finally with 25 mL of saturated NaCl. The dried solution was evaporated to constant weight at 35 °C (8 mm). From this weight and GC data the percent total recovery and product distribution were calculated.

Attempts to follow the rate of alkylation by titrating aliquots with acid and to determine C- vs. N-alkylation by back-titrating with base were frustrated by precipitation of salts, which prevented uniform sampling. However, the results obtained indicated that **12** was completely alkylated within 5 min, almost exclusively at nitrogen. Enamine **5** required 1 h for complete methylation and showed a small amount of C-alkylation, which could not be accurately determined. Both **6** and **13** were extremely slow in alkylating.

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Registry No. 1, 583-60-8; 2, 529-34-0; 3, 19816-92-3; 3 picrate, 79201-13-1; 5 (1-ene-2-methyl), 79201-14-2; 5 (1-ene-6-methyl), 79201-15-3; 6, 79201-16-4; 7, 105-56-6; 8, 1572-98-1; 9, 26734-09-8; 10, 79201-17-5; 11, 79201-18-6; 12 (1-ene-2-methyl), 5049-40-1; 12 (1-ene-6-methyl), 5049-51-4; 13, 7007-34-3; pyrrolidine, 123-75-1.

Reactions of Dimedone with Sulfur Chlorides

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A comparative study of the reactions of dimedone (1), as a representative β-diketone, with various simple sulfur chlorides has revealed that the product distribution observed can best be accounted for in terms of competing mechanisms of oxygen attack or carbon attack (at C-2) in the enol form. Oxygen attack is particularly important with SCl_2 and S_2Cl_2 and appears to involve a subsequent intramolecular transfer of Cl (or ClS) to C-2, via an intermediate such as **12**. The relative electrophilicity of the reagents and the facility with which **12** can be expected to rearrange to a C-2 substituted product appear to be among the factors influencing the course of these reactions. Some of the reactions show promise as synthetic routes to potentially useful dimedone derivatives.

The reactions of various classes of active methylene compounds with the simple chlorides of sulfur have frequently been reported, and, in particular, much recent work has focussed on the reactivity of thionyl chloride toward such substrates.[1,2] Less frequently, other recent reports have described the reactivity of the simple sulfur chlorides (SCl_2 and S_2Cl_2)[3] and of sulfenyl chlorides (RSCl)[4] with similar organic substrates. Curiously, given the potential mechanistic similarities, we are not aware of any systematic investigation of the comparative behavior of the above reagents with a common substrate. We have now carried out such an investigation, as an extension of our recent studies[5] on the behavior of malondiamides with disulfur dichloride. We decided to use the easily accessible, relatively simple β-diketone 5,5-dimethyl-1,3-cyclohexanedione (dimedone, **1**) as our standard substrate for reaction with disulfur dichloride (S_2Cl_2), sulfur dichloride (SCl_2), thionyl chloride, sulfuryl chloride,[6] and methanesulfenyl chloride, the results of which we now present.

Results and Discussion

Our initial experiments were carried out by using the reaction of disulfur dichloride with **1**, as Naik[7] had earlier reported the isolation of the thiosulfine (dithio ketone) **2** (Chart I) from the reaction of dimedone with disulfur dichloride under comparable conditions. We have recently shown[5] that other earlier claims by Naik et al. to have prepared thiosulfines from the reaction of substituted

Chart I

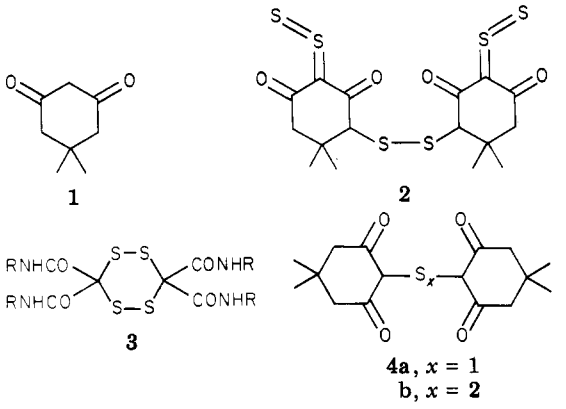


Table I.[a] Product Yields[b] from Reactions of 1 with Sulfur Chlorides

sulfur chloride	yield, % 4a	2-Cl-1 (5)	2,2-Cl_2-1 (6)	other
S_2Cl_2	84			
SCl_2	5	48		
$SOCl_2$[c]	5[d]			5[d] (7)
				2[d] (8)
SO_2Cl_2		26	66	

[a] All reactions were carried out in benzene at 25 °C for 18 h with 2 mol of the sulfur chloride, unless noted otherwise. [b] Isolated yields of chromatographically pure material. [c] A short reaction time (1 h) gave **15a** as the major product (58%) along with recovered **1** (62%). [d] Reaction allowed to proceed for 2 weeks at 25 °C.

(1) (a) Oka, K.; Hara, S. *Tetrahedon Lett.* **1977**, 695. (b) Oka, K.; Hara, S. *Ibid.* **1977**, 3059. (c) Oka, K.; Hara, S. *J. Org. Chem.* **1978**, *43*, 4533.

(2) (a) Senning, A. *Bull. Soc. Chim. Belg.* **1977**, *86*, 675. (b) Tsolomitis, A.; Sandris, C. *J. Heterocycl. Chem.* **1980**, *17*, 1645. (c) Sehgal, R. K.; Krubsack, A. J. *Synth. Commun.* **1980**, *10*, 245. (d) Adiwidjaja, G.; Günther, H.; Voss, J. *Angew. Chem., Int. Ed. Engl.* **1980**, *19*, 563. (e) Ireland, C. J.; Pizey, J. S. *J. Chem. Soc., Chem. Commun.* **1972**, 4.

(3) (a) Gompper, R.; Euchner, H.; Kast, H. *Justus Liebigs Ann. Chem.* **1964**, *675*, 151. (b) Gupta, S. K. *J. Org. Chem.* **1974**, *39*, 1944. (c) Senning, A. *Bull. Soc. Chim. Belg.* **1980**, *89*, 323. (d) Ito, S.; Mori, J. *Bull. Chem. Soc. Jpn.* **1978**, *51*, 3403.

(4) (a) Gustaffson, R.; Rappe, C.; Levin, J.-O. *Acta Chem. Scand.* **1969**, *23*, 1843. (b) Kay, I. T.; Lovejoy, D. J.; Glue, S. *J. Chem. Soc. C* **1970**, 445.

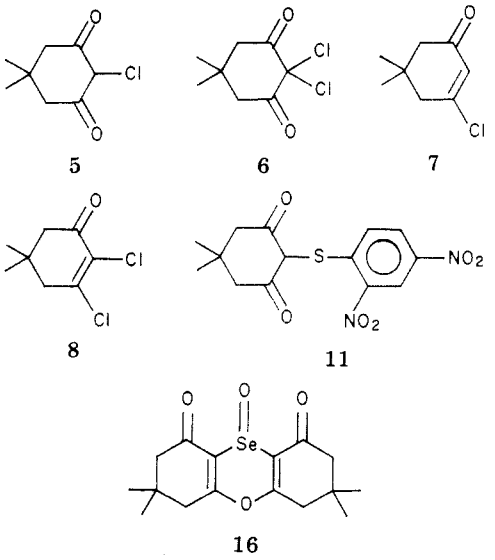
(5) Kutney, G. W.; Still, I. W. J. *Can. J. Chem.* **1980**, *58*, 1233.

(6) Sulfuryl chloride was included in the study essentially for completeness, as its well-documented behavior as an oxidizing agent makes it a rather unique sulfur chloride derivative.

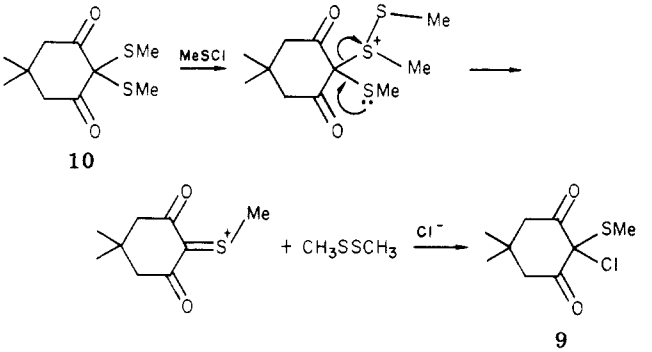
(7) Naik, K. G. *J. Chem. Soc.* **1921**, 1231.

0022-3263/81/1946-4911$01.25/0

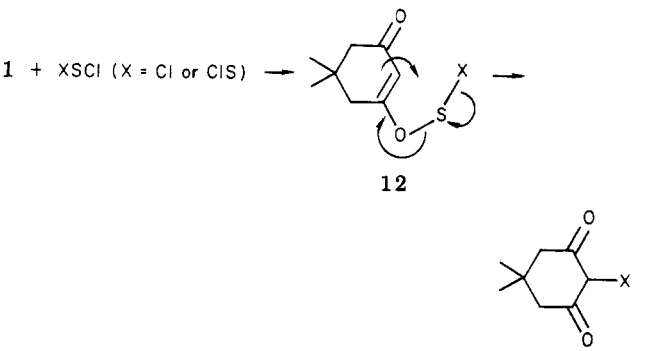
Chart II



Scheme I



Scheme II



malondiamides with disulfur dichloride were in error and that the products isolated are, in fact, the 1,2,4,5-tetrathiane derivatives **3**. In the current work, we found no evidence for compound **2** in the reaction of dimedone with disulfur dichloride.[8] Under our experimental conditions, the major product isolated (84%) is 2,2′-thiobisdimedone (**4a**). Even at reflux in benzene (Naik's conditions) we found evidence only for the presence of **4a** mixed with elemental sulfur. Since Naik's structural assignment relied heavily on elemental analysis and since we have found no simple way to separate the mixture, it is reasonable to conclude that the thiosulfine **2** is not formed in this reaction. The sulfide **4a** was also found by previous workers[3a] to be the major product (73%) from the reaction of **1** with S_2Cl_2 in acetic acid at 100 °C. Interestingly, we found no evidence for the expected 2,2′-dithiobisdimedone (**4b**) even on conducting the reaction of **1** with S_2Cl_2 at −78 °C, and we were also unable to form **4b** by the reaction of 2-chlorodimedone (**5**; Chart II) with Li_2S_2. The results of the reactions of dimedone with S_2Cl_2 and the other sulfur chlorides are summarized in Table I.

Although the simple sulfide **4a** was also isolated from the reaction of **1** with sulfur dichloride (Table I), the yield was surprisingly low, and the major product was 2-chlorodimedone (**5**). The reaction with 2 mol of sulfuryl chloride also yielded **5** as the minor product, the major product being the expected 2,2-dichlorodimedone (**6**). Compound **6** had earlier been reported as the major product from this reaction in 96% yield.[9] The reaction of dimedone with thionyl chloride under these conditions was comparatively slow, and even after 2 weeks almost 10% of **1** remained. The reaction mixture is exceedingly complex, and in addition to the low yields of the products reported in Table I, several other products were present in even smaller quantities. The rationale for the formation of **4a** and the initially unexpected chlorocyclohexenones **7** and **8** will be presented later.

Although the reaction of **1** with methanesulfenyl chloride[10] is not included in Table I, this reaction was found to give two products, 2-chloro-2-(methylthio)dimedone (**9**, 70%) and 2,2-bis(methylthio)dimedone (**10**, 11%), neither of which has been reported previously. The formation of 2-[(2,4-dinitrophenyl)thio]dimedone (**11**) by the reaction of dimedone with 2,4-dinitrobenzenesulfenyl chloride has been reported.[4a] It is worth noting, however, that these authors used a 2:1 ratio of dimedone to sulfenyl chloride to produce this result. A product analogous to **9** was previously reported[4b] from the reaction of ethyl 2-chloroacetoacetate with methanesulfenyl chloride. We believe that **10** is the primary product of the reaction, subsequently being converted to **9** by excess methanesulfenyl chloride, as outlined in Scheme I. Dimethyl disulfide was not isolated, but we have shown independently that **10** can be converted to **9** in essentially quantitative yield by using methanesulfenyl chloride. A similar mechanistic proposal has recently been made for the conversion of aromatic thiosulfonates to sulfonyl chlorides (eq 1) on the basis of earlier work by Douglass in the aliphatic series.[11,12]

$$RSO_2SR + RSCl \rightarrow RSO_2Cl + RSSR \qquad (1)$$

The most reasonable interpretation of the findings in Table I is that O attack of the partly enolized dimedone is the preferred pathway for reaction of **1** with disulfur dichloride and sulfur dichloride, followed by intramolecular transfer of ClS or Cl in the presumed intermediate **12** to form **13** or **5**, respectively, as shown in Scheme II. The reaction of dimedone with electrophilic reagents via the enolic oxygen atom appears to be well precedented.[13,14] In the case of the reaction with S_2Cl_2, the initial product **13**

(8) In attempting to duplicate Naik's results, we used 2 mol of the sulfur chloride and, for ease of comparison, have retained this ratio throughout the investigation.

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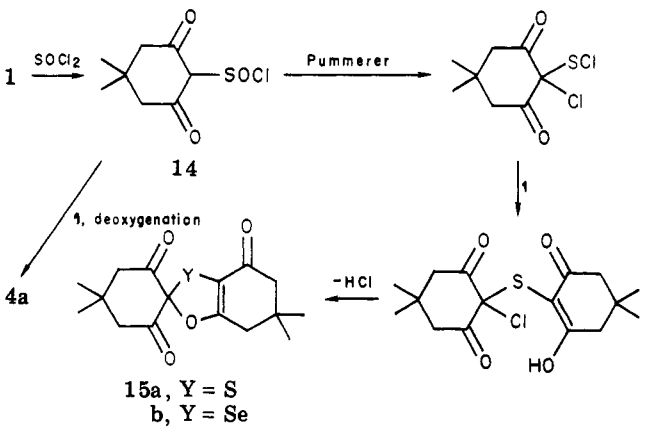
(14) Akhrem, A. A.; Lakhvich, F. A.; Budai, S. I.; Klebnicova, T. S.; Petrusevich, I. I. *Synthesis* **1978**, 925.

Scheme III



is itself a sulfenyl chloride and would be expected to react with a second molecule of 1 by C attack to give the observed sulfide **4a**.[15] by analogy with the results observed for the reaction with methanesulfenyl chloride.

In contrast to the above findings, the reaction of dimedone with methanesulfenyl chloride appears to involve mainly, if not exclusively, C attack, perhaps reflecting the softer acid character of the electrophile (CH_3SCl) in this instance. It is noteworthy that this reaction is quite slow by comparison with most of the other electrophiles studied, 73% of the starting dimedone being recoverable under our standard conditions.

The reaction of 1 with thionyl chloride is the most complex of those studied. As expected for dimedone, a vinylogous carboxylic acid, the simple chlorination product 3-chloro-5,5-dimethyl-2-cyclohexenone (**7**), as well as the dichloride 2,3-dichloro-5,5-dimethyl-2-cyclohexenone (**8**) are both formed, albeit in very low yield (Table I) and only after a prolonged reaction time. In contrast, a very short reaction period (1 h) produced the interesting tricyclic product **15a**, shown to be identical with the product obtained earlier by Koser et al.[16] Interestingly, the analogous selenium compound **15b**, first obtained by Stamm and Gossrau[17] from the selenium dioxide oxidation of **1** and wrongly formulated as structure **16**, has been shown by Laitalainen et al.[18] to have the unsymmetrical structure indicated (Chart II). A similar type of compound was recently obtained by Senning[2a] from the reaction of an acyclic β-diketone, 1,3-diphenyl-1,3-propanedione, with thionyl chloride. A reasonable mechanism for the formation of **15a**, involving initial attack of $SOCl_2$ at C-2 followed by Pummerer rearrangement, is shown in Scheme III.

The small amounts of **4a** formed in the reactions of **1** with both SCl_2 and $SOCl_2$ most likely result from attack on C-2 by the electrophile and subsequent reaction of the products **13** or **14**, respectively, with a second molecule of dimedone. In the case of **14** a subsequent deoxygenation step is required to product **4a**, rather than its sulfoxide, but thionyl chloride is well-known to be capable of deoxygenating sulfoxides.[19]

It is not necessary, of course, to postulate O attack in the formation of 2-chloro- and 2,2-dichlorodimedone (**5** and **6**) from the reaction of dimedone with sulfuryl chloride, since this reagent is well-known to effect the α-halogenation of ketones via the enol form and by an ionic mechanism.[20]

The mechanistic scheme which we have proposed on the basis of our study indicates that initial O attack of the enol form of β-diketones is certainly an important pathway in reactions with the simple sulfur chlorides. This pathway may be particularly important for cyclic β-diketones where strong internal hydrogen bonding is not possible. Although we have not attempted to optimize the conditions of our reactions from a synthetic standpoint, it seems likely that the reactions reported will prove useful as convenient sources of reactive derivatives of dimedone.

Experimental Section

The IR spectra were recorded on a Perkin-Elmer 298 grating spectrophotometer, UV spectra on a Unicam SP-8000 instrument, and ^1H NMR spectra on a Varian EM-360 spectrometer. Natural-abundance, proton-decoupled ^{13}C NMR spectra were obtained on a Varian XL-100-15 spectrometer at 25.16 MHz in the pulsed Fourier transform mode. The temperature of the probe was 32 ± 3 °C. Spectral widths of 6000 Hz were routinely used, with acquisition times of 0.666 s and pulse widths of 12 μs. Mass spectra were routinely recorded with a Bell and Howell 21-490 instrument.

Elemental analyses were performed by the Scandinavian Micro-analytical Laboratory. All melting points are uncorrected.

All reactions were carried out with dimedone (5.00 g, 35.7 mmol) and the sulfur chloride (71.4 mmol) in benzene (100 mL) and stirred for 18 h at 25 °C unless stated otherwise.

Reaction of 1 with Disulfur Dichloride. Isolation of 4a. Evaporation of the solvent under vacuum yielded a yellow solid (8.84 g). Removal of sulfur yielded 2,2′-thiobisdimedone (**4a**): 4.63 g (84%); mp 232–234 °C (95% EtOH) (lit.[3a] mp 234–236 °C; ^1H NMR ($CDCl_3$) δ 1.02 (s, 12 H), 2.35 (s, 8 H), 9.52 (s, 2 H) (the signal at δ 9.52 is concentration dependent; a recent report[21] shows this peak at δ 10.14); ^{13}C NMR ($CDCl_3$) δ 28.2 (CH_3), 31.5 (>C<), 46.3 (CH_2), 108.6 (CHS), 190.1 (CO); mass spectrum, *m/e* (relative intensity) 310 (54), 295 (17), 184 (12), 172 (25), 141 (20), 83 (100).

Reaction of 1 with Sulfur Dichloride. Isolation of 5. Filtration yielded 2-chlorodimedone (**5**): 3.00 g (48%); mp 159.5–161 °C (toluene) (lit.[22] mp 161–162 °C; ^1H NMR ($CDCl_3$) δ 1.09 (s, 6 H), 2.42 (s, 4 H), 7.22 (s, 1 H); mass spectrum, *m/e* (relative intensity) 176 (11), 174 (34), 159 (9), 146 (9), 118 (100).

Evaporation of the solvent yielded a yellow solid (3.90 g). Recrystallization of the crude solid yielded 2,2′-thiobisdimedone (0.25 g, 5%). The residue was a complex mixture.

Reaction of 1 with Sulfuryl Chloride. Isolation of 5 and 6. Filtration yielded 2-chlorodimedone (**5**; 1.64 g, 26%). Evaporation of the solvent yielded 2,2-dichlorodimedone (**6**); 4.88 g (66%); mp 111.5–112 °C (95% EtOH) (lit.[9] mp 113 °C); ^1H NMR ($CDCl_3$) δ 1.10 (s, 6 H), 2.98 (s, 4 H); mass spectrum, *m/e* (relative intensity) 210 (8), 208 (10), 118 (20), 110 (15), 100 (8), 89 (8), 83 (100).

Reaction of 1 with Thionyl Chloride. (A) Isolation of 4a, 7, and 8. The reaction mixture was stirred for 2 weeks instead of 18 h. Filtration yielded dimedone (0.44 g, 9%). Evaporation of the solvent and column chromatography (SiO_2, CCl_4) yielded many products of which the following were identified.

3-Chloro-5,5-dimethyl-2-cyclohexenone (7): colorless oil; 0.25 g (5%); ^1H NMR ($CDCl_3$) δ 1.10 (s, 6 H), 2.21 (s, 2 H, C-6), 2.52 (d, 2 H, C-4, J = 1 Hz), 6.15 (t, 1 H, J = 1 Hz); mass spectrum, *m/e* (relative intensity) 160 (9), 158 (25), 102 (100). This material was identical in all respects with an authentic sample prepared from dimedone and PCl_3 according to a literature procedure;[23] bp 72–74 °C (4 mm) [lit.[23] bp 98 °C (14 mm)].

(15) One of the referees has raised the possibility that 2-chlorodimedone (**5**) may be formed *directly* by attack of the C-2 carbon in 1 (enol form) at the Cl, rather than the S atom of SCl_2. Apart from the apparent lack of a precedent for such a suggestion, however, it is difficult to rationalize the totally different results observed for two reagents as formally similar as SCl_2 and S_2Cl_2 on this basis.

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(19) See: Pizey, J. S. "Synthetic Reagents"; Ellis Horwood Ltd.: Chichester, England, 1974; Vol. I, p 321 ff.

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(21) Koser, G. F.; Linden, S.-M.; Shih, Y.-J. *J. Org. Chem.* **1978**, *43*, 2676.

(22) Nielands, O.; Vanags, G. *Zh. Obshch. Khim.* **1960**, *30*, 510; *Chem. Abstr.* **1960**, *54*, 24469c.

2,3-Dichloro-5,5-dimethyl-2-cyclohexenone (8): 0.11 g (2%); mp 60.5–62 °C (petroleum ether, bp 60–80 °C) [lit.[24] mp 63 °C]; ^{1}H NMR ($CDCl_3$) δ 1.13 (s, 6 H), 2.43 (s, 2 H, C-6), 2.80 (s, 2 H, C-4); mass spectrum, m/e (relative intensity) 194 (19), 192 (29), 164 (29), 136 (100), 108 (17).

In addition, 2,2'-thiobisdimedone (**4a**; 0.26 g, 5%) was also isolated.

(B) Isolation of 15a. The reaction was carried out in benzene in the usual manner but stopped after 1 h. Filtration yielded dimedone (3.11 g, 62%). Evaporation and column chromatography (SiO_2, CH_2Cl_2) afforded first a small amount (0.05 g) of impure **7**, followed by the major fraction (1.23 g, 58%) consisting of a yellow solid (**15a**) which was recrystallized from dichloromethane–cyclohexane: mp 183–183.5 °C (lit.[16] mp 176–178 °C); ^{1}H NMR ($CDCl_3$) δ 0.87 (s, 3 H), 1.15 (s, 6 H), 1.22 (s, 3 H), 2.28 (s, 2 H), 2.45 (d, 2 H, ^2J = 14 Hz), 2.56 (s, 2 H), 3.03 (d, 2 H, ^2J = 14 Hz), in excellent agreement with the previously published ^{1}H NMR spectrum.[16]

Reaction of 1 with Methanesulfenyl Chloride. Isolation of 9 and 10. Chlorine (20.72 g, 0.296 mol) was slowly bubbled into dimethyl disulfide (27.84 g, 0.296 mol) in diglyme (60 mL). Vacuum distillation of 25 °C, with a receiver cooled in a dry ice–acetone bath, yielded methanesulfenyl chloride: 15.86 g (33%); ^{1}H NMR ($CDCl_3$) δ 2.82 (s) [lit.[10] (CCl_4) δ 2.91 (s)].

Reaction with dimedone was carried out by the standard procedure. Filtration yielded dimedone (3.63 g, 73%). Evaporation yielded a white solid. Recrystallization from petroleum ether (bp 60–80 °C) yielded 2-chloro-2-(methylthio)dimedone (**9**); 1.50 g (70%); mp 93–94 °C; ^{1}H NMR ($CDCl_3$) δ 0.90 (s, 3 H), 1.22 (s, 3 H), 2.21 (s, 3 H), 2.58 (d, 2 H, ^2J = 14 Hz), 3.28 (d, 2 H, ^2J = 14 Hz); IR ($CHCl_3$) ν_{max} 1740, 1755 cm^{-1} (C=O); mass spectrum, m/e (relative intensity) 222 (9), 220 (24), 186 (17), 130 (14), 83 (100).

Anal. Calcd for $C_9H_{13}ClO_2S$: C, 48.98; H, 5.94; Cl, 16.06; S, 14.53. Found: C, 48.86; H, 5.84; Cl, 16.24; S, 14.45.

The residual filtrate from the recrystallization was evaporated, yielding a clear oil. Purification by thick-layer chromatography (SiO_2, CH_2Cl_2) yielded 2,2-bis(methylthio)dimedone (**10**): 0.24 g (11%; mp 59–60 °C (petroleum ether, bp 60–80 °C); ^{1}H NMR ($CDCl_3$) δ 1.08 (s, 6 H), 2.10 (s, 6 H), 2.78 (s, 4 H); mass spectrum, m/e (relative intensity) 232 (46), 149 (24), 107 (18), 106 (10), 83 (100).

Anal. Calcd for $C_{10}H_{16}O_2S_2$: C, 51.69; H, 6.94; S, 27.60. Found: C, 51.89; H, 7.00; S 27.39.

Reaction of 10 with Methanesulfenyl Chloride. Methanesulfenyl chloride (0.10 g, 1.2 mmol) and compound **10** (0.15 g, 0.6 mmol) in chloroform (2 mL) were stirred for 18 h. Evaporation of the solvent yielded **9** (0.13 g, 93%).

Acknowledgment. We gratefully acknowledge financial support of this work by the Natural Sciences and Engineering Research Council of Canada and by the University of Toronto.

Registry No. **1**, 126-81-8; **4a**, 3359-52-2; **5**, 7298-89-7; **6**, 7298-86-4; **7**, 17530-69-7; **8**, 79255-35-9; **9**, 79255-36-0; **10**, 79255-37-1; **15a**, 56995-07-4; disulfur dichloride, 10025-67-9; sulfur dichloride, 10545-99-0; sulfuryl chloride, 7791-25-5; thionyl chloride, 7719-09-7; methanesulfenyl chloride, 5813-48-9.

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Iminium Salts from α-Amino Acid Decarbonylation. Application to the Synthesis of Octahydroindolo[2,3-*a*]quinolizines

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Iminium salts, formed regiospecifically by the decarbonylation of tertiary α-amino acids, have been applied to the synthesis of substituted tetrahydro-β-carbolines. In this manner the octahydroindolo[2,3-*a*]quinolizines **5–8** were prepared. Several useful methods for the synthesis of the requisite tertiary pipecolic acids **1–4** were developed. These include alkylation of secondary α-amino esters with tryptophyl bromide and alkylation of tryptophan methyl ester with α,ω-dibromo esters. Following deprotection, the resulting tertiary α-amino acids were heated breifly in phenylphosphonic dichloride to give the cyclized products in good yield. The presence of other substituents α or β to the basic nitrogen induces stereoselectivity in the ring closure. When this substituent is an α-carboxylic acid, it can be replaced by hydrogen through decarbonylation followed by reduction of the resulting iminium salt.

The tetrahydro-β-carboline nucleus is a structural feature present in many indole alkaloids. The most common methods for its synthesis are the Bischler–Napieralski and Pictet–Spengler reactions.[2] Application of the latter, however, is limited by the difficulty of regiospecifically generating the necessary iminium salt.

Recently we developed a convenient and regiospecific method for the preparation of iminium salts from tertiary α-amino acids.[3] Application to the synthesis of berbines,[4] a homotropane (anatoxin a),[5] and 1-azabicyclic systems[6] has demonstrated its value for the synthesis of nitrogen heterocylces. In this report we described the application of tertiary α-amino acid decarbonylation to the synthesis of some substituted tetrahydro-β-carbolines. Specifically, treatment of the tertiary pipecolic acids **1–4** with phenylphosphonic dichloride has resulted in the formation in high yield of the octahydroindolo[2,3-*a*]quinolizines **5–8**.

Results and Discussion

Synthesis of Tertiary Pipecolic Acids 1–4. Two conceptually different methods were used to synthesize the

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