An Improved Procedure for the Synthesis of 4,4-Disubstituted-3-oxo-1,2,5-thiadiazolidine 1,1-Dioxides

Zejun Xiao and Jack W. Timberlake*

Department of Chemistry, University of New Orleans, New Orleans, LA 70148 USA

Received July 30, 1999

An improved synthesis for the preparation of 3-oxo-1,2,5-thiadiazolidine 1,1-dioxides has been developed. This facile two-step procedure from α-amino acid esters and chlorosulfonyl isocyanate results in excellent yields of products.

J. Heterocyclic Chem., **37**, 773 (2000).

Introduction.

Sulfahydantoins, 3-oxo-1,2,5-thiadiazolidine 1,1-dioxides, have been studied for their potentially useful pharmacological properties and industrial utility [1,2]. They are structurally related to 2,4-imidazolidinediones (hydantoins), which are well known for their diverse chemical reactivity and biological activity, particularly as anticonvulsant drugs for the management of epilepsy. Sulfahydantoins are also functionally related to sweeteners (*e.g.*, sodium saccharin and potassium acesulfam) [2], and known herbicides (*e.g.*, bentazon) [3]. These compounds contain the common sulfonimide functional group, which provides the fundamental activity in saccharin and acesulfam-K. Thus, studies toward biological and industrial use of sulfahydantoins are attractive.

Results and Discussion.

Synthesis of α-Amino Acid Esters.

Condensation of carbonyl compounds, potassium cyanide, and ammonium carbonate in acetamide at high temperature results in the formation of hydantoins (Scheme 1) [4]. A series of 5,5-disubstituted hydantoins **1** were synthesized by the use of this modified Bucherer-Bergs reaction (Table 1). Generally, good yields of hydantoins were obtained.

Transformation of carbonyl derivatives to α-amino acids **2** can be achieved *via* hydrolysis of the corresponding hydantoins in the presence of concentrated aqueous base [5]. Hydrolysis of hydantoins (**1a**, **1b**, **1c**) gave good to excellent yields of the corresponding α-amino acids **2**.

α-Amino acids **2** were converted to the corresponding esters **3** by following the conventional approach using anhydrous alcohols and gaseous hydrogen chloride [5]. Experiments demonstrated that prolonged passage of hydrogen chloride with the addition of small amounts of sodium sulfate to the suspension of α-amino acids in the alcohols led to an increase in reaction yields. However, attempts to convert α-amino acids to the corresponding esters utilizing aqueous hydrochloric acid in 2,2-dimethoxypropane have proven unsuccessful [6].

Table 1

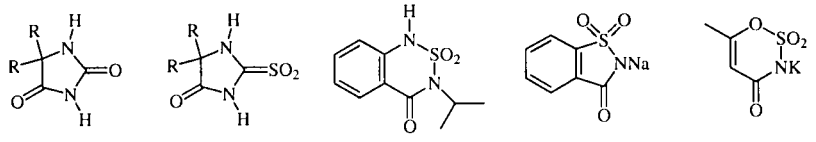
Synthesis of Hydantoins, α-Amino Acids **2** and α-Amino Acid Esters **3**

R1	R2	Yield (%)	Yield (%)	Yield (%)
4-methylphenyl	phenyl	66, **1a**	94, **2a**	55, **3a**
4-methylphenyl	4-methylphenyl	85, **1b**	99, **2b**	43, **3b**
4-chlorophenyl	4-chlorophenyl	96, **1c**	53, **2c**	49, **3c**

An Improved Synthesis of 3-Oxo-1,2,5-thiadiazolidine 1,1-Dioxides.

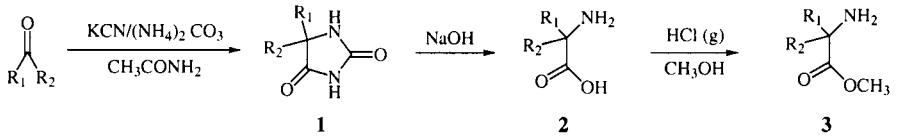
While a wide variety of methods for the synthesis of hydantoins are known, only a few synthetic routes to sulfahydantoins have been reported. A three-step procedure for the preparation of 4-monosubstituted-3-oxo-1,2,5-thiadiazolidin-1,1-dioxides was described by Kohn and co-workers [7]. The first step in this sequence was modeled after the Strecker [8] synthesis of hydantoins, in which a mixture of an aldehyde, a metal cyanide, and excess sulfamide in aqueous ethanol is refluxed to produce the corresponding 3-imino-1,2,5-thiadiazolidine 1,1-dioxide. However, this methodology is limited to 4-monosubstituted sulfahydantoins.

We previously described a general synthesis of 4,4-disubstituted sulfahydantoins [9], but the reaction conditions were not optimized, and overall yields were low. We suspected that thermal decomposition of *N*-carboalkoxysulfamoyl chloride at reflux induced side reactions, and/or addition of triethylamine and esters to the reaction mixture

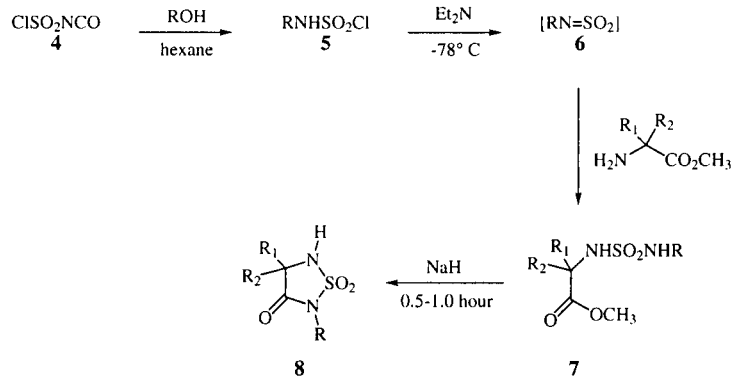


Hydantoin | Sulfahydantoin | Bentazon | Sodium saccharin | Acesulfam-K

Scheme 1



Scheme 2



at room temperature resulted in partial polymerization of *N*-sulfonylamine and gave low yields of the desired sulfamides. Thus, an improved synthetic procedure was devised to overcome these unfavorable features. The key improvement involves heating the reaction mixture of chlorosulfonyl isocyanate **4** and alcohols to only slightly above room temperature (less than 40° C) to produce sulfamoyl chloride **5**, followed by *in situ* generation and trapping of *N*-sulfonylamine **6** with triethylamine and α-amino acid esters at -78° C. One advantage of conducting the reaction at lower temperature is to prevent the side reaction of polymerization of **6** [10]. Subsequent treatment of sulfamides **7** with sodium hydride in tetrahydralfuran at room temperature, instead of prolonged heating, readily affords high yields of sulfahydantoins **8**. Generally, cyclization of **7** is achieved within one hour (Scheme 2). Note: Methyl 2,2-spiro {Dibenzo[*a,d*][1,4]cycloheptadiene-5} amino acid ester was prepared through a three step synthesis starting with dibenzosuberone [11].

The improved procedure results in the formation of good to excellent yields of sulfamides **7** and sulfahydantoins **8** (Table 2). However, sulfamide **7k** was obtained in low yield, presumably due to steric effects.

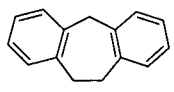
IR and NMR Spectra Analysis.

The carbonyl stretching frequencies in **7** observed at 1724-1741 cm^{-1} are higher than those of **8**, 1700-1739 cm^{-1}. Both sets of compounds show the diagnostic strong absorption bands at 1331-1393 cm^{-1} and 1137-1186 cm^{-1} for the sulfonyl group. The ^1H nmr peak position for amide protons in sulfamides **7** is located at 2.72-3.86 and 5.90-6.70 (ppm). The ^1H chemical shifts for the ester

Table 2

Yields of **7** and **8**

R_1	R_2	R	Yield (%)	Yield(%)
phenyl	phenyl	H	86, **7a**	82, **8a**
phenyl	phenyl	*t*-Bu	82, **7b**	91, **8b**
phenyl	phenyl	benzhydryl	95, **7c**	98, **8c**
4-methylphenyl	phenyl	*t*-Bu	79, **7d**	84, **8d**
4-methylphenyl	phenyl	benzhydryl	94, **7e**	98, **8e**
4-methylphenyl	4-methylphenyl	*t*-Bu	86, **7f**	95, **8f**
4-methylphenyl	4-methylphenyl	benzhydryl	93, **7g**	91, **8g**
4-chlorophenyl	4-chlorophenyl	*t*-Bu	87, **7h**	92, **8h**
spiro{Dibenzo[*a,d*][1,4]cycloheptadiene-5}		H	75, **7i**	82, **8i**
spiro{Dibenzo[*a,d*][1,4]cycloheptadiene-5}		*t*-Bu	92, **7j**	96, **8j**
spiro{Dibenzo[*a,d*][1,4]cycloheptadiene-5}		benzhydryl	38, **7k**	98, **8k**

a = 

groups range between 3.73-3.77 ppm, except that the proton signal of the ester groups of *N*-Spiro{Dibenzo-[*a,d*][1,4]cycloheptadiene-5}sulfamides comes around 3.55 ppm. Also, It should be noted that small upfield shifts for the hydrogens on cyclic amide groups are observed in comparison with the corresponding protons in open chain sulfamides **7**. The ^{13}C signals for the carbonyl groups in the esters **7** appear at lower field than those in the amides **8**.

EXPERIMENTAL

The nmr spectra were recorded on a Varian spectrometer operating at 300 MHz for ^{1}H and 75 MHz for ^{13}C in deuteriochloroform with either chloroform (7.26 ppm ^{1}H, 77.00 ppm ^{13}C) or tetramethylsilane as a reference peak. Coupling constants, J, are reported in Hz. Ir spectra were recorded on a Magna-IR^{TM} spectrometer 550. Elemental analyses were performed by Atlantic Microlab Inc. Norcross, GA.

All commercially available chemicals were purchased from Aldrich Chemical Company, Milwaukee, WI. *n*-Butyllithium was titrated before use [12]. THF and ether were freshly distilled from sodium/benzophenone. All reactions were carried out under an argon atmosphere in oven dried (140°) glassware.

General Experimental Procedure for the Preparation of Sulfamides (**7**).

In a 50 mL three-neck round bottom flask equipped with a gas inlet was placed chlorosulfonyl isocyanate (564 mg, 4 mmoles) and 5.0 mL of hexane. A solution of alcohol (4.00 mmoles, 2 equivalents) in hexane (5.0 mL) was added dropwise. The reaction mixture was warmed slightly above room temperature until the white suspension disappeared and bubbling stopped. The reaction mixture was cooled to –78°, and a solution of the ester **3** (2 mmoles) and triethylamine (0.55 mL, 4.0 mmoles) was added. The resultant mixture was stirred for 0.5 hour at –78°. Then, after removing the dry ice bath, the reaction mixture was further stirred over 2 hours and quenched with 20 mL of water. The aqueous layer was extracted with ether (3 x 30 mL), the combined organic layers dried over sodium sulfate, and evaporated to afford a crude product, which was purified by column chromatograph to give product **7**.

N-Diphenylmethyl-*N'*-[1,1-diphenyl-1-(methoxycarbonyl)-methyl]sulfamide (**7c**).

This compound was obtained as white power solid, mp 127-128°; ir (potassium bromide): 1741, 1335, 1156 cm^{-1}; ^{1}H nmr: 3.74 (s, 3H, OCH_3), 3.82 (d, 1H, J = 6.0 Hz), 5.44 (d, 1H, J = 6.0 Hz), 5.90 (s, 1H), 7.16-7.31 ppm (m, 20H, Ph); ^{13}C nmr: 53.5, 61.8, 71.7, 127.0, 127.4, 127.8, 128.1, 128.5, 128.9, 138.2, 141.2, 172.1 ppm.

Anal. Calcd. for $C_{28}H_{26}N_2O_4S$: C, 69.11; H, 5.40; N, 5.76. Found: C, 69.24; H, 5.36; N, 5.77.

N-tert-Butyl-*N'*-[1-phenyl-1-(4-methylphenyl)-1-(methoxycarbonyl)methyl]sulfamide (**7d**).

This compound was obtained as power solid, mp: 149-150°; ir (potassium bromide): 1735, 1393, 1138 cm^{-1}; ^{1}H nmr: 1.05 (s, 9H, *t*-Butyl), 2.35 (s, 3H, CH_3), 2.74 (s, 1H, *N-t*-Butyl), 3.75 (s, 3H, OCH_3), 6.05 (s, 1H, NH), 7.17 (d, 2H, J = 7.8, Ph), 7.30-7.40 (m, 5H, Ph), 7.50-7.53 ppm (m, 2H, Ph); ^{13}C nmr: 21.0, 29.3, 53.6, 53.7, 70.9, 128.0, 128.3, 128.7, 129.4. 135.4, 138.3, 138.5, 172.6 ppm.

Anal. Calcd. for $C_{20}H_{26}N_2O_4S$: C, 61.50; H, 6.72; N, 7.17. Found: C, 61.61; H, 6.75; N, 7.07.

N-Diphenylmethyl-*N'*-[1-phenyl-1-(4-methylphenyl)-1-(methoxycarbonyl)methyl]sulfamide (**7e**).

This compound was obtained as white solid, mp 97-98°; ir (potassium bromide): 1734, 1332, 1158 cm^{-1}; ^{1}H nmr: 2.25 (s, 3H, CH_3), 3.72 (d, 1H, J = 5.4 Hz), 3.75 (s, 3H, OCH_3), 5.41 (d, 1H, J = 4.8 Hz), 5.98 (s, 1H), 6.96 (d, 2H, J = 7.8, Ph), 7.15-7.40 ppm (m, 17H, Ph); ^{13}C nmr: 20.8, 53.4, 61.9, 71.4, 127.3, 127.8, 128.2, 128.4, 128.9, 129.2, 129.3, 135.5, 138.5, 138.7, 141.8, 172.6 ppm.

Anal. Calcd. for $C_{29}H_{28}N_2O_4S$: C, 69.57; H, 5.64; N, 5.60. Found: C, 69.46; H, 5.91; N, 5.39.

N-tert-Butyl-*N'*-[1,1-bis(4-methylphenyl)-1-(methoxycarbonyl)-methyl]sulfamide (**7f**).

This compound was obtained as white solid, mp 175-176°; ir (potassium bromide): 1740, 1392, 1190, 1137 cm^{-1}; ^{1}H nmr: 1.07 (s, 9H, *t*-Butyl), 2.35 (s, 6H, CH_3), 2.77 (s, 1H, *N-t*-Butyl), 3.75 (s, 3H, OCH_3), 6.06 (s, 1H, NH), 7.17 (d, 4H, J = 7.1 Hz, Ph), 7.40 ppm (dd, 4H, J = 6.6, 1.8 Hz, Ph); ^{13}C nmr: 20.9, 29.2, 53.5, 53.6, 70.6, 128.6, 129.2, 135.5, 138.2, 172.7 ppm.

Anal. Calcd. for $C_{21}H_{28}N_2O_4S$: C, 62.34; H, 6.99; N, 6.93. Found: C, 62.22; H, 6.99; N, 6.85.

N-Diphenylmethyl-*N'*-[1,1-bis(4-methylphenyl)-1-(methoxycarbonyl)methyl]sulfamide (**7g**).

This compound was obtained as white solid, mp 160-161°; ir (potassium bromide): 1735, 1333, 1159 cm^{-1}; ^{1}H nmr: 2.24 (s, 6H, CH_3), 3.61 (d, 1H, J = 5.1 Hz), 3.73 (s, 3H, OCH_3), 5.35 (d, 1H, J = 5.1 Hz), 5.98 (s, 1H, NH), 6.96 (d, 4H, J = 7.8 Hz, Ph), 7.15-7.40 ppm (m, 14H, Ph); ^{13}C nmr: 20.9, 53.5, 62.0, 71.1, 126.9, 127.4, 128.5, 128.8, 135.2, 138.1, 141.5, 172.4 ppm.

Anal. Calcd. for $C_{30}H_{30}N_2O_4S$: C, 70.00; H, 5.89; N, 5.44. Found: C, 69.46; H, 5.91; N, 5.39.

N-tert-Butyl-*N'*-[1,1-bis(4-chlorophenyl)-1-(methoxycarbonyl)-methyl]sulfamide (**7h**).

This compound was obtained as white solid, mp 189-190°; ir (potassium bromide): 1739, 1593, 1368, 1198, 1138 cm^{-1}; ^{1}H nmr: 1.10 (s, 9H, *t*-Butyl), 2.93 (s, 1H, *N-t*-Butyl), 3.76 (s, 3H, OCH_3), 6.04 (s, 1H, NH), 7.34 (d, 4H, J = 9.0 Hz, Ph), 7.42 ppm (d, 4H, J = 8.4 Hz, Ph); ^{13}C nmr: 29.3, 53.9, 54.0, 70.3, 128.2, 130.79, 134.7, 136.5, 171.7 ppm.

Anal. Calcd. for $C_{19}H_{22}N_2O_4SCl_2$: C, 51.23; H, 4.98; N, 6.29. Found: C, 51.14; H, 4.99; N, 6.20.

N-{1-spiro(dibenzo[*a,d*]cycloheptadiene-5)-1-(methoxycarbonyl)methyl}sulfamide (**7i**).

This compound was obtained as white solid, mp 168-170°; ir (potassium bromide): 1735, 1344, 1164 cm^{-1}; ^{1}H nmr: 3.05-3.17 (m, 2H), 3.21-3.30 (m, 2H), 3.50 (s, 2H, NH_2), 3.58 (s, 3H, OCH_3), 6.74 (s, 1H, NH), 7.10-7.30 (m, 6H, Ph), 7.53 ppm (d, 2H, J = 7.5 Hz, Ph); ^{13}C nmr: 36.3, 53.9, 71.8, 126.6, 128.2, 130.1, 130.5, 136.8, 143.3, 173.1 ppm.

Anal. Calcd. for $C_{17}H_{18}N_2O_4S$: C, 58.94; H, 5.25; N, 8.09. Found: C, 58.86; H, 5.30; N, 7.99.

N-tert-Butyl-*N'*-{1-spiro(dibenzo[*a,d*]cycloheptadiene-5)-1-(methoxycarbonyl)methyl}sulfamide (**7j**).

This compound was obtained as white solid, mp 168-170°; ir (potassium bromide): 1724, 1362 (m), 1334 (s), 1173 cm^{-1}; ^1H nmr: 1.13 (s, 9H, *t*-Butyl), 3.01 (s, 1H, *N-t*-Butyl), 3.05-3.17 (m, 2H), 3.24-3.34 (m, 2H), 3.53 (s, 3H, OCH_3), 6.70 (s, 1H, NH), 7.18-7.30 (m, 6H, Ph), 7.56 ppm (d, 2H, J = 7.6 Hz, Ph); ^{13}C nmr: 29.3, 36.1, 53.6, 53.8, 71.7, 126.2, 127.7, 130.0, 130.2, 137.2, 143.1, 173.3 ppm.

Anal. Calcd. for $C_{21}H_{26}N_2O_4S$: C, 62.65; H, 6.52; N, 6.96. Found: C, 62.55; H, 6.52; N, 6.91.

N-Diphenylmethyl-*N'*-{1-spiro(dibenzo[*a,d*]cycloheptadiene-5)-1-(methoxycarbonyl)methyl}sulfamide (**7k**).

This compound was obtained as white solid, mp 168-170°; ir (potassium bromide): 1735, 1334, 1164 cm^{-1}; ^1H nmr: 3.00-3.10 (m, 2H), 3.17-3.30 (m, 2H), 3.50 (s, 3H, OCH_3), 3.86 (d, 1H, J = 6.0 Hz), 5.36 (d, 1H, J = 6.0 Hz), 6.59 (s, 1H, NH), 6.90-7.00 (m, 2H, Ph), 7.10-7.36 ppm (m, 16H, Ph); ^{13}C nmr: 36.2, 53.8, 61.3, 72.0, 126.3, 127.1, 127.5, 127.8, 128.6, 129.8, 130.3, 137.2, 141.5, 143.2, 173.2 ppm.

Anal. Calcd. for $C_{30}H_{28}N_2O_4S$: C, 70.28; H, 5.52; N, 5.47. Found: C, 70.15; H, 5.43; N, 5.46.

General Experimental Procedure for the Synthesis of 4,4-Disubstituted-1,2,5-thiadiazolidin-3-one 1,1-Dioxides (**8**).

To a solution of the sulfamide **7** (1 mmole) and 10 mL of THF was added portionwise sodium hydride (57% oil dispersion, 63 mg, 1.5 mmoles). The reaction mixture was stirred 1 hour at room temperature. The reaction was quenched by 1% aqueous hydrochloric acid solution, and the aqueous layer was extracted with ether (3 x 10 mL). The combined extracts were dried with sodium sulfate, and evaporated under vacuum. The crude product was chromatographed on silica gel to give pure product **8**.

4,4-Diphenyl-2-diphenylmethyl-1,2,5-thiadiazolidin-3-one 1,1-Dioxide (**8c**).

This compound was obtained as white solid, mp 168-170°; ir (potassium bromide): 1739, 1384, 1186 cm^{-1}; ^1H nmr: 5.11 (s, 1H, NH), 6.39 (s, 1H, CH), 7.30-7.45 ppm (m, 20H, Ph); ^{13}C nmr: 62.8, 73.7, 127.2, 127.7, 128.4, 128.9, 130.0, 130.3, 135.9, 137.9, 168.3 ppm.

Anal. Calcd. for $C_{27}H_{22}N_2O_3S$: C, 71.34; H, 4.89; N, 6.16. Found: C, 71.42; H, 4.87; N, 6.21.

2-*tert*-Butyl-4-phenyl-4-(4-methylphenyl)-1,2,5-thiadiazolidin-3-one 1,1-Dioxide (**8d**).

This compound was obtained as white solid, mp 154-155°; ir (potassium bromide): 1727, 1396, 1332, 1165 cm^{-1}; ^1H nmr: 1.64 (s, 9H, *t*-Butyl), 2.35 (s, 3H, CH_3), 5.00 (s, 1H, NH), 7.15-7.5 ppm (m, 9H, Ph); ^{13}C nmr: 21.1, 27.0, 61.5, 72.8, 121.7, 127.5, 128.7, 128.9, 129.5, 135.8, 138.6, 139.0, 169.9 ppm.

Anal. Calcd. for $C_{19}H_{22}N_2O_3S$: C, 63.83; H, 6.17; N, 7.78. Found: C, 63.70; H, 6.20; N, 7.75.

2-Diphenylmethy-4-Phenyl-4-(4-methylphenyl)-1,2,5-thiadiazolidin-3-one 1,1-Dioxide (**8e**).

This compound was obtained as white solid, mp 209-210°; ir (potassium bromide): 1708, 1343, 1178 cm^{-1}; ^1H nmr: 2.37 (s, 3H, CH_3), 5.18 (s, 1H, NH), 6.41 (s, 1H, CH), 7.15-7.5 ppm (m, 19H, Ph); ^{13}C nmr: 21.0, 62.7, 73.6, 127.4, 128.2, 128.4, 128.8, 129.5, 135.2, 136.0, 139.0, 168.6 ppm.

Anal. Calcd. for $C_{28}H_{24}N_2O_3S$: C, 71.92; H, 5.17; N, 5.99. Found: C, 71.57; H, 5.35; N, 5.85.

2-*tert*-Butyl-4-bis(4-methylphenyl)-1,2,5-thiadiazolidin-3-one 1,1-Dioxide (**8f**).

This compound was obtained as white solid, mp 168-169°; ir (potassium bromide): 1728, 1396, 1331, 1173 cm^{-1}; ^1H nmr: 1.63 (s, 9H, *t*-Butyl), 2.34 (s, 6H, CH_3), 5.00 (s, 1H, NH), 7.17 (d, 4H, J = 7.8 Hz, Ph), 7.32 ppm (d, 4H, J = 7.8 Hz, Ph); ^{13}C nmr: 21.1, 27.0, 61.4, 72.7, 127.4, 129.5, 135.7, 138.9, 170.1 ppm.

Anal. Calcd. for $C_{20}H_{24}N_2O_3S$: C, 64.48; H, 6.51; N, 7.52. Found: C, 64.40; H, 6.49; N, 7.54.

2-Diphenylmethyl-4-bis(4-methylphenyl)-1,2,5-thiadiazolidin-3-one 1,1-Dioxide (**8g**).

This compound was obtained as white solid, mp 183-184°; ir (potassium bromide): 1709, 1341, 1177 cm^{-1}; ^1H nmr: 2.35 (s, 6H, CH_3), 5.08 (s, 1H, NH), 6.38 (s, 1H, CH), 7.15 (d, 4H, J = 7.1 Hz, Ph), 7.25-7.33 (m, 19H, Ph); ^{13}C nmr: 21.0, 62.8, 73.6, 127.5, 128.4, 128.8, 129.6, 135.3, 135.9, 137.9, 139.1, 168.4.

Anal. Calcd. for $C_{29}H_{26}N_2O_3S$: C, 71.02; H, 5.23; N, 5.81. Found: C, 71.10; H, 5.21; N, 6.06.

2-*tert*-Butyl-4-bis(4-chlorophenyl)-1,2,5-thiadiazolidin-3-one 1,1 Dioxide (**8h**).

This compound was obtained as white solid, mp 138-139°; ir (potassium bromide): 1731, 1337, 1175 cm^{-1}; ^1H nmr: 1.61 (s, 9H, *t*-Butyl), 5.19 (s, 1H, NH), 7.36 ppm (s, 8H, Ph); ^{13}C nmr: 27.0, 61.9, 71.8, 129.1, 130.0, 135.5, 136.6, 169.1 ppm.

Anal. Calcd. for $C_{18}H_{18}N_2O_3SCl_2$: C, 52.30; H, 4.40; N, 6.78. Found: C, 52.41; H, 4.42; N, 6.68.

4-Spiro(dibenzo[*a,d*]cycloheptadiene-5')-1,2,5-thiadiazolidin-3-one 1,1-Dioxide (**8i**).

This compound was obtained as white solid, mp 219-220°; ir (potassium bromide): 1727, 1345, 1173, 1160 cm^{-1}; ^1H nmr: 3.04 (m, 2H, CH_2), 3.46 (m, 2H, CH_2), 5.50 (BR, 1H, NH), 7.20-7.35 (m, 6H, Ph), 7.60-7.70 (m, 2H, Ph), 9.40 (br, 1H, NH); ^{13}C nmr: 34.7, 77.6, 126.7, 129.1, 129.6, 131.3, 137.0, 143.0, 172.5. MS: 314.1, 235.1, 220.1, 207.1, 180.1, 165.1, 91.1, 64.0.

Anal. Calcd. HRMS for $C_{16}H_{14}N_2O_3S$: 314.07252. Found: 314.07255.

2-*tert*-Butyl-4-spiro(dibenzo[*a,d*]cycloheptadiene-5')-1,2,5-thiadiazolidin-3-one 1,1-Dioxide (**8j**).

This compound was obtained as white solid, mp 192-193°; ir (potassium bromide): 1700, 1341, 1173 cm^{-1}; ^1H nmr: 1.79 (s, 9H, *t*-Butyl), 3.04 (m, 2H, CH_2), 3.46 (m, 2H, CH_2), 5.47 (s, 1H, NH), 7.15-7.31 (m, 6H, Ph), 7.50 ppm (d, 2H, J = 7.2 Hz); ^{13}C nmr: 27.2, 34.2, 61.7, 74.5, 126.6, 128.3, 129.3, 131.3, 135.1, 142.4, 170.48 ppm.

Anal. Calcd. for $C_{20}H_{22}N_2O_3S$: C, 64.83; H, 6.00; N, 7.56. Found: C, 64.66; H, 5.95; N, 7.52.

2-Diphenylmethyl-4-spiro(dibenzo[*a,d*]cycloheptadiene-5')-1,2,5-thiadiazolidin-3-one 1,1-Dioxide (**8k**).

This compound was obtained as white solid, mp 247-248°; ir (potassium bromide): 1726, 1382 cm^{-1}; ^1H nmr: 3.04 (m, 2H,

CH_2), 3.46 (m, 2H, CH_2), 5.32 (s, 1H, NH), 6.53 (s, 1H, CH), 7.10-7.50 ppm (m, 18H, Ph); ^{13}C nmr: 34.0, 63.2, 126.7, 128.6, 129.3, 129.6, 131.5, 134.4, 135.9, 142.4, 169.02 ppm.

Anal. Calcd. for $C_{16}H_{14}N_2O_3S$: C, 72.47; H, 5.04; N, 5.83. Found: C, 71.86; H 4.97; N, 5.78.

REFERENCES AND NOTES

[1a] W.C. Groutas, R. Kuang and R. Venkataraman, *Biochem. Biophys. Res. Comm.*, **194**, 341 (1994); [b] B. Unterhalt and G. A. Hanewacker, *Arch. Pharm.*, **321**, 375 (1988).

[2] G. W. Muller and G. E. DuBois, *J. Org. Chem.*, **54**, 4471 (1989).

[3] H. J. Sanders, *Chem. Eng. News*, 20 (1981).

[4a] H. R. Henze and L. M. Long, *J. Am. Chem. Soc.*, **63**, 1941 (1941); [b] H. R. Henze and R. J. Speer, *J. Am. Chem. Soc.*, **64**, 522 (1942);. [c] H. R. Henze and A. F. Isbell, *J. Am. Chem. Soc.*, **76**, 4152 (1954).

[5] P. D. Skelly, W. J. Ray and J. W. Timberlake, *J. Org. Chem.*, **50**, 267 (1985).

[6] J. R. Rachele, *J. Org. Chem.*, **28**, 2898 (1963).

[7] C. H. Lee, J. D. Korp and H. Kohn, *J. Org. Chem.*, **54**, 3077 (1989).

[8a] J. N. Coker, W. L. Kohlhase, A. O. Rogers and G. G. Allan, *J. Org. Chem.*, **84**, 3077 (1962); [b] D. D. I. Ugi, *Angew, Chem. Int. Ed. Engl.*, **1**, 8 (1962).

[9] J. W. Timberlake, W. J. Ray, E. D. Stevens and C. L. Klein, *J. Org. Chem.*, **54**, 5824 (1989).

[10a] G. M. Atkins and E. M. Burgess, *J. Am. Chem. Soc.*, **94**, 6135 (1972); [b] G. M. Atkins and E. M. Burgess, *J. Am. Chem. Soc.*, **90**, 4745 (1968); [c] E. M. Burgess and W. M. Williams, *J. Org. Chem.*, **38**, 1249 (1973); [d] E. M. Burgess and W. M. Williams, *J. Am. Chem. Soc.*, **94**, 4386 (1972); [e] J. A. Kloek and K. L. Leschinsky, *J. Org. Chem.*, **44**, 305 (1979); [f] G. M. Atkins and E. M. Burgess, *J. Am. Chem. Soc.*, **89**, 2502 (1967).

[11a] B. Tao, Ph. D. Dissertation, University of New Orleans, 1997; [b] T. A. Dobson, M. A. Davis, A. M. Hartung and J. M. Manson, *Can. J. Chem.*, **46**, 2843 (1968); [c] S. Selman and J. F. Eastham, *J. Org. Chem.*, **30**, 3804 (1965).

[12] W. G. Kofron and L. M. Baclawski, *J. Am. Chem. Soc.*, **47**, 2002 (1925).