ordinates. In the final refinements anisotropic temperature factors were used for the carbon and oxygen atoms and isotropic temperature factors were used for the hydrogen and solvent atoms. The hydrogen atoms were included in the structure factor calculations at their calculated positions, and were not refined. Computer drawings were done by using ORTEP[18] (see Figure 4). The primary hydroxyl group in the E ring was found to be disordered, occupying two positions with an approximate relative weight of 0.6–0.4.

**Acknowledgment.** We are grateful to Dr. S. P. Hubbell (Department of Zoology, University of Iowa) for collection of the plant material. We thank the National Science Foundation for financial support (Grant No. DEB 8010638) and instrumentation awards for the purchase of mass (Grant No. CHE 8007937) and NMR (Grant No. CHE 8201836) spectrometers.

**Registry No.** **3a**, 64652-15-9; **3b**, 86782-62-9; **3c**, 86727-48-2; **3d**, 86783-77-9; **4a**, 86747-46-8; **4b**, 25671-04-9; **5**, 25671-07-2; **6a**, 86727-49-3; **6b**, 86727-50-6; **9**, 86727-51-7; **10**, 86727-52-8; **11a**, 86727-53-9; **11b**, 86727-54-0.

**Supplementary Material Available:** Table II listing the positional and thermal parameters in 3 (2 pages). Ordering information is given on any current masthead page.

(18) Johnson, C. K. "ORTEP: A Fortran Thermal Ellipsoid Plot Program for Crystal Structure Illustrations", Report ORNL-3794; Oak Ridge National Laboratory: Oak Ridge, TN, 1965.

# Studies on the Preparation and Reactions of Tritylsulfenimines[1]

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Carbonyl compounds react with stable, crystalline triphenylmethanesulfenamide ($TrSNH_2$, **4**) under mild conditions to form tritylsulfenimines **5** and **6**. Lithiation of acetone tritylsulfenimine (**5c**) at 0 °C led to a novel rearrangement–decomposition producing tritylacetone (**8**). Lithiated tritylsulfenimines were found to undergo temperature-dependent ambident alkylation reactions leading to carbon-alkylated products **9** at −78 °C and nitrogen-alkylated products **10** at −20 °C. Lithiated tritylsulfenimines **5** reacted with carbonyl compounds at −78 °C to form adducts **11** from which the sulfenimine could be hydrolytically cleaved under mild conditions ($AgNO_3/H_2O$–THF), thus effecting "directed aldol" condensation. Tritylsulfenimines **5** and **6** were reduced with $NaBH_3CN$ under mildly acidic conditions to form stable triphenylmethanesulfenamides **13** and **14**.

The sulfenamide functional group[3] has until recently not been exploited for synthetic purposes. Davis has developed a preparation of phenylsulfenimines, useful as secondary imine equivalents, which does not rely on the isolation of the intermediate primary sulfenamide **1**.[4,5] The scope of Davis' reaction is somewhat limited; for example, the phenylsulfenimine of crotonaldehyde cannot be prepared due to the polymerization of crotonaldehyde under the reaction conditions.[4a] Nevertheless, Davis' work demonstrated that the sulfenimine functional group could be useful for the construction of nitrogen-containing molecules and that the potential utility of the sulfenimine group could not be fully realized with phenylsulfenimines.

It seemed that utilization of a stable, isolable primary sulfenamide could greatly extend the scope of sulfenamide-based synthetic methodology. Many primary sulfenamides are known[3] although not all qualify as stable, isolable substances. Many preparations which should in principle lead to the formation of the primary sulfenamide often lead instead to the formation of the apparently more stable corresponding sulfenimide **2** (eq 1).

$$\underset{X=Cl,Br,SR\ldots etc.}{RSX} \xrightarrow{NH_3} \underset{\underline{1}}{RSNH_2} \longrightarrow \underset{\underline{2}}{\tfrac{1}{2}(RS)_2NH} + \tfrac{1}{2}NH_3 \qquad (1)$$

We describe in this and the accompanying paper various studies on the preparation and reactions of triphenylmethanesulfenamides and tritylsulfenimines and applications (1) of tritylsulfenimines for carbon–carbon bond-forming alkylation, (2) of tritylsulfenimines for "directed aldol" condensation, (3) of tritylsulfenimines and triphenylmethanesulfenamides for reductive amination of carbonyl compounds, and (4) of triphenylmethanesulfenamides for the protection of nitrogen.

## Results and Discussion

Our attention was focused upon triphenylmethanesulfenamide ($TrSNH_2$, **4**) as a stable primary sulfenamide. Crystalline **4** can be easily prepared (eq 2) by a modification of the original preparation[6] from crystalline, commercially available trityl mercaptan (TrSH) via crystalline

$$Ph_3CSH = TrSH \xrightarrow{SO_2Cl_2} \underset{\underline{3}}{TrSCl} \xrightarrow{NH_4OH} \underset{\underline{4}}{TrSNH_2} \qquad (2)$$

(1) Taken from the Ph.D. thesis of B.P.B., Harvard University, 1981.

(2) Present address: Department of Chemistry, Massachusetts Institute of Technology, Cambridge, MA 02139. Address correspondence to the Department of Chemistry, University of Oregon, Eugene, OR 97403.

(3) Reviews of sulfenamide chemistry include: (a) Davis, F. A.; Nadir, V. K. *Org. Prep. Proced. Int.* **1979**, *11*, 13. (b) Davis, F. A. *Int. J. Sulfur Chem.* **1973**, *8*, 71. (c) Kuhle, E. *Synthesis* **1971**, 617. (d) Brown, C.; Grayson, B. T. *Mech. React. Sulfur Compd.* **1970**, *5*, 93. (e) Riesz, E. *Bull. Soc. Chim. Fr.* **1966**, 1449. (f) Chabrier, P.; Renard, S. H. *Ibid.* **1950**, 13. (g) Kharasch, N.; et al. *Chem. Rev.* **1946**, *39*, 269. Primary sulfenamides not mentioned in review articles: (a) Davis, F. A., et al. *J. Org. Chem.* **1977**, *42*, 967. (b) Sartori, P.; Golloch, A. *Chem. Ber.* **1971**, *104*, 967. (c) Carr, E. L.; et al. *J. Org. Chem.* **1949**, *14*, 921. (d) Baltrop, J. A.; Morgan, K. J. *J. Chem. Soc.* **1957**, 3072. (e) Emeleus, H. J.; Haas, A. *Ibid.* **1963**, 1272. (f) Smith, G. E. P.; et al. *J. Org. Chem.* **1949**, *14*, 935. (g) Khromov-Broisov, N. V.; Kolesova, M. B. *J. Gen. Chem. USSR (Engl. Transl.)* **1955**, *25*, 361. (h) Greenbaum, S. B. *J. Am. Chem. Soc.* **1954**, *76*, 6052.

(4) (a) Davis, F. A.; et al. *J. Org. Chem.* **1973**, *38*, 2809. (b) David, F. A.; Manicinelli, P. *Ibid.* **1977**, *42*, 398. (c) Davis, F. A.; Mancinelli, P. *Ibid.* **1978**, *43*, 1797. (d) Davis, F. A.; Mancinelli, P. *Ibid* **1980**, *45*, 2597.

(5) Ommision of the carbonyl compound from Davis' reaction leads to the formation of bis(benzenesulfenimide). For bis(benzenesulfenimide) chemistry (see: (a) Mukaiyama, T.; Taguchi, T. *Tetrahedron Lett.* **1970**, 3411. (b) Mukaiyama, T.; Taguchi, T.; Nishi, M. *Bull. Chem. Soc. Jpn.* **1971**, *44*, 2797. (c) Lecher, H. *Chem. Ber.* **1925**, *58*, 409.

(6) Vorlander, D.; Mittag, E. *Chem. Ber.* **1919**, *52*, 413.

0022-3263/83/1948-3531$01.50/0 

Table I. Preparation of Tritylsulfenimines from the Corresponding Carbonyl Compounds

| entry | $R_1$ | $R_2$ | $R_3$ | tritylsulfenimine (isolated yield,[a] %) | mp,[b] °C |
|---|---|---|---|---|---|
| 1 | H | $CH_3$ | H | **5a** (96-97) | 110-111[c] |
| 2 | H | $(CH_2)_7CH_3$ | H | **5b** (98-100) | oil |
| 3 | $CH_3$ | H | H | **5c** (93-98) | 135-138[d] |
| 4 | $CH_3$ | $CH_3$ | H | **5d** (97) | 74.5-76[d] |
| 5 | | $-(CH_2)_4-$ | H | **5e** (96-99) | 140-141[e] |
| 6 | | $-(CH_2)_2CH(C(CH_3)_3)CH_2-$ | H | **5f** (92-99) | 110.5-111.5[c] |
| 7 | | $-(CH_2)_4-$ | $CH_3$ | **5g** (98) | 98-101[c] |
| 8 | $CH_3$ | $COOCH_3$ | H | **5h** (93) | 100-101[c] |
| 9 | $CH_3$ | $COOCH_2CH_3$ | H | **5i** (100) | oil |
| 10 | $CH_3$ | $(CH_2)_2OSi(CH_3)_2C(CH_3)_3$ | H | **5j** (70[f]) | oil |

[a] After filtration through Florisil. [b] Uncorrected. [c] Recrystallized by trituration from $CHCl_3$ with *t*-BuOH. [d] Recrystallized by trituration from THF with EtOH. [e] Recrystallized by trituration from THF with EtOH and then from $CHCl_3$ with pentane. [f] Modified procedure; see Experimental Section.

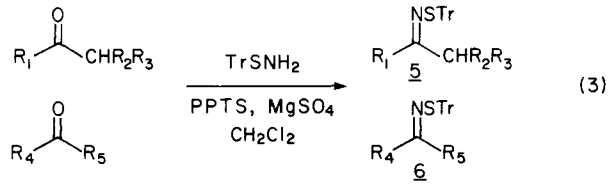
Table II. Preparation of Tritylsulfenimines from the Corresponding Carbonyl Compounds

| entry | $R_4$ | $R_5$ | tritylsulfenimine (isolated yield,[a] %) | mp,[b] °C |
|---|---|---|---|---|
| 1 | H | $CH=CHCH_3$ | **6a** (92-97) | 137-140[c] |
| 2 | H | $CH=C(CH_3)_2$ | **6b** (92) | 128-132[d] |
| 3 | H | Ph | **6c** (98-99) | 132-134[e] |
| 4 | H | 4-$CH_3OPh$ | **6d** (98) | 159-160[c] |
| 5 | $CH_3$ | $COOCH_3$ | **6e** (89) | 131-134[f] |
| 6 | $CH_3$ | Ph | **6f** (59[g]) | 141-145[c] |
| 7 | $-(CH_2)_3C(CH_3)=CH-$ | | **6g** (44[g]) | 147-150[h] |

[a] After filtration through Florisil. [b] Uncorrected. [c] Recrystallized by trituration from $CHCl_3$ with *t*-BuOH. [d] Crude product. [e] Recrystallized by trituration from $CHCl_3$ with EtOH. [f] Recrystallized by trituration from $CH_2Cl_2$ with $Et_2O$. [g] Modified procedure; see Experimental Section. [h] Recrystallized by trituration from $Et_2O$ with pentane.

triphenylmethanesulfenyl chloride (TrSCl, **3**). Both TrSCl and $TrSNH_2$ are air-stable substances which can be stored for months at room temperature.

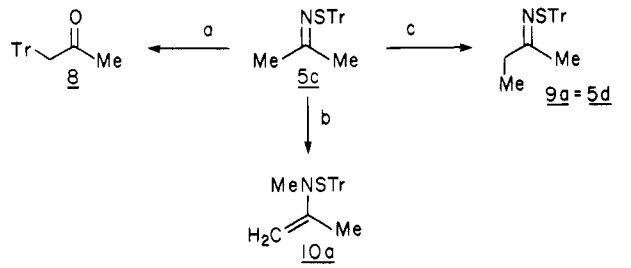
In reactions with carbonyl compounds to form imines, **4** is less reactive than the analogous hydroxylamines or hydrazines. Nevertheless, treatment of a carbonyl compound with **4** in $CH_2Cl_2$ with anhydrous $MgSO_4$ as a drying agent–catalyst and pyridinium *p*-toluenesulfonate (PPTS)[7] as a catalyst (eq 3) was found to be a general practical preparation of tritylsulfenimines **5** and **6** as shown in Tables I and II.




(3)

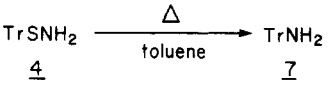
Under these conditions it is not possible to efficiently form the tritylsulfenimines of aromatic ketones or $\alpha,\beta$-unsaturated ketones in reasonable yields. This problem, apparently thermodynamic in nature, is also encountered in the synthesis of alkyl and aryl imines and dimethylhydrazones of aromatic and $\alpha,\beta$-unsaturated ketones.[8g,9b]

Scheme I[a]




[a] (a) (1) LDA/THF, 0 °C; 2 h; (2) $NH_4Cl/H_2O$. (b) (1) *sec*-BuLi/THF, −20 °C; (2) MeI, −20 °C. (c) (1) *sec*-BuLi/THF, −78 °C; (2) MeI, −78 °C.

Attempts to drive the reactions to completion were hampered by the instability of **4** to prolonged heating (eq 4) and to strong acid in nonhydroxylic solvents.




(4)

The tritylsulfenimine of acetophenone (**6f**) could be formed in modest yield (59%) by allowing the $CH_2Cl_2$ solution to reflux through $CaH_2$ in a Soxhlet extractor or Dean–Stark trap to remove $H_2O$. The tritylsulfenimine of 3-methylcyclohexenone (**6g**) was also prepared (44%) by using these modified conditions.

Several synthetic transformations are possible by utilizing metalated tritylsulfenimines as reactive intermediates. The course of various reactions of the tritylsulfenimine of acetone (**5c**) with strong bases illustrates its stability and reactivity under various conditions (Scheme I).

The decomposition of lithiated **5c** at 0 °C to form tritylacetone (**8**) after an aqueous extractive workup was clearly a temperature-dependent process since stable solutions of lithiated **5c** formed at lower temperatures (vide infra) produced **8** upon warming to near room temperature.

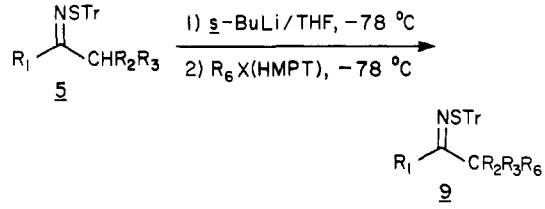
The reaction of lithiated tritylsulfenimines with highly reactive alkylating agents such as methyl iodide (MeI) or allyl iodide in THF at −78 °C to form carbon-alkylated products proceeded at a practical rate (eq 5, Table III). Reaction of lithiated **5c** with *n*-butyl bromide (*n*-BuBr) to form carbon-alkylated product **9b** was impractical at −78 °C in the absence of hexamethylphosphoric triamide (HMPT); the use of TMEDA or $Me_2SO$ was ineffective at significantly accelerating the rate of this reaction.

Carbon alkylation of a lithiated tritylsulfenimine followed by reduction of the sulfenimine to a sulfenamide

(7) Grieco, P. A.; et al. *J. Org. Chem.* **1977**, *42*, 3772.

(8) Representative works include: (a) Wittig, G. *Top. Curr. Chem.* **1976**, *67*, 1–14. (b) Normant, H.; et al. *Tetrahedron Lett.* **1976**, 1379. (c) Normant, H.; et al. *Synthesis*, **1975**, 256. (d) Reiff, H. In "Newer Methods of Preparative Organic Chemistry"; Foerst, W., Ed.; Verlag Chemie: New York, 1971; Vol. VI, pp 48–65. (e) Wittig, G.; Reiff, H. *Angew. Chem., Int. Ed. Engl.* **1968**, *7*, 7. (f) Stork, G.; Dowd, S. R. *J. Am. Chem. Soc.* **1963**, *85*, 2178. (g) Eissenstat, M. A. Ph.D. Thesis, Harvard University, 1978, pp 13–15, 20–22, 41–57 and references therein.

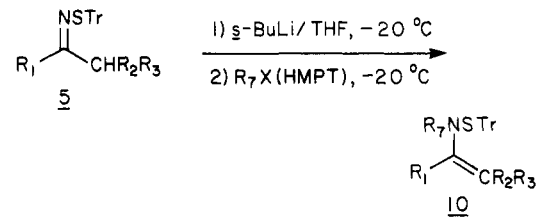
(9) (a) Ludwig, J. W.; Newcomb, M.; Bergbreiter, D. E. *J. Org. Chem.* **1980**, *45*, 4666. (b) Corey, E. J.; Enders, D. *Chem. Ber.* **1978**, *111*, 1337, 1362. (c) Corey, E. J.; Boger, D. L. *Tetrahedron Lett.* **1978**, 4597. (d) Normant, H.; et al. *Synthesis* **1976**, 237, 238.



(5)

(vide infra) and cleavage of the triphenylmethanesulfenamide to an amine (see accompanying paper) results in the overall formation of a carbon–carbon bond which, in terms of retrosynthetic analysis as a key bond relative to the nitrogen atom, is a key bond rarely formed with conventional amine synthetic methodology. The sequence of sulfenimine-mediated carbon–carbon bond formation followed by retention of the imine nitrogen in the final product through reduction of the carbon–nitrogen double bond to a single bond may prove to be a useful, general strategy for alkaloid synthesis.

When the temperature of an alkylation reaction of lithiated **5c** with *n*-BuBr in THF was raised to −20 °C in an attempt to accelerate the reaction while avoiding the use of HMPT, alkylation occurred on nitrogen. Nitrogen alkylation of lithiated **5c** with *n*-BuBr was favored with or without the introduction of TMEDA, HMPT, or $Me_2SO$. In general, lithiation of tritylsulfenimines **5** in THF at −20 °C followed by the addition of an alkylating agent, with HMPT in some cases, produced the nitrogen-alkylated product **10** (eq 6, Table IV) along with some



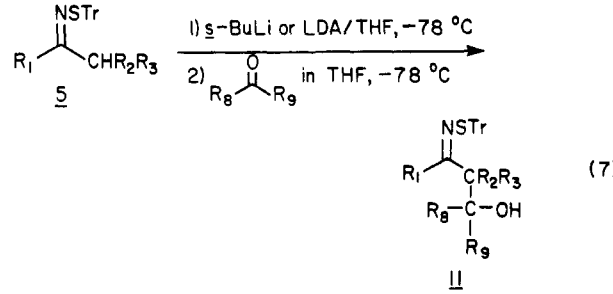
(6)

decomposition products (mainly tritylacetone or tritylbutanone by NMR). These results can be contrasted with the clean carbon monoalkylation observed at −78 °C.

The propensity for nitrogen vs. carbon alkylation appears in the one case examined in detail to be primarily determined by the temperatures to which the lithiated tritylsulfenimine had been exposed prior to the addition of the alkylating agent. Lithiation of **5c** at −78 °C in THF, as would be done for the carbon alkylation reaction, followed by warming to −20 °C, cooling to −78 °C, and addition of MeI produced significant, and sometimes predominant, amounts of the nitrogen alkylated product.

The ambident reactivity of lithiated tritylsulfenimines can be contrasted with the reactivity observed with the analogous aliphatic and aryl imines,[8] dimethylhydrazones,[9] and, in particular, phenylsulfenimines,[4c,d] which all undergo clean carbon alkylation under a variety of conditions. For example, Davis reported that the reaction of lithiated acetone phenylsulfenimine with MeI in $Et_2O$ at 0 °C to reflux led solely to the carbon-alkylated product in 95% yield.[4c] It is at present unclear what factors are important in determining the ambident reactivity of metalated imines.

Carbonyl electrophiles react almost instantaneously with lithiated tritylsulfenimines at −78 °C to generate "directed aldol" adducts[8a,d,e] **11** (eq 7, Table V). The tritylsulfenimine of propionaldehyde (**5a**) decomposed upon treatment with alkyllithium reagents at −78 °C; even rapid quenching with carbonyl electrophiles such as benzaldehyde and benzophenone did not produce any aldol adduct **11**. Lithium diisopropylamide (LDA) was found

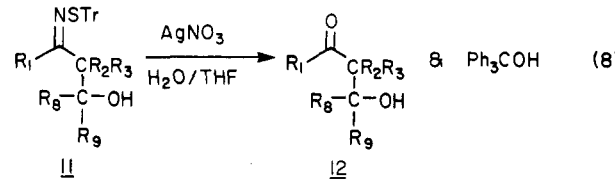


(7)

to deprotonate **5a** as desired to form, after reaction with benzophenone, the aldol adduct **11a**. This can be rationalized as preferential deprotonation at the $sp^2$ carbon by the highly reactive alkyllithium reagent followed by secondary decomposition reactions rather than deprotonation at the $sp^3$ carbon as desired. The deprotonation of dimethylhydrazones[1d] and phenylsulfenimines[4d] of aldehydes is complicated by two sites of deprotonation.

The hydrolysis of carbonyl derivatives such as oximes and hydrazones and their derivatives is usually kinetically facile but thermodynamically unfavorable and must be driven to completion. Attempted hydrolyses of the tritylsulfenimine group from "directed aldol" adducts **11** under various catalytic conditions resulted in rapid partial hydrolysis which was incomplete even after 24 h.

Treatment of tritylsulfenimine "directed aldol" adducts **11** with silver nitrate ($AgNO_3$), in this case apparently a mild metal-cation one-electron oxidant, in buffered aqueous THF at room temperature led to the corresponding carbonyl compound (eq 8, Table VI). The use

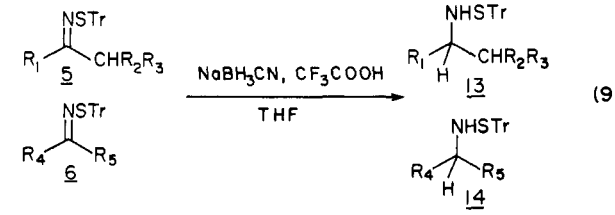


(8)

of a buffer is preferred since unbuffered reactions become acidic (pH 3). The use of $AgNO_3$ for this cleavage reaction was suggested by the observation that treatment of triphenylmethanesulfenamides with $AgNO_3$ led to the formation of a silver mirror and precipitate.

Various other oxidizing reagents were also surveyed for the hydrolysis of tritylsulfenimine **11c** since it possessed the potentially most sensitive functionality. Useful reagents include $HgCl_2$, $FeCl_3$, $HClO_4$, and $H_5IO_6$, which led to complete reaction within minutes. Nevertheless, $AgNO_3$ appears to be the best reagent in regard to efficiency, mildness of conditions, and compatibility of the reagent with numerous functional groups.

Tritylsulfenimines were found to be unreactive toward borohydride reduction under standard conditions ($NaBH_4$/THF–EtOH). Sodium cyanoborohydride ($NaBH_3CN$)[10] and trifluoroacetic acid under mildly acidic conditions (pH 3–6) in THF were found to reduce tritylsulfenimines **5** and **6** to the corresponding triphenylmethanesulfenamides **13** and **14** as shown in eq 9 and



(9)

(10) A review on $NaBH_3CN$: Lane, C. F. *Synthesis* **1975**, 135.

Table III. Carbon-Carbon Bond Formation by Alkylation of Lithiated Tritylsulfenimines at −78 °C

| starting tritylsulfenimine[b] | $R_2$ | $R_6$ | X | product tritylsulfenimine (isolated yield,[a] %) |
|---|---|---|---|---|
| 5c | H | $CH_3$ | I | 9a = 5d (~100) |
| 5c | H | $(CH_2)_3CH_3$ | Br | 9b (92) |
| 5c | H | $(CH_2)_2OSi(CH_3)_2C(CH_3)_3$ | Br | 9c = 5k (52-77) |
| 5k = 9c | $(CH_2)_2OSi(CH_3)_2C(CH_3)_3$ | $CH_2CH=CH_2$ | I | 9d (~100) |

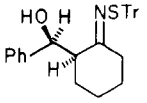
[a] See Experimental Section for details in each case. [b] $R_1 = CH_3$ and $R_3 = H$ in all cases.

Table IV. Carbon-Nitrogen Bond Formation by Alkylation of Lithiated Tritylsulfenimines at −20 °C

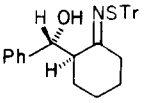
| starting tritylsulfenimine[b] | $R_1$ | $R_7$ | X | product tritylsulfenenamine (isolated yield,[a] %) |
|---|---|---|---|---|
| 5c | $CH_3$ | $CH_3$ | I | 10a (62) |
| 5c | $CH_3$ | $(CH_2)_3CH_3$ | Br | 10b (56) |
| 5c | $CH_3$ | $(CH_2)_2OSi(CH_3)_2C(CH_3)_3$ | Br | 10c (48) |
| 5d | $CH_2CH_3$ | $CH(CH_3)_2$ | I | 10d (63) |

[a] After chromatography on silica gel. [b] $R_2 = R_3 = H$ in all cases.

Table V. Formation of Directed Aldol Adducts by the Reaction of Lithiated Tritylsulfenimines with Carbonyl Electrophiles at −78 °C




11e

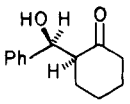



11f

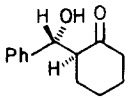
| starting tritylsulfenimine[h] | $R_1$ | $R_2$ | base | $R_8$ | product-directed aldol adduct (isolated yield,[a] %) | mp,[b] °C |
|---|---|---|---|---|---|---|
| 5a | H | $CH_3$ | LDA | Ph | 11a (79) | |
| 5c | $CH_3$ | H | *sec*-BuLi | H | 11b (89) | 100-110[c] |
| 5c | $CH_3$ | H | *sec*-BuLi | Ph | 11c (72[d]) | 168-170[e] |
| 5d | $CH_2CH_3$ | H | *sec*-BuLi | H | 11d (81) | 119-121[f] |
| 5e | $-(CH_2)_4-$ | | *sec*-BuLi | H | 11e (46) | 54-57[g] |
| | | | | | 11f (31) | 149-151[f,g] |

[a] After chromatography on silica gel unless otherwise noted. [b] Uncorrected. [c] Amorphous solid. [d] Recrystallized yield. [e] Recrystallized-digested with $Et_2O$. [f] Recrystallized by trituration from $CHCl_3$ with *t*-BuOH. [g] After chromatographic separation from the diastereomer. [h] $R_3 = H$ and $R_9 = Ph$ in all cases.

Table VI. Conversion of Tritylsulfenimines to the Corresponding Carbonyl Compounds with Silver Nitrate




12c




12d

| starting trityl-sulfenimine[c] | $R_1$ | $R_2$ | $R_8$ | "directed aldol" product (isolated yield,[a] %) |
|---|---|---|---|---|
| 11b | $CH_3$ | H | H | 12a (67) |
| 11c | $CH_3$ | H | Ph | 12b (93) |
| 11e | $-(CH_2)_4-$ | | H | 12c (86)[b] |
| 11f | $-(CH_2)_4-$ | | H | 12d (83)[b] |

[a] After chromatography on silica gel. [b] See ref 15. [c] $R_3 = H$ and $R_9 = Ph$ in all cases.

Table VII. Triphenylmethanesulfenamides possess useful and interesting properties as described in the accompanying paper.

Various unsuccessful attempts were made to effect nucleophilic addition of organometallic reagents across the carbon–nitrogen double bond in **5c**. When an attempt was made to accelerate the reaction of MeLi–LiBr with **5c** in $Et_2O$ by maintaining the reaction mixture at 40 °C (3 h), predominant deprotonation occurred as evidenced by the formation of tritylacetone (**8**) as the major product.

In general, differences in the conditions necessary to promote nucleophilic addition or $\alpha$ deprotonation are often fairly subtle. For example, the addition of organolithium reagents to simple imines, dimethylhydrazones, and oxime ethers can be accomplished by refluxing the compounds in $Et_2O$ for several hours,[11] whereas dimethylhydrazones can be deprotonated with organolithium reagents at −78 °C in THF.[9]

In conclusion, our results presented in this paper (in conjunction with results in the accompanying paper) suggest that tritylsulfenimines should be useful for carbon monoalkylation of metalated tritylsulfenimines with eventual incorporation of the nitrogen into the final product, for use in a mild method for directed aldol condensation, and for use in a mild method for reductive ammination of a carbonyl to a primary amine. In the course of these studies some interesting reactions were discovered including the thermal extrusion of a sulfur from triphenylmethanesulfenamides, the thermal decomposition of lithiated tritylsulfenimines, and the temperature-dependent ambident alkylation of lithiated tritylsulfenimines.

## Experimental Section

**General Methods.** Melting points (determined on a Kofler hot-stage apparatus) and boiling points are uncorrected. $^1H$ NMR spectra were run with Varian T-60 (60 MHz), Varian A-60 (60 MHz), and Varian HFT-80 (80 MHz) instruments. IR spectra (calibrated with the 1601-$cm^{-1}$ absorption of a polystyrene film) were obtained with a Perkin-Elmer Model 137 instrument and are reported in wave numbers ($cm^{-1}$). High-resolution mass

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Table VII. Preparation of Triphenylmethanesulfenamides by $NaBH_3CN$ Reduction of the Corresponding Tritylsulfenimines

| tritylsulfenimine[i] | $R_1$ | $R_2$ | pH reduction[a] | triphenylmethanesulfenamide (isolated yield,[b] %) | mp,[c] °C |
|---|---|---|---|---|---|
| 5b | H | $(CH_2)_7CH_3$ | 4-5 | 13a (95) | oil |
| 5c | $CH_3$ | H | 4-5 | 13b (98) | 58-65[d] |
| 5e | | $-(CH_2)_4-$ | 4-5 | 13c (97) | oil |
| 5f | | $-(CH_2)_2CH(C(CH_3)_3)CH_2-$ | 4-5 | 13d (94)[e] | 108-110[f] |
| 5i | $CH_3$ | $CO_2CH_2CH_3$ | 3-4, 4-5 | 13e (91-96) | oil |

| tritylsulfenimine[j] | $R_5$ | pH reduction[a] | triphenylmethanesulfenamide (isolated yield,[b] %) | mp,[c] °C |
|---|---|---|---|---|
| 6a | $CH=CHCH_3$ | 4-5 | 14a (95)[g] | 76-80[h] |
| 6c | Ph | 4-5, 5-6 | 14b (95-97) | 98.5-100[f] |
| 6d | 4-$CH_3OPh$ | 4-5 | 14c (99-100) | 108-110[f] |

[a] Nominally the aqueous transition pH of the acid-base indicator. [b] After filtration through silica gel. [c] Uncorrected. [d] Crude solid. [e] The thermodynamically more stable trans isomer was obtained. [f] Recrystallized by trituration from $CHCl_3$ with *t*-BuOH. [g] Contamined with 30% of the fully reduced product. [h] After purification by silica gel chromatography. [i] $R_3$ = H in all cases. [j] $R_4$ = H in all cases.

spectra (MS) were obtained with a Kratos MS-50 instrument. Low-resolution mass spectra were obtained with an AEI MS-9 or Kratos MS-50 instrument. Elemental microanalyses were performed by either Scandinavian Microanalytical Laboratories, Herlev, Denmark, or Galbraith Laboratories, Inc., Knoxville, TN. Thin-layer chromatography was performed with Merck silica gel 60 F-254 or Merck aluminum oxide 150 F-254 (Type T). Preparative chromatography was performed with Florisil (100–200 mesh), Merck silica gel 60 (70–230 mesh), and Merck silica gel 60 (230–400 mesh). Commercial reagent grade solvents and chemicals were used as obtained unless otherwise noted. THF was freshly distilled under argon from sodium benzophenone ketyl immediately prior to use. Dry $CH_2Cl_2$ was either distilled from $CaH_2$ or filtered through dry basic alumina.

IR data for compounds containing the tritylsulfenyl group were very similar with absorptions at approximately 3050–2850, 2000–1700, 1600, 1495, and 1440 $cm^{-1}$. Low-resolution mass spectra for compounds containing the triphenylmethanesulfenamide group were generally uninformative since the highest mass/charge peak was usually at $m/z$ 243 (trityl).

**Preparation of TrSCl (3).** To a magnetically stirred solution of TrSH (20.00 g, 72.5 mmol) in toluene (50 mL) and anhydrous $Et_2O$ (225 mL) maintained near 0 °C was added by syringe sulfuryl chloride ($SO_2Cl_2$; 11.7 mL, 19.5 g, 144 mmol) in a slow stream. The reaction vessel was sealed, and as the solution was stirred 2 h at 0 °C yellow solid crystallized out. The heterogeneous mixture was treated with toluene (300 mL), leading to a homogeneous solution which was washed with $H_2O$ (3 × 200 mL), a 1:1 mixture of saturated $NaHCO_3/H_2O$ and saturated $NaCl/H_2O$ (200 mL), and saturated $NaCl/H_2O$ (200 mL). Drying of the solution ($MgSO_4$) followed by removal of the volatiles in vacuo at or below 50 °C led to yellow solid; residual volatiles were removed on a vacuum line. The crude solid (22.83 g 101%) was shown by silica gel TLC (20% $Et_2O$/hexanes) to contain TrSCl ($R_f$ 0.63) and a more polar contaminant ($R_f$ 0.36) which could be removed by digestion with $Et_2O$ (100 mL, 30 min, 65% overall), by digestion with anhydrous MeOH (100 mL, 30 min, 68% overall), or by recrystallization.

**Recrystallization of 3.** Crude TrSCl (17.69 g) was dissolved in $CHCl_3$ (75 mL) with stirring. The addition of *t*-BuOH (50 mL) caused rapid microcrystallization in solution. The suspension was stirred and then allowed to stand at room temperature until the yellow solution was no longer cloudy (ca. 1 h), and then *t*-BuOH (50 mL) was stirred in. After 3 h at room temperature the yellow solid was collected by suction filtration, washed with *t*-BuOH (50 mL), and washed with anhydrous EtOH (25 mL), and then residual volatiles were removed on a vacuum line, leading to yellow, crystalline solid (11.31 g, 64%). Removal of most of the $CHCl_3$ from the combined filtrates in vacuo followed by overnight crystallization, led to more product (4.18 g, 24%). For recrystallized TrSCl: mp 133–137 °C (exceptional samples), 125–133 °C (range for typical samples) (lit.[6] mp 137 °C); NMR $\delta$ 7.15–7.35 (m); IR ($CH_2Cl_2$) 3010 (aromatic CH), 1975, 1920, 1830, and 1780 (monosubstituted aromatic), 1610, 1495, 1445; MS, $m/z$ (relative intensity) 275 (8, TrS), 244 (49), 243 (100, Tr), 165 (94).

**Preparation of $TrSNH_2$ (4).** A three-necked, 2-L flask equipped with a mechanical stirrer, a stopcock vented to the atmosphere, and a *non*-pressure-equalizing addition funnel (necessary to avoid entry of $NH_3$ vapor into the TrSCl solution) was charged with 29% $NH_4OH/H_2O$ (430 mL) which was cooled with stirring to near 0 °C. A solution of recrystallized TrSCl (21.58 g, 69.5 mmol) in $CH_2Cl_2$ (325 mL) was placed in the addition funnel then was added in a slow stream to the rapidly (nearly violently) stirred cold $NH_4OH/H_2O$ solution. Additional $CH_2Cl_2$ (100 mL) was used to effect complete transfer of the TrSCl. At the end of the addition the $CH_2Cl_2$ layer was separated out and dried ($MgSO_4$), and the volatiles were removed in vacuo. Residual volatiles were removed on a vacuum line from the white microcrystalline residue (19.77 g, 97.8%). Such material is suitable for most purposes; it is pure by criteria such as NMR, TLC, and use in reactions in comparison with recrystallized, analytically pure material (vide infra).

**Recrystallization of 4.** A solution of crude $TrSNH_2$ (19.77 g), prepared from recrystallized TrSCl, in $CHCl_3$ (100 mL) was treated with *t*-BuOH (150 mL). The resulting solution–suspension was concentrated in vacuo at or below room temperature until most of the $CHCl_3$ had evaporated away. The suspension was treated with *t*-BuOH (50 mL) and then was stirred several hours at room temperature. The solid was collected by suction filtration and washed with anhydrous EtOH (100 mL), and then the volatiles were removed on a vacuum line, leaving white crystals (15.51 g, 78% recovery). In an identical preparation crude $TrSNH_2$ (23.22 g, 100.4%) was recrystallized, leading to analytically pure material (17.88 g, 77%). For recrystallized 4: mp 119–122 °C (lit.[6] mp 126 °C); NMR $\delta$ 2.30 (br s, 2 H), 7.10–7.40 (m, 15 H); IR ($CH_2Cl_2$) 3350 (NH), 3290 (NH), 3000 (aromatic CH), 1975, 1910, 1820, and 1770 (monosubstituted aromatic), 1600, 1580, 1485, 1438; MS, $m/z$ (relative intensity) 275 (1, TrS), 244 (40), 243 (100, Tr), 165 (65). Anal. Calcd for $C_{19}H_{17}NS$: C, 78.31; H, 5.88; N, 4.81; S, 11.00. Found: C, 78.12; H, 5.95; N, 4.67; S, 11.23.

Pure $TrSNH_2$ can also be prepared by using crude TrSCl followed by recrystallization of the crude $TrSNH_2$ in 65–70% overall yield from TrSH.

**General Procedure for the Preparation of Tritylsulfenimines (5 and 6) from the Corresponding Carbonyl Compounds.** A solution of $TrSNH_2$ (1.0 equiv, 0.07 M), carbonyl compound (ca. 1.1 equiv), and PPTS (0.05 equiv) in dry $CH_2Cl_2$ was stirred at room temperature at least 2 h over anhydrous $MgSO_4$ (5 equiv). Suction filtration through Celite followed by removal of volatiles in vacuo produced crude oil which was dissolved in a small amount of $CH_2Cl_2$ and filtered through Florisil (5.0 g/g of $TrSNH_2$) to remove the PPTS. Removal of volatiles in vacuo produced an oil which was freed from residual $CH_2Cl_2$, which inhibits crystallization, by dissolving the oil in $Et_2O$ and/or pentane several times followed by removal of volatiles in vacuo each time. Crude tritylsulfenimines **5** and **6** were pure (NMR, TLC) for most purposes and were usually used directly for subsequent reactions.

Representative $^1H$ NMR data are as follows. **Acetone tritylsulfenimine (5c)**: δ 1.87 and 1.92 (2 s, 6 H), 7.10–7.35 (m, 15 H). **2-Butanone tritylsulfenimine (5d)**: δ 0.67–0.86 (t, 3 H, $J$ = 8 Hz), 1.91 (s, 3 H), 2.02–2.30 (q, 2 H, $J$ = 8 Hz), 7.05–7.45 (m, 15 H). **Cyclohexanone tritylsulfenimine (5e)**: δ 1.33–1.75 (m, 6 H), 1.95–2.50 (2 m, centered at 2.15 and 2.35, 4 H), 7.05–7.40 (m, 15 H). **Benzaldehyde tritylsulfenimine (6c)**: δ 7.10–7.40 (m, 20 H), 8.31 (s, 1 H).

**Acetone Tritylsulfenimine (5c) and 2-Butanone Tritylsulfenimine (5d).** A preparation as in the general procedure led to incomplete reaction (**5c**, 90%; **5d**, 84%). Preferably the reaction was performed in neat carbonyl compound: $TrSNH_2$ (1.00 g, 3.44 mmol), PPTS (43 mg, 0.17 mmol), and reagent grade ketone (25 mL) were combined and left at room temperature for 1–2 h. After removal of volatiles in vacuo, the residue was dissolved in $CH_2Cl_2$ and filtered through Florisil as in the general procedure, the remainder of which was then followed.

**5-[(*tert*-Butyldimethylsilyl)oxy]-2-pentanone Tritylsulfenimine (5j).** This was prepared as in the general procedure with $TrSNH_2$ (2.45 g, 8.42 mmol) except that the reaction mixture was stirred 4 h over 10 equiv of $MgSO_4$ (incomplete reaction by TLC) followed by removal of the $MgSO_4$ by suction filtration and stirring of the filtrate over 10 equiv of fresh $MgSO_4$ for 3 h (complete reaction by TLC). Silica gel flash chromatography (3% $Et_2O$/hexanes) led to pure (NMR, TLC) oil (2.89 g, 70%).

**Preparation of Acetophenone Tritylsulfenimine (6f).** A 50-mL one-neck flask was equipped with a Dean–Stark trap (filled with 3-Å molecular sieves, $CaH_2$, and $CH_2Cl_2$) fitted with a reflux condenser and $CaSO_4$ drying tube. The flask was charged with $TrSNH_2$ (500 mg, 1.72 mmol), acetophenone (258 mg, 2.15 mmol), PPTS (22 mg, 0.088 mmol), anhydrous $MgSO_4$ (1.03 g, 8.6 mmol), and dry $CH_2Cl_2$ (25 mL). The solution–suspension was refluxed; additional PPTS was added periodically when $H_2O$ evolution (gas evolution from $CaH_2$) appeared to subside since it was suspected that $CaH_2$ was slowly getting into the reaction to kill the catalyst. At the end of 3 days the still incomplete reaction was worked up as in the general preparation. The crude product was purified by preparative TLC (silica gel, 10% $Et_2O$/hexanes, extraction with $CH_2Cl_2$; 400 mg, 59%).

**Preparation of 3-Methylcyclohexenone Tritylsulfenimine (6g).** This was prepared as in the preparation of acetophenone tritylsulfenimine (**6f**) with $TrSNH_2$ (1.00 g, 3.44 mmol), 3-methylcyclohexenone (473 mg, 4.30 mmol), PPTS (44 mg, 0.18 mmol), anhydrous $MgSO_4$ (2.06 g, 17.2 mmol), and $CH_2Cl_2$ (25 mL). The crude product was purified by silica gel flash chromatography (2% $Et_2O$/hexanes), leading to solid **6g** (733 mg, 44%).

**Thermolysis of 4.** A solution of $TrSNH_2$ (500 mg, 1.72 mmol) in toluene (25 mL) was brought to reflux. The initially colorless solution had already become yellow when reflux was achieved. After 1 h at reflux much decomposition was evident by TLC (silica gel, 20% $Et_2O$/hexanes). After 20 h at reflux no $TrSNH_2$ remained. Removal of volatiles in vacuo followed by filtration through silica gel with $CH_2Cl_2$ led to an oil (500 mg) which contained numerous products by TLC and NMR. Tritylamine (**7**) was isolated by preparative silica gel TLC as a solid: 167 mg (37%); mp 102–104 °C; mp (analytical sample) 102–104 °C (lit.[12] mp 97–100 °C); NMR δ 2.20–2.50 (br s, 2 H), 7.05–7.45 (m, 15 H); IR ($CH_2Cl_2$) 3360 and 3300 (w, NH); MS (EI), $m/z$ (relative intensity) 259 (5, $TrNH_2$), 182 (100, $TrNH_2$ – Ph), 104 (182 – Ph, H). Anal. (purified by extraction into aqueous HCl followed by neutralization and back-extraction into $Et_2O$, 88% recovery) Calcd for $C_{19}H_{17}N$: C, 87.99; H, 6.61; N, 5.40. Found: C, 87.98; H, 6.87; N, 5.31.

**Preparation of Tritylacetone (8) from Acetone Tritylsulfenimine (5c).** To a solution of **5c** (500 mg, 1.51 mmol) and diisopropylamine (230 mg, 2.27 mmol, 0.319 mL) in dry THF (10 mL) at 0 °C under argon in a flame-dried flask was added dropwise a solution of *n*-butyllithium/hexanes (1.6 M, 1.42 mL, 2.27 mmol). The solution (red initially, clear brown after 1 h) was stirred 2 h at 0 °C, and then 5% $NH_4Cl/H_2O$ (10 mL) and $Et_2O$ (25 mL) were added. The organic phase was washed with $H_2O$ (2 × 10 mL) and saturated $NaCl/H_2O$ (10 mL) and then dried ($MgSO_4$), and the volatiles were removed in vacuo, resulting in a yellow oil (474 mg). NMR and TLC (silica gel, 50% $Et_2O$/hexanes) indicated that **5c** had been consumed and that **8** was the predominant product along with other minor uncharacterized products. Preparative TLC on silica gel (25% THF/pentane, extraction with $CH_2Cl_2$) and then alumina (25% THF/pentane, extraction with $CH_2Cl_2$) followed by recrystallization from 95% EtOH and then anhydrous EtOH led to analytically pure product: mp (analytical sample) 140–143 °C (lit.[13] mp 141–142 °C; NMR δ 1.85 (s, 3 H), 3.82 (s, 2 H), 7.00–7.35 (m, 15 H); IR ($CH_2Cl_2$) 1730 (carbonyl); MS, $m/z$ (relative intensity) 300 (12, parent), 243 (100, Tr), 165 (61). Anal. Calcd for $C_{22}H_{20}O$: C, 87.96; H, 6.71. Found: C, 87.77; H, 6.75.

**General Procedure for the Lithiation of Tritylsulfenimines.** All reactions with organometallic reagents were performed under a continuous slow stream of argon. Syringes and needles were stored at 110 °C and were allowed to cool in a desiccator immediately prior to use. Glassware in constructed experimental setups was heated (flame or heat gun) intensely and allowed to cool twice with a rapid stream of argon flowing through immediately prior to use.

Into a briefly opened flask equipped with a rubber septum, argon inlet, argon outlet, and magnetic stir bar was placed solid tritylsulfenimine (1.51 mmol) at room temperature. To the resealed system was added dry THF (10 mL) by syringe. The resulting stirred solution was cooled to −78 °C (dry ice/acetone) over 15 min. The addition of a solution of *sec*-butyllithium (*n*-butyllithium has also been used successfully) in cyclohexane (1.3 M, 1.45 mL, 1.88 mmol) dropwise by syringe led eventually to a persistent red color in the solution. The red solution was stirred 1 h at −78 °C followed by the addition of the electrophile (carbonyl compound or alkyl halide) either neat or as a solution in THF.

**General Procedure for the Carbon Alkylation of Lithiated Tritylsulfenimines at −78 °C.** To a solution of the lithiated sulfenimine in THF at −78 °C was added the alkylating agent (1.25–1.50 equiv) either neat or as a solution in THF dropwise by syringe followed in several instances by the addition of hexamethylphosphoric triamide (HMPT, 1.25–1.50 equiv) dropwise by syringe. The red solutions usually became yellow after several min. After the solution was stirred at −78 °C for 1–6 h, the reaction was quenched at −78 °C by the addition of either $H_2O$, dilute $NH_4Cl/H_2O$, or anhydrous EtOH followed by warming to near room temperature. After the addition of $Et_2O$ the organic phase was washed with saturated $NaCl/H_2O$ (one time when no HMPT was used and five times when HMPT was used) and was dried ($MgSO_4$), and the volatiles were removed in vacuo. The crude product was purified by either silica gel preparative TLC, silica gel flash chromatography, or alumina preparative TLC. Alumina chromatography is recommended since partial hydrolysis of tritylsulfenimines can occur on silica gel, a problem not found with alumina as a chromatographic adsorbent. These reactions were run on 250-mg to 1.00-g scales.

**2-Butanone Tritylsulfenimine (9a).** This was obtained as in the general procedure by reaction of lithiated **5c** with MeI (no HMPT) for 1 h at −78 °C. Crude product from several reactions (ca. 100% yield) was cleanly and completely the C-alkylated product, having a $^1H$ NMR identical with that of **5d** prepared from 2-butanone with $TrSNH_2$.

**2-Heptanone Tritylsulfenimine (9b).** This was obtained as in the general procedure by reaction of lithiated **5c** with *n*-BuBr (HMPT added) for 3 h at −78 °C. The crude product was purified by preparative TLC (alumina, 5% $Et_2O$/hexanes, extraction with $CH_2Cl_2$; 92% isolated yield).

**5-[(*tert*-Butyldimethylsilyl)oxy]-2-pentanone Tritylsulfenimine (9c).** This was obtained as in the general procedure by reaction of lithiated **5c** with $BrCH_2CH_2OSi(CH_3)_2C(CH_3)_3$ (HMPT added) for 3 h at −78 °C. Chromatography on silica gel resulted in material loss due to hydrolysis several times (52–77% yield). An analytical sample was purified by preparative TLC on alumina. The NMR of this **9c** was identical in all respects with that of a sample of **5k** prepared from the corresponding ketone.

(12) Sisti, A. J.; Milstein, S. R. *J. Org. Chem.* **1974**, *39*, 3932.

(13) House, H. O.; Respess, W. L.; Whitesides, G. M. *J. Org. Chem.* **1966**, *31*, 3128.

Compound **9d** was prepared as in the general procedure except that **5k** (=**9c**) was treated with *sec*-butyllithium for 90 min and then was reacted with allyl iodide (no HMPT) for 90 min at −78 °C. TLC (silica gel, 5% $Et_2O$/pentane) of the crude product (104%) showed no **5k** (=**9c**, $R_f$ 0.56) and only one product (**9d**, $R_f$ 0.66).

**General Procedure for the Nitrogen Alkylation of Lithiated Tritylsulfenimines at −20 °C.** The reactions were performed as described for reactions at −78 °C except that the −20 °C cooling bath was dry ice/aqueous $CaCl_2$,[14] the lithiation was performed for only 10–15 min, and the alkylation reaction (with or without HMPT) was stirred only 1 h at −20 °C before the workup. All crude tritylsulfenenamines were purified by silica gel preparative TLC. All reactions were performed with 500 mg of **5**.

Compound **10a** was prepared as in the general procedure. Lithiated **5c** was reacted with MeI (no HMPT) leading to **10a**: 62% (after chromatography); NMR δ 1.36 (s, 3 H), 2.38 (s, 3 H), 3.50–3.65 (pseudo s, 2 H), 6.90–7.40 (m, 15 H); high-resolution MS (CI), calcd for $C_{23}H_{24}NS$ (parent + H) $m/z$ 346.1629; found $m/z$ 346.1626.

Compound **10b** was prepared as in the general procedure. Lithiated **5c** was reacted with *n*-BuBr (HMPT added) leading to **10b**: 56% (after chromatography); NMR δ 0.70–1.00 (t, 3 H, $J$ = 7 Hz), 1.05–1.50 (m) and 1.37 (s, 7 H total), 2.50–2.80 (t, 2 H, $J$ = 7 Hz), 3.50–3.65 (pseudo s, 2 H), 6.90–7.35 (m, 15 H); high-resolution MS (CI), calcd for $C_{26}H_{30}NS$ (parent + H) $m/z$ 388.2099, found, 388.2106.

Compound **10c** was prepared as in the general procedure. Lithiated **5c** was reacted with $BrCH_2CH_2OSi(CH_3)_2C(CH_3)_3$ (HMPT added) leading to **10c**: 48% (after chromatography); NMR δ 0.00 (s, 6 H), 0.85 (s, 9 H), 1.34 (s, 3 H), 2.61–2.91 (t, 2 H, $J$ = 7 Hz), 3.40–3.65 (pseudo s and t, 4 H), 7.00–7.40 (m, 15 H); high-resolution MS (CI), calcd for $C_{30}H_{40}NOSSi$ (parent + H) $m/z$ 490.2600, found $m/z$ 490.2580.

Compound **10d** was prepared as in the general procedure. Lithiated **5c** was reacted with $ICH(CH_3)_2$ (HMPT added) leading to **10d**: 63% (after chromatography); NMR δ 0.70–1.10 (d and t, 9 H), 1.70–2.00 (q, 2 H, $J$ = 7 Hz), 2.65–3.15 (septet, 1 H, $J$ = 7 Hz), 3.55–3.70 (pseudo s, 2 H), 7.00–7.40 (m, 15 H); high-resolution MS (CI), calcd for $C_{26}H_{30}NS$ (parent + H) $m/z$ 388.2099, found $m/z$ 388.2093.

**Deprotonation of Propionaldehyde Tritylsulfenimine (5a) with LDA. Reaction with Benzophenone.** A stirred solution of diisopropylamine (0.085 mL, 61 mg, 0.604 mmol) in dry THF (1 mL) at room temperature was treated with a solution of *sec*-butyllithium/cyclohexane (1.3 M, 0.47 mL, 0.61 mmol) dropwise by syringe. The solution was immediately cooled to −78 °C with stirring for 15 min. To the stirred solution at −78 °C was added a solution of **6a** (100 mg, 0.302 mmol) in dry THF (1 mL); additional THF (1 mL) was used to effect complete transfer. After the solution was stirred 30 min at −78 °C, a solution of benzophenone (110 mg, 0.61 mmol) in THF (2 mL) was added dropwise by syringe. After this mixture was stirred 30 min at −78 °C, anhydrous EtOH was added and the solution warmed to near room temperature. $Et_2O$ (25 mL) was added, and the organic phase was washed with $H_2O$ (15 mL) and saturated $NaCl/H_2O$ (15 mL) and then was dried ($Na_2SO_4$), followed by removal of the volatiles in vacuo. Silica gel preparative TLC of the crude product led to **11a** (123 mg, 79%) which was pure (vide infra) by TLC and NMR. The product loses water readily on silica gel, and attempts at further chromatography led to the production of significant amounts of elimination product: NMR δ 0.80 (d, 3 H, $J$ = 7 Hz), 1.59 (s, allylic Me of elimination product), 3.30–3.75 (m and s, 2 H), 6.90–7.60 (m, 25 H), 7.99 (d, 1 H, $J$ = 5 Hz, imine CH); IR ($CH_2Cl_2$) 3600, 3550–3200 (OH).

**General Procedure for the Reaction of Lithiated Tritylsulfenimines with Carbonyl Electrophiles at −78 °C.** To a solution of the lithiated tritylsulfenimine at −78 °C in THF was added the carbonyl compound (1.25 equiv) either neat or as a solution in THF. After 10–30 min at −78 °C the reactions were quenched and worked up as in the alkylation reactions. The crude products were purified by silica gel preparative TLC. Reactions were run by using 250 mg to 2.00 g of **5**.

**General Procedure for the Silver Nitrate Mediated Cleavage of Tritylsulfenimines to the Corresponding Carbonyl Compounds.** To a solution of tritylsulfenimine (0.029 M, 1.0 equiv) in 10% 0.05 M pH 7 phosphate buffer/THF was added a solution of $AgNO_3$ (0.20 M, 1–4 equiv) in 10% $H_2O$/THF either all at once or in 1-equiv aliquots periodically through the reaction. Within a few minutes black precipitate began to fall out of solution. After 1–1.5 h the reaction mixture was filtered through Celite with THF. Removal of volatiles in vacuo led to crude product which was purified directly by silica gel preparative TLC to free the carbonyl compound from the triphenylcarbinol byproduct (isolated in 74% yield after chromatography from a reaction performed on **11c** and identified by TLC and NMR comparison with authentic material).

Compound **12a** was produced by treatment of **11b** (25 mg) with $AgNO_3$ (2 equiv) for 1.5 h (67% **12a** after chromatography).

Compound **12b** was produced by treatment of **11c** with $AgNO_3$ for either 3 days (93% **12b** after chromatography) or 6 h (78% **12b** after chromatography).

Compound **12c** was produced by treatment of **11e** (24 mg) with $AgNO_3$ (4 equiv) for 1.5 h (86% **12c** after chromatography).

Compound **12d** was produced by treatment of **11f** (22 mg) with $AgNO_3$ (3 equiv) for 1.5 h (83% after chromatography).

**Conversion of 11c to 12b with Various Oxidants.** A solution of **11c** (10–25 mg, 0.0195–0.049 mmol) in 10% $H_2O$/THF (1–2 mL) was treated with the various oxidants (1–2 equiv). The reactions were monitored by TLC (silica gel, 25% $CH_2Cl_2$/toluene) for the disappearance of **11c** and the appearance of **12b**.

**General Procedure for the Reduction of Tritylsulfenimines to the Corresponding Triphenylmethanesulfenamides.** To a stirred solution of the tritylsulfenimine **5** or **6** (1.0 equiv, 0.067 M), $NaBH_3CN$ (2.0 equiv, 6.0 equiv of hydride), and a trace of acid–base indicator (Chlorophenol Red for pH 5–6, Bromocresol Green for pH 4–5, Bromophenol Blue for pH 3–4) in dry THF at room temperature was added dropwise a solution of trifluoroacetic acid/THF (1%) periodically as needed to maintain the pH near the transition pH of the indicator. When acid consumption had ceased (constant indicator color for ca. 10 min), saturated $NaHCO_3$ (1 volume) was added with stirring. The aqueous phase was extraced with $Et_2O$ (2 volumes). The organic phase was washed with $H_2O$, dilute (0.1–1 N) $HCl/H_2O$, saturated $NaHCO_3/H_2O$, and saturated $NaCl/H_2O$ and then was dried ($MgSO_4$ or $NaSO_4$), and the volatiles were removed in vacuo. The crude product was dissolved in $CH_2Cl_2$ and was filtered through silica gel (2 g/g of starting sulfenimine) to remove residual inorganic material. Removal of volatiles in vacuo led to an oil which was freed from residual $CH_2Cl_2$, which inhibits crystallization, by dissolving the oil in $Et_2O$ and/or pentane followed by removal of volatiles in vacuo several times. These triphenylmethanesulfenamides (**13** and **14**) were pure (TLC, NMR) for most purposes and were usually used directly for subsequent reactions.

Representative triphenylmethanesulfenamide $^1H$ NMR data are as follows. ***N*-Isopropyl-1,1,1-triphenylmethanesulfenamide (13b)**: δ 0.86 (d, 6 H, $J$ = 6 Hz), 2.25–2.65 (m, 2 H), 7.05–7.50 (m, 15 H). **Cyclohexyl-1,1,1-triphenylmethanesulfenamide (13c)**: δ 0.75–1.85 (m, 10 H), 1.85–2.25 (m, 1 H), 2.25–2.55 (m, 1 H, NH as determined by $D_2O$ wash), 7.00–7.50 (m, 15 H). ***N*-Benzyl-1,1,1-triphenylmethanesulfenamide (14b)**: δ 2.60–2.85 (t, 1 H, $J$ = 6 Hz), 3.65 (d, 2 H, $J$ = 6 Hz), 6.90–7.50 (m, 20 H).

**13d**: The stereochemistry and stereochemical purity of **13d** were determined by analysis of the phenylthiourea derivative (86% after chromatography) of the corresponding amine (obtained by treatment of **13d** with $HI/THF–H_2O$). For the phenylthiourea: NMR δ 0.84 (s, 9 H), 0.95–2.40 (m, 9 H), 3.75–4.50 (m, 1 H), 5.60–5.95 (d, 1 H, $J$ = 8 Hz), 6.80–7.55 (m, 5 H), 7.55–7.90 (br s, 1 H). The stereochemical assignment was made by an analysis of the shape and width of the signal at δ 3.75–4.50. The stereochemical purity was determined by the occurrence of only one *tert*-butyl signal and by the lack of any other signal in the δ 4.5–2.5 region.

**14a**: The crude product contained **14b** (70% by NMR) contaminated with the fully reduced product ($TrSNHCH_2CH_2CH_2CH_3$, 30% by NMR). A sample containing mainly **14a** could be obtained by careful silica gel preparative TLC.

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(15) House, H. O.; et al. *J. Am. Chem. Soc.* **1973**, *95*, 3310.

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**Registry No.** 4, 38499-08-0; **5a**, 86864-24-6; **5b**, 86864-25-7; **5c**, 86864-26-8; **5d**, 86864-27-9; **5e**, 86864-28-0; **5f**, 86864-29-1; **5g**, 86884-72-2; **5h**, 86884-73-3; **5i**, 86864-30-4; **5j**, 86864-31-5; **6a**, 86864-32-6; **6b**, 86864-33-7; **6c**, 86864-34-8; **6d**, 86864-35-9; **6e**, 86864-36-0; **6f**, 86864-37-1; **6g**, 86864-38-2; **7**, 5824-40-8; **8**, 13733-56-7; **9b**, 86864-39-3; **9d**, 86864-40-6; **10a**, 86864-41-7; **10b**, 86864-42-8; **10c**, 86864-43-9; **10d**, 86864-44-0; **11a**, 86864-45-1; **11b**, 86864-46-2; **11c**, 86864-47-3; **11d**, 86864-48-4; **11e**, 86864-49-5; **11f**, 86864-50-8; **12a**, 5381-93-1; **12b**, 14035-54-2; **12c**, 13161-18-7; **12d**, 42052-56-2; **13a**, 86864-51-9; **13b**, 86864-52-0; **13c**, 86864-53-1; **13d**, 86864-54-2; **13e**, 86864-55-3; **14a**, 86864-56-4; **14b**, 86864-57-5; **14c**, 86864-58-6; $OHCCH_2CH_3$, 123-38-6; $OHCCH_2(CH_2)_7CH_3$, 112-31-2; $H_3CCOCH_3$, 67-64-1; $H_3CCOCH_2CH_3$, 78-93-3; $-(CH_2)_4COCH_2-$, 108-94-1; $-(CH_2)_2CH(C(CH_3)_3)CH_2COCH_2-$, 936-99-2; $-(CH_2)_4COCH(CH_3)-$, 583-60-8; $H_3CCOCH_2COOCH_3$, 105-45-3; $H_3CCOCH_2COOCH_2CH_3$, 141-97-9; $H_3CCOCH_2(CH_2)_2OSi(CH_3)_2C(CH_3)_3$, 86864-59-7; $OHCCH{=}CHCH_3$, 4170-30-3; $OHCCH{=}C(CH_3)_2$, 107-86-8; OHCPh, 100-52-7; $OHCC_6H_4OCH_3$-4, 123-11-5; $H_3CCOCOOCH_3$, 600-22-6; $H_3CCOPh$, 98-86-2; $-(CH_2)_2C(CH_3){=}CHCO-$, 2758-18-1; $CH_3F$, 74-88-4; $H_3C(CH_2)_3Br$, 109-65-9; $(CH_3)_3CSi(CH_3)_2O(CH_2)_2Br$, 86864-60-0; $H_2C{=}CHCH_2I$, 556-56-9; $Ph_2CO$, 119-61-9.

**Supplementary Material Available:** Tabulations of $^1H$ NMR and elemental microanalysis data of compounds **5a-j**, **6a-g**, **9b,d**, **11b-f**, **12a-d**, **13a-e**, and **14a-c** (11 pages). Ordering information is given on any current masthead page.

# Studies on the Development of the Tritylsulfenyl Group as a Nitrogen Protecting Group and Application in a Synthesis of δ-Coniceine[1]

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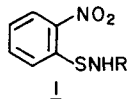
The (triphenylmethyl)sulfenyl (tritylsulfenyl, TRS) group was found to possess properties which should make it useful as a nitrogen protecting group. The almost instantaneous reaction of TrSCl (**6**) with amines produced the corresponding triphenylmethanesulfenamides. The TRS group was found to render the nitrogen atom nonbasic and relatively nonnucleophilic, was stable to aqueous acid, aqueous base, and various reducing agents, and was moderately stable to Moffat oxidation conditions. The TRS group could be cleaved under mild conditions, generating the amine with either $CuCl_2$/EtOH-THF, HI/THF-$H_2O$, or trimethylsilyl iodide ($Me_3SiI$)/$CH_2Cl_2$. A synthesis of δ-coniceine (**16**) illustrates carbon-carbon bond formation with tritylsulfenimine methodology and the utility of the tritylsulfenyl group as a nitrogen protecting group.

The sulfenamide functional group, in particular the *o*-nitrophenylsulfenyl (*o*-NPS) group (see **1**), is known to




**1**

$Ph_3CSNHR$ = TrSNHR

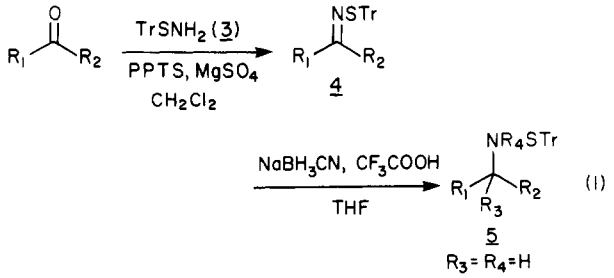
**2**

be useful as a nitrogen protecting group for peptide synthesis.[3] Zervas[3] examined the (triphenylmethyl)sulfenyl (tritylsulfenyl, TRS) group (see **2**) as an amine protecting group for peptide synthesis, for which it was useful, but the methodology was never widely used due to the superior properties of the *o*-NPS group.

We have found that the TRS group possesses properties which make it useful as an amine protecting group in contexts other than peptide synthesis and in situations where the *o*-NPS group would be inapplicable due to incompatibility of the nitro group with various reagents, in particular strong reducing agents and organometallic reagents.

## Results and Discussion

Triphenylmethanesulfenamides are now readily available by reduction of tritylsulfenimines as described in the accompanying paper (eq 1), but the general utility of the




TRS group as a nitrogen protecting group arises from the ease of preparation of triphenylmethanesulfenamides from the corresponding amines. Treatment of an amine with triphenylmethanesulfenyl chloride (TrSCl, **6**)[4] at room

(1) Taken from the Ph.D. thesis of B.P.B., Harvard University, 1981.

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(3) Zervas, L.; Borovas, D.; Gazis, E. *J. Am. Chem. Soc.* **1963**, *85*, 3660.

(4) See accompanying paper.

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