33. I. O. Sutherland, in: Annual Reports on NMR Spectroscopy, Vol. 4, Academic Press, London–New York (1971), p. 71.

HETEROATOMIC DERIVATIVES OF AZIRIDINE.

13.* NEW MACROHETEROCYCLIC COMPOUNDS CONTAINING ARYLALKYL AND FUNCTIONAL GROUPS ATTACHED TO THE ENDOCYCLIC NITROGEN ATOMS

M. G. Voronkov, V. I. Knutov,
M. K. Butin, and O. B. Bannikova

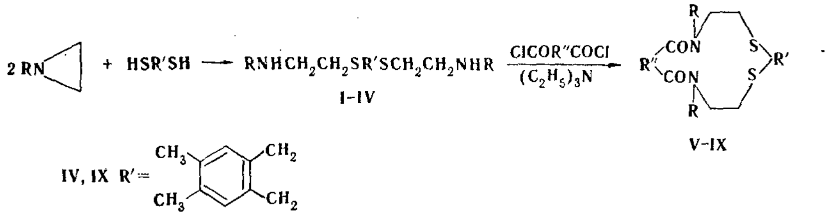
UDC 547.717'898

The reaction of N-substituted aziridines with 1,2-ethanedithiol and 1,2-bis(mercaptomethyl)-4,5-dimethylbenzene leads to N-substituted diamines. The reaction of the latter with adipic and phthalic acid dichlorides gives N-substituted macroheterocycles.

The introduction of alkyl and functional groups in the rings of macroheterocyclic compounds leads to an increase in their lipophilic and complexing properties [2-4]. Syntheses of cryptands and their polymacroheterocyclic analogs have been accomplished on the basis of functionally substituted macroheterocycles [5, 6]. Macroheterocycles with functional groups have been investigated as biologically active compounds [7, 8]. Immobilized on polymeric materials, they are used as new heterogeneous catalysts [9].

We have previously synthesized unsubstituted and functionally substituted macroheterocycles from primary and secondary diamines and dicarboxylic acid dichlorides. The diamines were obtained by the reaction of aziridine and 1-(2-carbomethoxyethyl)aziridine with dithiols [10-13].

In order to obtain arylalkyl- and functionally substituted macroheterocycles we synthesized diamines I-IV and studied their reaction with adipic and phthalic acid dichlorides.



I $R=C_6H_5CH_2CH_2$, $R'=CH_2CH_2$; II $R=CH_3OOCCH_2CH_2$, $R'=CH_2CH_2$; III $R=NCCH_2CH_2$, $R'=CH_2CH_2$; IV $R=CH_3OOCCH_2CH_2$; V $R=C_6H_5CH_2CH_2$, $R'=CH_2CH_2$, $R''=-(CH_2)_4-$; VI $R=CH_3OOCCH_2CH_2$, $R'=CH_2CH_2$, $R''=-(CH_2)_4-$; VII $R=NCCH_2CH_2$, $R'=CH_2CH_2$, $R''=-(CH_2)_4-$; VIII $R=C_6H_5CH_2CH_2$; $R'=CH_2CH_2$, $R''=C_6H_4$-*o*; IX $R=CH_3OOCCH_2CH_2$, $R''=C_6H_4$-*o*

Linear diamines I-IV were obtained in 70-80% yields by the reaction of N-substituted aziridines with 1,2-ethanedithiol and 1,2-bis(mercaptomethyl)-4,5-dimethylbenzene. The structure of diamines I-IV was proved by the preparation of their dihydrochlorides and by acid hydrolysis of 1,8-bis[2-(carbomethoxy)ethylamino]-3,6-dithiaoctane (II) and 1,8-bis(2-cyanoethylamino)-3,6-dithiaoctane (III) to the amino acid dihydrochloride (X).

$$\text{II, III} \xrightarrow[CH_3COOH]{HCl} \underset{X}{(HOOCCH_2CH_2NHCH_2CH_2SCH_2-)_2 \cdot 2\,HCl}$$

Diamines I-IV react readily with adipic and phthalic acid dichlorides in a large volume of dry benzene in the presence of triethylamine to give macroheterocycles V-IX in 55-70% yields.

---

*See [1] for Communication 12.

Irkutsk Institute of Organic Chemistry, Siberian Branch, Academy of Sciences of the USSR, Irkutsk 664033. Translated from Khimiya Geterotsiklicheskikh Soedinenii, No. 9, pp. 1228-1230, September, 1981. Original article submitted January 13, 1981.

0009-3122/81/1709-0916$07.50

EXPERIMENTAL

The IR spectra of the compounds were obtained with a UR-20 spectrometer. The PMR spectra of solutions of the compounds in $CDCl_3$ were recorded with a Tesla BS-487C spectrometer (80 MHz). Thin-layer chromatography (TLC) was carried out on Silufol [elution with benzene—methanol (5:1)].

1,8-Bis(2-phenylethylamino)-3,6-dithiaoctane (I). A mixture of 14.7 g (0.1 mole) of 1-(2-phenylethyl)aziridine and 4.7 g (0.05 mole) of 1,2-ethanedithiol in 100 ml of methanol was heated at 55-60°C for 6 h, after which the methanol was removed by distillation, and the residue was dissolved in chloroform and precipitated by means of petroleum ether in the cold to give 15.5 g (80%) of an oil. IR spectrum: 3310 (NH); 3030, 1600 (=CH); 755 cm^{-1} (CH_2SCH_2). The dihydrochloride had mp 248-249°C. Found: Cl 15.1; N 5.9; S 14.1%. $C_{22}H_{32}N_2S_2 \cdot 2HCl$. Calculated: Cl 15.4; N 6.1; S 13.9%.

1,8-Bis(2-cyanoethylamino)-3,6-dithiaoctane (III). This compound was obtained as an oil from 9.6 g (0.1 mole) of 1-(2-cyanoethyl)aziridine and 4.7 g (0.05 mole) of 1,2-ethanediol by the method used to prepare diamine II [12]. The yield was 11.7 g (82%). IR spectrum: 3320 (NH), 2260 (CN), and 760 cm^{-1} (CH_2SCH_2). PMR spectrum: 2.70 (2H, s, NH) and 3.26 ppm (16H, m, CH_2N, CH_2S). The dihydrochloride had mp 183-184°C. Found: Cl 20.1; S 17.6%. $C_{12}H_{22}N_4S_2 \cdot 2HCl$. Calculated: Cl 19.6; S 17.8%.

1,2-Bis{2-[(2-carbomethoxyethyl)amino]ethylthiomethyl}-4,5-dimethylbenzene (IV). This compound was similarly obtained as an oil from 12.9 g (0.1 mole) of 1-(2-carbomethoxyethyl)aziridine and 9.9 g (0.05 mole) of 1,2-bis(mercaptomethyl)-4,5-dimethylbenzene. The yield was 16.5 g (72%). IR spectrum: 3320 (NH), 1740 ($COOCH_3$), and 760 cm^{-1} (CH_2SCH_2). PMR spectrum: 2.18 (6H, s, CH_3), 2.74 (16H, m, CH_2N, CH_2S), 3.62 (6H, s, OCH_3), 3.80 (2H, s, NH), and 7.15 ppm (2H, s, C_6H_2). Found: N 5.8%; $C_{22}H_{36}N_2O_4S_2$. Calculated: N 6.14% The dihydrochloride had mp 185-187°C.

8,13-Dioxo-1,4-dithia-7,14-bis(2-phenylethyl)-7,14-diazacyclohexadecane (V). A mixture of 9.7 g (0.025 mole) of diamine I and 5.0 g (0.05 mole) of triethylamine in 500 ml of dry benzene and a solution of 4.6 g (0.025 mole) of adipic acid dichloride in 500 ml of dry benzene were added separately in the course of 6 h at room temperature with vigorous stirring to 1 liter of dry benzene, after which the precipitate was removed by filtration, and the solvent was removed by distillation at reduced pressure. The residue was purified by chromatography on aluminum oxide [elution with benzene—methanol (5:1)]. The solvent was removed by distillation, and the residue was recrystallized from methanol to give 8.6 g (70%) of a product with mp 134-135°C. IR spectrum: 3030, 1600 (=CH); 1640 (CO); 760 cm^{-1} (CH_2SCH_2). PMR spectrum: 2.70 (16H, m, CH_2N, CH_2S), 3.47 (8H, m, CH_2CH_2CO), and 7.16 (10H, s, C_6H_5). The product had R_f 0.3. Found: C 67.2; H 7.4; N 5.4; S 13.0%; M (by cryoscopy) 475. $C_{28}H_{38}N_2O_2S_2$. Calculated: C 67.5; H 7.6; N 5.6; S 12.9%; M 498.

8,13-Dioxo-1,4-dithia-7,14-bis[(2-carbomethoxy)ethyl]-7,14-diazacyclohexadecane (VI). This compound was similarly obtained from 8.8 g (0.025 mole) of diamine II and 4.6 g (0.025 mole) of adipic acid dichloride. The yield of product with mp 105-107°C was 9.7 g (68%). IR spectrum: 1640 (CO), 1730 ($COOCH_3$), and 760 cm^{-1} (CH_2SCH_2). The product had R_f 0.31. Found: C 51.5; H 7.0; N 5.6; S 13.8%; M 440. $C_{20}H_{34}N_2O_6S_2$. Calculated: C 51.9; H 7.3; N 6.1; S 13.8%; M 462.

8,13-Dioxo-1,4-dithia-7,14-bis(2-cyanoethyl)-7,14-diazacyclohexadecane (VII). This compound was similarly obtained from 7.1 g (0.025 mole) of diamine III and 4.6 g (0.025 mole) of adipic acid dichloride. The yield of product with mp 184-185°C was 6.8 g (70%). IR spectrum: 1645 (CO), 2260 (CN), and 760 cm^{-1} (CH_2SCH_2). The product had R_f 0.28. Found: C 54.0; H 6.9; N 14.3; S 16.7%; M 376. $C_{18}H_{18}N_4O_2S_2$. Calculated: C 54.4; H 7.1; N 14.1; S 16.4%; M 396.

9,10-Benzo-8,11-dioxo-1,4-dithia-7,12-bis(2-phenylethyl)-7,12-diazacyclotetradec-9-ene (VIII). This compound was similarly obtained from 9.7 g (0.025 mole) of diamine I and 5.0 g (0.025 mole) of phthalic acid dichloride. The yield of product with mp 190-191°C was 9.1 g (70%). IR spectrum: 1640 (CO); 3030, 1600 (=CH); 760 cm^{-1} (CH_2SCH_2). PMR spectrum: 2.76 (16H, m, CH_2N, CH_2S), 3.67 (4H, d, $C_6H_5CH_2$), and 7.19 ppm (14H, m, C_6H_5, C_6H_4). The product had R_f 0.51. Found: C 69.4; H 6.9; N 5.5; S 12.4%; M 492. $C_{30}H_{34}N_2O_2S_2$. Calculated: C 69.4; H 6.6; H 5.4; S 12.3%; M 518.

11,12-Benzo-3,4-(4,5-dimethylbenzo)-10,13-dioxo-1,6-dithia-9,14-bis[2-(carbomethoxy)-ethyl]-9,14-diazacyclohexadeca-3,11-diene (IX). This compound was similarly obtained from 11.2 g (0.025 mole) of diamine IV and 5.0 g (0.025 mole) of phthalic acid dichloride. The yield of product with mp 72-73°C was 7.8 g (55%). IR spectrum: 1640 (CO); 1735 ($COOCH_3$); 3030, 1605 (=CH); 760 cm^{-1} (CH_2SCH_2). Found: C 61.2; H 6.2; N 4.5; S 11.0%; M 556. $C_{30}H_{38}N_2O_6S_2$. Calculated: C 61.4; H 6.4; N 4.8; S 10.9%; M 586.

1,8-Bis(2-carboxyethylamine)-3,6-dithiaoctane Dihydrochloride (X). A mixture of 0.05 mole of diamine II or III and 10 ml of concentrated HCl in 50 ml of acetic acid was heated at 100°C for 2 h, after which the solvent was evaporated, and the residue was recrystallized from methanol to give dihydrochloride X, with mp 134-135°C, in 90-93% yield. IR spectrum: 1740, 1410 (COOH); 2460, 2600-3030 cm^{-1} ($NH_2^+Cl^-$). Found: Cl 17.3; S 13.5%. $C_{12}H_{24}N_2O_4S_2 \cdot 2HCl$. Calculated: Cl 17.7; S 13.9%.

LITERATURE CITED

1. M. G. Voronkov and V. I. Knutov, Khim. Geterotsikl. Soedin., No. 7, 921 (1981).
2. J. J. Cristensen, D. J. Eatough, and R. M. Izatt, Chem. Rev., 74, 351 (1974).
3. G. R. Newkome, J. D. Sauer, J. M. Roper, and D. C. Hager, Chem. Rev., 77, 513 (1977).
4. J. S. Bradshaw and P. E. Stott, Tetrahedron, 36, 461 (1980).
5. N. Wester and F. Vögtle, Chem. Ber., 112, 3723 (1979).
6. C. K. Chang, J. Amer. Chem. Soc., 99, 2819 (1977).
7. F. Vögtle and U. Elben, Chem. Ber., 111, 1434 (1978).
8. U. Elben, H. B. Fuchs, K. Frensch, and F. Vögtle, Ann., 1102 (1979).
9. A. V. Bogat-skii, N. G. Luk'yanenko, and V. N. Pastushok, Dokl. Akad. Nauk SSSR, 247, 1153 (1979).
10. V. I. Knutov, M. K. Butin, and M. G. Voronkov, 15th Scientific Session on the Chemistry and Technology of Organic Sulfur Compounds and Sulfurous Petroleum Oils (Summaries of Papers) [in Russian], Ufa (1979), p. 97.
11. V. I. Knutov, M. K. Butin, L. M. Chudesova, V. A. Usov, and M. G. Voronkov, News in the Chemistry of Nitrogen-Containing Heterocycles [in Russian], Vol. 1, Zinatne, Riga (1979), p. 63.
12. M. G. Voronkov, V. I. Knutov, V. A. Usov, M. K. Butin, and O. B. Bannikova, Khim. Geterotsikl. Soedin., No. 11, 1474 (1979).
13. V. I. Knutov, M. K. Butin, and M. G. Voronkov, Khim. Geterotsikl. Soedin., No. 1, 123 (1980).