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Bromination and Thiocyanation of 4-Cyano-2-methyl-1,3,6-triazacycl[3.3.3]azine under Photochemical Conditions

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The bromination and thiocyanation of 4-cyano-2-methyl-1,3,6-triazacycl[3.3.3]azine, *1a*, with free bromine and with thiocyanogen in the presence of light, results in ring as well as in side-chain substitution. The structures of eight brominated compounds, *5–12*, and of three thiocyanocyclazines, *16–18*, are reported. In chlorinated solvents the bromination yields mixtures of chlorinated and brominated compounds. The photochemical displacement of chlorine for bromine is briefly discussed.

We have recently described the electrophilic bromination of 4-cyano-2-methyl-1,3,6-triazacycl[3.3.3]azine, *1a*, with *N*-bromosuccinimide in chloroform and with bromine in glacial acetic acid, in both cases in the absence of light and peroxides.[1]

In agreement with results from HMO calculations [2] (performed on *1b*) the electrophilic substitution in *1a* occurred exclusively in positions 7 and 9. Free-valence values estimated by the same method [2] suggested that free-radical attack would be preferred in the same positions and also at C-5 (*cf.* Fig. 1).

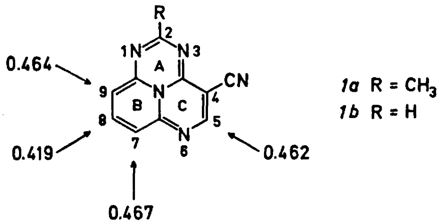
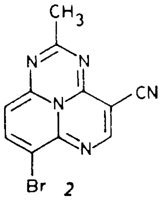


Fig. 1. Free-valence values at positions 5, 7, 8, and 9 in *1b*.

The first part of the present communication describes the isolation and structural assignment of eight bromine-containing compounds formed when a solution of the easily prepared cyclazine *1a* [2] was treated with free bromine under the influence of light from a medium pressure mercury arc (Hanau Q-81). The rate of the dark reaction under the conditions used in this investigation is considerable and all compounds described are probably not formed exclusively by a free-radical path. This point will be elaborated later in the present paper.

The following compounds substituted in the ring (*2*–*4*), in the side-chain (*5*–*6*), or in both (*7*–*11*) were isolated.



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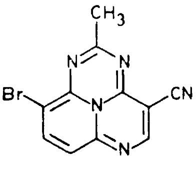

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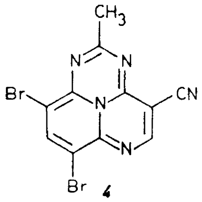

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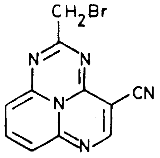

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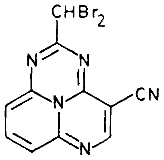

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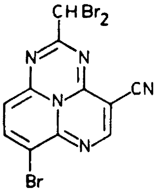

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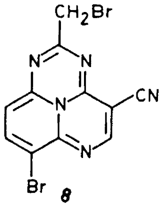

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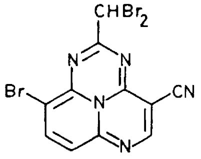

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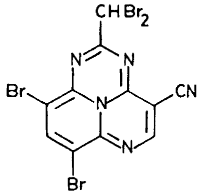

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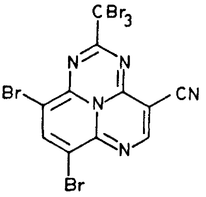

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The structures of the new compounds (*5*–*11*) were supported by mass-spectral, infrared, ultraviolet, and, where sufficient amounts were available, by NMR data. The details are to be found in the Experimental section. In some cases, where the substitution pattern could not be unambiguously determined from the spectra of the compounds, the structures were derived by synthesis from a derivative with an already secured structure. These correlations are outlined in Chart 1.

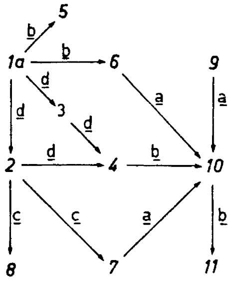

Chart 1. Reagents: *a* Br_2 in $CHCl_3$ or CCl_4; *b* Br_2 in $CHCl_3$ or CCl_4, $h\nu$; *c* NBS in "non-purified" $CHCl_3$; (*cf.* the Experimental section); *d* NBS in $CHCl_3$.[1]

The number of bromine atoms in a molecule was immediately determined from the element profile in the molecular-ion region, showing doublets (intensities 1:1), triplets (1:2:1), quartets (1:3:3), quintets (1:4:6:4:1), and sextets (1:5:10:10:5:1) for mono-, di-, tri-, tetra-, and pentasubstituted derivatives, respectively.[3]

All the brominated compounds have, like *1a*, high melting points (*2 – 11* melt above 350°). Their solubilities and chromatographic mobilities are rather similar to those of *1a*.

The electronic spectra of the brominated compounds show the pattern typical of a 1,3,6-triazacycl[3.3.3]azine with about seven high-intensity absorption maxima between 220 and 400 nm and low-intensity bands at 450 – 700 nm (*cf.* the Experimental section). Compounds with bromine in the side-chain are blue to violet in the solid state and in solution; compounds with bromine in the aromatic positions are green in the solid state but blue in solution; finally, compounds brominated both in the methyl group and in the ring are green both in the solid state and in solution.

The IR spectra of compounds *2 – 11* all show the strong absorption band characteristic of the cyano group (2210 – 2230 cm^{-1}).

The mass spectra of *5 – 11* are characterized by successive losses of bromine atoms (*cf.* Ref. 1, p. 631), eventually leading to bromine-free fragments, whose fragmentation patterns are very similar to those obtained from *1a – 4*.[1,4] The spectrum of *5* with assignments of fragment structures and proposed modes of fragmentation, supported by metastable ion peaks, is illustrated in Fig. 2.

In the mass spectra of *2* and *3*,[1] one atom of bromine is lost from the molecular ion and the resulting fragment then loses CH_3CN, which is supported by a metastable ion at $m/e = 135.2$. This type of fragmentation is observed for *N*-heteroaromatic systems with a methyl group on the adjacent ring-carbon atom.* In the mass spectrum of *5*, however, this metastable ion is found at $m/e = 135.6$, corresponding to a loss of CH_2CN, which indicates that the bromine atom in *5* was originally located in the side chain.

The NMR-spectra of *6 – 11* are easily interpreted, and the chemical shift values and coupling constants are summarized in Table 1.

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* see Ref. 4, p. 614 and further references therein.

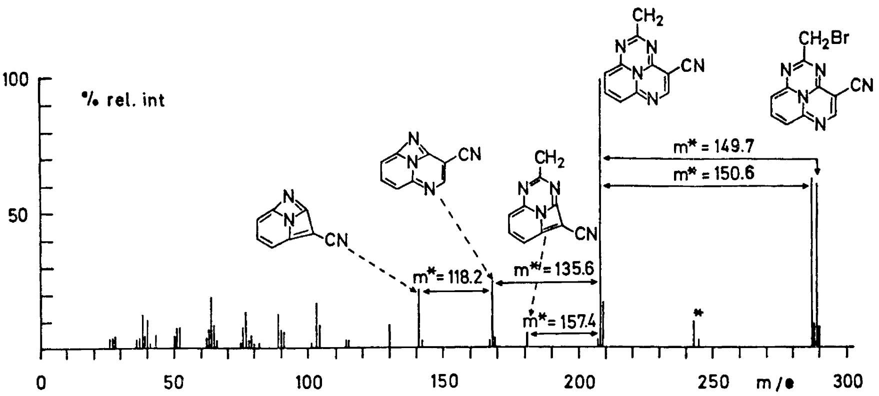


Fig. 2. Mass spectrum of *5*. The sample contained *ca.* 10 % of $C_{11}H_6N_5Cl$.

Table 1. NMR spectral data (δ-values and coupling constants) for compounds *6–11* (solvent: trifluoroacetic acid).

Compound	Side-chain protons	H-5	H-7	H-8	H-9	J_{7-8} (Hz)	J_{8-9} (Hz)	J_{7-9} (Hz)
6	6.12	7.83	7.12 or 7.04	8.08	7.04 or 7.12	7.5 or 8.8	8.8 or 7.5	0.9
7	6.07	7.84	–	8.20	7.04	–	9.0	–
8	4.07	7.93	–	8.17	6.95	–	9.0	–
9	6.09	7.77	6.88	8.19	–	9.0	–	–
10	6.13	7.85	–	8.45	–	–	–	–
11	–	7.86	–	8.52	–	–	–	–

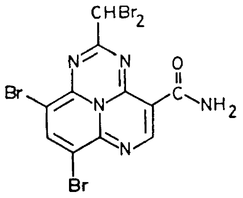
Solutions of *1a* in carbon tetrachloride, chloroform, and methylene chloride were used for the photochemical brominations. The following solvents were also tried but found unsuitable: hydrocarbons like hexane (low solubility of *1a* and generation of HBr leading to the formation of insoluble cyclazine hydrobromides), methanol (formation of methoxy derivatives), and ethyl acetate (destruction of the cyclazine system). In all these three solvents, however, low yields of compounds *2–11* were obtained.

The composition of the reaction mixtures varied depending on the solvent, as well as on the irradiation time. In chloroform, aromatic substitution dominated in the beginning of the irradiation period with initial formation of *2*, *3*, and *4*. In carbon tetrachloride, *5* and *6* were formed after a short induction period (*ca.* 15 min) together with small amounts of *2* and *3*. After longer irradiation times (in chloroform, carbon tetrachloride and mixtures thereof) *7*, *9*, *10*, and *11* were formed, *10* being the major product.

Bromination of *1a* with NBS or bromine in the absence of radical promoters gave exclusively substitution in the aromatic ring.[1] Under the conditions used in the present investigation it was found, however, that after a longer period (several months), *10* and *11* could sometimes be obtained from the dark reaction in fairly good yields.

The marked acceleration of the side-chain substitution under the influence of light and the induction period observed for the formation of *5* and *6*, clearly demonstrate that a free-radical mechanism is operating. The description of the reaction path for the aromatic substitution is not equally simple. Attempts were made to find conditions under which no "dark bromination" would occur (in methylene chloride at −80° and in carbon tetrachloride at −15°), but *2*, *3*, and *4* were always detected. Irradiation of *1a* in carbon tetrachloride at −15° gave the same products and, in addition, *5*, which is monobrominated in the side chain. A small increase in the yield of products substituted in the ring was observed when the reaction mixture was irradiated. Under the conditions used in this investigation, however, it has not been possible to separate homolytic and heterolytic aromatic substitution.

A compound formed in low yield in the photochemical bromination reaction of *1a* was shown by spectrometric methods (IR, MS, *cf.* the Experimental section) to be the amide *12*. The same compound was also obtained from irradiation of *10*; therefore the positions of the bromine atoms in the proposed structure seem to be correct. It is possible that this represents a photochemical conversion of a nitrile to an amide, but we are not aware of any other cases of the same type. Attempts to achieve the same reaction by irradiation of *10* in a chloroform solution containing dilute hydrochloric acid were, however, unsuccessful.



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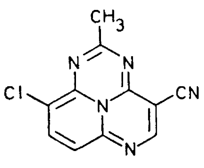
When the monobromo compound *3* was irradiated in a bromine-containing chloroform solution, *3* was completely converted to two chlorinated compounds.* For these we propose structures *13* and *14*, since their mass spectro-



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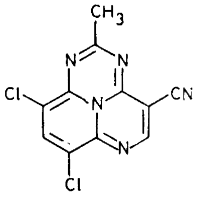

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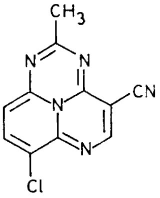
[*] A compound containing one chlorine and one bromine atom was also formed, though in very low yield (less than 1 % of the yield of *14*, as estimated from the mass spectrum).

metrical fragmentation patterns are analogous with those of the corresponding bromine derivatives *3* and *4*.[1] When the 7-bromo isomer *2* was irradiated under the above-mentioned conditions, *14* was formed, plus a compound very similar to *13* (TLC), which we believe is the 7-chloro isomer *15*. In addition, partly chlorinated compounds were observed as impurities (MS) in the brominated analogues, when these were formed in chlorinated solvents.



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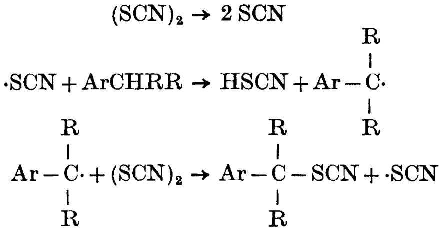
Similar observations for the system bromobenzene-chlorine were originally reported by Eibner [5] and the same reaction was later studied by Miller and Walling [6] and by Milligan *et al.*[7] In their studies free chlorine (dissolved in carbon tetrachloride) was present, and in the mechanism proposed the chlorine atom is attached to the aromatic ring *via* a π-complex type of bond. To our knowledge no reports on similar photochemical aromatic halogen exchange in chloroform or carbon tetrachloride solutions in the absence of added chlorine have appeared. It is not unlikely, however, that sufficient amounts of free chlorine (or bromine chloride) are formed during the irradiation to cause a halogen exchange in compounds substituted with bromine in the aromatic nucleus.

Arylalkyl hydrocarbons have been successfully thiocyanated with thiocyanogen in light-induced reactions [8] giving products substituted exclusively in the side-chain. The mechanism has been depicted [8] as a photo-initiated, radical chain reaction:

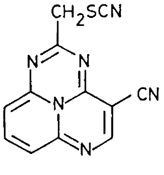


$$\mathrm{(SCN)_2 \rightarrow 2\,SCN}$$

$$\mathrm{\cdot SCN + ArCHRR \rightarrow HSCN + Ar-\overset{R}{\underset{R}{C}}\cdot}$$

$$\mathrm{Ar-\overset{R}{\underset{R}{C}}\cdot + (SCN)_2 \rightarrow Ar-\overset{R}{\underset{R}{C}}-SCN + \cdot SCN}$$

With *1a* as substrate a similar reaction with thiocyanogen occurred in the presence of light, and a low yield of *16* was isolated. Compound *16* was the only product obtained in detectable amounts from photolysis in benzene, but in chlorinated solvents (methylene chloride, chloroform, and carbon tetrachloride) products substituted in the aromatic nucleus were also formed. Two of these, *17* and *18*, were isolated, but at least five other products, probably thiocyanated or isothiocyanated in the ring and/or in the side chain, were



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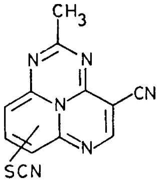

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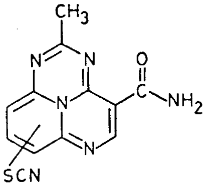

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detected. Compounds *16*–*18* were characterized by spectrometrical methods and by comparison with spectra for the corresponding bromo compound.

The side-chain substituted compound *16* was easily identified from its mass spectrum by a reasoning analogous with that used for compound *5* above. For *17* and *18*, the exact positions of the thiocyanate groups could not be determined, but *17* and *18* must be substituted in the *B*-ring, since the substituents can be placed neither at the methyl carbon (loss of CH_3CN in the mass spectra) nor at position 5 (loss of HCN from the *C*-ring). The mass spectrum of *18* differs from the spectra of *16* and *17*, since loss of CO as well as of S is observed here.

The UV spectra of compounds *16*, *17*, and *18* show the typical pattern with six to seven high-intensity bands at 500–220 nm and low-intensity peaks at 700–500 nm (*cf.* Table 2). Characteristic peaks in the infrared region are presented in the Experimental section.

Table 2. Electronic spectral data for *5*–*7*, *9*–*12*, and *16*–*18*.

	nm ($\varepsilon \times 10^{-4}$)						
5	388 (0.82)	371 (0.92)	354s(0.74)	335 (1.09)	271 (1.35)	237 (1.39)	216s(1.13)
6	389 (1.55)	380 (1.48)	372 (1.71)	355 (1.41)	338 (1.94)	272 (2.62)	236 (2.38)
7	397 (1.03)	388s(1.10)	378 (1.27)	346 (2.01)	282 (2.13)	241 (1.82)	222 (1.99)
9	398 (1.14)	381 (1.28)	363 (1.05)	345 (1.48)	285 (1.54)	234 (2.03)	224 (2.03)
10	404 (1.18)	398s(1.22)	387 (1.44)	353 (2.24)	292 (2.10)	243s(1.92)	231 (2.20)
11	398s(1.35)	385s(1.60)	370s(1.82)	354 (2.21)	293 (2.36)	242s(2.41)	227 (2.93)
12	400 (1.56)	382 (1.86)	360s(1.97)	346 (2.41)	285 (2.30)	241 (2.91)	224 (2.78)
16	390 (0.75)	372 (0.80)	356 (0.67)	333 (0.94)	269 (1.05)	234 (1.62)	
17	402s(0.75)	387 (0.80)	363s(1.17)	346 (1.68)	293 (0.69)	287 (0.67)	239 (1.90)
18	383 (0.40)	342 (0.44)	327 (0.58)	383 (0.52)	277s(0.50)	228 (1.40)	
	nm (ε).						
5	662s(111)	610 (260)	575 (277)	535s(190)			
6	670s(145)	621 (367)	578 (412)	544s(296)	455 (87)		
7	696s(205)	641 (413)	595 (401)	558s(257)	474 (45)		
9	698s(140)	645 (342)	596 (342)	554s(205)			
10	720 (155)	662 (406)	611 (302)	568s(157)			
11	719 (272)	660 (491)	614 (695)	575s(462)	512 (226)	479 (83)	
12	690s(268)	636 (532)	600 (501)	497 (338)	467 (359)		
16	642 (1400)	602 (2384)	572 (2400)	526s(895)			
17	665 (864)	614 (1183)	580s(895)				
18	550 (1323)	519 (1195)	483s(770)				

EXPERIMENTAL

General. The NMR spectra have been measured in trifluoroacetic acid with tetramethyl silane as internal reference using a Varian Model A-60 spectrometer. Mass spectra were recorded with a GEC–AEI 902 mass spectrometer at the Department of Medical Biochemistry, University of Göteborg. The IR spectra were determined in KBr with a Beckman IR 9 spectrophotometer or with a Perkin-Elmer 337 infrared spectrophotometer, and the UV and visible spectra in absolute ethanol with a Cary Model 15 spectrophotometer. For column chromatography, silica gel (0.02 – 0.5 mm) was used, and for TLC, Silica Gel GF_{254} (Merck) according to Stahl. The irradiations were carried out with a medium-pressure mercury arc (Hanau Q-81) placed in a quartz container cooled with water. The solution in the reaction vessel was magnetically stirred, and a stream of nitrogen was bubbled through the solution.

Methylene chloride, chloroform, and carbon tetrachloride used in the photochemical reactions were distilled and passed over aluminium oxide, if not otherwise stated. 4-Cyano-2-methyl-1,3,6-triazacycl[3.3.3]azine was prepared as described in Ref.2.

General bromination procedure

The conditions chosen for the photochemical bromination reactions varied slightly, but in general the following procedure was used. A solution (1 – 5 mM) of *1a* in carbon tetrachloride and/or chloroform was irradiated with ultraviolet light. The irradiation time varied from one to several hours, and the composition of the reaction mixture was followed by TLC. Before this analysis could be performed, the reaction solution, in which the products were present as cyclazine hydrobromides, was evaporated to dryness. An ethanol solution of the residue was stirred with the weakly basic ion-exchange resin Amberlite IR-4B (OH form). The mixture of the free bases of the bromocyclazines was then separated by chromatography (column or TLC).

Bromination of *1a*

Under "dark" conditions; (a) with excess of bromine. The dark-blue solution of 150 mg (0.72 mmol) of *1a* in 50 ml of chloroform was mixed with a solution of 300 mg (1.87 mmol) of bromine in 50 ml of chloroform. A red precipitate was immediately formed, and after a few minutes the solution became colourless. Three products, *2*, *3*, and *4*, had been formed; they were identified by comparison with authentic samples (TLC).

(b) At low temperatures with bromine. (i) In methylene chloride at – 80°. A solution of 6 mg of *1a* in 50 ml of methylene chloride was cooled to – 80° and 5 ml of methylene chloride, containing 1 drop of bromine, was slowly added. After 10 min, *2* and *3* had formed and after 1 h, *4* was also detected (TLC). (ii) In carbon tetrachloride at – 15°. A solution containing 7 mg of *1a* and 1 drop of bromine in 100 ml of carbon tetrachloride was left at – 15° for 1 h. Small amounts of *2* – *4* could be detected by TLC.

Under photochemical conditions; (a) with excess of bromine. A solution of 140 mg (0.67 mmol) of *1a* and 400 mg (2.5 mmol) of bromine in 100 ml of carbon tetrachloride reacted as described under (a) above. This heterogeneous mixture was irradiated for 17 h. The red precipitate of hydrobromides, treated as described above, and the green-violet solution were investigated by TLC. About half a dozen compounds were detected, among them *7* and *10*, identified by TLC.

(b) With continuously added bromine. To avoid extensive electrophilic bromination by having excess of halogen present, the bromine was introduced continuously over the entire period in the following way. A thin stream of nitrogen was passed through a gas-washing bottle containing bromine, and the mixture of nitrogen and bromine was bubbled *via* a gas-inlet tube through the solution of *1a*. This procedure resulted in lower initial yields of *2*, *3*, and *4* (substituted in the *B*-ring). (i) In carbon tetrachloride. A solution of 200 mg of *1a* in 500 ml of carbon tetrachloride was brominated with *ca.* 0.5 ml of bromine as just described. After 5 h, when the starting material was almost consumed (TLC), the irradiation was interrupted. The reaction mixture, containing a red-green precipitate, was evaporated to dryness under reduced pressure. The residue was then dissolved in 50 ml of absolute ethanol, and treated over-night with 5 g of IR-4B resin (OH form). After filtration the solvent was evaporated *in vacuo* and the residue chromatographed on 20 g of silica gel, using chloroform-ethyl acetate 10:1 as the eluent. Further purification was performed with TLC. The following compounds were isolated: *5* (10 mg; 3.6 %), *6* (40 mg; 11 %), *7* (main product; *ca.* 30 %), *8* and *9* (30 mg together; 7 %), *10* (20 mg; 4 %), and *12* (5 mg; 1 %).

The above procedure was repeated until enough material was obtained for identification of the compounds by spectroscopic methods. Infrared data for the cyano groups, chromatographic mobilities, and molecular weights (MS) for compounds *5*–*10* are summarized in Table 3.

Compound *12* had infrared absorption at 3340, 3150, and 1650 ($CONH_2$) cm^{-1}. TLC: $R_F = 0.38$ ($CHCl_3$–EtOAc, 6:1). MS: $M^+ = 542.713 \pm 0.011$. Calc. for $C_{11}H_5N_5O^{79}Br_2{}^{81}Br_2$: 542.719.

The NMR data of *6*–*10* are summarized in Table 1 and the electronic spectra of *5*–*12* in Table 2.

Table 3. Infrared, chromatographic, and mass spectral properties of *5*–*10*.

	5	*6*	*7*	*8*	*9*	*10*
–CN (IR)	2220	2220	2210	2220	2220	2215
R_F (TLC)	0.30[a]	0.47[a]	0.37[b]	0.21[b]	0.21[b]	0.57[b]
M^+ (MS)	287–289	365–369	443–449	365–369	443–449	521–529

[a] Eluent EtOAc. [b] Eluent $CHCl_3$–EtOAc, 6:1.

(ii) In chloroform. To a solution of 100 mg of *1a* in 100 ml of chloroform, 2 ml of bromine was added continuously, as described above, during irradiation for 4 h. After evaporation and ion exchange as described under (i), 214 mg of a bromocyclazine mixture was obtained. Preparative TLC ($CHCl_3$–EtOAc, 6:1) of 5.2 mg of the crude product gave six bands, which were extracted with chloroform. Compounds *4*–*12* were obtained in the following yields, determined from UV-measurements: *4*, 62 %; *4*+*12*, 20 % (mainly *4*); *7*, 6 %; *10*, 8 %. Only very minute amounts of *8* and *9* were formed. No compounds with less than two bromine atoms could be detected (TLC).

In this experiment, the concentration of bromine was considerable, which probably accounts for the high percentage of *4* formed. However, in other experiments in chloroform, the initial yield of *4* was also substantial, but after prolonged irradiation time the amount of *4* decreased and mainly *10* was obtained.

(iii) In mixtures of chloroform and carbon tetrachloride. Over a period of 3.5 h, 1 ml of bromine was bubbled with a stream of nitrogen into a solution of 209 mg of *1a* in 500 ml of a 1:1 mixture of chloroform and carbon tetrachloride. After 1 h, *5* and *6* were detected (TLC) but after 3.5 h, only traces of these compounds could be observed and mainly *7* and *10* were present. After purification by column chromatography 265 mg (54 %) of *10* was isolated.

In a second experiment a solution of 200 mg of *1a* in a mixture of 350 ml of chloroform and 150 ml of carbon tetrachloride was irradiated for 50 min, while 0.5 ml of bromine was continuously added as described above. Only the mono- and dibromosubstituted compounds *2*–*6* were obtained (TLC).

(c) At low temperature with bromine. In an open vessel 7 mg of *1a* in 50 ml of carbon tetrachloride at −15° was irradiated and 3 drops of bromine in 50 ml of carbon tetrachloride was slowly added during the irradiation. After 1 h, the reaction mixture was analyzed by TLC. Three monobromides, *2*, *3*, and *5*, and one dibromide, *4*, were detected (TLC).

Bromination of derivatives of *1a*

Under "dark" conditions; (a) of *6* to *7* and *10* with bromine. A mixture of 5 mg of *6* and 1 drop of bromine in 10 ml of chloroform was stirred for 1 h. Isolation by preparative TLC yielded mainly *10* plus minor amounts of *7* (TLC).

(b) of *7* to *10* with bromine. A solution of 5 mg of *7* and 1 drop of bromine in 25 ml of carbon tetrachloride was stirred in the dark. After 4 h no new products could be detected and all starting material remained unreacted (TLC). After 1 week compound *10* had been formed in about 50 % yield (TLC).

(c) of *9* to *10* with bromine. Compound *9* brominated as described under (b) gave after 3 h *10* in about 50 % yield.

(d) of *2* to *7*, *8*, and *10* with NBS in "non-purified" chloroform.* Refluxing of 9.3 mg of NBS and 10 mg of *2* in 2 ml of chloroform for 30 min gave *7*, *8*, and *10* (TLC).

(e) of *3* to *4* with NBS in "non-purified" chloroform. Compound *3* was treated as described under (d). Only the ring-substituted compound *4* was formed.

Under photochemical conditions; (a) of *10* to *11* and *12* with bromine. To 25 mg of *10* in 50 ml of chloroform, 200 mg of bromine dissolved in 50 ml of chloroform was added and the mixture irradiated for 3.5 h. After evaporation and ion-exchange as described above, *11* and *12* (MS, TLC) were isolated. Separation of unreacted *10* and *11* was performed on a silica gel plate (CH_2Cl_2), developed twice.

Compound *11* was identified as a pentabromide from its mass spectrum. MS: $M^+ = 599-609$ (sextet: relative intensities 1:5:10:10:5:1). IR: 2230 (CN) cm^{-1}. TLC: $R_F = 0.57$ ($CHCl_3-EtOAc$, 6:1). For NMR and electronic spectra, see Tables 1 and 2, respectively.

A colour change from green to red, observed when the TLC-plates were left in the air for some minutes, was earlier in this investigation attributed to *10*, but was here discovered to come from *11*. Apparently, *11* had been formed in many photochemical experiments described above, but it had been destroyed upon standing on a column of silica gel, or on the TLC-plate. The red conversion product of *11* could not be eluted with chloroform, ethyl acetate, or methanol and its nature has not been investigated.

(b) of *3* to *13* and *14* with bromine. Irradiation for 30 min of 12 mg of *3* and 1 drop of bromine dissolved in 100 ml of chloroform gave two products, which were separated by preparative TLC and identified as *13* and *14* by mass spectrometry. No brominated compounds and no starting material could be detected by TLC.

(c) of *2* to *14* and *15* with bromine. The same procedure was followed as described under (b). All starting material was consumed and *14* (TLC) plus a compound having almost the same R_F-value as *13* (0.24 compared to 0.26 for *13*; EtOAc) were formed. The new compound is supposed to have the structure *15*.

(d) of *4* to *10* with bromine. A solution of 10 mg of *4* and 1 drop of bromine in 100 ml of chloroform was irradiated for 45 min. The following compounds, separated by preparative TLC, were isolated and identified: *10* (MS, TLC), *12* (TLC), one compound with $R_F = 0.50$ ($CHCl_3$-EtOAc, 6:1) and with the molecular formula $C_{11}H_3N_5Br_2Cl_2$ and one with $R_F = 0.54$ and the molecular formula $C_{11}H_3N_5Br_3Cl$ (MS). Minor amounts of a not identified compound ($R_F = 0.40$; $CHCl_3$-EtOAc, 6:1) were also isolated.

Irradiation of *10* in the presence of H_2O/HCl.

In 100 ml of chloroform, containing 0.1 ml 2 M HCl, 39 mg of *10* was dissolved and irradiated for 50 min. No amide, *12*, was formed (TLC). Two products were observed and separated by TLC, but both showed strong infrared absorption at 2220 (CN) cm^{-1}.

General thiocyanation procedure

Thiocyanogen was prepared from bromine and lead thiocyanate as described by Söderbäck.[9] Addition of thiocyanogen in equimolar amounts to a solution of *1a* immediately resulted in the formation of a red precipitate and gradual decolourization of the

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* Analytical grade, not passed over Al_2O_3.

blue solution. The solid was shown (by IR, NMR, and elemental analysis) to be the thiocyanate *19*, $C_{11}H_7N_5.(HSCN)_n$; $n \approx 2$.

The formation of *19* probably depends on the formation of HSCN from thiocyanogen and small amounts of water present in the solvents.[10] When these were carefully dried and the thiocyanogen solution, protected from moisture, was added slowly to the reaction mixture in portions, no formation of *19* was observed.

Salt formation between *1a* and HSCN

Addition of 5 mmol of thiocyanogen in 50 ml of carbon tetrachloride to 500 mg (2.4 mmol) of *1a* in 50 ml of carbon tetrachloride immediately led to the precipitation of a red solid. The solution, which initially was strongly coloured, gradually became pale, and after 15 min it was almost colourless. The reaction mixture was filtered, the solid washed repeatedly with chloroform, and the remaining material dried in the air. The red solid was identified as *19*. IR: 2060 (SCN), 2230 (CN), 2300–2800 (broad absorption peak, $-\overset{|}{\underset{|}{N}}{}^{+}-H$) cm^{-1}. M.p.: sublimation, accompanied by loss of HSCN, gives a blue material, which melts at 265°(=m.p. of *1a*). NMR ($AsCl_3$): singlet at 2.30 (3 H), multiplet at 7.02 (2 H), triplet at 7.80 (1 H), singlet at 7.98 (1 H), and $-\overset{|}{\underset{|}{N}}{}^{+}-H$ at 8.17 (2–3 H). The coupling pattern of *19* is analogous with that observed for *1a*. (Found: S 20.3. Calc. for $C_{13}H_9N_7S_2$: S 19.6).*

Thiocyanation of *1a*

Under photochemical conditions; (a) in carbon tetrachloride. A solution of 0.24 mmol (50 mg) of *1a* in 350 ml of carbon tetrachloride and 0.50 mmol of thiocyanogen in 50 ml of the same solvent (the thiocyanogen solution added dropwise over a period of 1 h) was irradiated for 3 h, after which no starting material remained (TLC). The larger portion of the solvent was evaporated *in vacuo* and the residue was dissolved in methylene chloride and allowed to stand for 2 days (to complete the polymerization of unreacted thiocyanogen).[10] Chromatography on 20 g of silica gel with methylene chloride removed a large amount of yellow impurities, and ethyl acetate eluted a blue-green band, which was further purified by preparative TLC (CH_2Cl_2-EtOAc, 6:1). Three products, *16*–*18*, were isolated, but at least five other coloured bands (blue, green, violet, and red) were observed on TLC.** The yield of *16* was 3 % (1.9 mg), and *17* and *18* were isolated in less than 1.5 % each. M.p.: for *16*, 206–208°; for *17*, 213–215°; for *18*, 235–237°.*** IR: for *16* and *17*, 2220 (CN) and 2160 (sharp peak, –SCN) cm^{-1}; for *18*, 2165 (–SCN), 3370, 3290, 3210, and 1655 ($CONH_2$) cm^{-1}. TLC: for *16*, $R_F = 0.36$; for *17*, $R_F = 0.62$; for *18*, $R_F = 0.55$ (EtOAc). The compounds are violet (*16*), blue (*17*), and red (*18*). Electronic spectral data are summarized in Table 2.

(b) In benzene. Over a period of 1 h 0.5 mmol of thiocyanogen in 10 ml of benzene was added to an irradiated solution of 50 mg (0.24 mmol) of *1a* in 100 ml of benzene. No coloured products were formed during this time (TLC). Another 0.25 mmol of thiocyanogen in 5 ml of benzene was added and the irradiation was continued for 5 h. The reaction mixture was worked up as described above, and *16* was the only product formed (< 2 %).

Several irradiation experiments in carbon tetrachloride and in methylene chloride with varying concentrations of the reactants were performed, giving the same products and the same low yields. Attempts to scale up the thiocyanation procedure were not successful. This resulted only in increasing amounts of the yellow by-products.

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* The results obtained are in poor agreement with the calculated values, probably because of inhomogeneity of the material.

** Under "dark" conditions no coloured products were obtained.

*** Melting points are uncorrected.

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