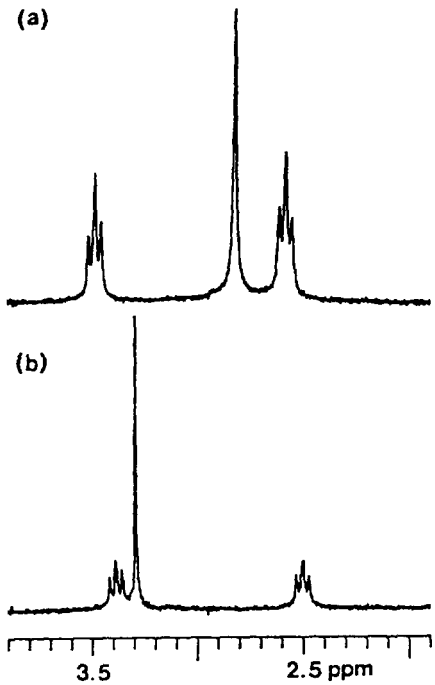


Figure 4. ^{1}H NMR spectra of D_2O solutions containing ethylenediamine and $BW_{11}Co$ in (a) 1 : 2 mole ratio at pH = 7.6, and (b) 2 : 1 mole ratio at pH = 8.0. Chemical shifts in ppm from TMS. The singlet at 3.29 ppm is attributed to the free ligand.

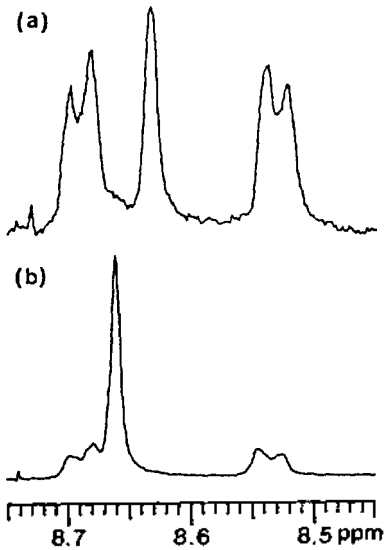


Figure 5. ^{1}H NMR spectrum of a D_2O solutions containing pyrazine and $BW_{11}Co$ in (a) 1 : 2 and (b) 4 : 1 mole ratio at pH = 6.9. Chemical shifts in ppm from TMS.

When these ligands are coordinated to the heteropolyanions, the 2-H lines are always shifted upfield. Heteropolyanions exhibit some difference in the ability to form dumbbell-shaped 1 : 2 ligand-heteropolyanion complexes: $BW_{11}Co$ forms 1 : 2 complexes better than $SiW_{11}Co$ does. These bidentate ligands may be useful in preparing extended systems from appropriate cobalt complexes.

Acknowledgment. The financial support of the Korea Science and Engineering Foundation is gratefully acknowledged. The use of an NMR spectrometer is financially supported by the Organic Chemistry Research Center.

References

1. T. J. R. Weakley, H. T. Evans, Jr., J. S. Showell, G. F. Tourné, and C. M. Tourné, *J. Chem. Soc., Chem. Commun.*, 139 (1973).
2. R. G. Finke, M. Droege, J. R. Hutchinson, and O. Gansow, *J. Amer. Chem. Soc.*, **103**, 1587 (1981).
3. W. H. Knoth, P. J. Domaille, and R. L. Harlow, *Inorg. Chem.*, **25**, 1577 (1986).
4. M. Ko, G. I. Rhyu, and H. So, *Bull. Korean Chem. Soc.*, **14**, 519 (1993).
5. T. J. R. Weakley and S. A. Malik, *J. Inorg. Nucl. Chem.*, **29**, 2935 (1967).
6. T. J. R. Weakley, *J. Chem. Soc., Dalton*, 341 (1973).
7. L. C. W. Baker and J. S. Figgis, *J. Amer. Chem. Soc.*, **92**, 3794 (1970).
8. E. Pretsch, J. Seibl, W. Simon, and T. Clerc, *Tables of Spectral Data for Structure Determination of Organic Compounds*, 2nd Ed., Springer-Verlag, Berlin, 1989, p. H275.

A Convenient Synthesis of *N*-Alkyl-*N'*-(1-carboalkoxyalkyl)sulfamides

Chai-Ho Lee, Jin Soo Song, Young-Haeng Lee, Won Sik Choi†, and Bong Young Chung*

Department of Chemistry, Won Kwang University, Iri 570-479
†Department of Genetic Engineering, Soon Chun Hyang University, Asan, Chungnam 337-880
**Department of Chemistry, Korea University, Seoul 136-701, Korea*

Received July 23, 1993

3-Oxo-1,2,5-thiadiazolidine 1,1-dioxides(**3**) which can be easily obtained by the cyclization of *N*-(1-carboalkoxyalkyl)sulfamides **2** under the basic condition have been found to possess some pharmacological properties.[1] Three procedures have been reported for the preparation of **2**; successive reactions of chlorosulfonyl isocyanate with formic acid or benzyl alcohol followed by α-amino acid alkyl esters,[2] treatment of α-amino acid alkyl esters with sulfamoyl chloride,[3] and ethanolysis of 3-imino-1,2,5-thiadiazolidine 1,1-dioxides.[4] These methods are, however, very tedious and complicated.

We now wish to report a new method to prepare the unsymmetrical sulfamides **2** from 2-hydroxyphenyl *N*-alkylsulfamates **1** which are easily obtainable from catechol sulfate and alkylamines by DuBois' procedure.[5] Reaction of sulfamates **1** with various α-amino acid alkyl esters in the presence of *N,N*-dimethylaminopyridine (DMAP) in refluxing dioxane afforded the unsymmetrical sulfamides **2** in excellent to good yields. When DMAP was absent, the yield was quite low. This route thus represents a very convenient and general method to prepare unsymmetrical *N*-alkyl-*N'*-arylsulfamides which are valuable key intermediates for many heterocycles

containing N-SO_2-N moiety.[6]

Experimental

General Methods. Infrared spectra were obtained on a Perkin Elmer 710B spectrophotometer and NMR spectra were recorded on Bruker AC 100(100 MHz) and JMN-EX 400(400 MHz) FT NMR spectrometers. Chemical shifts(δ) are given in ppm relative to TMS. Reagents and solvents were used without further purification.

General Procedure for the Preparation of 2-Hydroxyphenyl Sulfamates 1.[5]

To a DMF (10 m*l*) solution of amine (3.0 mmol) and triethylamine (0.30 g, 3.0 mmol) was added methylene chloride (3.0 m*l*) solution of catechol sulfate (0.50 g, 3.0 mmol) dropwise with vigorous stirring at 0℃ for 2 hr under dry nitrogen. The solution was poured into a 1% aqueous HCl solution (100 m*l*) and the precipitate was filtered and dried to give **1** as a white solid.

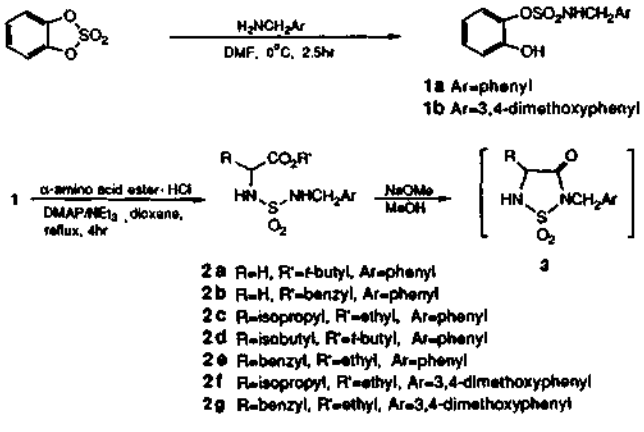
2-Hydroxyphenyl *N*-Benzylsulfamates(1a). From benzylamine (0.32 g) **1a** was obtained in 93% yield (0.75 g): mp. 116-118℃ (lit.[5a] mp. 116.5-117.5℃); IR (KBr) 1155, 1355, 3240, 3385 cm^{-1}; ^{1}H-NMR ($CDCl_3$) δ 4.27 (d, 2H, J=6.0 Hz), 6.75 (t, 2H, J=6.0 Hz), 7.20-7.50 ppm (m, 9H).

2-Hydroxyphenyl *N*-(3,4-Dimethoxybenzyl)sulfamates(1b). From 3,4-dimethoxybenzylamine(0.50 g) **1b** was obtained in 97% yield (0.99 g); mp. 82-84℃ (lit.[5c] mp. 78-80 ℃); IR (KBr) 1180, 1370, 3235, 3385 cm^{-1}; ^{1}H-NMR ($CDCl_3$) δ 3.72 (s, 6H), 4.22 (d, 2H, J=6.1 Hz), 5.80-6.15 (m, 2H), 6.70-7.20 ppm (m, 8H).

General Procedure for the Amination of Sulfamates 1

A dry dioxane (5 m*l*) solution containing **1** (1.00 mmol), α-amino acid alkyl ester hydrochloride (1.10 mmol), triethylamine (1.10 mmol) and DMAP (0.15 mmol) was refluxed for 4 hr under dry nitrogen, allowed to cool and poured into a 5% aqueous HCl solution (50 m*l*). The solid product was recrystallized from ethanol and the oily product was purified by column chromatography.

***N*-Benzyl-*N'*-carbo-*t*-butoxymethylsulfamide (2a).** Reaction of **1a** with glycine *t*-butyl ester hydrochloride gave **2a** in 61% yield; mp. 115-117℃; IR (KBr) 1160, 1350, 1730, 3300 cm^{-1}; ^{1}H-NMR ($CDCl_3$) δ 1.46 (s, 9H), 3.70 (s, 2H), 4.26 (s, 2H), 4.70 (brd s, 1H), 4.90 (brd s, 1H), 7.30 ppm (s, 5H). ^{13}C-NMR (DMSO-d_6) δ 25.64, 45.01, 47.05, 83.54, 127.31, 128.03, 129.30, 138.47, 169.13 ppm.



***N*-Benzyl-*N'*-carbobenzyloxymethylsulfamide(2b).** Reaction of **1a** with glycine benzyl ester hydrochloride gave **2b** in 53% yield; mp. 112-114℃; IR (KBr) 1140, 1330, 1728, 3250 cm^{-1}; ^{1}H-NMR ($CDCl_3$) δ 3.84 (d, 2H, J=5.2 Hz), 4.22 (d, 2H, J=4.8 Hz), 4.78 (t, 2H, J=5.2 Hz), 5.07 (t, 1H, J=4.8 Hz), 5.18 (s, 2H), 7.24-7.35 ppm (m, 10H). ^{13}C-NMR (DMSO-d_6) δ 44.31, 47.16, 66.92, 127.11, 127.96, 128.09, 128.13, 128.22, 128.34, 136.72, 138.06, 169.92 ppm.

***N*-Benzyl-*N'*-(1-carbethoxyisobutyl)sulfamide(2c).** Reaction of **1a** with valine ethyl ester hydrochloride gave **2c** in 85% yield; mp. 48-49℃; $[\alpha]_D^{20}$ = +2.1 (c=2.28, $CHCl_3$); IR (KBr) 1140, 1340, 1735, 3325 cm^{-1}; ^{1}H-NMR ($CDCl_3$) δ 0.98 (d, 3H, J=6.8 Hz), 1.06 (d, 3H, J=6.4 Hz), 1.13 (t, 3H, J=7.0 Hz), 2.05-2.18 (m, 1H), 3.90 (dd, 1H, J=4.8, 6.8 Hz), 4.16-4.24 (m, 4H), 4.49 (t, 1H, J=5.6 Hz), 5.09 (d, 1H, J=6.8 Hz), 7.22-7.31 ppm (m, 5H). ^{13}C-NMR (DMSO-d_6) δ 14.64, 17.92, 18.25, 32.06, 46.52, 62.01, 62.64, 127.17, 127.64, 128.11, 138.12, 172.49 ppm.

***N*-Benzyl-*N'*-(1-carbo-*t*-butoxyisopentyl)sulfamide(2d).** Reaction of **1a** with leucine *t*-butyl ester hydrochloride gave **2d** in 76% yield; mp. 110-112℃; $[\alpha]_D^{20}$ = −5.0° (c=2.0, $CHCl_3$); IR (KBr) 1120, 1330, 1720, 3350 cm^{-1}; ^{1}H-NMR ($CDCl_3$) δ 0.93 (d, 6H, J=6.5 Hz), 0.99 (d, 3H, J=6.1 Hz), 1.47 (s, 9H), 1.43-1.52 (m, 2H), 1.72-1.91 (m, 1H), 3.83-3.96 (m, 1H), 4.21 (d, 2H, J=5.3 Hz), 4.86 (t, 1H, J=5.3 Hz), 5.32 (d, 1H, J=6.2 Hz), 7.23-7.37 ppm (m, 5H). ^{13}C-NMR ($CDCl_3$) δ 22.24, 23.22, 25.02, 28.39, 42.53, 47.73, 55.69, 82.87, 128.27, 128.53, 129.14, 137.30, 173.33 ppm.

***N*-Benzyl-*N'*-(1-carbethoxyphenethyl)sulfamide(2e).** Reaction of **1a** with phenylalanine ethyl ester hydrochloride gave **2a** as an oil in 68% yield; $[\alpha]_D^{20}$ = −4.4° (c=2.00, $CHCl_3$); IR (KBr) 1150, 1340, 1730, 3320 cm^{-1}; ^{1}H-NMR ($CDCl_3$) δ 1.18 (t, 3H, J=7.2 Hz), 2.99-3.11 (m, 2H), 3.78-4.02 (m, 1H), 4.03-4.28 (m, 4H), 4.70 (t, 1H, J=5.1 Hz), 5.19 (m, 1H, J=6.2 Hz), 7.12-7.35 ppm (m, 10H), ^{13}C-NMR (DMSO-d_6) δ 14.52, 39.45, 47.44, 57.70, 62.33, 127.74, 128.32, 128.43, 128.95, 129.11, 130.02, 136.12, 137.05, 172.40 ppm.

***N*-(1-Carbethoxyisobutyl)-*N'*-(3,4-dimethoxybenzyl) sulfamide(2f).** Reaction of **1b** with valine ethyl ester hydrochloride gave **2f** as an oil in 67% yield; $[\alpha]_D^{20}$ = +1.8° (c=1.20, $CHCl_3$); IR (KBr) 1160, 1320, 1720, 3260 cm^{-1}; ^{1}H-NMR ($CDCl_3$) δ 0.88 (d, 3H, J=6.8 Hz), 1.03 (d, 3H, J=6.6 Hz), 1.17 (t, 3H, J=7.0 Hz), 1.95-2.02 (m, 1H), 3.82 (dd, 1H, J=5.5, 7.2 Hz), 3.85 (s, 3H), 3.86 (s, 3H), 4.08-4.25 (m, 4H), 4.73 (t, 1H, J=5.1 Hz), 5.21 (d, 1H, J=7.2 Hz), 6.78-6.86 ppm (m, 3H). ^{13}C-NMR ($CDCl_3$) δ 14.63, 17.94, 19.51, 31.78, 47.61, 56.37, 61.76, 62.10, 111.69, 111.73, 120.77, 129.56, 149.21, 149.62, 172.87 ppm.

***N*-(1-Carbethoxyphenethyl)-*N'*-(3,4-dimethoxybenzyl)sulfamide(2g).** Reaction of **1b** with phenylalanine ethyl ester hydrochloride gave **2g** in 88% yield; mp. 52-54℃; $[\alpha]_D^{20}$ = +7.0° (c=0.47, $CHCl_3$); IR (KBr) 1160, 1370, 1728, 3250 cm^{-1}; ^{1}H-NMR ($CDCl_3$) δ 1.02 (t, 3H, J=7.0 Hz), 2.93 (m, 2H), 3.65-3.88 (m, 1H), 3.72 (s, 3H), 3.73 (s, 3H), 3.92-4.03 (m, 2H), 4.11-4.19 (m, 2H), 5.22 (t, 1H, J=5.0 Hz), 5.53 (d, 1H, J=6.3 Hz), 6.63-6.71 (m, 3H), 7.10-7.11 ppm (m, 5H). ^{13}C-NMR ($CDCl_3$) δ 14.69, 39.02, 47.24, 56.52, 58.01, 61.98, 112.71, 112.75, 120.11, 127.08, 128.91, 130.11, 130.45, 147.52, 139.01, 139.83, 177.25 ppm.

Acknowledgement. This research was supported by the Korea Science and Engineering Foundation (Grant No.

911-0302-001-2).

References

1. (a) J. L. Archibald, D. R. Beardsley, T. J. Ward, J. F. Waterfall, and J. F. White, *J. Med. Chem.*, **26**, 416 (1983); (b) A. A. Algieri, G. M. Luke, R. T. Standridge, M. Brown, R. A. Partyka, and R. R. Crenshew, *J. Med. Chem.*, **25**, 211 (1982); (c) P. Goya, R. Nieves, and C. Ochoa, *Rev. R. Acad. Cienc. Exactas, Fis. Nat. Madrid*, **78**, 373 (1984); *Chem. Abstr.*, **104**, 207234r (1986); (d) J. A. Kloek and K. L. Leschinsky, *J. Org. Chem.*, **43**, 3824 (1978); (e) C.-H. Lee and H. Kohn, *J. Pharm. Sci.*, **79**, 716 (1990).
2. (a) G. W. Muller and G. E. DuBois, *J. Org. Chem.*, **54**, 4471 (1989); (b) G. Dewynter, N. Aouf, M. Criton, and J.-L. Montero, *Tetrahrdron*, **49**, 65 (1993).
3. (a) J. W. Timberlake, W. J. Ray, and E. D. Stevens, *J. Org. Chem.*, **54**, 5824 (1989); (b) B. Unterhalt and G.-A. Hanewacker, *Arch. Pharm. (Weinheim)*, **321**, 749 (1988).
4. (a) C.-H. Lee, J. D. Korp, and H. Kohn, *J. Org. Chem.*, **54**, 3077 (1989); (b) C.-H. Lee, S.-Y. Jin, C. Y. Lee, and B. Y. Chung, *Bull. Korean Chem. Soc.*, **13**, 8 (1992).
5. (a) G. E. DuBois and R. A. Stephenson, *J. Org. Chem.*, **45**, 5371 (1980); (b) G. E. DuBois, *J. Org. Chem.*, **45**, 5373 (1980); (c) C.-H. Lee, M. S. Lee, Y. H. Lee, and B. Y. Chung, *Bull. Korean Chem. Soc.*, **13**, 357 (1992).
6. (a) CIBA Ltd., *Belg. Patent* 640,160, May 19 (1964); *Chem. Abstr.*, **62**, 16134e (1965); (b) G. E. DuBois, *J. Org. Chem.*, **45**, 5374 (1980); (c) E. Ziegler and W. Ruf, *Naturforsch*, **30B**, 951 (1975).