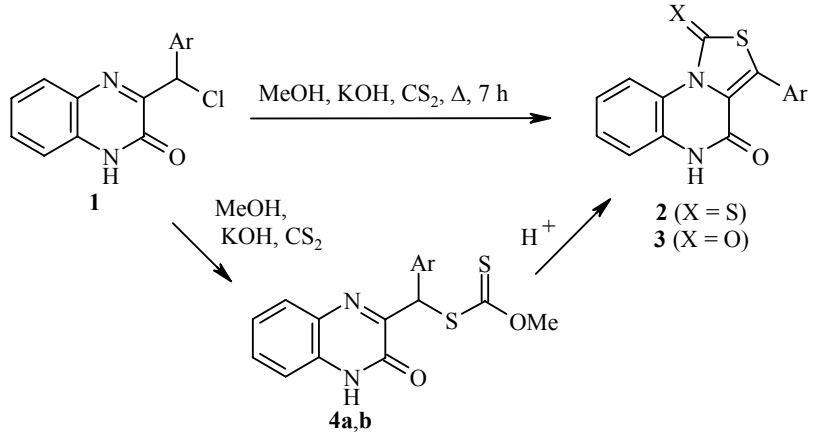
Chemistry of Heterocyclic Compounds, Vol. 40, No. 1, 2004

CARBON DISULFIDE IN SYNTHESIS OF THIAZOLO[3,4-*a*]QUINOXALINES BASED ON 3-(α-CHLOROBENZYL)QUINOXALIN-2-(1H)-ONES

A. A. Kalinin and V. A. Mamedov

Keywords: xanthogenates, carbon disulfide, thiazolo[3,4-*a*]quinoxalines, quinoxalines, thiazoles.

A widely used method for obtaining thiazole derivatives is the Cook–Heilbron synthesis [1], in which C–S and C–C–N moieties are used to construct the ring in condensation of carbon disulfide with α-amino nitriles and α-amino amides, leading to 5-aminothiazole derivatives that are either unsubstituted or substituted in the position 4. We have found that 3-(α-chlorobenzyl)quinoxalin-2-(1H)-ones **1** [2], because of the α-chlorobenzylimine moieties which function as a triatomic synthon C^+–C–N^-, when reacted with hydrogen disulfide yield condensed thiazole derivatives: thiazolo[3,4-*a*]quinoxalines **2, 3**. Since the reactions are carried out in the presence of KOH in methanol solution, formation of a thiazoloquinoxaline system probably occurs via xanthogenates **4**, which then undergo intramolecular cyclocondensation. In order to confirm this hypothesis, we synthesized the xanthogenates **4a,b** and showed that they can undergo ring closure to form thiazolo[3,4-*a*]-quinoxalines under conditions of not only base catalysis but also acid catalysis, and the latter variant is preferred. Depending on both the reaction conditions and the nature of the aryl group of the substituent at the position 3, 1-thioxo (**2**) or 1-oxo (**3**) derivatives of thiazolo[3,4-*a*]quinoxalines are formed. The best yields of thiazolo[3,4-*a*]quinoxalines are achieved when the reactions are carried out in CF_3COOH; in this case, boiling solutions of xanthogenates **4a,b** in CF_3COOH for two hours leads exclusively to 1-oxothiazolo[3,4-*a*]-quinoxalines **3a,b**, while boiling for half an hour makes it possible, when Ar = Ph, to obtain the 1-thioxo



4 a Ar = Ph, **b** Ar = 2,4-$Cl_2C_6H_3$

A. E. Arbuzov Institute of Organic and Physical Chemistry, Kazan Science Center, Russian Academy of Sciences, Kazan 420088; e-mail: mamedov@iopc.kcn.ru. Translated from Khimiya Geterotsiklicheskikh Soedinenii, No. 1, pp. 133-135, January, 2004. Original article submitted July 23, 2003.

derivative **2a**. We do not get good results if instead of CF_3COOH we use AcOH or 6.1 M HCl, in which thiocyanate and diphenylisothioureide analogs of compound **4a** readily undergo intramolecular cyclization to form 1-iminothiazoloquinoxalines [3]: we can obtain thiazoloquinoxaline **2a** only if we boil xanthogenate **4a** for 4 h.

In the ^1H NMR spectrum of thiazoloquinoxalines **2, 3**, there is a diagnostic doublet signal [3-5] from the $H_{(9)}$ proton of the azolo[*a*]quinoxalines, which resonates downfield (8.8-10.5 ppm), in contrast to other protons of the aromatic rings.

3-Phenyl-1-thioxothiazolo[3,4-*a*]quinoxalin-4(5H)-one (2a). A. KOH (0.20 g, 3.6 mmol) and CS_2 (0.9 ml) were dissolved in methyl alcohol (10 ml). Quinoxaline **1a** (0.40 g, 1.5 mmol) was added to the solution and it was boiled for 7 h. The precipitated crystals were filtered out and washed with methanol. Yield 30 mg (6.5%).

B. A solution of compound **4a** (0.60 g, 1.8 mmol) in AcOH (10 ml) was boiled for 4 h and allowed to stand overnight. The precipitated crystals were filtered out and washed with 2-propanol. Yield 60 mg (11%).

C. A solution of compound **4a** (0.30 g, 0.9 mmol) in CF_3COOH (5 ml) was boiled for 40 min and allowed to stand overnight. The precipitated crystals were filtered out and washed with 2-propanol. Yield 0.11 g (40%); mp 300-302°C. IR spectrum (vaseline oil), ν, cm^{-1}: 689, 738, 1075, 1130, 1165, 1224, 1398, 1489, 1606, 1687, 2500-3220. ^1H NMR spectrum (DMSO-d_6), δ, ppm (*J*, Hz): 7.13-7.63 (8H, m, C_6H_5, $H_{(6-8)}$); 10.48 (H, d, *J* = 8.33, $H_{(9)}$); 11.55 (1H, br. s, NH). Found, %: C 61.85; H 3.07; N 9.18; S 20.84. $C_{16}H_{10}N_2OS_2$. Calculated, %: C 61.91; H 3.25; N 9.03; S 20.66.

3-Phenylthiazolo[3,4-*a*]quinoxaline-1,4(5H)-dione (3a). A solution of compound **4a** (0.30 g, 0.9 mmol) in CF_3COOH (5 ml) was boiled for 2 h. The precipitated crystals was filtered out and washed with 2-propanol. Yield 0.11 g (40.5%); mp 313-315°C (AcOH). The characteristics of **3a** match those described in [3].

3-(2,4-Dichlorophenyl)thiazolo[3,4-*a*]quinoxaline-1,4(5H)-dione (3b). Obtained as for tricycle **3a** from quinoxaline **4b**. Yield 41%; mp >360°C (DMSO). IR spectrum (vaseline oil), ν, cm^{-1}: 478, 587, 756, 814, 842, 878, 1097, 1226, 1317, 1435, 1496, 1578, 1633, 1689, 2500-3220. ^1H NMR spectrum (DMSO-d_6), δ, ppm (*J*, Hz): 7.16-7.24 (2H, m, $H_{(6)}$ or $H_{(7)}$, $H_{(8)}$); 7.31 (1H, dd, *J* = 8.04, *J* = 6.68, $H_{(6)}$ or $H_{(7)}$); 7.51 (1H, dd, *J* = 8.70, *J* = 2.00, $H_{(5)}$ in $C_6H_3Cl_2$); 7.59 (1H, d, *J* = 8.70, $H_{(6)}$); 7.73 (1H, d, *J* = 2.00, $H_{(3)}$ in $C_6H_3Cl_2$); 8.83 (1H, d, *J* = 8.04, $H_{(9)}$); 11.28 (1H, br. s, NH). Found, %: C 52.99; H 2.38; N 7.63; S 8.69; Cl 19.32. $C_{16}H_8Cl_2N_2O_2S$. Calculated, %: C 52.91; H 2.22; N 7.71; S 8.83; Cl 19.52.

3-(α-Methoxythiocarbonylthiobenzyl)quinoxalin-2(1H)-one (4a). KOH (0.40 g, 7.1 mmol) and CS_2 (1.0 ml) were dissolved in methyl alcohol (30 ml) and then the mixture was stirred for 0.5 h. Quinoxaline **1a** (1.00 g, 3.7 mmol) was added to the solution and it was stirred for 4 h and allowed to standard overnight. The crystals were filtered out and washed with 2-propanol. Yield 1.13 g (90%); mp 165-167°C (*i*-PrOH). IR spectrum (vaseline oil), ν, cm^{-1}: 698, 755, 1075, 1101, 1280, 1492, 1560, 1612, 1663, 2500-3220. ^1H NMR spectrum (DMSO-d_6), δ, ppm (*J*, Hz): 4.14 (3H, s, CH_3); 6.63 (1H, s, PhC<u>H</u>); 7.25-7.38 (5H, m); 7.55-7.65 (3H, m); 7.84 (1H, d, *J* = 8.20, $H_{(5)}$), 12.45 (1H, br. s, NH). Found, %: C 59.47; H 4.21; N 8.25; S 18.74. $C_{17}H_{14}N_2O_2S_2$. Calculated, %: C 59.63; H 4.12; N 8.18; S 18.72.

3-(α-Methoxythiocarbonylthio-2,4-dichlorobenzyl)quinoxalin-2(1H)-one (4b). Obtained as for compound **4a** from quinoxaline **1b**. Yield 89%; mp 217-219°C (acetone). IR spectrum (vaseline oil), ν, cm^{-1}: 469, 577, 749, 855, 891, 946, 1058, 1100, 1235, 1432, 1559, 1612, 1660, 2500-3220. ^1H (DMSO-d6) NMR spectrum, δ, ppm (*J*, Hz): 4.14 (3H, s, CH_3); 6.93 (1H, s, ArCH); 7.28-7.39 (2H, m); 7.42 (1H, dd, *J* = 8.58, *J* = 2.38, $H_{(5)}$ in $C_6H_3Cl_2$); 7.52-7.62 (2H, m); 7.68 (1H, d, *J* = 2.38, $H_{(3)}$ in $C_6H_3Cl_2$); 7.78 (1H, dd, *J* = 8.10, *J* = 0.95, $H_{(8)}$); 12.64 (1H, br. s, NH). Found, %: C 49.68; H 2.88; N 6.67; S 15.97; Cl 17.32. $C_{17}H_{12}Cl_2N_2O_2S_2$. Calculated, %: C 49.64; H 2.94; N 6.81; S 15.59; Cl 17.24.

This work was done with the financial support of the Russian Foundation for Basic Research (grant No. 03-03-32865).

REFERENCES

1. C. Roussel, in: *Thiazole and Its Derivatives* (J. V. Metzger, ed.), Wiley, New York (1979), Pt. 2, p. 393.
2. V. A. Mamedov, I. A. Nuretdinov, and F. G. Sibgatullina, *Izv. Akad. Nauk, Ser. Khim.*, 1412 (1988).
3. V. A. Mamedov, A. A. Kalinin, A. T. Gubaidullin, I. A. Litvinov, and Ya. A. Levin, *Khim. Geterotsikl. Soedin.*, 1664 (1999).
4. V. A. Mamedov, A. A. Kalinin, I. Kh. Rizvanov, N. M. Azancheev, Yu. Ya. Efremov, and Ya. A. Levin, *Khim. Geterotsikl. Soedin.*, 1279 (2002).
5. G. W. H. Cheeseman and B. Tuck, *J. Chem. Soc. (C)*, **13**, 1164 (1967).

ERRATUM

The authors of the article "^{1}H and ^{13}C NMR Spectra of 9H-Pyrimido[4,5-*b*]indoles", Vol. 39, No. 10, pp. 1348-1354, are V. P. Borovik, M. M. Shakirov, and O. P. Shkurko. The paper was presented of and on behalf of N. N. Vorozhtsov Novosibirsk Institute of Organic Chemistry.