

99. Reaction of 3-Amino-2*H*-azirines with 2-Amino-4,6-dinitrophenol (Picramic Acid): Synthesis of Quinazoline- and 1,3-Benzoxazole Derivatives¹⁾

by José M. Villalgordo²⁾, Beverly R. Vincent³⁾, and Heinz Heimgartner*

Organisch-chemisches Institut der Universität Zürich Winterthurerstrasse 190, 8057–Zürich

(17.IV.90)

The reaction of 3-(dimethylamino)-2*H*-azirines **1a–c** and 2-amino-4,6-dinitrophenol (picramic acid, **2**) in MeCN at 0° to room temperature leads to a mixture of the corresponding 1,2,3,4-tetrahydroquinazoline-2-one **5**, 3-(dimethylamino)-1,2-dihydroquinazoline **6**, 2-(1-aminoalkyl)-1,3-benzoxazole **7**, and *N*-[2-(dimethylamino)phenyl]- α -aminocarboxamide **8** (Scheme 3). Under the same conditions, 3-(*N*-methyl-*N*-phenyl-amino)-2*H*-azirines **1d** and **1e** react with **2** to give exclusively the 1,3-benzoxazole derivative **7**. The structure of the products has been established by X-ray crystallography. Two different reaction mechanisms for the formation of **7** are discussed in Scheme 6. Treatment of **7** with phenyl isocyanate, 4-nitrobenzoyl chloride, tosyl chloride, and HCl leads to a derivatization of the NH₂-group of **7** (Scheme 4). With NaOH or NaOMe as well as with morpholine, **7** is transformed into quinazoline derivatives **5**, **14**, and **15**, respectively, *via* ring expansion (Scheme 5). In case of the reaction with morpholine, a second product **16**, corresponding to structure **8**, is isolated. With these results, the reaction of **1** and **2** is interpreted as the primary formation of **7**, which, under the reaction conditions, reacts with Me₂NH to yield the secondary products **5**, **6**, and **8** (Scheme 7).

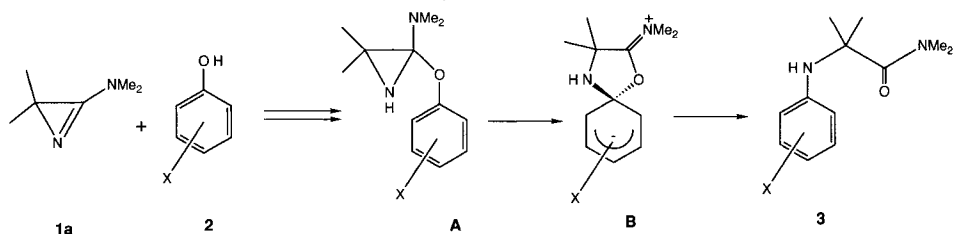
1. Introduction. – Several years ago, we have reported that phenols with $pK_a < ca. 8$ and 3-(dimethylamino)-2,2-dimethyl-2*H*-azirine (**1a**) in benzene at reflux temperature react to give substituted anilines of type **3** [1] (Scheme 1). The mechanism of this reaction was formulated in analogy to that of the reaction of **1a** and carboxylic acids (*cf.* [2][3]): protonation of the ring-N-atom of **1a** by the acidic phenol and nucleophilic attack of the phenolate at the amidinium-C-atom leads to the aziridine **A** which rearranges to give the spiro-*Meisenheimer* compound **B**. Re-aromatization *via* cleavage of the C–O bond and formation of the amide group than yields **3**; *i.e.* the transformation **2** $\rightarrow$ **3** proceeds *via* a nucleophilic aromatic substitution.

¹⁾ Presented (H.H.) at the 'Internationales Symposium über Stickstoff-Ringe und -Ketten', Heidelberg, March 19–21, 1990.

²⁾ Part of the planned thesis of J.M.V., Universität Zürich.

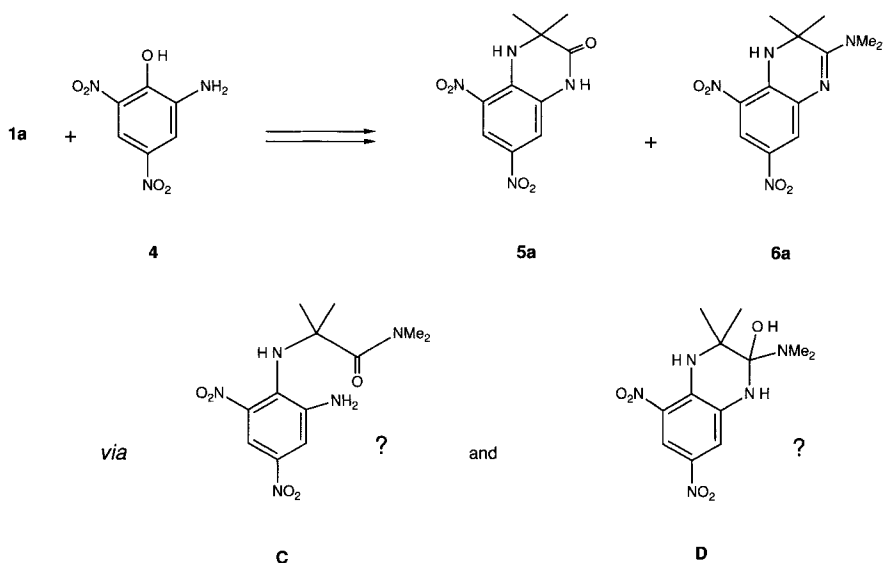
³⁾ Present address: Molecular Structure Corp., 3200A Research Forest Drive, The Woodlands, Texas 77381, USA.

Scheme 1



Under similar conditions (MeCN, reflux), the reaction of 2-amino-4,6-dinitrophenol (picramic acid, $pK_a = 4.2^4$, **4**) and **1a** gave a mixture of the quinazoline derivatives **5a** and **6a** in *ca.* 10 and 25% yield, respectively (Scheme 2). We have proposed [4] a reaction mechanism similar to that of other activated phenols, *i.e.* the α -(arylamino)isobutyramide **C** should be an intermediate. Intramolecular nucleophilic attack of the aromatic NH_2 group onto the *N,N*-dimethylamide function could give **D** which, after elimination of either Me_2NH or H_2O , yields the isolated products **5a** and **6a**.

Scheme 2

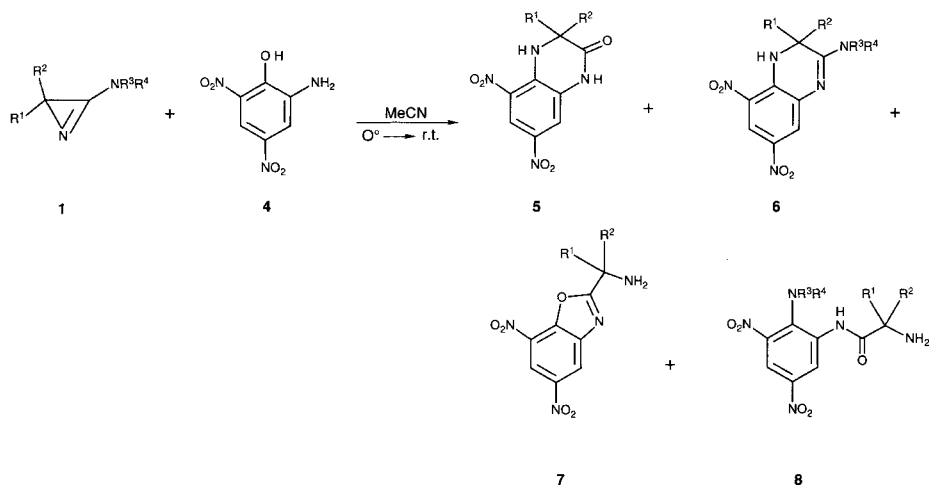


Recently, we tried to establish the proposed reaction mechanism by proceeding the reaction at lower temperature and with differently substituted 3-amino-2*H*-azirines **1** in order to isolate the postulated intermediate **C**.

⁴) Determined by potentiometric titration.

2. Results. – A solution of 3-(dimethylamino)-2,2-dimethyl-2*H*-azirine (**1a**) in MeCN was added to a suspension of picramic acid (**2**) in MeCN at 0° and stirred at room temperature. After 24 h, a complex mixture of products was detected by TLC. Separation by flash chromatography yielded **5a** and **6a** as yellow and red crystals, respectively, in small amounts (*Scheme 3* and *Tab. 1*).

Scheme 3



After crystallization, the main product **7a**, which is an isomer of **5a**, was isolated in *ca.* 45% yield as an orange powder. The remaining product **8a**, isolated in *ca.* 26% yield as yellow prisms, has been proved to be the only 1:1 adduct of **1a** and **2** (MS, elemental analysis) formed in this reaction.

Table. 1. Reaction of 3-Amino-2*H*-azirines **1** with 2-Amino-4,6-dinitrophenol (**2**) in MeCN at 0° → Room Temperature

1	R ¹	R ²	R ³	R ⁴	5 [%]	6 [%]	7 [%]	8 [%]
a	Me	Me	Me	Me	a (7–8)	a (14–25)	a (34–52)	a (24–29)
b	–(CH ₂) ₄ –		Me	Me	b (4)	b (32)	b (40)	b (16)
c	–(CH ₂) ₅ –		Me	Me	c (3)	c (7)	c (50)	c (26)
d	Me	Me	Me	Ph	–	–	a (83)	–
e	–(CH ₂) ₄ –		Me	Ph	–	–	b (81)	–

Similar results were obtained with the 3-(dimethylamino)-substituted ‘spiro-azirines’ **1b** and **1c** (*Table. 1*). In contrast, the two aminoazirines **1d** and **1e**, bearing an *N*-methyl-*N*-(phenylamino) group at C(3), react with **2** under analogous conditions to give exclusively the 1,3-benzoxazole derivatives of type **7**.

The structures of the products **5–8** have been elucidated from their spectral data and, in case of **5b**, **6b**, and **8b**, established by X-ray crystallography (*Figs. 1–3*; *cf. Exper. Part*).

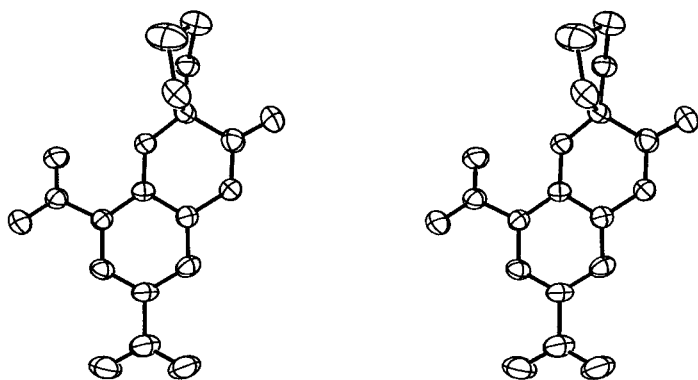


Fig. 1. Stereoview of the crystal structure of **5b**



Fig. 2. Packing of **5b**

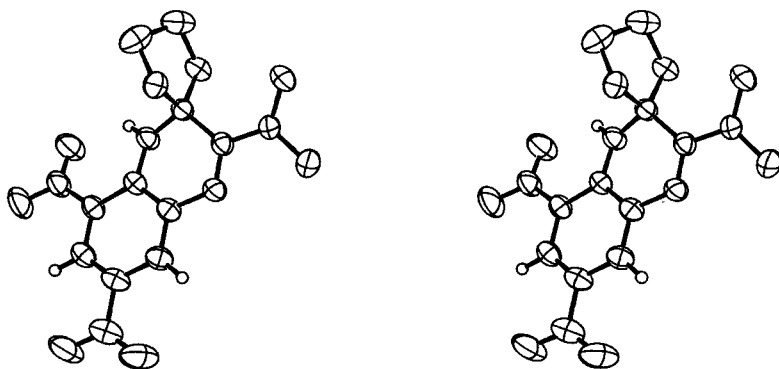
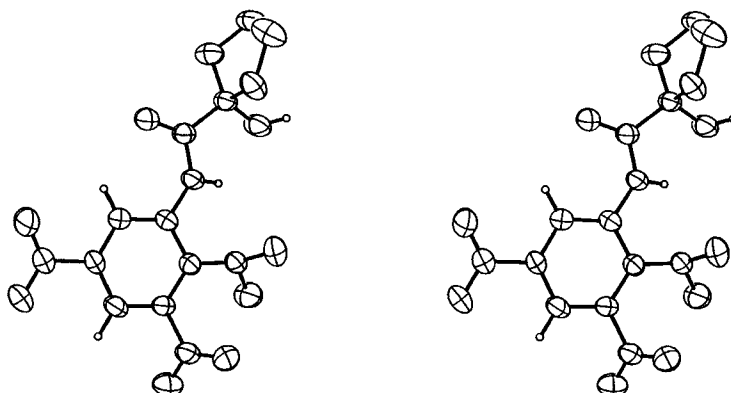


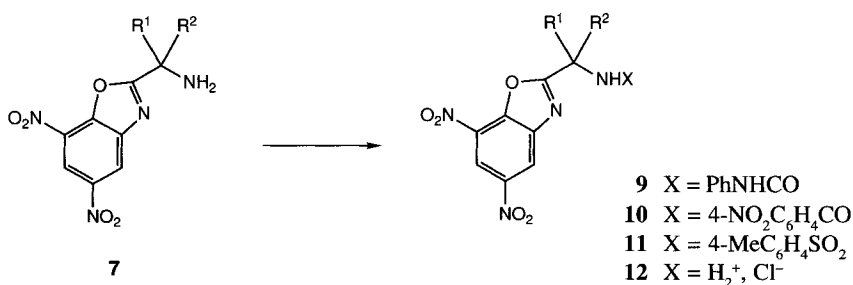
Fig. 3. Stereoview of the crystal structure of **6b**

Fig. 4. Stereoview of the crystal structure of **8b**

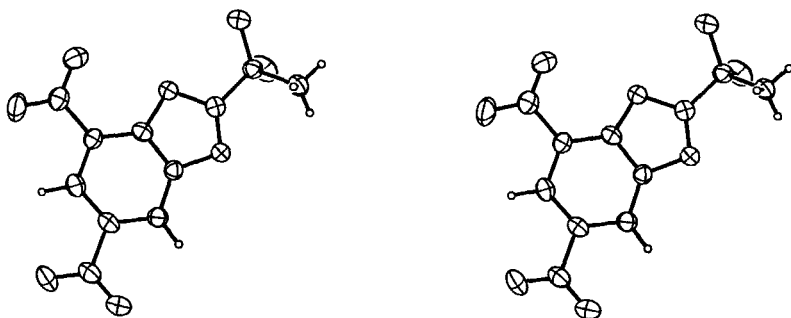
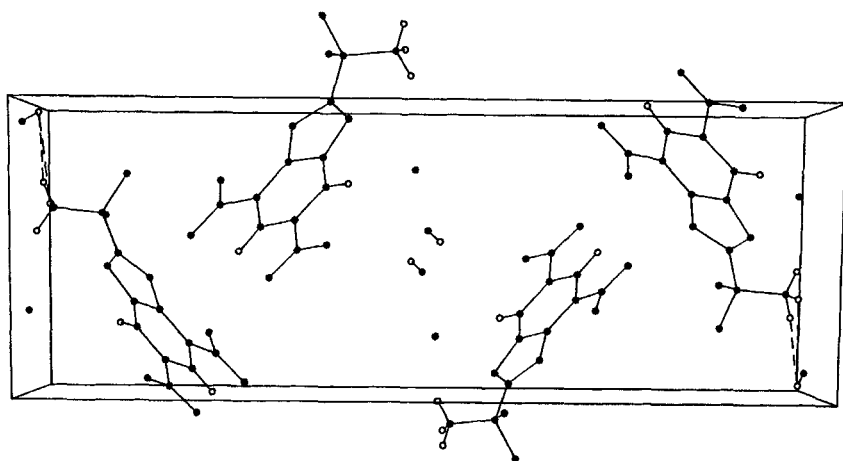
In case of **7**, we were not able to grow suitable crystals for an X-ray analysis. Crystallization from different solvents led either to amorphous material (with CH_2Cl_2 , Et_2O , hexane, AcOEt) or to transformations of the product into new compounds (with alcohols).

With the aim to prove the presence of a primary NH_2 group in **7** and with the hope to obtain a derivative suitable for crystal-structure determination, we treated a solution of **7a** in CH_2Cl_2 with phenyl isocyanate, with 4-nitrobenzoyl chloride and pyridine, with TsCl and Et_3N , and with HCl (Scheme 4).

Scheme 4

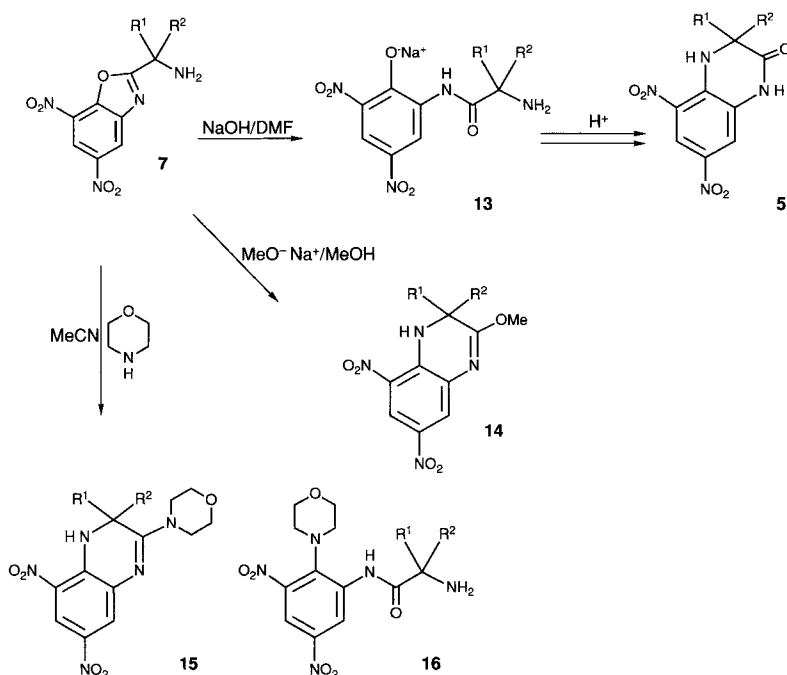


In all these reactions, the 1,3-benzoxazole skeleton was conserved. Although products **9–12** have been isolated as pure materials and in good yield, single crystals of good quality could be obtained only from hydrochloride **12a**. The result of the X-ray structure determination is shown in Fig. 4.

Fig. 5. Stereoview of the crystal structure of **12a**Fig. 6. Packing of **12a**

Treatment of 1,3-benzoxazoles of type **7** with nucleophiles led to ring transformations (*Scheme 5*). With NaOMe in MeOH, a ring expansion to the quinazoline derivative **14** occurred. A similar reaction was observed with morpholine, leading to **15**, which corresponds to structure **6**. In this case, a second product **16** was isolated. The structure of the latter corresponds to that of **8**. Again, a ring expansion was observed, when a solution of **7** in THF was treated with aqueous 1N NaOH at room temperature. The sole product of this reaction, formed in high yield, was the quinazolinone **5**. In DMF at room temperature, **7** reacted with 1N NaOH to an orange, solide material in quantitative yield. The structure of this product, which could not be isolated in pure form, most likely corresponds to that of phenolate **13**. Protonation with dilute aqueous HCl led to a product which, in DMSO solution, underwent a cyclization to give also **5**.

Scheme 5



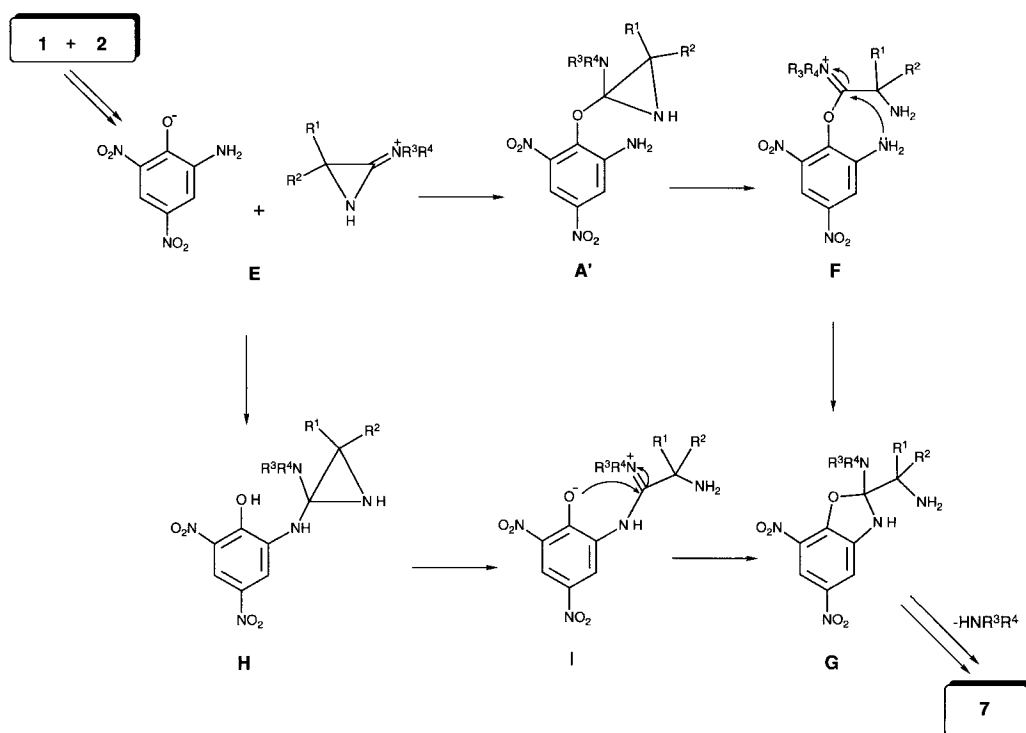
3. Discussion. – The most surprising result of the present study is the formation of **7** as the main or sole product. All attempts to detect an intermediate of type **C** (Scheme 2) failed. Therefore, we conclude that there is no such intermediate formed at 0° . Probably the reaction of **A'** to a spiro-*Meisenheimer* compound of type **B** (Scheme 1) does not take place due to steric hindrance⁵⁾. Instead of the expected intermediate **C**⁶⁾, the 1,3-benzoxazole **7** is formed.

Reaction mechanisms for the formation of **7** are presented in Scheme 6. It is likely that an aziridine **A'** is produced in the usual way. Cleavage of a C–N bond of the three-membered ring leads to intermediate **F**. Nucleophilic attack of the aromatic NH_2 group then gives the 2,3-dihydro-1,3-benzoxazole **G** and elimination of $\text{R}^3\text{R}^4\text{NH}$ yields **7**. An alternative reaction mechanism could lead to the formation of **H** via a nucleophilic attack of the aromatic NH_2 group onto the aziridinium ion of **E**. In analogy to $\text{A}' \rightarrow \text{F} \rightarrow \text{G}$, **H** can undergo a ring opening to **I**, which again can react via **G** to give **7**.

⁵⁾ This suggestion is supported by the previously reported results of reactions of **1** with 2,6-disubstituted phenols [1], which indeed proceed very slowly.

⁶⁾ The reaction of **1a** and 2,4-dinitrophenol gave the corresponding aniline derivative in 22% yield [1].

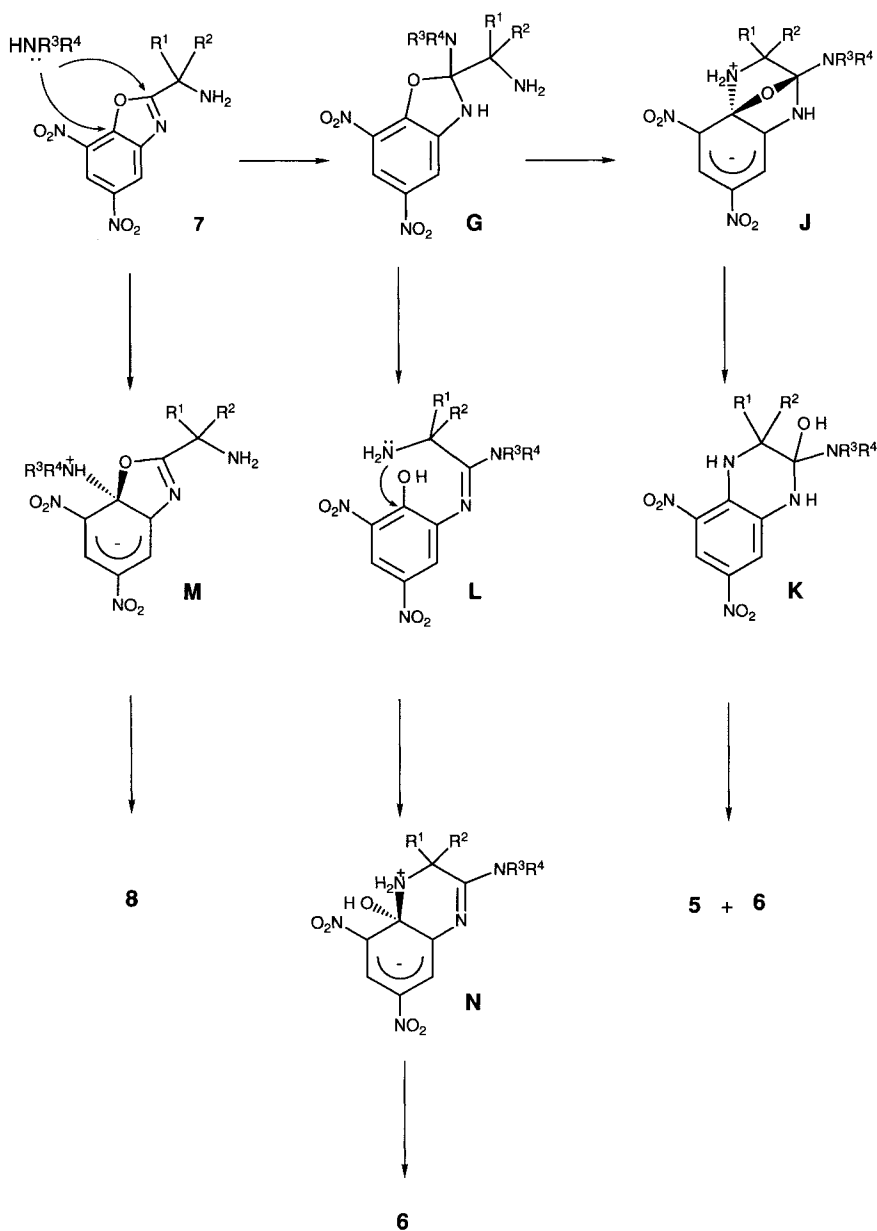
Scheme 6



The ring expansions observed by treatment of **7** with nucleophiles (Scheme 5) can be explained with the reaction sequence depicted in Scheme 7: the attack of the nucleophile onto C(2) of the oxazole yields **G**, which, via **J** and **K**, leads to **5** and **6**. The latter can also be formed via opening of the five-membered ring of **G** and intramolecular nucleophilic aromatic substitution ($\rightarrow$ **L** $\rightarrow$ **N** $\rightarrow$ **6**). The direct substitution of the aromatic oxygen function by an amine and cleavage of the oxazole ring leads via **M** to **8**.

The difference of the reactions of the 3-(dimethylamino)- and the 3-(*N*-methyl-*N*-phenylamino)-2*H*-azirines **1a–c** and **1d** and **1e**, respectively, is in accordance with the proposed reaction mechanisms: *N*-methylaniline is a better leaving group than Me_2NH (cf. also [5]) and a poorer nucleophile. Whereas **7**, under the conditions of its formation, reacts with the produced nucleophile Me_2NH to give **5**, **6**, and **8**, *N*-methylaniline is not nucleophilic enough to attack the 1,3-oxazole ring (Scheme 7).

Scheme 7



Our thanks are due to the analytical services of our institute, especially to Mr. *H. Frohofer* for elemental analyses, Mrs. *E. Patterson-Vykoukal* for running IR spectra, Mr. *M. Vöhler* for NMR spectra, Dr. *A. Lorenzi* for mass spectra, and to Dr. *B.P. Chandrasekhar BASF, India, Bombay*, for carrying out some preliminary experiments. Financial support by the *Swiss National Science Foundation* and by *F. Hoffmann-La Roche AG, Basel*, is gratefully acknowledged.

Experimental Part

General. See [6][7]. IR spectra in KBr. ^1H - (200 MHz) and ^{13}C -NMR (50.4 MHz) spectra in CDCl_3 , MS at 70 eV, CI-MS with 2-methylpropane; peaks in m/z [%] (>40, >5%).

1. *Reaction of 2,2-Dialkyl-3-(dimethylamino)-2H-azirines (1) and 2-Amino-4,6-dinitrophenol (2). General Procedure.* To a suspension of 199 mg (1 mmol) of **2** (prepared according to [8]) in 3 ml of dry MeCN, a soln. of 1.15 mmol of **1** in 0.5 ml of MeCN was added at 0° under Ar. The mixture was stirred for 24 h, raising the temp. from 0° to r.t. The solvent was removed under reduced pressure ($T < 30^\circ$), and the resulting residue purified by flash chromatography ($\text{AcOEt}/\text{CH}_2\text{Cl}_2$ 2:3) [9]. By this means, compounds **7a–c** were isolated in spectroscopically pure form and crystallized to obtain anal. pure products. The remaining material was separated by prep. TLC (hexane/ AcOEt 1:1, two plates), except in the case of **6b** and **8b**, which, after TLC separation, were dissolved in 8 ml of CH_2Cl_2 and washed twice with 4 ml of 2N HCl. The org. layer containing **8b** was dried (MgSO_4), and the aq. layer was brought to pH 8 with 5% aq. K_2CO_3 and extracted with AcOEt to give **6b**.

1.1. *With 3-(Dimethylamino)-2,2-dimethyl-2H-azirine (1a).* 1.1.1. 2-(1-Amino-1-methylethyl)-5,7-dinitro-1,3-benzoxazole (**7a**). Isolated as a yellow oil, crystallized from CH_2Cl_2 /hexane: orange powder, 34–52% yield. For spectroscopical data see *Exper. 1.4*.

1.1.2. 1,2,3,4-Tetrahydro-3,3-dimethyl-5,7-dinitroquinazolin-2-one (**5a**). Isolated as an amorphous yellow solid, crystallized from EtOH/xylene: yellow prisms, 7–8% yield. M.p. $274\text{--}275^\circ$. IR: 3320m, 3195w, 3110w, 2960w, 2930m, 2850w, 1695s, 1625s, 1605m, 1545s, 1520s, 1515s, 1470m, 1435m, 1400m, 1395m, 1360s, 1330s, 1240m, 1215m, 1160m, 1095m, 1050w, 950m, 905w, 895m, 845w, 830w, 770w, 750w, 740w, 720m, 680m, 660m. ^1H -NMR ($(\text{D}_6)\text{DMSO}$): 11.15 (s, NH); 8.60 (s, NH); 8.48 (d, $J = 2.5$, 1 arom. H); 7.74 (d, $J = 2.5$, 1 arom. H); 1.54 (s, $(\text{CH}_3)_2\text{C}$). ^{13}C -NMR ($(\text{D}_6)\text{DMSO}$): 168.1 (s, C=O); 135.9, 135.7, 129.6, 128.9 (4s, 4 arom. C); 116.5, 111.6 (2d, 2 arom. C); 56.5 (s, C(3)); 26.8 (q, $(\text{CH}_3)_2\text{C}$). EI-MS: 266 (26, M^+), 251 (100), 223 (20), 205 (23), 177 (16), 159 (26), 131 (10), 43 (25), 42 (10), 41 (15). Anal. calc. for $\text{C}_{10}\text{H}_{10}\text{N}_4\text{O}_5$ (266.21): C 45.12, H 3.78, N 21.04; found: C 45.01, H 4.01, N 21.08.

1.1.3. 2-(Dimethylamino)-3,4-dihydro-3,3-dimethyl-5,7-dinitroquinazoline (**6a**). Isolated as a red solid, crystallized from acetone/hexane: red prisms, 14–25% yield. M.p. $205.8\text{--}206.9^\circ$. IR: 3360m, 3100m, 2965w, 2920w, 1605s, 1590s, 1550s, 1520s, 1500s, 1420s, 1395w, 1385m, 1375m, 1360s, 1330s, 1320s, 1290s, 1230w, 1210w, 1200w, 1165w, 1150m, 1130m, 1080s, 1020w, 935m, 930m, 895w, 880w, 810m, 770w, 740m, 730w, 710w. ^1H -NMR: 8.72 (d, $J = 2.5$, 1 arom. H); 8.20 (br. s, NH); 7.97 (dd, $J = 2.5$, 0.9, 1 arom. H); 3.15 (s, $(\text{CH}_3)_2\text{N}$); 1.64 (s, $(\text{CH}_3)_2\text{C}$). EI-MS: 293 (37, M^+), 278 (100), 249 (19), 247 (6), 246 (8), 232 (14), 186 (20), 172 (6), 157 (6), 130 (6), 93 (6), 70 (7), 63 (6), 57 (10), 56 (8), 44 (23), 43 (15), 42 (22), 41 (12), 40 (7). Anal. calc. for $\text{C}_{15}\text{H}_{15}\text{N}_5\text{O}_4$ (293.28): C 49.14, H 5.15, N 23.88; found: C 48.95, H 5.07, N 23.62.

1.1.4. 2-Amino-N-[2-(dimethylamino)-3,5-dinitrophenyl]-2-methylpropanamide (**8a**). Isolated as a yellow solid, crystallized from i-PrOH: yellow prisms, 24–29% yield. M.p. $205.8\text{--}206.9^\circ$. IR: 3380w, 3340w, 3240m, 3120w, 3100w, 2980w, 2940w, 2860w, 2810w, 1685s, 1605m, 1595m, 1540s, 1530s, 1455m, 1440w, 1420m, 1350s, 1340s, 1215m, 1180w, 1145m, 1100w, 1080m, 950m, 910m, 885m, 805m, 770w, 755m, 735m. ^1H -NMR: 10.82 (br. s, NH); 9.54 (d, $J = 2.7$, 1 arom. H); 8.23 (d, $J = 2.7$, 1 arom. H); 2.85 (s, $(\text{CH}_3)_2\text{N}$); 1.66 (br. s, NH_2); 1.50 (s, $(\text{CH}_3)_2\text{C}$). ^{13}C -NMR: 176.5 (s, C=O); 146.0, 142.9, 140.5, 135.6 (4s, 4 arom. C); 116.7, 114.5 (2d, 2 arom. C); 55.7 (s, C(2)); 41.7 (q, $(\text{CH}_3)_2\text{N}$); 29.0 (q, $(\text{CH}_3)_2\text{C}$). CI-MS: 313 (15, $[M + 2]^+$), 312 (100, $[M + 1]^+$), 285 (3), 281 (5). Anal. calc. for $\text{C}_{12}\text{H}_{17}\text{N}_5\text{O}_5$ (311.29): C 46.30, H 5.50, N 22.50; found: C 46.54, H 5.71, N 22.39.

1.2. *With 2-(Dimethylamino)-1-azaspiro[2.4]hept-1-ene (1b).* 1.2.1. 2-(1-Aminocyclopentyl)-5,7-dinitro-1,3-benzoxazole (**7b**). Isolated as a colourless oil, crystallized from CH_2Cl_2 /hexane: orange powder, 40% yield. For spectroscopical data, see *Exper. 1.5*.

1.2.2. 1',2',3',4'-Tetrahydro-5',7'-dinitrospiro[cyclopentane-1,3'-quinazolin]-2'-one (**5b**). Isolated as a yellow solid, crystallized from EtOH: yellow prisms, 3–4% yield. M.p. $210\text{--}211^\circ$. IR: 3320s, 3200w, 3100w, 2960w, 1695s, 1620s, 1545s, 1515s, 1490w, 1355s, 1330s, 1310s, 1285m, 1260w, 1215w, 1190w, 1170w, 1105m, 1090m, 1055w, 1030w, 955w, 940m, 900w, 890m, 835m, 770w, 750w, 740m, 720w. ^1H -NMR ($(\text{D}_6)\text{DMSO}$): 11.10 (br. s, NH); 8.53 (br. s, NH); 8.48 (d, $J = 2.6$, 1 arom. H); 7.75 (d, $J = 2.6$, 1 arom. H); 2.3–1.7 (m, 4 CH_2). EI-MS: 292 (100, M^+), 275 (35), 263 (43), 250 (18), 245 (18), 235 (84), 217 (16), 171 (25), 85 (42). Anal. calc. for $\text{C}_{12}\text{H}_{12}\text{N}_4\text{O}_5$ (292.24): C 49.32, H 4.14, N 19.17; found: C 49.34, H 4.14, N 19.00.

1.2.3. 2'-(Dimethylamino)-3',4'-dihydro-5',7'-dinitrospiro[cyclopentane-1,3'-quinazoline] (**6b**). Isolated as a red solid, crystallized from i-PrOH: red prisms, 32% yield. M.p. $165.4\text{--}166.4^\circ$. IR: 3340m, 3110w, 2930m, 2860w, 1605s, 1590s, 1550s, 1520s, 1500s, 1450w, 1425m, 1385m, 1360s, 1335s, 1320s, 1310s, 1290m,

1270m, 1210w, 1185w, 1165w, 1140m, 1080m, 1010w, 940m, 910w, 905w, 880m, 860w, 770w, 740m, 730m, 710m. ¹H-NMR: 8.70 (*d*, *J* = 2.6, 1 arom. H); 8.52 (br. *s*, NH); 7.94 (*dd*, *J* = 2.6, 0.8, 1 arom. H); 3.08 (*s*, (CH₃)₂N); 2.5–1.8 (*m*, 4 CH₂). ¹³C-NMR: 159.2 (*s*, C(2)); 137.1, 136.5, 136.2, 132.2 (4*s*, 4 arom. C); 120.5, 116.2 (2*d*, 2 arom. C); 61.3 (*s*, C(3')); 31.9 (*q*, (CH₃)₂N); 41.0, 24.7 (2*t*, 4 CH₂). EI-MS: 319 (100, *M*⁺), 303 (12), 302 (57), 290 (21), 275 (50), 272 (27), 246 (20), 244 (23), 226 (13), 198 (23), 84 (80). Anal. calc. for C₁₄H₁₉N₅O₄ (319.32): C 52.66, H 5.36, N 21.93; found: C 52.62, H 5.38, N 21.70.

1.2.4. *1-Amino-N-[2-(dimethylamino)-3,5-dinitrophenyl]cyclopentanecarboxamide (8b)*. Isolated as a yellow solid, crystallized from *i*-PrOH: yellow prisms, 16% yield. M.p. 142.3–143.1°. IR: 3370m, 3320m, 3200m, 3100m, 2980w, 2960m, 2880w, 1680s (br.), 1600m, 1595m, 1540s, 1530s, 1505s, 1484s, 1450s, 1414s, 1413s, 1370s, 1345s, 1210w, 1175w, 1160w, 1140w, 1085w, 1070w, 1055w, 945s, 910s, 895w, 830w, 895w, 780w, 755w, 735w. ¹H-NMR: 10.94 (br. *s*, NH); 9.56 (*d*, *J* = 2.7, 1 arom. H); 8.22 (*d*, *J* = 2.7, 1 arom. H); 2.85 (*s*, (CH₃)₂N); 2.4–1.4 (*m*, 10H). ¹³C-NMR: 176.4 (*s*, C=O); 145.9, 142.7, 140.4, 137.5 (4*s*, 4 arom. C); 116.6, 114.3 (2*d*, 2 arom. C); 65.9 (*s*, C(1)); 41.6 (*q*, (CH₃)₂N); 40.7, 24.5 (2*t*, 4 CH₂). CI-MS: 339 (17, [*M* + 2]⁺), 338 (100, [*M* + 1]⁺), 84 (13). Anal. calc. for C₁₄H₁₉N₅O₅ (337.33): C 49.85, H 5.67, N 20.76; found: C 49.73, H 5.49, N 20.51.

1.3. With 2-(Dimethylamino)-1-azaspiro[2.5]oct-1-ene (**1c**). 1.3.1. 2-(1-Aminocyclohexyl)-5,7-dinitro-1,3-benzoxazole (**7c**). Isolated as a yellow oil which was crystallized from CH₂Cl₂/hexane: orange powder, 47–54 % yield. M.p. 100° (dec.). IR: 3400w, 3330w, 3100m, 2940s, 2860s, 1635m, 1615s, 1545s, 1535s, 1530s, 1460m, 1445m, 1375m, 1350s, 1275m, 1260m, 1250m, 1190m, 1175w, 1155w, 1070w, 1050w, 1035m, 935w, 920s, 900m, 895m, 850m, 835m, 810w, 790w, 740m, 730m, 720s. ¹H-NMR (CDCl₃): 9.09 (*d*, *J* = 2.1, 1 arom. H); 8.87 (*d*, *J* = 2.1, 1 arom. H); 2.6–1.3 (*m*, 5 CH₂). ¹³C-NMR (CDCl₃): 177.6 (*s*, C=N); 146.9, 145.1, 144.5, 144.2 (4*s*, 4 arom. C); 121.4, 116.8 (2*d*, 2 arom. C); 54.0 (*s*, C(1')); 36.4, 36.4, 25.1 (3*t*, 5 CH₂). EI-MS: 306 (9, *M*⁺), 263 (9), 166 (8), 123 (11), 122 (9), 111 (13), 100 (8), 98 (100), 97 (18), 96 (8), 95 (13), 94 (15), 85 (30), 84 (83), 83 (24), 82 (11), 81 (15), 69 (25), 68 (37), 67 (34), 60 (21).

1.3.2. 1',2',3',4'-Tetrahydro-5',7'-dinitrospiro[cyclohexane-1,3'-quinazolin]-2'-one (**5c**). Isolated as a yellow solid, crystallized from *i*-PrOH: yellow needles, 3% yield. M.p. 220.3–220.8°. IR: 3360m, 3340m, 3090w, 2990m, 2860m, 1690s, 1525m, 1600w, 1545s, 1515s, 1470w, 1455w, 1435w, 1390w, 1365m, 1335s, 1320s, 1290s, 1250w, 1210w, 1175w, 1140w, 1100m, 1080m, 1030w, 1000w, 950w, 930w, 910w, 900w, 890m, 870w, 860w, 820w, 770w, 760w, 740m, 730w. ¹H-NMR ((D₆)DMSO): 11.10 (br. *s*, NH); 8.70 (br. *s*, NH); 8.49 (*d*, *J* = 2.6, 1 arom. H); 7.75 (*d*, *J* = 2.6, 1 arom. H); 1.9–1.2 (*m*, 5 CH₂). EI-MS: 306 (100, *M*⁺), 289 (22), 263 (52), 259 (13), 251 (10), 250 (40), 235 (38), 217 (11), 205 (12), 171 (12), 158 (13), 56 (18), 42 (21), 40 (14). Anal. calc. for C₁₃H₁₄N₄O₅ (306.27): C 50.98, H 4.61, N 18.30; found: C 51.03, H 4.75, N 18.05.

1.3.3. 2'-(Dimethylamino)-3',4'-dihydro-5',7'-dinitrospiro[cyclohexane-1,3'-quinazoline] (**6c**). Isolated as a red solid, crystallized from *i*-PrOH: red microcrystals, 6–8% yield. M.p. 187–187.7°. IR: 3370s, 3110w, 3000w, 2950m, 2930s, 2860m, 1610s, 1590s, 1550s, 1525s, 1500s, 1470m, 1445w, 1420s, 1370s, 1330s, 1320s, 1290s, 1275s, 1250w, 1205w, 1165m, 1130s, 1080m, 1050w, 1015w, 999m, 945w, 935s, 910w, 890m, 880w, 860w, 840w, 815m, 770w, 740m, 730m, 715m. ¹H-NMR (CDCl₃): 9.04 (br. *s*, NH); 8.74 (*d*, *J* = 2.5, 1 arom. H); 7.96 (*dd*, *J* = 2.5, 0.8, 1 arom. H); 3.15 (*s*, (CH₃)₂N); 2.2–1.2 (*m*, 5 CH₂). EI-MS: 334 (24, [*M* + 1]⁺), 333 (100, *M*⁺), 316 (55), 286 (17), 56 (18), 47 (30), 45 (34), 43 (30), 42 (38). Anal. calc. for C₁₅H₁₉N₅O₄ (333.34): C 54.05, H 5.74, N 21.01; found: C 53.97, H 5.79, N 20.84.

1.3.4. 1-Amino-N-[2-(dimethylamino)-3,5-dinitrophenyl]cyclohexanecarboxamide (**8c**). Isolated as a yellow solid, crystallized from EtOH: yellow prisms, 25–27% yield. M.p. 118.6–119.3°. IR: 3400m, 3260s, 3100m, 2930s, 2860s, 2800m, 1690m (br.), 1595s, 1545s, 1540s, 1530s, 1400s, 1485s, 1450s, 1420s, 1340s, 1215m, 1180m, 1170m, 1155m, 1145m, 1120m, 1100m, 1080s, 1065s, 1000w, 950s, 920m, 910m, 880m, 860m, 835w, 820w, 780w, 760w, 755m, 740s. ¹H-NMR (CDCl₃): 10.94 (br. *s*, NH); 9.55 (*d*, *J* = 2.7, 1 arom. H); 8.22 (*d*, *J* = 2.7, 1 arom. H); 2.84 (*s*, (CH₃)₂N); 2.3–1.4 (*m*, 12 H). ¹³C-NMR (CDCl₃): 176.9 (*s*, C=O); 145.9, 142.8, 140.5, 137.5 (4*s*, 4 arom. C); 116.7, 114.3 (2*d*, 2 arom. C); 58.3 (*s*, C(1)); 41.6 (*q*, (CH₃)₂N); 34.3, 25.0, 21.0 (3*t*, 5 CH₂). CI-MS: 353 (51, [*M* + 2]⁺), 352 (96, [*M* + 1]⁺), 322 (5), 321 (5), 307 (14), 99 (11), 98 (100). Anal. calc. for C₁₅H₂₁N₅O₅ (351.36): C 51.27, H 6.02, N 19.93; found: C 51.11, H 5.89, N 19.70.

1.4. With 2,2-Dimethyl-3-(*N*-methyl-*N*-phenylamino)-2H-azirine (**1d**). A soln. of 113 mg (0.65 mmol) of **1d** in 1 ml of dry MeCN was added, at 0° under Ar, to a suspension of 99.5 mg (0.5 mmol) of **2** in 1.5 ml of MeCN. The mixture was stirred for 24 h between 0° and r.t., the solvent evaporated (*T* < 30°) and the residue purified by flash chromatography (AcOEt/CH₂Cl₂ 2:3). Crystallization from CH₂Cl₂/hexane yielded 110 mg (83%) of **7a** as orange powder. M.p. 90° (dec.). IR: 3370w, 3320w, 2980w, 2930w, 1630m, 1615m, 1565w, 1540s, 1530s, 1460m, 1430w, 1385m, 1375m, 1350s, 1340s, 1270w, 1250w, 1220w, 1105m, 1095m, 1065m, 1025m, 990w, 935m, 915m, 900m, 810m, 745m, 720m. ¹H-NMR ((CD₃)₂CO): 8.98 (*d*, *J* = 2.2, 1 arom. H); 8.94

(*d*, *J* = 2.2, 1 arom. H); 2.91 (br. s, NH₂); 1.68 (s, (CH₃)₂C). ¹³C-NMR ((D₆)DMSO): 176.6 (s, C=N); 146.7 (s, C=O); 146.7, 144.2, 143.8, 132.1 (4s, 4 arom. C); 121.5, 116.7 (2*d*, 2 arom. C); 51.0 (s, C(1')); 39.5 (*q*, (CH₃)₂C). CI-MS: 267 (100, [*M* + 1]⁺), 58 (20), 57 (67). EI-MS: 251 (100, [*M* - CH₃]⁺), 210 (16), 164 (8), 159 (6), 118 (5), 58 (20), 42 (9).

1.5. With 2-(*N*-Methyl-*N*-phenylamino)-1-azaspiro[2.5]hept-1-ene (**1e**). In analogy to *Exper. 1.4*, 130 mg (0.65 mmol) of **1e** in 1 ml of MeCN were treated with **2**: 118 mg (81%) of **7b** as orange powder. M.p. 105° (dec.). IR: 3400w, 3325w, 3105m, 2945m, 2865m, 1630m, 1615m, 1565m, 1545s, 1535s, 1460m, 1385m, 1305s, 1265m, 1250m, 1145m, 1065m, 1035m, 990m, 935m, 915m, 895m, 810s, 740m, 720s. ¹H-NMR ((CD₃)₂CO): 8.97 (*d*, *J* = 2.1, 1 arom. H); 8.92 (*d*, *J* = 2.1, 1 arom. H); 2.45–1.75 (*m*, 10 H). ¹³C-NMR ((D₆)MeOH): 178.3 (s, C=N); 148.6, 146.3, 145.7, 145.6 (4s, 4 arom. C); 121.1, 117.7 (2*d*, 2 arom. C); 62.5 (s, C(1')); 41.0, 25.5 (2*t*, 4 CH₂). EI-MS: 292 (52, *M*⁺), 276 (16), 275 (100), 264 (19), 263 (84), 217 (21), 210 (18), 84 (24), 42 (15).

2. Reactions of 2-(1-Aminoalkyl)-1,3-benzoxazoles **7** with Electrophiles. 2.1. With Phenyl Isocyanate.

2.1.1. *N*-[1-(5,7-Dinitro-1,3-benzoxazol-2-yl)cyclopentyl]-*N*'-phenylurea (**9b**). To a well stirred soln. of 58 mg (0.19 mmol) of **7b** in 2 ml of CH₂Cl₂ at r.t. under Ar, 22 ml (0.20 mmol) of phenyl isocyanate were added. The reaction mixture was stirred overnight, the formed solid collected by filtration, washed with cold MeOH, Et₂O and dried: 75 mg (96%) of **9b**. Colourless solid, m.p. 200.6–202.8°. IR: 3350m, 3320m, 3100m, 2980m, 2940w, 2880w, 1640s, 1620s, 1600s, 1565s, 1550s, 1535s, 1500s, 1460w, 1445m, 1370w, 1350s, 1320s, 1300w, 1255m, 1250m, 1230m, 1195w, 1180w, 1145w, 1120w, 1100w, 1070w, 1025m, 970w, 935w, 915w, 900m, 810m, 755m, 740m, 725m, 695m. ¹H-NMR ((D₆)DMSO): 9.07 (*d*, *J* = 2.2, 1 arom. H); 8.84 (*d*, *J* = 2.2, 1 arom. H); 8.56 (s, PhNH); 7.35–6.85 (*m*, 6 arom. H); 2.5–1.85 (*m*, 4 CH₂). ¹³C-NMR ((D₆)DMSO): 175.1 (s, C=N); 154.5 (s, C=O); 144.4, 144.5, 143.7, 139.7, 139.6 (5s, 5 arom. C); 128.7, 128.5, 121.7, 118.0, 117.7 (5*d*, 7 arom. C); 61.5 (s, C(1')); 38.1, 23.4 (2*t*, 4 CH₂). EI-MS: 411 (34, *M*⁺), 371 (21), 370 (100), 188 (11), 119 (12), 93 (60), 77 (10).

2.1.2. *N*-[1-(5,7-Dinitro-1,3-benzoxazol-2-yl)cyclohexyl]-*N*'-phenylurea (**9c**). According to *Exper. 2.1.1*, 50 mg (0.16 mmol) of **7c** were reacted with phenyl isocyanate: 60 mg (88%) of **9c**. Colorless solid, m.p. 225.4–226°. IR: 3350m, 3320m, 3100w, 2950w, 2940w, 2930w, 2860w, 1645s, 1615m, 1600s, 1560s, 1550s, 1540s, 1500s, 1465w, 1445m, 1345s, 1320s, 1250s, 1205w, 1190w, 1150w, 1130w, 1115m, 1075w, 1065w, 1035w, 1020w, 980w, 940w, 930w, 900m, 870w, 810m, 755m, 745m, 725m, 695m. ¹H-NMR ((D₆)DMSO): 9.07 (*d*, *J* = 2.2, 1 arom. H); 8.85 (*d*, *J* = 2.2, 1 arom. H); 8.63 (s, PhNH); 7.3–6.8 (*m*, 6 arom. H); 2.35–1.65 (*m*, 5 CH₂). ¹³C-NMR ((D₆)DMSO): 175.5 (s, C=N); 145.0 (s, C=O); 146.4, 144.5, 143.8, 139.7, 132.0 (5s, 5 arom. C); 128.6, 121.4, 117.5, 116.4, 116.4 (5*d*, 7 arom. C); 54.1 (s, C(1')); 33.9, 24.7, 20.9 (3*t*, 5 CH₂). EI-MS: 425 (57, *M*⁺), 370 (16), 119 (26), 94 (11), 93 (100), 81 (11), 77 (12), 55 (10).

2.2. With 4-Nitrobenzoyl Chloride: *N*-[1-(5,7-Dinitro-1,3-benzoxazol-2-yl)cyclopentyl]-4-nitrobenzamide (**10**). A soln. of 80 mg (0.43 mmol) of 4-nitrobenzoyl chloride in 5 ml of CH₂Cl₂ was added dropwise to a soln. of 120 mg (0.40 mmol) of **7b** in 3.5 ml of pyridine. The soln. was refluxed for 8 h and stirred at r.t. overnight. Then, 15 ml of CH₂Cl₂ were added, the soln. was washed three times with 15 ml of 3*N* HCl and once with ice/H₂O. The org. layer was dried (MgSO₄), evaporated, and the residue chromatographed (hexane/AcOEt 1:1): 130 mg (74%) **10**. White foam, m.p. 81.1–82.2°. IR: 3400w, 3100w, 2960w, 2870w, 1650m (br.), 1620m, 1605m, 1545s, 1535s, 1525s, 1495w, 1460w, 1350s, 1300m, 1255m, 1190w, 1140w, 1110w, 1070w, 1050w, 1030m, 980w, 940w, 905w, 870w, 850w, 810m, 780w, 725m. ¹H-NMR (CDCl₃): 9.06 (*d*, *J* = 2.1, 1 arom. H); 8.87 (*d*, *J* = 2.1, 1 arom. H); 8.30 (*m*, 2 arom. H); 7.96 (*m*, 2 arom. H); 6.92 (s, NH); 2.75–2.65 (*m*, CH₂); 2.55–2.35 (*m*, CH₂); 2.2–2.0 (*m*, 2 CH₂). ¹³C-NMR (CDCl₃): 174.0 (s, C=N); 166.1 (s, C=O); 149.4, 146.8, 144.9, 144.0, 139.1, 132.1 (6s, 6 arom. C); 128.2, 123.5, 121.3, 116.5 (4*d*, 6 arom. C); 63.1 (s, C(1')); 38.6, 23.9 (2*t*, 4 CH₂). EI-MS: 441 (4, *M*⁺), 424 (20), 291 (20), 275 (48), 233 (13), 150 (100), 104 (33), 92 (11), 76 (10).

2.3. With TsCl: *N*-[1-(5,7-Dinitro-1,3-benzoxazol-2-yl)cyclopentyl]-*p*-toluenesulfonamide (**11**). To a soln. of 35 mg (0.12 mmol) of **7b** and 25 mg (0.13 mmol) of TsCl in 3 ml of abs. CH₂Cl₂ at r.t., a slight excess of Et₃N was added and the reaction mixture refluxed for 4 h. Then 7 ml of CH₂Cl₂ were added, the soln. was washed with H₂O, the org. layer dried (MgSO₄), the solvent evaporated, and the residue chromatographed (hexane/AcOEt 9:1): 38 mg (71%) of **11**, which was crystallized from toluene. Colourless microcrystals, m.p. 235–235.5°. IR: 3350s, 3130m, 3100m, 2990w, 2960w, 2880w, 1670m, 1600m, 1575w, 1545s, 1535s, 1495w, 1460m, 1445w, 1430w, 1410m, 1370m, 1345s, 1310m, 1250w, 1190w, 1170s, 1150m, 1120m, 1090m, 1020m, 935m, 930m, 905w, 900w, 870w, 845w, 815s, 810s, 770w, 745w, 730s, 720s, 705w. ¹H-NMR ((D₆)DMSO): 9.02 (*d*, *J* = 2.2, 1 arom. H); 8.83 (*d*, *J* = 2.2, 1 arom. H, NH); 7.36 (*d*, *J* = 8.1, 2 arom. H); 6.93 (*d*, *J* = 8.1, 2 arom. H); 2.49–2.35 (*m*, 4H); 2.05 (s, CH₃); 1.85–1.65 (*m*, 4 H). CI-MS: 447 (100, [*M* + 1]⁺). EI-MS: 291 (36, *M* - OTs), 238 (11), 159 (35), 155 (20), 92 (17), 91 (93), 85 (11), 83 (6), 75 (26), 67 (10), 65 (24), 59

(41), 56 (21), 55 (12), 45 (24), 44 (22), 42 (22), 41 (24), 40 (17), 34 (100). Anal. calc. for $C_{19}H_{18}N_4SO_7$ (446.44): C 51.11, H 4.06, N 12.55, S 7.18; found C 51.33, H 4.24, N 12.43, S 7.19.

2.4. With HCl. 2.4.1. 2-(1-Amino-1-methylethyl)-5,7-dinitro-1,3-benzoxazole Hydrochloride (**12a**). Dry HCl gas was bubbled through a soln. of 50 mg (0.18 mmol) of **7a** in 5 ml of abs. CH_2Cl_2 at r.t. for 5 min. Filtration of the formed solid and crystallization in EtOH yielded 48 mg (88%) of **12a**. Colorless needles, m.p. 116° (dec.). IR: 3420m (br.), 2910m (br.), 1650m, 1620m, 1590w, 1555s, 1535s, 1460w, 1440w, 1360m, 1350s, 1265m, 1255m, 1190m, 1150s, 1070m, 1020m, 950m, 935m, 905m, 805m, 735m, 720s. 1H -NMR ((D_6) DMSO): 9.40 (br. s, 3 H); 9.19 (d, $J = 2.1$, 1 arom. H); 8.95 (d, $J = 2.1$, 1 arom. H); 1.84 (s, $(CH_3)_2C$). Cl-MS: 267 (100, $[M - HCl]^+$), 268 (11), 71 (7).

2.4.2. 2-(1-Aminocyclopentyl)-5,7-dinitro-1,3-benzoxazole Hydrochloride (**12b**). Dry HCl gas was bubbled through a soln. of 130 mg (0.44 mmol) **7b** in 8 ml of abs. CH_2Cl_2 at r.t. for 5 min. The colorless solid was filtered and crystallized from EtOH: 130 mg (90%) of **12b**. Colourless microcrystals, m.p. 127–128° (dec.). IR: 3440m (br.), 2930m (br.), 1640m, 1625m, 1595w, 1550s, 1540s, 1505m, 1465w, 1440w, 1370m, 1350s, 1250m, 1195m, 1150s, 1070m, 1025m, 950m, 940m, 900m, 860w, 800m, 770w, 735m, 725s. 1H -NMR ((D_6) DMSO): 9.45 (br. s, 3 H); 9.19 (d, $J = 2.1$, 1 arom. H); 8.94 (d, $J = 2.1$, 1 arom. H); 2.45–1.9 (m, 4 CH_2). ^{13}C -NMR ((D_6) DMSO): 170.3 (s, C=N), 146.9, 144.3, 143.5, 132.4 (4s, 4 arom. C); 121.9, 117.3 (2d, 2 arom. C); 61.2 (s, C(1')); 37.1, 24.4 (2t, 4 CH_2). EI-MS: 292 (27, $[M - HCl]^+$), 276 (10), 275 (61), 265 (12), 263 (57), 250 (11), 217 (19), 210 (17), 172 (11), 171 (13), 164 (15), 118 (17), 91 (17), 90 (13), 85 (11), 84 (82), 77 (13), 69 (15), 67 (40), 65 (11), 63 (15), 62 (20), 58 (14), 57 (38), 56 (24), 55 (50), 54 (13), 51 (10), 46 (13), 44 (17), 43 (100), 42 (71), 40 (21).

3. Reactions of 2-(1-Aminoalkyl)-1,3-benzoxazoles **7** with Nucleophiles. 3.1. Treatment of **7b** with NaOH. a) To a soln. of 80 mg (0.27 mmol) of **7b** in 2 ml DMF, several drops of 1N NaOH were added at r.t., and the mixture was stirred overnight. The solvent was evaporated, the resulting solid washed with MeOH and dried to yield quantitatively sodium 2,4-dinitro-6-[(2-amino-2-methyl)propanoyl]aminophenolate (**13**) as an orange powder. Cl-MS: 333 (5, $[M + 1]^+$), 237 (18), 232 (16), 231 (11), 230 (42), 229 (83), 221 (12), 219 (13), 215 (24), 212 (14), 211 (100), 209 (17), 194 (28), 174 (11), 172 (37), 85 (15), 71 (27), 69 (21). This material was treated with 5% HCl and then extracted with CH_2Cl_2 . The combined org. layers were dried ($MgSO_4$) and the solvent evaporated to give the corresponding phenol in 98% yield, which, in DMSO, rearranges partially to **5b**.

b) In analogy to a, a soln. of **7b** in THF was treated with 1N NaOH at r.t. and the solvent evaporated. After addition of H_2O , the soln. was extracted with CH_2Cl_2 ; 90% of **5b** (see Exper. 1.2.2).

3.2. Treatment of **7c** with NaOH. According to Exper. 3.1.b, 80 mg (0.26 mmol) of **7c** in 2 ml of THF were treated with 1N NaOH at r.t.: 66 mg (89%) of **5c** (s. Exper. 1.3.2).

3.3. Treatment of **7** with NaOMe. 3.3.1. 3',4'-Dihydro-2'-methoxy-5',7'-dinitrospiro[cyclopentane-1,3'-quinazoline] (**14b**). To a well stirred soln. of NaOMe in MeOH, 80 mg (0.27 mmol) of **7b** were added at r.t. After 5 min, the reaction was complete (TLC), the solvent was removed, the residue dissolved in H_2O , saturated with NaCl, and extracted twice with CH_2Cl_2 . The org. layers were dried ($MgSO_4$), the solvent evaporated and the residue crystallized from i-PrOH: 81 mg (98%) of **14b**. Orange microcrystals, m.p. 182.7–184°. IR: 3340s, 3100m, 3000w, 2960m, 2930m, 2880m, 2860m, 1615s, 1610s, 1595m, 1540s, 1525s, 1505s, 1450s, 1430m, 1370s, 1350s, 1335s, 1305s, 1290s, 1250m, 1210s, 1080s, 1025m, 970s, 950w, 940m, 905s, 835w, 770w, 750m, 740m, 730m, 720m, 705w. 1H -NMR ($CDCl_3$): 8.83 (d, $J = 2.6$, 1 arom. H); 8.55 (br. s, NH); 8.04 (dd, $J = 2.6$, 0.8, 1 arom. H); 3.94 (s, CH_3O); 2.4–2.3 (m, 2 H); 1.9–1.85 (m, 6 H). EI-MS: 306 (22, M^+), 278 (16), 277 (82), 275 (15), 231 (20), 186 (12), 185 (17), 159 (10), 149 (17), 127 (12), 113 (14), 111 (15), 99 (19), 97 (28), 91 (21), 85 (46), 83 (30), 71 (43), 70 (21), 69 (40), 59 (35), 58 (100), 57 (30), 56 (51), 42 (56). Anal. calc. for $C_{13}H_{14}N_4O_5$ (306.27): C 51.15, H 4.62, N 18.35; found: C 51.12, H 4.73, N 18.56.

3.3.2. 3',4'-Dihydro-2'-methoxy-5',7'-dinitrospiro[cyclohexane-1,3'-quinazoline] (**14c**). According to Exper. 3.3.1, 120 mg (0.39 mmol) of **7c** were added to a soln. of NaOMe in MeOH within 5 min at r.t. Crystallization from i-PrOH yielded 121 mg (97%) of **14c**. Orange needles, m.p. 167.6–167.9°. IR: 3360m, 3110w, 3080w, 2970w, 2940s, 2860m, 1645s, 1610s, 1590s, 1530s, 1500s, 1475w, 1455m, 1440m, 1425m, 1370s, 1360s, 1340s, 1325s, 1285s, 1260s, 1240s, 1200w, 1180s, 1170s, 1160s, 1140w, 1090m, 1065w, 1020w, 1005w, 975s, 950w, 925s, 910w, 905w, 895w, 860w, 845w, 770w, 750m, 740m, 730m, 720m. 1H -NMR ($CDCl_3$): 8.99 (s, NH); 8.82 (d, $J = 2.6$, 1 arom. H); 8.00 (dd, $J = 2.6$, 0.8, 1 arom. H); 3.94 (s, CH_3O); 2.1–1.3 (m, 5 CH_2). ^{13}C -NMR ($CDCl_3$): 165.5 (s, C=N); 138.8, 136.7, 134.0, 129.6 (4s, 4 arom. C); 123.3, 119.3 (2d, 2 arom. C); 54.6 (s, C(1')); 54.4 (q, CH_3O); 34.0, 24.4, 20.7 (3t, 5 CH_2). EI-MS: 320 (33, M^+), 278 (17), 277 (100), 264 (6), 231 (13), 185 (9), 56 (7), 54 (5), 44 (17), 42 (15), 40 (11). Anal. calc. for $C_{14}H_{16}N_4O_5$ (320.30): C 52.50, H 5.03, N 17.49; found: C 52.29, H 5.08, N 17.30.

4. *Reaction of 7b and Morpholine.* To a soln. of 85 mg (0.25 mmol) of **7b** in 2 ml of abs. MeCN under Ar, 50 μ l of morpholine were added at 0°, and the mixture was stirred at r.t. overnight. Removal of the solvent and flash chromatography (hexane/AcOEt 4:1) yielded 30 mg (35%) **7b** and 57 mg (64% with respect to consumed **7b**) of a ca. 1:1.5 mixture (¹H-NMR) of *1-Amino-N-[2-(morpholin-4-yl)-3,5-dinitrophenyl]cyclopentane-carboxamide (16)* and *3',4'-Dihydro-2'-(morpholin-4-yl)-5',7'-dinitrospiro[cyclopentane-1,3'-quinazoline] (15)*. Isolation of **15** in pure form was achieved by washing a CH₂Cl₂ soln. of the mixture with 2*N* HCl. The org. layer was dried (MgSO₄), the solvent evaporated, and the residue crystallized from EtOH: 34 mg of **15** in anal. pure form. Orange crystals, m.p. 237.7–238.3°. IR: 3360s, 3100w, 2980w, 2920w, 2850w, 1605s, 1590s, 1550s, 1520m, 1500s, 1490s, 1480m, 1395w, 1365m, 1355s, 1330s, 1290w, 1270w, 1260w, 1250w, 1230w, 1200s, 1170m, 1120s, 1110m, 1080m, 1020w, 1000w, 990m, 900w, 885w, 855w, 805w, 740w, 730w, 715m. ¹H-NMR (CDCl₃): 8.76 (*d*, *J* = 2.2, 1 arom. H); 8.47 (br. *s*, NH); 8.00 (*dd*, *J* = 2.2, 0.5, 1 arom. H); 3.81 (*m*, 2 CH₂O); 3.52 (*m*, 2 CH₂N); 2.2–1.6 (*m*, 4 CH₂). EI-MS: 361 (19, *M*⁺), 344 (9), 113 (10), 99 (15), 97 (21), 85 (50), 84 (10), 83 (25), 71 (68), 70 (14), 69 (26), 57 (100), 56 (17), 55 (28), 43 (59), 41 (21). Anal. calc. for C₁₆H₁₉N₅O₅ (361.35): C 53.18, H 5.30, N 19.38; found: C 53.22, H 5.58, N 19.13.

Spectroscopical Data for 16 (from mixtures with 15): ¹H-NMR (CDCl₃): 11.00 (br. *s*, NH); 9.63 (*d*, *J* = 2.7, 1 arom. H); 8.16 (*d*, *J* = 2.7, 1 arom. H); 3.95–3.9 (*m*, 4 H); 3.08 (br. *s*, 4 H); 2.5–1.6 (*m*, 10 H). CI-MS: 380 (15, [*M* + 1]⁺), 362 (100), 363 (21), 361 (22), 88 (23), 84 (71).

5. *X-Ray Structure Determination of 5b, 6b, 8b, and 12a (see Fig. 1–6)*⁷⁾. Data were collected on a Nicolet-R3 diffractometer using the Wyckoff ω -scan mode and graphite monochromated MoK α radiation at 294 K. Data collection and refinement parameters are listed in Tab. 2. The usual corrections except for absorptions were applied. The structures were determined by direct methods and refined by blocked-cascade refinements with ca. 100 variables per block using SHELXTL [10]. The non-H-atoms were refined with anisotropic temp. factors. Individual isotropic temp. factors were refined for the H-atoms.

For **5b**, most non-H-atoms were located by direct methods. The structure was expanded using *Fourier* techniques. Atoms were identified by a combination of stereochemical and crystallographic information. All H-atoms could be located in a difference *Fourier* map. Only the positions for the NH-atoms were refined, the remaining H-atoms were included using a riding model. There is one molecule of DMSO per molecule of **5b** in the packing. H–N(1) is involved in an asymmetrically bifurcated H-bond with O(5) (intramolecular) and O(5) of an adjacent molecule. H–N(2) binds to the O-atom of the DMSO molecule. The molecular structure and the packing of **5b** are shown in Fig. 1 and 2.

All non-H-atoms of **6b** were located by direct methods, and all H-atoms in a subsequent difference *Fourier* map. Only the position for the NH-atom was allowed to refine, while all other H-atoms were included in the refinement using a riding model. The NH forms an intramolecular H-bond with one of the NO₂ O-atoms. The molecular structure of **6b** is shown in Fig. 3.

For **8b**, most non-H-atoms were located by direct methods. The structure was expanded using *Fourier* techniques. Atoms were identified on the basis of bond lengths, number of attached H-atoms, and configuration. All H-atoms could be located in a difference map. The positions of the NH-atoms were allowed to refine, while all others were included in the refinement using a riding model. There was no evidence for the presence of H-bonding. The molecular structure of **8b** is shown in Fig. 4.

All non-H-atoms of **12a** were located by direct methods. There is one molecule of H₂O per molecule of **12a** in the packing. All H-atoms could be located in a difference map except one belonging to the H₂O molecule. Only the positions of the N–H-atom and the one H₂O H-atom were allowed to refine; all other H-atoms were included in the refinement using a riding model. The NH₃⁺ group forms three H-bonds: two of the NH-atoms bind to different Cl[–] ions, while the third forms a H-bond to the H₂O molecule. The latter, in turn, forms H-bonds to two other Cl[–] ions. The missing H-atom is probably disordered between these two H-bonds. The molecular structure and the packing of **12a** are shown in Fig. 5 and 6.

⁷⁾ All crystallographic data are deposited with the Cambridge Crystallographic Data Centre, University Chemical Laboratory, Lensfield Road, Cambridge CB2 1EW, England.

Table 2. Crystallographic data of **5b**, **6b**, **8b**, and **12a**.

	5b	6b
Crystallized from	MeCN	acetone/hexane
Colour	yellow	red
Crystal temp. (<i>ca.</i>) [K]	294	294
Space group	<i>P</i> 1 triclinc	<i>P</i> 1 triclinc
<i>Z</i>	2	2
Atoms in the asymmetric unit	C ₁₂ H ₁₂ N ₄ O ₅ · C ₂ H ₆ OS	C ₁₄ H ₁₇ N ₅ O ₄
Formula Weight	292.25 + 78.13	319.32
Cell parameters ^{a)}		
<i>a</i> [Å]	5.897(2)	8.867(4)
<i>b</i> [Å]	8.384(1)	11.413(5)
<i>c</i> [Å]	17.105(3)	8.214(4)
α [°]	81.61(1)	105.37(3)
β [°]	85.87(2)	107.18(4)
γ [°]	89.07(2)	74.21(5)
<i>V</i> [Å ³]	834.5(3)	749(1)
Calc. density [Mg/m ³]	1.474	1.416
2 θ (max)	46°	52°
Reflections measured	3182	3173
Symmetry-independent reflections	2319	2748
Reflections used in the refinement (<i>I</i> > 2.5 σ (<i>I</i>))	1853	2158
Variables	251	228
<i>R</i>	0.038	0.059
<i>R_w</i>	0.042	0.067
Weighting scheme <i>w</i>	($\sigma^2(F) + 0.00031F^2$) ⁻¹	($\sigma^2(F) + 0.00038F^2$) ⁻¹
	8b	12a
Crystallized from	i-PrOH	EtOH
Colour	yellow	colourless
Crystal temp. (<i>ca.</i>) [K]	294	294
Space group	<i>C</i> 2/ <i>c</i> monoclinic	<i>P</i> 2 ₁ / <i>n</i> monoclinic
<i>Z</i>	8	4
Atoms in the asymmetric unit	C ₁₄ H ₁₉ N ₅ O ₅	C ₁₀ H ₁₁ ClN ₄ O ₅ · H ₂ O
Formula Weight	337.33	302.67 + 18.01
Cell parameters ^{a)}		
<i>a</i> [Å]	19.059(4)	6.477(5)
<i>b</i> [Å]	10.967(3)	24.123(9)
<i>c</i> [Å]	19.010(3)	8.872(5)
α [°]	90	90
β [°]	126.11(1)	96.17(4)
γ [°]	90	90
<i>V</i> [Å ³]	3216(1)	1378(2)
Calc. density [Mg/m ³]	1.393	1.545
2 θ (max)	46°	46°
Reflections measured	2476	2196
Symmetry-independent reflections	2198	1920
Reflections used in the refinement (<i>I</i> > 2.5 σ (<i>I</i>))	1684	1696
Variables	246	218
<i>R</i>	0.043	0.034
<i>R_w</i>	0.048	0.040
Weighting scheme <i>w</i>	($\sigma^2(F) + 0.0006F^2$) ⁻¹	($\sigma^2(F) + 0.00041F^2$) ⁻¹

^{a)} The cell dimensions were obtained from 25 accurately centered reflections with 25° < 2 θ < 35° (**5b**), 20° < 2 θ < 28° (**6b**), 20° < 2 θ < 25° (**8b**), and 20° < 2 θ < 24° (**12a**), respectively.

REFERENCES

- [1] B. P. Chandrasekhar, H. Heimgartner, H. Schmid, *Helv. Chim. Acta* **1977**, *60*, 2270.
- [2] P. Vittorelli, H. Heimgartner, H. Schmid, P. Hoet, L. Ghosez, *Tetrahedron* **1974**, *30*, 3737.
- [3] D. Obrecht, H. Heimgartner, *Helv. Chim. Acta* **1981**, *64*, 482; *ibid.* **1987**, *70*, 102.
- [4] H. Heimgartner, *Isr. J. Chem.* **1981**, *21*, 151.
- [5] P. Wipf, H. Heimgartner, *Helv. Chim. Acta* **1987**, *70*, 354.
- [6] K. Dietliker, H. Heimgartner, *Helv. Chim. Acta* **1983**, *66*, 262.
- [7] P. Wipf, H. Heimgartner, *Helv. Chim. Acta* **1986**, *69*, 1153.
- [8] H. E. Fierz-David, 'Farbenchemie', 3. Aufl., Berlin 1924, S. 87; *cf.* Beilstein, *Handbuch der Organischen Chemie*, *E I 13*, S. 123; *E III 13*, S. 899.
- [9] W. C. Still, M. Kahn, A. Mitra, *J. Org. Chem.* **1978**, *43*, 2923.
- [10] G. M. Sheldrick, SHELXTL, an integrated system for solving, refining and displaying crystal structures from diffractometer data, version 5.1, 1986.