Photochemistry of heterocycles
XIX.* Preparation and photochemistry of isoxazolines fused with naphthalene ring

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Received 1 October 1986

1,3-Dipolar cycloaddition of X-substituted benzonitrile oxides, where X stands for H, 4-CH_3, 4-Cl, 4-Br, 4-F, 4-NO_2, and 3-Cl, with 1,4-dihydronaphthalene is described. Photolysis of the thus prepared 3-aryl-3a,4,11,11a-tetrahydronaphthaleno[2,3-*d*]isoxazoles was studied and quantum yields measured from the diminishing concentration of the starting material. Preparation of benzodiazocino[3,4-*d*]isoxazoles is described.

Описано 1,3-диполярное циклоприсоединение X-замещенных бензонитрил-оксидов, где X = H, 4-CH_3, 4-Cl, 4-Br, 4-F, 4-NO_2 и 3-Cl с 1,4-дигидронафталином. Изучен фотолиз полученных таким образом 3-арил-3a,4,11,11a-тетрагидронафталино[2,3-*d*]изоксазолов, и измерены квантовые выходы реакций, исходя из убывания концентрации исходного материала. Описывается получение бензодиазоцино[3,4-*d*]изоксазолов.

Isoxazoline derivatives proved to be very useful intermediates in organic synthesis [1], especially for the preparation of γ-amino alcohols and β-hydroxycarbonyl compounds. The photochemistry of isoxazolines has received also due attention; their photorearrangements proceed usually nonselectively [2—5]. Recently we have found [6—12], that the photorearrangement can be made selective, giving cyclic enamino aldehydes, *e.g.* $I \xrightarrow{h\nu} III$, or $IV \xrightarrow{h\nu} VI$, if there is an oxygen atom, or a double C=C bond in the β-position with respect to isoxazoline oxygen. The thus gained selectivity is due to the stabilization of the biradical by *p*-electrons of the oxygen in the intermediate [6—11], or by the π-electrons of the double bond, respectively (intermediate *V*) (Scheme 1).

Our further aim has been to test the possibility of using the 6π-electrons of the benzene ring for the stabilization of the radical (a benzyl type of radical X). The key step therefore was the synthesis of isoxazolines fused with the tetrahydronaphthalene ring.

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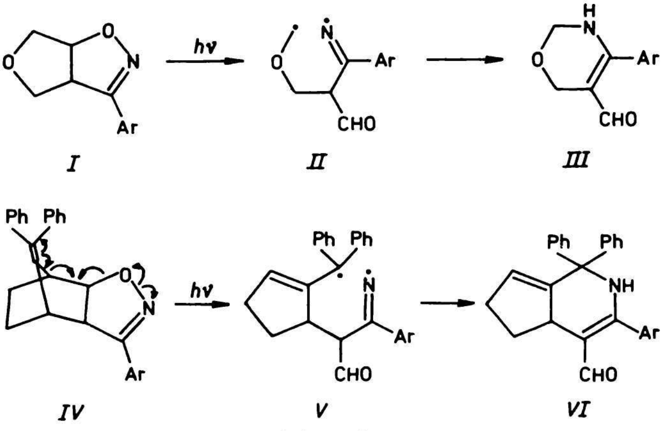
* For Part *XVIII* see *J. Prakt. Chem.*, in press.

The requisite 3-(X-phenyl)-3a,4,11,11a-tetrahydronaphthaleno[ᒧ,3-*d*]isoxazoles *VIIIa*—*VIIIg*, where X stands for H, 3-Cl, 4-Cl, 4-CH_3, 4-F, 4-NO_2, 4-Br were prepared by 1,3-dipolar cycloaddition of the corresponding benzonitrile oxides and 1,4-dihydronaphthalene. As precursors for the dipoles served substituted benzohydroximoyl chlorides, prepared in turn by the liquid chlorine chlorination. The required nitrile oxides were generated *in situ* by the action of triethylamine (see Experimental), since the simpler and faster generation of nitrile oxides by hypochlorite [13] did not work with 1,4-dihydronaphthalenes. The best yields 30 to 45 %, were achieved when fivefold excess of the dipolarophile was used in the cycloaddition. The rest of the reaction mixture were nitrile oxide dimers; the dimers became a major product, when only a molar amount of 1,4-dihydronaphthalene was used.



Scheme 1

The structure of the derivative *VIIIa* was confirmed by spectral data. In its ^{1}H NMR spectrum multiplets of the bridge isoxazoline protons were found at $\delta = 3.90$—4.34 ppm (H-3a), and at $\delta = 5.0$—5.28 ppm (H-11a). The spectrum further showed two doublets at $\delta = 2.82$ ppm and $\delta = 3.00$ ppm, belonging to methylene protons. ^{13}C NMR spectrum contained characteristic signals of isoxazoline ring, *e.g.* a singlet at $\delta = 152.51$ ppm (C=N) and doublets at $\delta = 81.07$ ppm (C-11a) and $\delta = 47.75$ ppm (C-3a). The triplets of methylene group were found at $\delta = 33.59$ ppm and $\delta = 30.01$ ppm. The structure of other isoxazolines *VIIIb*—*VIIIg* was confirmed analogously.

All derivatives *VIIIa*—*VIIIg* possess in their UV spectra a band at a wavelength characteristic of isoxazoline derivatives [5, 6]. Their IR spectra displayed characteristic stretching vibrations ν(C=N) at $\tilde{\nu} \approx 1500\ \mathrm{cm}^{-1}$, the band at $\tilde{\nu} \approx 1400\ \mathrm{cm}^{-1}$ was assigned to the skeletal vibrations of the isoxazoline ring [14].

As can be seen from the UV spectra of isoxazolines *VIII* the irradiation would require a wavelength under 300 nm. We have therefore performed our experiments using a low-pressure Hg lamp emitting a nearly monochromatic light with $\lambda = 253.7$ nm. In contrast to our previous successful irradiation in methanol solutions [6—12], irradiation of *VIII* did not furnish any cyclic enamino aldehydes *XII*; the only products were polymers. The situation did not improve when we used benzene or ether as solvent. HPLC monitoring of the irradiation revealed that both in methanol and ether the irradiation proceeded in the same manner, with slightly higher reaction rate in ether. However, products formed faster in ether decomposed faster as well. The irradiation in benzene proceeded at much slower pace, leading, as in the previous cases to very unstable photoproducts, which decomposed fast by further irradiation. To the same conclusion have led also attempts to monitor the irradiation by UV spectroscopy, using 5×10^{-5} mol dm^{-3} concentration. The consumption of the starting *VIIIa* and the formation of a maximum, corresponding to cyclic enamino aldehyde *XII* can clearly be seen [6—12] (Fig. 1). Based on the dwindling concentration of starting material we have measured the following quantum yields Φ: 0.046 (*VIIIa*), 0.012 (*VIIIb*), 0.012 (*VIIIc*). The Φ values tally with

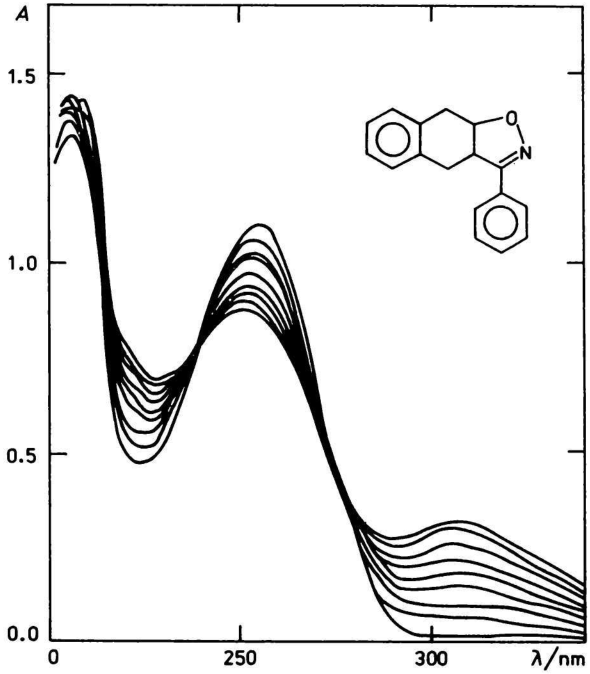
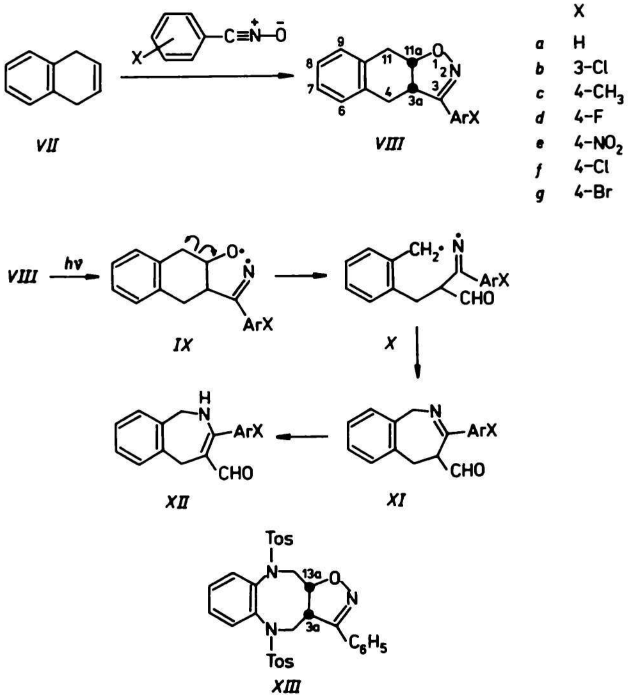


Fig. 1. UV monitoring of the irradiation of *VIIIa*.

those measured for the reaction $I \xrightarrow{h\nu} III$ and $IV \xrightarrow{h\nu} VI$ and indicate a stabilization of the intermediary radical X by the benzene ring. The products of the photorearrangement, however, are photo- and thermolabile and decompose quickly (Scheme 2).



Scheme 2

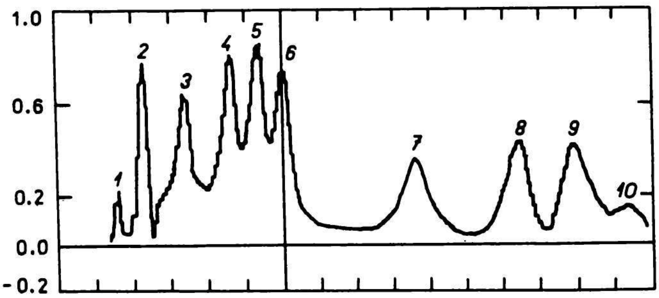


Fig. 2. HPLC chromatogram of the reaction mixture after irradiation of *VIIIa* ($\lambda = 220$ nm).

Having failed to separate the photolyzed solution and isolate its components in pure state in order to identify them, we resorted to a combination of liquid chromatography and rapid spectral detector (see Experimental) allowing the measurements of UV spectra of the separated peaks. The method could separate 10 components (Fig. 2), with one of them having a maximum at $\lambda_{max} = 310$ nm, just as the monitoring of the overall reaction indicated. The component was assigned a *XIIa* structure. Varying the irradiation conditions did not improve the yield of the expected enamino aldehyde.

In order to assess the possible stabilizing influence of the nitrogen atom on the intermediary biradical, we have prepared a model isoxazoline *XIII* by cycloaddition of benzonitrile oxide and *N*,*N'*-ditosylbenzo-1,6-diazocine [15]. Structure of the thus prepared benzoazocino[3,4-*d*]isoxazole *XIII* was also confirmed by spectral data (see Experimental). Its irradiation however, produced only polymeric material.

Experimental

Melting points were determined according to Kofler. ^{1}H NMR spectra were measured on a 80 MHz Tesla 487 C, ^{13}C NMR spectra on the Jeol JX-100, in deuteriochloroform, using tetramethylsilane as internal standard. Electronic spectra were taken with a Perkin—Elmer model 323, methanolic solutions were measured in temperature-controlled cuvettes. ε Values are in $m^2\,mol^{-1}$.

The progress of cycloaddition was monitored by TLC on Silufol plates (detection with UV_{214} light). Hydroximoyl chlorides were prepared by chlorination of the corresponding aldoximes in chloroform according to [16] but by a 120 % excess of liquid chlorine. 1,4-Dihydronaphthalene was prepared by reduction of naphthalene with sodium in ethanol according to [17].

Photochemical experiments were performed in a reaction vessel described previously [6—12]. For the HPLC check a Spectra Physics chromatograph equipped with Lichrosorb RP-18 150 × 4 mm, 5 μm particles (Merck) was used; as a mobile phase served methanol—water mixture (volume ratio = 7 : 3). For the measurements of UV spectra of the separated chromatographic peaks an arrangement consisting of LKB 2150 pump, Rapid scan detector 2140 connected on line to Olivetti M-24 microcomputer equipped with Canon colour printer was used. Quantum yields measurements based on the concentration of the starting material have been described elsewhere [9].

3-Phenyl-3a,4,11,11a-tetrahydronaphthaleno[2,3-d]isoxazole (VIIIa)

To 1,4-dihydronaphthalene (6.5 g; 0.05 mol) in 25 cm^3 of dry ether benzohydroximoyl chloride (1.55 g; 0.01 mol) in 20 cm^3 of dry ether was added. Reaction mixture was cooled to 0—5 °C and stirred during the dropwise addition of triethylamine (1.41 g; 0.014 mol) in 10 cm^3 of ether. After the addition was complete the reaction mixture was further stirred for 24 h at laboratory temperature. Triethylammonium chloride was then filtered off, the filtrate concentrated *in vacuo* and covered with hexane. Colourless crystals thus obtained were recrystallized from ethanol. Yield = 1 g (41 %), m.p. = 102—104 °C. For $C_{17}H_{15}NO$ (M_r = 249.30) w_i(calc.): 81.90 % C, 6.06 % H, 5.62 % N; w_i(found): 81.74 % C, 6.21 % H, 5.58 % N. UV spectrum, λ_{max}/nm ($\log\{\varepsilon\}$): 263 (2.96). IR spectrum, $\tilde{\nu}$/cm^{-1}: 920, 1100, 1450, 1490, 1500, 1590, 2980. ^{1}H NMR spectrum, δ/ppm: 2.82 (d, 2H, H_2-4), 3.00 (d, 2H, H_2-11), 3.90—4.34 (m, 1H, H-3a), 5.00—5.28 (m, 1H, H-11a), 6.96—7.42 (m, 9H, H_{ar}). ^{13}C NMR spectrum, δ/ppm: 152.51 (s, C=N), 135.85, 135.01, 129.82, 128.84, 127.54, 127.15, 126.83 (C_{ar}), 81.07 (d, C-11a), 47.75 (d, C-3a), 33.59 (t, C-11), 30.01 (t, C-4).

By the same procedure the substituted benzohydroximoyl chlorides were converted to derivatives *VIIIb—VIIIg*:

3-(3-Chlorophenyl)-3a,4,11,11a-tetrahydronaphthaleno[2,3-d]isoxazole (VIIIb), m.p. = = 110—112 °C, yield = 38 %. For $C_{17}H_{14}ClNO$ (M_r = 283.75) w_i(calc.): 71.95 % C, 4.93 % H, 4.93 % N; w_i(found): 72.06 % C, 5.17 % H, 5.11 % N. UV spectrum, λ_{max}/nm ($\log\{\varepsilon\}$): 273 (3.50). IR spectrum, $\tilde{\nu}$/cm^{-1}: 800, 920, 1420, 1450, 1595, 1490, 2980. ^{1}H NMR spectrum, δ/ppm: 2.82 (d, 2H, H_2-4), 3.05 (d, 2H, H_2-11), 3.93—4.23 (m, 1H, H-3a), 5.08—5.38 (m, 1H, H-11a), 6.96—7.61 (m, 8H, H_{ar}). ^{13}C NMR spectrum, δ/ppm: 157.28 (s, C=N), 137.01, 135.48, 134.72, 129.12, 128.12, 127.32, 125.02 (C_{ar}), 81.35 (d, C-11a), 47.22 (d, C-3a), 32.49 (t, C-11), 29.13 (t, C-4).

3-(Methylphenyl)-3a,4,11,11a-tetrahydronaphthaleno[2,3-d]isoxazole (VIIIc), m.p. = = 80—82 °C, yield = 36 %. For $C_{18}H_{17}NO$ (M_r = 263.32) w_i(calc.): 82.10 % C, 6.51 % H, 5.32 % N; w_i(found): 81.96 % C, 6.59 % H, 5.08 % N. UV spectrum, λ_{max}/nm ($\log\{\varepsilon\}$): 258 (3.16). IR spectrum, $\tilde{\nu}$/cm^{-1}: 920, 1420, 1460, 1515, 1595, 2990. ^{1}H NMR spectrum, δ/ppm: 2.35 (s, 3H, CH_3), 2.87 (d, 2H, H_2-4), 3.02 (d, 2H, H_2-11), 3.90—4.22 (m, 1H, H-3a), 5.06—5.35 (m, 1H, H-11a), 7.02—7.55 (m, 8H, H_{ar}).

3-(4-Fluorophenyl)-3a,4,11,11a-tetrahydronaphthaleno[2,3-d]isoxazole (VIIId), m.p. = = 114—115 °C, yield = 39 %. For $C_{17}H_{14}FNO$ (M_r = 267.31) w_i(calc.): 76.38 % C, 5.23 % H, 5.23 % N; w_i(found): 76.52 % C, 5.15 % H, 5.25 % N. UV spectrum, λ_{max}/nm ($\log\{\varepsilon\}$): 266 (3.28). IR spectrum, $\tilde{\nu}$/cm^{-1}: 920, 1130, 1350, 1400, 1450, 1480, 1500, 1600, 2980. ^{1}H NMR spectrum, δ/ppm: 2.83 (d, 2H, H_2-4), 3.05 (d, 2H, H_2-11), 6.95—7.75 (m, 8H, H_{ar}). ^{13}C NMR spectrum, δ/ppm: 157.62 (s, C=N), 154.34 (s, C—F), 135.60, 134.95, 129.30, 128.65, 127.48, 126.83 (C_{ar}), 81.15 (d, C-11a), 47.69 (d, C-3a), 33.53 (t, C-11), 29.82 (t, C-4).

3-(4-Nitrophenyl)-3a,4,11,11a-tetrahydronaphthaleno[2,3-d]isoxazole (VIIIe), m.p. = = 184—186 °C, yield = 42 %. For $C_{17}H_{14}N_2O_3$ (M_r = 294.30) w_i(calc.): 69.37 % C, 4.80 % H, 9.52 % N; w_i(found): 69.12 % C, 5.03 % H, 9.74 % N. UV spectrum, λ_{max}/nm ($\log\{\varepsilon\}$): 278 (3.35). IR spectrum, $\tilde{\nu}$/cm^{-1}: 920, 1330, 1505, 1560, 1595, 2980. ^{1}H NMR spectrum, δ/ppm: 2.87 (d, 2H, H-4), 3.06 (d, 2H, H_2-11), 3.93—4.12 (m, 1H, H-3a), 5.09—5.25 (m, 1H, H-11a), 6.98—8.29 (m, 8H, H_{ar}). ^{13}C NMR spectrum, δ/ppm: 157.11 (s, C=N), 148.53 (s, C—NO_2), 135.53, 135.14, 132.02, 129.68, 128.17, 127.13, 127.47, 124.62 (C_{ar}), 82.25 (d, C-11a), 47.08 (d, C-3a), 33.39 (t, C-11), 29.75 (t, C-4).

3-(4-Chlorophenyl)-3a,4,11,11a-tetrahydronaphthaleno[2,3-d]isoxazole (VIIIf), m.p. =

= 112—116 °C, yield = 27 %. For $C_{17}H_{14}ClNO$ (M_r = 283.75) w_i(calc.): 71.95 % C, 4.93 % H, 4.93 % N; w_i(found): 72.14 % C, 4.85 % H, 5.14 % N. UV spectrum, λ_{max}/nm (log{ε}): 255 (3.65). IR spectrum, $\tilde{\nu}$/cm^{-1}: 760, 910, 1390, 1420, 1500, 1600, 3000. ^{1}H NMR spectrum, δ/ppm: 2.87 (d, 2H, H_2-4), 3.06 (d, 2H, H_2-11), 3.91—4.12 (m, 1H, H-3a), 5.10—5.25 (m, 1H, H-11a), 6.98—7.71 (m, 8H, H_{ar}). ^{13}C NMR spectrum, δ/ppm: 157.61 (s, C=N), 136.98, 135.55, 134.88, 129.17, 128.26, 127.48, 126.83 (C_{ar}), 81.35 (d, C-11a), 47.56 (d, C-3a), 33.53 (t, C-11), 29.76 (t, C-4).

3-(4-Bromophenyl)-3a,4,11,11a-tetrahydronaphthaleno[2,3-d]isoxazole (VIIIg), m.p. = = 120—121 °C, yield = 40 %. For $C_{17}H_{14}BrNO$ (M_r = 328.22) w_i(calc.): 62.20 % C, 4.26 % H, 4.26 % N; w_i(found): 62.18 % C, 4.31 % H, 4.49 % N. IR spectrum, $\tilde{\nu}$/cm^{-1}: 760, 920, 1430, 1450, 1500, 1600, 2980. ^{1}H NMR spectrum, δ/ppm: 2.80 (d, 2H, H_2-4), 3.05 (d, 2H, H_2-11), 3.93—4.11 (m, 1H, H-3a), 5.11—5.23 (m, 1H, H-11a), 6.91—7.88 (m, C_{ar}).

N,N'-Ditosylbenzodiazocino[3,4-d]isoxazole (XIII)

To the solution of *N,N'*-ditosylbenzodehydrodiazocine (2 g; 0.004 mol) in 10 cm^3 of dry tetrahydrofuran benzohydroximoyl chloride (1.3 g; 0.008 mol) in 15 cm^3 of dry tetrahydrofuran was added. To the stirred mixture, kept at 0—5 °C a solution of triethylamine (0.9 g; 0.009 mol) in 10 cm^3 of tetrahydrofuran was added. After 24 h stirring at laboratory temperature the triethylammonium chloride was filtered off and the filtrate was concentrated. The residue was triturated with 5 cm^3 of methanol, the crystals recrystallized from methanol. M.p. = 68—70 °C, yield = 0.6 g (15 %). For $C_{31}H_{29}N_3O_5S_2$ (M_r = 587.34) w_i(calc.): 63.39 % C, 4.93 % H, 7.15 % N; w_i(found): 63.13 % C, 5.17 % H, 7.18 % N. ^{1}H NMR spectrum, δ/ppm: 2.37 (s, 3H, CH_3), 2.41 (s, 3H, CH_3), 3.37—3.50 (m, 4H, H_2-4, H_2-13), 3.70—3.85 (m, 1H, H-3a), 4.05—4.30 (m, 1H, H-13a), 7.22—7.92 (m, 12H, H_{ar}).

References

1. Kozikowski, A. P., *Accounts Chem. Res. 17*, 410 (1984).
2. Ito, Y. and Matsuura, T., *Tetrahedron Lett. 31*, 1373 (1975).
3. Mukai, T., Kumagai, T., and Seshimoto, O., *Pure Appl. Chem. 49*, 287 (1977).
4. Seshimoto, O., Kumagai, T., Shimizu, K., and Mukai, T., *Chem. Lett. 1977*, 1195.
5. Kumagai, T., Shimizu, K., Kawamura, Y., and Mukai, T., *Tetrahedron Lett. 37*, 3365 (1981).
6. Fišera, Ľ., Laudár, S., Timpe, H.-J., Zálupský, P., and Štibrányi, L., *Collect. Czechoslov. Chem. Commun. 49*, 1193 (1984).
7. Fišera, Ľ., Štibrányi, L., Máťušová, A., Oremus, V., and Timpe, H.-J., *Tetrahedron Lett. 1984*, 2731.
8. Fišera, Ľ., Oremus, V., Štibrányi, L., Timpe, H.-J., and Máťušová, A., *Collect. Czechoslov. Chem. Commun. 50*, 1982 (1985).
9. Fišera, Ľ., Oremus, V., Timpe, H.-J., Štibrányi, L., and Zálupský, P., *Collect. Czechoslov. Chem. Commun.*, in press.
10. Fišera, Ľ., Konopíková, M., Štibrányi, L., and Timpe, H.-J., *Collect. Czechoslov. Chem. Commun. 50*, 1971 (1985).

11. Fišera, Ľ., Oravec, P., Štibrányi, L., Kožina, N. D., and Badovskaya, L. A., *Synthesis 1986*, 565.
12. Zálupský, P., Fišera, Ľ., and Timpe, H.-J., *Z. Chem.*, in press.
13. Lee, G. A., *Synthesis 1982*, 508.
14. Horák, M. and Papoušek, D., *IČ spektra a struktura molekul.* (IR Spectra and the Structure of Molecules.) Academia, Prague, 1976.
15. Schroth, W., Reinhardt, J., Urähke, K., and Strechenbach, B., *Z. Chem. 3*, 228 (1963).
16. Werner, A. and Buss, H., *Ber. 27*, 2193 (1894).
17. Bamberg, E. and Lodter, W., *Ber. 20*, 3073 (1887).

Translated by P. Zálupský