acid (Scheme 9).

4. Conclusion

In conclusion, a number of new neonicotinoids have been synthesized by twofold S_NVin reactions of nitropolychlorobutadienes with bioactive heterocycles, carrying bisnucleophile-sidechains with a structurally and electronically varied C_2-backbone. Additionally, due to the stepped reactivity of the introduced nitropolychlorobutadienes, the primary substitution products prepare the ground for subsequent synthetic steps towards reduced compounds, enamines, ketones, vinyl thioethers and dichloronitro compounds. Most of the described neonicotinoids were tested against some agronomical important pests. Especially compound **13** and **29** were broadly active against aphids like green peach aphid *Myzus persicae* and cotton aphid *Aphis gossypii* in foliar and soil application. Additional efficacy against cotton whitefly *Bemisia tabaci* and mustard beetle *Phaedon cochleariae* was observed with **29**. The latter compound showed also a moderate-to-good efficacy against cat fleas *Ctenocephalides felis*, houseflies *Musca domestica* and blowfly larvae *Lucilia cuprina* with concentrations of 100 ppm.[14d]

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