Heteroatom Chemistry
Volume 7, Number 3, 1996

Synthetic Approaches Toward Macrocyclic Sulfonyl Crown Formazans

Yehia A. Ibrahim,* Ahmed H. M. Elwahy, and Ashraf A. Abbas

Department of Chemistry, Faculty of Science, Cairo University, Giza, A R Egypt

Received 8 December 1995

ABSTRACT

Coupling of diazonium salts with ethyl sulfonylpyruvates **1–3** *or arenesulfonylacetic acids* **14,15** *afforded good yields of the corresponding 1,5-symmetrically disubstituted-3-sulfonylformazans* **4–11**. *The new sulfonyl macrocyclic crown formazans* **25–32** *were prepared by coupling of the appropriate bisdiazonium salts* **22–24** *with compounds* **1–3** *or* **14,15**. © *1996 John Wiley & Sons, Inc.*

INTRODUCTION

The chemistry and diverse applications of formazans have been the subject of a large number of reviews that have been cited previously [1]. Moreover, there is recent growing interest in the synthesis of macrocyclic crown formazans due to their useful applications in selective metal extraction [2–5] and determination [6–15]. Such applications depend mainly on the cavity size of the macrocyclic crown formazans as well as on the substituents in the macrocycle. Thus, for example, compounds I [R = NO_2, CN, X = $(CH_2)_3$] were used for selective spectrophotometric determination of lithium [6,8]. Also, I [R = CN, X = $(CH_2)_3$] forms a useful cesium ion selective electrode [11]. On the other hand, compounds I [R = Ph, CN, X = $C_2H_4(OC_2H_4)_n$, n = 0–2] were reported [3,5] to be useful for selective extraction of Cu and Hg. The present study offers synthetic approaches to new crown formazans with methanesulfonyl or arenesulfonyl substituents at the formazyl carbon that are expected to have useful applications.

RESULTS AND DISCUSSION

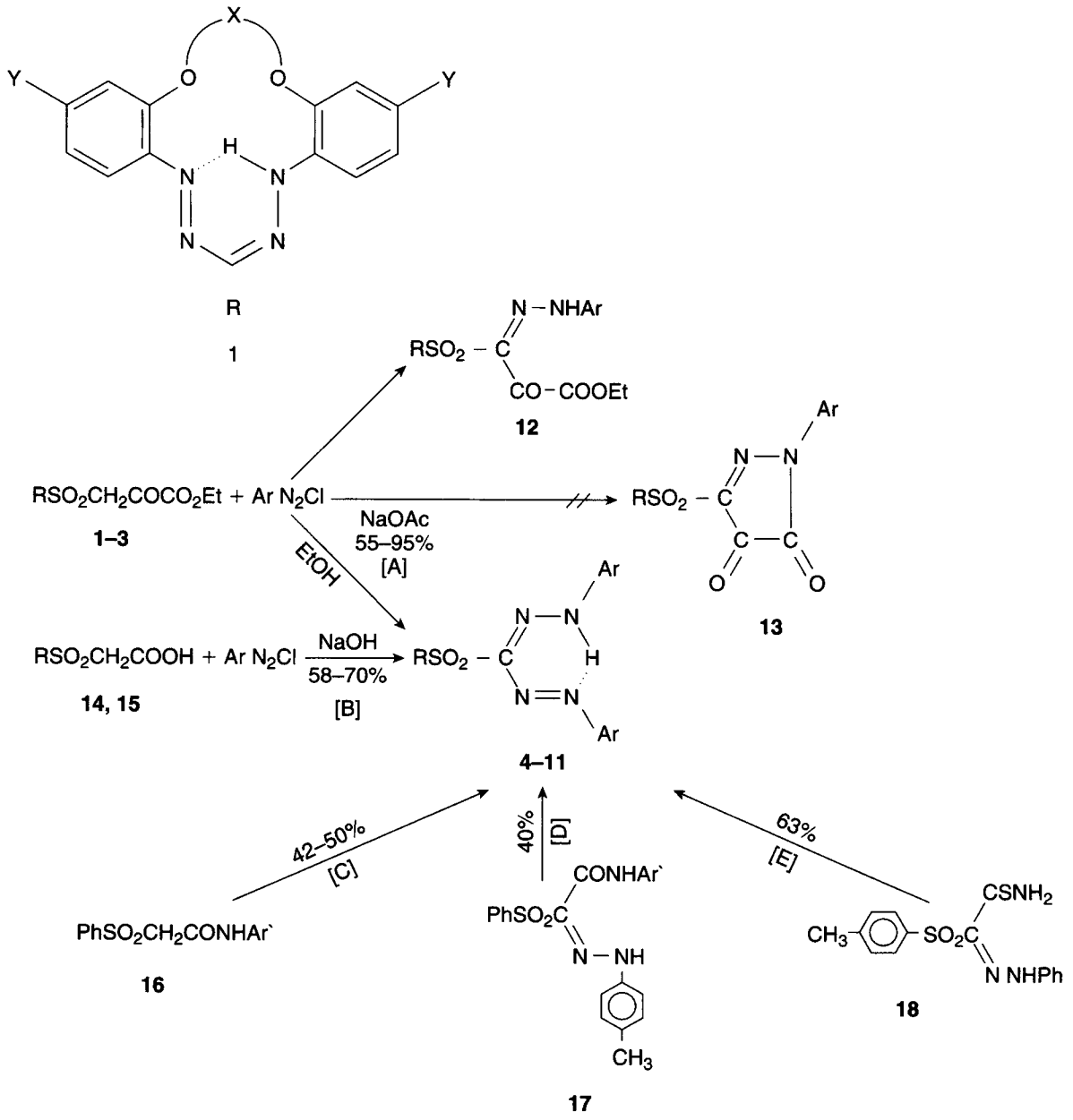
We recently reported the synthesis of 3-arylformazans and their macrocyclic crown derivatives by the coupling of diazonium salts with arylpyruvic acids [1]. Similarly, lariat crown formazans were recently [16] prepared from phenylpyruvic acid. In continuation of these interesting findings, we studied the possible utility of sulfonylpyruvates **1–3** in the synthesis of 3-substituted formazans and their macrocyclic crown counterparts. Thus, coupling of each of the ethyl sulfonylpyruvates **1–3** with the appropriate arenediazonium chlorides in ethanolic sodium acetate solution (method A, Scheme 1) afforded the corresponding formazans **4–11** in 55–95% yields. Attempts to isolate the hydrazone derivatives **12** or the pyrazolinediones **13** were unsuccessful even by variation of the molar ratios of the reactants. Moreover, under more basic conditions (by using aqueous NaOH), no identifiable products could be isolated from those reactions.

In the present study, compounds **4–11** were obtained in 58–70% yields by coupling each of benzenesulfonylacetic acid **14** and *p*-toluenesulfonylacetic acid **15** with the appropriate diazonium salts in aqueous sodium hydroxide solution. Our results contradict previously reported failures in attempts to obtain the formazans **4–11** despite the successful formation of *o*-methyl and *o*-methoxy derivatives [17].

The literature contains reports of the synthesis of **7,8** in 42–50% yields by the coupling of the respective benzenesulfonylacetylarylamides **16** and

*To whom all correspondence should be addressed.

CCC 1042-7163/96/030215-05



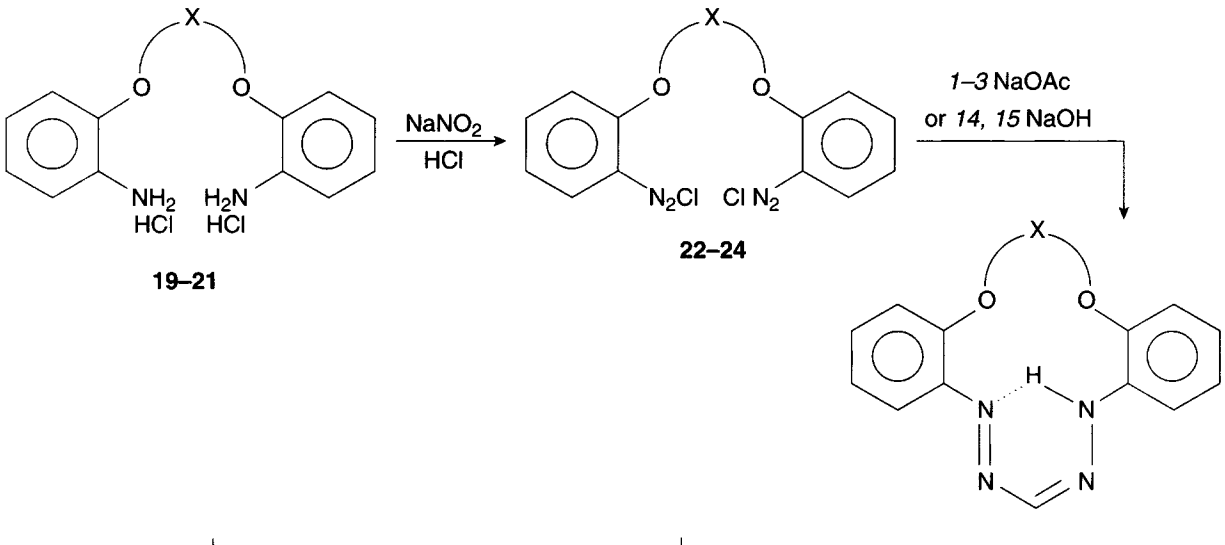
Compd. no.	R
1, 4, 5, 6	CH_3
2, 7, 8, 14	C_6H_5
3, 9, 10, 11, 15	p-$CH_3C_6H_4$

Compd. no.	Ar
4, 9	Ph
5, 7, 10	p-$CH_3C_6H_4$
6, 8, 11	p-$CH_3OC_6H_4$

SCHEME 1

the synthesis of **7** by the coupling of the phenylhydrazone **17** with the appropriate diazonium salts in aqueous sodium hydroxide [18] (methods C and D, Scheme 1). Also, compound **9** was obtained in 63% yield by coupling of the thioglyoxylamidephenylhydrazone **18** with benzenediazonium chloride (method E, Scheme 1) [19].

The previous findings for the synthesis of 1,5-symmetrically disubstituted 3-sulfonylformazans **4–11** from **1–3** and **14,15** have now been extended to



Compd. no.	X
19, 22, 25, 26, 27	$(CH_2)_3$
20, 23, 28, 29	H_2C CH_2
21, 24, 30, 31, 32	H_2C CH_2

Compd. no.	R
25, 30	CH_3
26, 28, 31	Ph
27, 29, 32	p-$CH_3C_6H_4$

SCHEME 2

the synthesis of macrocyclic crown formazans **25–32** with a methanesulfonyl or arenesulfonyl group at the formazyl carbon. Thus, diazotization of the diamines **19–21** gave the corresponding bisdiazonium salts **22–24**. Coupling of the latter with the appropriate pyruvates **1–3** in ethanolic sodium acetate solution afforded the corresponding macrocycles **25–32** in 4–6% yields after chromatographic separation by preparative thin-layer chromatography. Alternatively, compounds **26–29** and **31,32** were obtained in 8–11% yields by coupling of each of the bisdiazonium salts **22–24** with benzenesulfonylacetic acid **14** or *p*-toluenesulfonylacetic acid **15** in aqueous sodium hydroxide solution (Scheme 2). The structure of each of the macrocycles was confirmed by the appearance of the parent peaks corresponding to the molecular ion peak in their mass spectra. Moreover, all new formazans showed the expected characteristic signals in their ^1H NMR spectra.

EXPERIMENTAL

All melting points are uncorrected. The IR spectra (KBr) were recorded with a Unicam SP 1200 infrared spectrophotometer. The NMR spectra were measured in $CDCl_3$ on a Varian Gemini 200 Spectrometer (200 MHz). The UV spectra were recorded in dioxan on a Perkin Elmer Lambda 4B UV/VIS spectrophotometer. Mass spectra were determined on Finigan Mat 312, or GCMS-QP 1000 EX (70 eV) instruments. Microanalyses were carried out at the Microanalytical Centre, Cairo University. The starting compounds **1** [20], **2,3** [21,22], **14,15** [23], and **19–21** [9,15] were prepared as described previously.

1,5-Diaryl-3-methane(or arene)sulfonylformazans **4–11**

General Procedure. A solution of the appropriate aromatic amine (10 mmol) in water (5 mL) and HCl (3 mL, 10N) was diazotized at −5°C with a solution of $NaNO_2$ (0.8 g) in water (5 mL) during 5 minutes. This was then added to a solution of the appropriate pyruvate **1–3** (5 mmol) in ethanol (10 mL) containing NaOAc (2 g) or to the arenesulfonylacetic acid **14,15** (5 mmol) in aqueous NaOH (10 mL, 15%) dropwise with stirring over a period of 10 minutes at 0–5°C. The reaction mixture was then kept in the freezer for about 12 hours. The solid that had precipitated was collected and crystallized from ethanol (in the case of **4,5**) or acetic acid to give red crystals of the corresponding formazan derivative **4–11**.

1,5-Diphenyl-3-methanesulfonylformazan (**4**). MP 182–184°C (95%); ^{1}H NMR δ 3.33 (s, 3H, CH_3SO_2), 7.26–7.7 (m, 10H, ArH's), 14.95 (s, 1H, NH) ppm. Calcd for $C_{14}H_{14}N_4O_2S$: C, 55.61, H, 4.67, N, 18.53; S, 10.60. Found: C, 55.30; H, 5.00; N, 18.20; S, 10.90.

1,5-Di-p-tolyl-3-methanesulfonylformazan (**5**). MP 180–182°C (60%); ^{1}H NMR δ 2.4 (s, 6H, CH_3Ar), 3.32 (s, 3H, CH_3SO_2), 7.27–7.55 (m, 8H, ArH's), 15.03 (s, 1H, NH) ppm. Calcd for $C_{16}H_{18}N_4O_2S$: C, 58.16; H, 5.49; N, 16.96; S, 9.70. Found: C, 57.80; H, 5.70; N, 17.20; S, 9.90.

1,5-Di-p-methoxyphenyl-3-methanesulfonylformazan (**6**). Mp 165–167°C (58%), ^{1}H NMR δ 3.26 (s, 3H, CH_3SO_2), 3.87 (s, 6H, OCH_3), 6.97–7.62 (m, 8H, ArH's), 15.03 (s, 1H, NH) ppm. Calcd for $C_{16}H_{18}N_4O_4S$: C, 53.02; H, 5.00; N, 15.46; S, 8.85. Found: C, 52.70; H, 5.30; N, 15.60; S, 9.10.

1,5-Di-p-tolyl-3-benzenesulfonylformazan (**7**). Mp 200–202°C (Ref. [19] mp 200°C) (60% from **2**, 70% from **14**).

1,5-Di-p-methoxyphenyl-3-benzenesulfonylformazan (**8**). Mp 175–177°C (Ref. [18] mp 176°C) (60% from **2**, 69% from **14**).

1,5-Diphenyl-3-p-toluenesulfonylformazan (**9**). Mp 160–162°C (Ref. [20] mp 159–60°C) (70% from **3**, 64% from **15**).

1,5-Di-p-tolyl-3-toluenesulfonylformazan (**10**). Mp 197–199°C (61% from **3**, 66% from **15**); ^{1}H NMR δ 2.39 (s, 6H, $C\underline{H}_3C_6H_4N$), 2.42 (s, 3H, $C\underline{H}_3C_6H_4SO_2$), 7.21–8.03 (m, 12H, ArH's), 15.0 (s, 1H, NH) ppm. Calcd for $C_{22}H_{22}N_4O_2S$: C, 65.00; H, 5.46; N, 13.78; S, 7.89. Found: C, 64.70; H, 5.80; N, 13.40; S, 8.10.

1,5-Di-p-methoxyphenyl-3-p-toluenesulfonylformazan (**11**). Mp 157–159°C (55% from **3**, 58% from **15**); ^{1}H NMR δ 2.41 (s, 3H, $C\underline{H}_3Ar$), 3.63 (s, 6H, OCH_3), 6.92–8.0 (m, 12H, ArH's), 15.03 (s, 1H, NH) ppm. Calcd for $C_{22}H_{22}N_4O_4S$: C, 60.26; H, 5.06; N, 12.78; S, 7.31. Found: C, 59.90; H, 5.40; N, 13.00; S, 7.60.

Synthesis of Macrocyclic Crown Formazans 25–32

General Procedure. A solution of the appropriate diamine dihydrochloride **19–21** (1 mmol) in water (5 mL) and HCl (3 mL, 10N) was diazotized at −5°C with a solution of sodium nitrite (0.23 g in 5 mL of water) during 1/2 hour. Stirring was continued for 1 hour at −5°C and then added dropwise with stirring to a solution containing the appropriate pyruvate **1–3** (1 mmol in 10 mL of ethanol containing 2 g of NaOAc) or arenesulfonylacetic acid **14,15** (1 mmol in 10 mL of water containing 1.5 g of NaOH) over a period of 1 hour. The reaction mixture was then kept in the freezer for about 12 hours. After acidification with HCl (1N), the solid that precipitated was collected and purified on preparative TLC using silica gel (60 F_{254}) with the proper eluent for each derivative.

16,17-Dihydro-5H,15H-7-methanesulfonyldibenzo[b,i][1,11,4,5,7,8]dioxatetraazacyclotetradecine (**25**) was purified using dichloromethane as an eluent (R_f = 0.70, red spot) mp 200–202°C (6%); Ms: *m/z* 374 (M^+, 62.2%); UV: λ_{max} (log ε_{max}) = 482 nm (4.24); IR: 1308, 1158 (SO_2) cm^{-1}; ^{1}H NMR δ 2.64 (quintet, 2H, $CH_2C\underline{H}_2CH_2$), 3.59 (s, 3H, CH_3SO_2), 4.66 (t, 4H, $OC\underline{H}_2CH_2$), 7.26–8.19 (m, 8H, ArH's), 15.84 (s, 1H, NH) ppm. Calcd for $C_{17}H_{18}N_4O_4S$: C, 54.53; H, 4.85; N, 14.96; S, 8.56. Found: C, 54.20; H, 5.00; N, 14.70; S, 8.20.

16,17-Dihydro-5H,15H-7-benzenesulfonyldibenzo[b,i][1,11,4,5,7,8]dioxatetraazacyclotetradecine (**26**) was purified using dichloromethane as an eluent (R_f = 0.8, red spot) mp 267–269°C (5% from **14**, 9% from **2**); Ms: *m/z* 436 (M^+, 52%); UV: λ_{max} (log ε_{max}) = 482 nm (4.2); IR: 1312, 1157 (SO_2) cm^{-1}; ^{1}H NMR δ 2.35 (quintet, 2H, $CH_2C\underline{H}_2CH_2$), 4.36 (t, 4H, $OC\underline{H}_2CH_2$), 6.9–8.14 (m, 13H, ArH's), 15.54 (s, 1H, NH) ppm. Calcd for $C_{22}H_{20}N_4O_4S$: C, 60.54; H, 4.62; N, 12.84; S, 7.35. Found: C, 60.20; H, 4.40; N. 12.90; S, 7.60.

16,17-Dihydro-5H,15H-7-*p*-toluenesulfonyldibenzo[b,i][1,11,4,5,7,8]dioxatetraazacyclotetradecine (**27**) was purified using dichloromethane as an eluent (R_f = 0.73, red spot) mp 264–266°C (4% from **3**, 10% from **15**); Ms: *m/z* 450 (M^+, 44%); UV: λ_{max}(log ε_{max}) = 483 nm (4.24); IR: 1312, 1156 (SO_2) cm^{-1}; ^{1}H NMR δ 2.34 (quintet, 2H, $CH_2C\underline{H}_2CH_2$), 2.39 (s, 3H, CH_3), 4.36 (t, 4H, $OC\underline{H}_2CH_2$), 6.90–8.02 (m, 12H, ArH's), 15.50 (s, 1H, NH) ppm. Calcd for $C_{23}H_{22}N_4O_4S$: C, 61.32; H, 4.92; N, 12.44; S, 7.11. Found: C, 61.10; H, 4.60; N, 12.10; S, 6.80.

16-Methylene-16,17-dihydro-5H,15H-7-benzenesulfonyldibenzo[b,i][1,11,4,5,7,8]dioxatetraazacyclotetradecine (**28**) was purified using dichloromethane as an eluent (R_f = 0.77, red spot) mp 250–252°C (4.5% from **2**, 8.5% from **14**); Ms: *m/z* 448 (M^+, 33%); UV: λ_{max} (log ε_{max}) = 481 nm (4.15); IR: 1312, 1156 (SO_2) cm^{-1}; ^{1}H NMR δ 4.79 (s, 4H, OCH_2), 5.54 (s, 2H, $=CH_2$) 7.0–8.1 (m, 13H, ArH's), 15.60 (s, 1H, NH) ppm. Calcd for $C_{23}H_{20}N_4O_4S$: C, 61.59; H, 4.49; N, 12.49; S, 7.15. Found: C, 61.30; H, 4.20; N, 12.70; S, 6.90.

16-Methylene-16,17-dihydro-5H,15-7-*p*-toluenesulfonyldibenzo[b,i][1,11,4,5,7,8]dioxatetraazacyclotetradecine (**29**) was purified using dichloromethane as an eluent (R_f = 0.77, red spot) mp 252–254°C (4% from **3**, 9.5% from **15**); Ms: *m/z* 462 (M^+, 16%); ^1H NMR δ 2.39 (s, 3H, CH_3), 4.79 (s, 4H, OCH_2), 5.54 (s, 2H, $=CH_2$), 7.0–8.02 (m, 12H, ArH's), 15.59 (s, 1H, NH) ppm. Calcd for $C_{24}H_{22}N_4O_4S$: C, 62.32; H, 4.79; N, 12.11; S, 6.93. Found: C, 62.60; H, 4.90; N, 11.80; S, 6.80.

5,21-Dihydro-11H-13-methanesulfonyltribenzo-[b,i,m][1,11,4,5,7,8]dioxatetraazacyclopentadecine (**30**) was purified using dichloromethane as an eluent (R_f = 0.66, red spot) mp 233–235°C (7%); Ms: *m/z* 436 (M^+, 43%); UV: λ_{max} (log ε_{max}) = 479.8 nm (4.21); IR: 1311, 1157 (SO_2) cm^{-1}; ^1H NMR δ 3.27 (s, 3H, CH_3SO_2), 5.37 (s, 4H, OCH_2), 7.0–7.8 (m, 12H, ArH's), 15.66 (s, 1H, NH) ppm. Calcd for $C_{22}H_{20}N_4O_4S$: C, 60.54; H, 4.62; N, 12.84; S, 7.35. Found: C, 60.20; H, 4.90; N, 13.00; S, 7.50.

5,21-Dihydro-11H-13-benzenesulfonyltribenzo-[b,i,m][1,11,4,5,7,8]dioxatetraazacyclopentadecine (**31**) was purified using dichloromethane as an eluent (R_f = 0.8, red spot) mp 184–186°C (5% from **2**, 8% from **14**), Ms: *m/z* 498 (M^+, 33%); UV: λ_{max}(log ε_{max}) = 480 nm (4.21); IR: 1310, 1156 (SO_2) cm^{-1}; ^1H NMR δ 5.30 (s, 4H, OCH_2), 6.9–8.1 (m, 17H, ArH's), 15.6 (s, 1H, NH) ppm. Calcd for $C_{27}H_{22}N_4O_4S$: C, 65.06; H, 4.45; N, 11.24; S, 6.43. Found: C, 64.70; H, 4.20; N, 11.50; S, 6.10.

5,21-Dihydro-11H-13-*p*-toluenesulfonyltribenzo[b,i,m][1,11,4,5,7,8]dioxatetraazacyclopentadecine (**32**) was purified using dichloromethane as an eluent (R_f = 0.83, red spot) mp 227–229°C (4% from **3**), 11% from **15**) Ms: *m/z* 512 (M^+, 17%); UV: λ_{max} (log ε_{max}) = 480 nm (4.16); IR: 1311, 1157 (SO_2) cm^{-1}; ^1H NMR δ 2.38 (s, 3H, CH3), 5.31 (s, 4H, OCH_2), 7.0–7.9 (m, 16H, ArH's), 15.5 (s, 1H, NH) ppm. Calcd for $C_{28}H_{24}N_4O_4S$: C, 65.61; H, 4.72; N, 10.93; S, 6.26. Found: C, 65.30; H, 4.50; N, 11.20; S, 5.90.

REFERENCES

[1] Y. A. Ibrahim, A. H. M. Elwahy, A. A. Abbas, *Tetrahedron, 50,* 1994, 11489.

[2] Yu. A. Zolotov, N. V. Niz'eva, P. V. Iono, V. M. Dziomko, V. M. Ostrovskaya, I. A. D'yakonova, *Otkrytiya, Izobret., Prom. Obraztsy, Tovamye Znaki,* 1983, 16; *Chem. Abstr., 100,* 1984, 158896.

[3] N. V. Niz'eva, V. P. Ionov, I. V. Pletnev, D. M. Kumina, V. M. Ostrovskaya, I. A. D'yakonova, Yu. A. Zolotov, *Dokl. Akad. Nauk SSSR, 274,* 1984, 611; *Chem. Abstr., 101,* 1984, 47705.

[4] Yu. A. Zolotov, V. P. Ionov, A. V. Bodnyav, G. A. Larikova, N. V. Niz' eva, G. E. Vlasova, E. V. Rybakova, *Zr. Anal. Khim., 37,* 1982, 1543; *Chem. Abstr., 98,* 1983, 78972.

[5] N. V. Isakova, Yu. A. Zolotov, V. P. Ionov, *Zr. Anal. Khim., 44,* 1989, 1045; *Chem. Abstr., 112,* 1990, 47893.

[6] I. C. Lin, M. Pirio, U.S. Patent 4,742,010; *Chem. Abstr., 110,* 1989, 88600.

[7] V. M. Dziomko, V. M. Ostrovskaya, T. E. Zhukova, Yu. S. Ryabokobylko, *Zh. Obshch. Khim., 51,* 1981, 2324; *Chem. Abstr., 96,* 1982, 52283.

[8] R. V. Sitnikova, A. N. Krylova, *Lab. Delo.,* 1980, 142; *Chem. Abstr., 93,* 1980, 21812.

[9] E. Yu. Misionzhnik, M. G. Uzbekov, V. M. Ostrovskaya, G. I. Sitnikova, G. Ya. Avrutskii, A. A. Neduva, I. I. Ettinger, *Lab. Delo.,* 1990, 19; *Chem. Abstr., 114,* 1991, 135424.

[10] A. S. Attiyat, Y. A. Ibrahim, G. D. Christain, *Microchem. J., 37,* 1988, 114.

[11] A. S. Attiyat, Y. A. Ibrahim, G. D. Christain, *Microchem. J., 37,* 1988, 122.

[12] R. V. Sitnikova, A. N. Krylova, S. L. Zelichenok, V. M. Dziomko, V. M. Ostrovskaya, T. E. Zhukova, E. I. Tolmacheva, *Zr. Anal. Khim., 37,* 1982, 611; *Chem. Abstr., 97,* 1982, 174017.

[13] G. D. Christian, *Lithium, 3,* 1990, 181.

[14] V. M. Ostrovskaya, G. I. Sitnikova, I. A. D'yakonova, Yu. S. Ryabokobylko, V. M. Dziomko, R. V. Sitnikova, G. Ya. Avrutskii, A. A. Neduva, E. Yu. Misionzhnik, *Otkrytiya, Izobret.,* 1989, 185; *Chem. Abstr., 111,* 1989, 224523.

[15] M. S. Kravchenko, V. M. Ostrovskaya, M. Sh. Fumarova, *Vysokochist. Veshchestva,* 1990, 52; *Chem. Abstr., 114,* 1991, 239405.

[16] A. R. Katritzky, S. A. Belyakov, H. D. Durst, *Tetrahedron Lett., 35,* 1994, 6465.

[17] J. Troger, A. Berndt, *J. Prakt. Chem., 102,* 1921, 1.

[18] A. S. Shwali, A. L. Elansari, *Bull. Soc. Chem. Jpn., 47,* 1974, 2627.

[19] V. M. Neplyuev, M. G. Lekar, R. G. Dubenko, P. S. Pel Kis, *Ukr. Khim. Zh., 10,* 1974, 311.

[20] M. P. Sokolov, G. E. Avakyan, *Zr. Org. Khim., 22,* 1986, 721; *Chem. Abstr., 106,* 1987, 83975.

[21] Yu. S. Andreichikov, A. L. Fridman, V. L. Gein, E. I. Pidemskii, *Khim. Farm. Zh., 11,* 1977, 85; *Chem. Abstr., 88,* 1978, 22837.

[22] Yu. S. Andreichikov, A. L. Fridman, V. L. Gein, L. F. Gein, *Zr. Org. Khim., 13,* 1977, 2070; *Chem. Abstr., 88,* 1978, 120741.

[23] S. Gabriel, *Chem. Ber., 14,* 1881, 833.