spectra. We also wish to thank Professor A. Moscowitz for helpful discussions.

Registry No.—Dimethyl disulfide, 624-92-0.

References and Notes

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(7) See, for instance, H. O. House and B. M. Trost, *J. Org. Chem.*, **30,** 2502 (1965).
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(10) A multiplet was observed at δ 3.17–2.62, which consisted primarily of a pair of doublets superimposed on a broad peak. These doublets were centered at δ 3.04 (J = 3.5 Hz) and 2.84 (J = 6.0 Hz). To the extent that the doublet which was most intense had the smaller coupling constant, one is tempted to speculate that the major isomer has the cis stereochemistry. This would be consistent with a slight preference for pseudoaxial addition of the reagent to the enolate anion.[7,9,11]
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(19) Boiling points are uncorrected. Spectral data were obtained through the use of the following instruments: Varian A-60-D nuclear magnetic resonance spectrometer; Perkin-Elmer R-24-B nuclear magnetic resonance spectrometer; Perkin-Elmer Model 137 Infracord; AEI MS-30 mass spectrometer. Microanalyses were performed by the Scandinavian Microanalytical Laboratories, Herlev, Denmark. We wish to acknowledge financial assistance from the General Electric Foundation in the purchase of the Perkin-Elmer R-24-B NMR spectrometer.
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Sulfenylation of Amides

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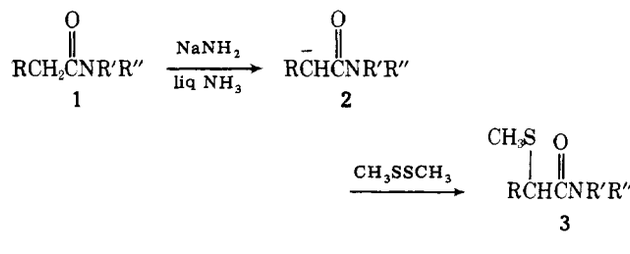
A variety of amides and lactams have been sulfenylated. It was found that, in general, lithium diisopropylamide in tetrahydrofuran was a useful base–solvent system for the α-monosulfenylation of N,N-disubstituted amides. In contrast, sodium amide in liquid ammonia was a superior base–solvent system for polysulfenylation of such amides.

Recently, we have described in detail the [2,3] sigmatropic rearrangement of ylides derived from azasulfonium salts as part of our general synthesis of indoles[1] and oxindoles.[2] Crucial to the preparation of the requisite azasulfonium salt precursors was the availability of a variety of sulfides. In connection with the synthesis of oxindoles, we were particularly concerned with the preparation of α-methylthioamides.[2] Of the various methods available for the introduction of an α-methylthio moiety, we were attracted to the possibility of directly sulfenylating anions of the appropriate amide or lactam with dimethyl disulfide. The recent comprehensive report on the sulfenylation of ketones and esters,[3,4] and of more direct relationship, the phenyl sulfenylation of 1-methyl-2-pyrrolidone and 1-methyl-2-piperidone recently described by Zoretic and Soja,[5] prompted us to report herein our results on the methyl sulfenylation of amides. Of particular interest in this regard are the major differences between the findings of Zoretic and Soja and those from our laboratory, especially those associated with the effect of different solvents on the nature of the reaction.

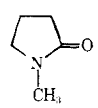
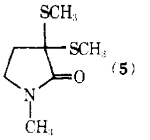
Previously, we[6] and others[7] had demonstrated the suitability of sodium amide as a base for the α-alkylation of amides. Thus, it seemed reasonable that treatment of **1** with sodium amide in liquid ammonia would produce **2,** which on reaction with dimethyl disulfide would yield **3.** In practice, this



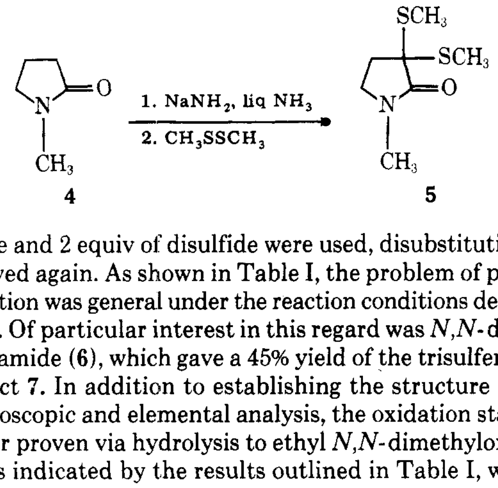
1 2 3

reaction was not suitable for monosulfenylation of amides. When 1 equiv of *N*-methylpyrrolidone (**4**) was treated with 1 equiv of sodium amide in liquid ammonia, followed by the addition of 1 equiv of dimethyl disulfide, only the disubstituted lactam **5** and unreacted **4** were obtained. When 2 equiv

Table I. Polysulfenylation of Amides with Sodium Amide–Dimethyl Disulfide in Liquid Ammonia[a]

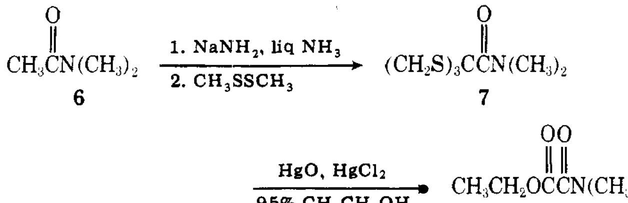
Starting amide	Registry no.	Product(s)	Registry no.	% yield(s)
	872-50-4	 (5)	63017-89-0	45
$CH_3C(O)N(CH_3)_2$	127-19-5	$(CH_3S)_3CC(O)N(CH_3)_2$ (7)	63017-90-3	45
$CH_3CH_2C(O)N(CH_3)C_6H_5$	5827-78-1	$(CH_3S)_2C(CH_3)C(O)N(CH_3)C_6H_5$	63017-91-4	60
$CH_3CH_2CH_2C(O)N(CH_3)C_6H_5$	42883-79-4	$(CH_3S)_2C(C_2H_5)C(O)N(CH_3)C_6H_5$ +	63017-92-5	43
		$C_2H_5CH(SCH_3)C(O)N(CH_3)C_6H_5$	63017-93-6	40
$C_6H_5CH_2C(O)N(CH_3)C_6H_5$	40669-47-4	$(CH_3S)_2C(C_6H_5)C(O)N(CH_3)C_6H_5$ +	63017-94-7	40[b]
		$C_6H_5CH(SCH_3)C(O)N(CH_3)C_6H_5$	63017-95-8	60[b]

[a] All yields listed resulted from the reaction of 1 equiv of amide or lactam with 2 equiv each of base and dimethyl disulfide. [b] Yields were determined by NMR spectroscopy.



4 5

of base and 2 equiv of disulfide were used, disubstitution was observed again. As shown in Table I, the problem of polysulfenylation was general under the reaction conditions described above. Of particular interest in this regard was *N,N*-dimethylacetamide (**6**), which gave a 45% yield of the trisulfenylated product **7**. In addition to establishing the structure of **7** by spectroscopic and elemental analysis, the oxidation state was further proven via hydrolysis to ethyl *N,N*-dimethyloxamate (**8**). As indicated by the results outlined in Table I, with so-



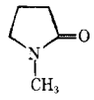
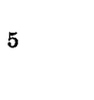
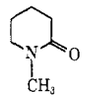
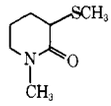
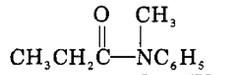
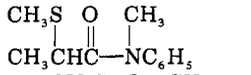
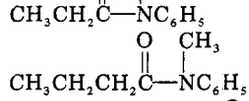
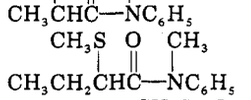
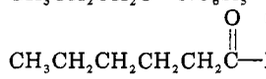
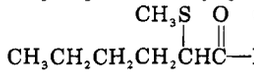
6 7 8

dium amide in liquid ammonia as the solvent–base system, a propensity for polysulfenylation existed. This tendency toward polysulfenylation appeared to be sensitive to the steric effect of the environment. Whereas *N*-methylpyrrolidone, *N,N*-dimethylacetamide, and *N*-methyl-*N*-phenylpropionamide gave only polysulfenylation, those amides with more hindered methylenes adjacent to the carbonyl, namely *N*-methyl-*N*-phenylbutyramide and α,*N*-diphenyl-*N*-methylacetamide, gave mixtures of monosubstitution and disubstitution. From the data in hand, it cannot be determined whether the shift from selective polysulfenylation to partial monosulfenylation was due solely to the increased steric hindrance at the reaction site or whether this change was due to a combination of steric and electronic effects. These results correlate quite well with those of Zoretic and Soja in THF–HMPA using an amide–base–disulfide ratio of 1:2:2.[5]

In view of the problems associated with polysulfenylation when sodium amide in liquid ammonia was used as the base–solvent system, we decided to explore other base–solvent systems. Since lithium dialkylamides have been used previously to promote sulfenylations,[3–5] we investigated the reaction of amines with lithium diisopropylamide (LDA) in tetrahydrofuran, while maintaining the 1 equiv excess of both base and sulfenylating agent in order to observe any tendency to produce polysulfenylation. As shown in Table II, our results with excess LDA and excess sulfenylating agent both differ from and parallel those of Zoretic and Soja. Whereas Zoretic and Soja found that a 1:2:2 ratio of amide–base–diphenyl disulfide afforded bissulfenylation, we found that this ratio gave monosulfenylation in most of the cases which we have studied in THF. However, it should be stressed that Zoretic and Soja were using a different solvent system and a different sulfenylating agent. We found good to excellent yields of monosulfenylation products in most cases (only with *N*-methylpyrrolidone was polysulfenylation observed). The reason for the dichotomy between our two base–solvent systems was not intuitively obvious. The possibility that the contrasting behavior was due to the difference in gegenion was ruled out when it was demonstrated that lithium amide in liquid ammonia gave essentially the same results as sodium amide in liquid ammonia.

It would appear that the differences discussed above were associated primarily with the use of tetrahydrofuran as sol-

Table II. Sulfenylation of Amides with Lithium Diisopropylamide in Tetrahydrofuran[a]

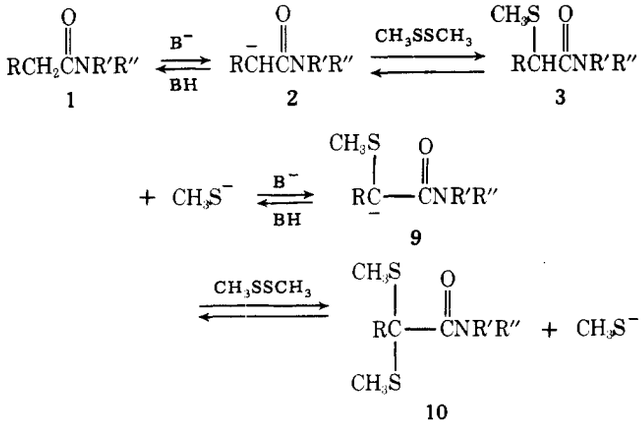
Starting amide	Registry no.	Product	Registry no.	% yield
		 5		87
	931-20-4		63017-97-0	69
			63017-98-1	87
				80
	63017-96-9		63017-99-2	65

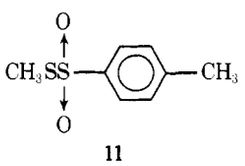
[a] All yields listed resulted from the reaction of 1 equiv of amide with 2 equiv of base and 2 equiv of dimethyl disulfide.

vent. As noted by other workers:[3] "In THF solutions, bissulfenylation of ketone enolates with diphenyl disulfide or of ester enolates with dimethyl disulfide were not observed regardless of the amount of excess base or disulfide. In THF–HMPA mixtures, bissulfenylation of ketone enolates can occur." The overall mechanistic picture can best be discussed in terms of Scheme I. There is little doubt that both base–solvent systems result in the conversion of **1** into **2** and that this is probably reversible. Dimethyl disulfide undoubtedly reacts with **2** to yield **3** and thiomethoxide. Since the α proton on **3** should be more readily removed by base than that on **1**, it would be anticipated that **3** would be rapidly converted into **9**, especially in the presence of excess base. Apparently when the base–solvent system was sodium amide–liquid ammonia, **9** was readily formed and subsequently reacted with the excess dimethyl disulfide to form **10** and thiomethoxide. In contrast, with LDA in tetrahydrofuran, **10** was not formed. The possibility of **10** being formed reversibly was ruled out by the experimental demonstration that the reaction of **10** with thiomethoxide to give **9** was a very slow reaction in tetrahydrofuran, giving only 20% conversion of **10** into **9** during the normal reaction time. Furthermore, when methylthio tosylate (**11**) was used as the sulfenylating agent in tetrahydrofuran, only monosulfenylation was observed. Similar results were observed when *N*-methylthiosuccinimide (**12**) was used as the sulfenylating agent. Thus, it would appear that the lack of disulfenylation in tetrahydrofuran was due primarily to the relative stability of the lithium salt of **9** in tetrahydrofuran.

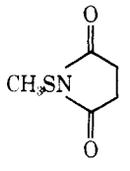
An interesting side aspect of this study was the curious difference in behavior noted for *N*-methylpyrrolidone vs. *N*-methylpiperidone. Whereas *N*-methylpyrrolidone gave disulfenylated products in both base–solvent systems, *N*-methylpiperidone afforded the monosulfenylated product (69%) in tetrahydrofuran. This demonstrated a sharp contrast in reactivity between the five- and six-membered lactams under identical conditions. Presumably, this was a consequence of the different geometries of the two rings in question.

Scheme I





11



12

In summary, it appears that lithium diisopropylamide in tetrahydrofuran is a useful base–solvent system for the α-monosulfenylation of N,N-disubstituted amides. In contrast, sodium amide in liquid ammonia is a superior base–solvent system for polysulfenylation of such amides.

Experimental Section[8]

General Procedure for Sulfenylation Utilizing Sodium Amide in Liquid Ammonia with Dimethyl Disulfide. Sodium amide was formed through the portionwise addition of 4.6 g (0.20 mol) of sodium into 100 mL of dry liquid ammonia containing a catalytic amount of ferric chloride. When the formation of sodium amide was complete, 10.0 g (0.10 mol) of *N*-methyl-2-pyrrolidone was added dropwise. The resulting green suspension was stirred for 20 min, then 19.0 g (0.20 mol) of dimethyl disulfide was added dropwise. After stirring for 2 h, the ammonia was allowed to evaporate, water was added carefully, and the solution was acidified with concentrated hydrochloric acid. The solution was extracted with four 50-mL portions of chloroform, dried over anhydrous magnesium sulfate, and filtered, and the filtrate was concentrated by rotatory evaporation. The residue was fractionally distilled to yield 2.1 g of starting lactam, bp 35–40 °C (0.4 mm), and 8.5 g (45%) of *N*-methyl-3,3-di(methylthio)-2-pyrrolidone, bp 115 °C (0.4 mm), which crystallized on standing, mp 33–35 °C, after recrystallization from *n*-hexane: NMR (CCl_4) δ 3.35 (2 H, t, J = 7 Hz), 2.82 (3 H, s), 2.28 (2 H, t, J = 7 Hz), 2.12 (6 H, s); *m/e* calcd for $C_7H_{13}NOS_2$ 191.044, found 191.045.

Anal. Calcd for $C_7H_{13}NOS_2$: C, 43.98; H, 6.81; N, 7.32. Found: C, 43.87; H, 6.83; N, 7.23.

***N,N*-Dimethyl-2,2,2-tri(methylthio)acetamide (7).** The general procedure outlined above was used with 8.7 g (0.10 mol) of *N,N*-dimethylacetamide to give 6.8 g (45%) of *N,N*-dimethyl-2,2,2-tri(methylthio)acetamide (**7**) after recrystallization from *n*-hexane, mp 84–86 °C: IR (KBr) 6.20 μm; NMR (CCl_4) δ 3.23 (6 H, s), 2.03 (9 H, s); *m/e* calcd for $C_7H_{15}NOS_3$ 225.032, found 225.037.

Anal. Calcd for $C_7H_{15}NOS_3$: C, 37.33; H, 6.67; N, 6.22. Found: C, 37.49; H, 6.78; N, 6.13.

N-Methyl-N-phenyl-2,2-di(methylthio)propionamide. The general procedure described above was used with 8.0 g (0.05 mol) of N-methyl-N-phenylpropionamide. Utilization of 2 equiv of sodium amide and 2 equiv of dimethyl disulfide gave 10 g of crude product, which on distillation gave 7.5 g (60%) of N-methyl-N-phenyl-2,2-di(methylthio)propionamide: bp 105–110 °C (0.13 mm); IR (neat) 6.10 μm; NMR (CCl_4) δ 7.30 (5 H, s), 3.39 (3 H, s), 2.05 (6 H, s), 1.44 (3 H, s); *m/e* calcd for $C_{12}H_{17}NOS_2$ 255.075, found 255.073.

Anal. Calcd for $C_{12}H_{17}NOS_2$: C, 56.47; H, 6.66; N, 5.49. Found: C, 56.75; H, 6.76; N, 5.69.

N-Methyl-N-phenyl-2,2-di(methylthio)butyramide and N-Methyl-N-phenyl-2-methylthiobutyramide. The general procedure described above was used with 9.0 g (0.05 mol) of N-methyl-N-phenylbutyramide. The crude product was distilled to yield 4.45 g (40%) of N-methyl-N-phenyl-2-methylthiobutyramide, bp 105–135 °C (0.3 mm), and 5.75 g (43%) of N-methyl-N-phenyl-2,2-di(methylthio)butyramide as a crystalline pot residue, mp 65–70 °C. Recrystallization from n-hexane gave an analytical sample: mp 72–73 °C; IR (KBr) 6.14 μm; NMR ($CDCl_3$) δ 7.31 (5 H, s), 3.37 (3 H, s), 1.94 (6 H, s), 1.47 (2 H, q, J = 7.2 Hz), 1.00 (3 H, t, J = 7.2 Hz); *m/e* calcd for $C_{13}H_{19}NOS_2$ 269.091, found 269.090.

Anal. Calcd for $C_{13}H_{19}NOS_2$: C, 57.99, H, 7.06; N, 5.24. Found: C, 57.97; H, 7.14; N, 5.19.

N-Methyl-2,N-diphenyl-2,2-di(methylthio)acetamide and N-Methyl-2,N-diphenyl-2-methylthioacetamide. The general procedure described above was used with 11.3 g (0.05 mol) of N-methyl-2,N-diphenylacetamide to give a quantitative yield of a mixture of mono- and disulfenylated product. The mixture was not readily separated by standard techniques on a preparative scale. Analysis by NMR spectroscopy indicated 60% monosulfenylation and 40% disulfenylation. The two products were separated by thin layer chromatography on silica gel. The separated products were then molecularly distilled.

N-Methyl-2,N-diphenyl-2,2-di(methylthio)acetamide was distilled at 150 °C (1.5×10^{-4} mm): IR (neat) 6.10 μm; NMR ($CDCl_3$) δ 7.5–6.7 (10 H, br m), 3.10 (3 H, s), 1.95 (6 H, s); *m/e* calcd for $C_{17}H_{19}NOS_2$ 317.091, found 317.092.

Anal. Calcd for $C_{17}H_{19}NOS_2$: C, 64.35; H, 5.99; N, 4.42. Found: C, 64.40; H, 6.16; N, 4.42.

N-Methyl-2,N-diphenyl-2-methylthioacetamide was distilled at 110 °C (0.15 mm): IR (neat) 6.05 μm; NMR (CCl_4) δ 7.5–7.0 (10 H, br m), 4.25 (1 H, s), 3.22 (3 H, s), 1.82 (3 H, s); *m/e* calcd for $C_{16}H_{17}NOS$ 271.103, found 271.104.

Anal. Calcd for $C_{16}H_{17}NOS$: C, 70.85; H, 6.27; N, 5.17. Found: C, 70.59; H, 6.44; N, 5.02.

Ethyl N,N-Dimethyloxamate (8). To a solution of 450 mg (2 mmol) of N,N-dimethyl-2,2,2-tri(methylthio)acetamide in 55 mL of 95% ethanol was added 2.28 g of mercuric chloride and 706 mg of mercuric oxide. The resulting suspension was refluxed for 5.5 h under an atmosphere of nitrogen. After cooling, the reaction mixture was filtered and the separated solids were washed with methylene chloride. The filtrate was diluted with water, ammonium chloride solution was added, and the methylene chloride solution was separated, dried over Drierite, and filtered, and the filtrate was evaporated to yield 257 mg (88%) of ethyl N,N-dimethyloxamate (8), which showed no impurities by NMR analysis.

General Procedure for Sulfenylation Utilizing Lithium Diisopropylamide in Tetrahydrofuran. N-Methyl-N-phenyl-2-methylthiopropionamide. A tetrahydrofuran solution of lithium diisopropylamide (LDA) was prepared by the slow addition of 9 mL of 2.2 M methyllithium to 2.0 g (0.02 mol) of dry diisopropylamine in 50 mL of tetrahydrofuran (THF) at −78 °C under nitrogen. To this solution was added dropwise 1.63 g (0.01 mol) of N-methyl-N-phenylpropionamide in 10 mL of THF at −78 °C. The solution was stirred at −78 °C for 30 min, after which 2.0 g (~0.02 mol) of dimethyl disulfide was added. After stirring for 2 h at −78 °C, the solution was allowed to warm to room temperature and quenched by the addition of 50 mL of water. The reaction mixture was extracted with four 50-mL portions of chloroform. The organic extracts were combined, washed with dilute hydrochloric acid and saturated sodium chloride, and dried over Drierite. After filtration, the solvent was removed and the crystalline residue was recrystallized from n-hexane to give 1.83 g (87%) of N-methyl-N-phenyl-2-methylthiopropionamide, mp 71.5–73.0 °C: IR (KBr) 6.08 μm; NMR (CCl_4) δ 7.28 (5 H, s), 3.22 (3 H, s), 3.12 (1 H, q, J = 7 Hz), 2.03 (3 H, s), 1.32 (3 H, d, J = 7 Hz); *m/e* calcd for $C_{11}H_{15}NOS$ 209.087, found 209.086.

Anal. Calcd for $C_{11}H_{15}NOS$: C, 63.16; H, 7.18; N, 6.70. Found: C, 63.24; H, 7.29; N, 6.68.

N-Methyl-N-phenyl-2-methylthiobutyramide. According to the general procedure described above, 1.7 g (0.01 mol) of N-methyl-N-phenylbutyramide was treated with 2 equiv of LDA and dimethyl disulfide. Workup afforded 2.35 g, which was purified by molecular distillation (60 °C pot temperature, 0.12 mm) to give 1.73 g (80%) of N-methyl-N-phenyl-2-methylthiobutyramide as a light yellow oil: IR (neat) 6.05 μm; NMR (CCl_4) δ 7.40 (5 H, s), 3.27 (3 H, s), 2.87 (1 H, d of d, J = 9 and 7 Hz), 2.25–1.25 (2 H, complex m), 2.02 (3 H, s), 0.88 (3 H, t, J = 7 Hz); *m/e* calcd for $C_{12}H_{17}NOS$ 223.103, found 223.102.

Anal. Calcd for $C_{12}H_{17}NOS$: C, 64.57; H, 7.62; N, 6.28. Found: C, 64.27; H, 7.75; N, 6.14.

N-Methyl-N-phenyl-2-methylthiohexanamide. According to the general procedure outlined above, 2.0 g (0.1 mol) of N-methyl-N-phenylhexanamide was treated with 2 equiv each of LDA and dimethyl disulfide. Workup gave an oil which crystallized on cooling in n-hexane to yield 1.6 g (65%) of N-methyl-N-phenyl-2-methylthiohexanamide as yellow prisms, mp 46–48 °C: IR (KBr) 6.11 μm; NMR (CCl_4) δ 7.31 (5 H, s), 3.21 (3 H, s), 2.85 (1 H, d of d, J = 9 and 6 Hz), 2.20–0.50 (9 H, complex m), 2.01 (3 H, s); *m/e* calcd for $C_{14}H_{21}NOS$ 251.134, found 251.134.

Anal. Calcd for $C_{14}H_{21}NOS$: C, 66.93; H, 8.37; N, 5.58. Found: C, 66.85; H, 8.39; N, 5.59.

N-Methyl-3-methylthiopiperidone. As described above, 1.13 g (0.01 mol) of N-methylpiperidone was treated with 2 equiv each of LDA and dimethyl disulfide. The crude product was purified by chromatography on silica gel (ether eluent) to give 1.10 g (69%) of N-methyl-3-methylthiopiperidone. Molecular distillation (60 °C pot temperature, 0.15 mm) gave an analytical sample: IR (neat) 6.15 μm; NMR (CCl_4) δ 3.40–3.00 (3 H, m), 2.82 (3 H, s), 2.22 (3 H, s), 2.22–1.50 (4 H, complex m); *m/e* calcd for $C_7H_{13}NOS$ 159.072, found 159.073.

Anal. Calcd for $C_7H_{13}NOS$: C, 52.83; H, 8.18; N, 8.81. Found: C, 52.83; H, 8.30; N, 8.71.

N-Methyl-3,3-di(methylthio)-2-pyrrolidone (5). Utilizing the procedure outlined above, 1.0 g (0.01 mol) of N-methylpyrrolidone was treated with 2 equiv each of LDA and dimethyl disulfide. Workup gave 1.70 g of an oil, which crystallized on standing. This material was identical in all respects with the N-methyl-3,3-di(methylthio)-2-pyrrolidone described above.

Desulfenylation of N-Methyl-N-phenyl-2,2-di(methylthio)-propionamide with Lithium Thiomethoxide. Methanethiol (500 mg, 0.01 mol) was added to 1 equiv of LDA in 50 mL of THF and the solution was stirred for 30 min at −78 °C under nitrogen. N-Methyl-N-phenyl-2,2-di(methylthio)propionamide (1.2 g, 5 mmol) was added to the solution and the reaction mixture was stirred for 2 h at −78 °C and then allowed to warm to room temperature. Water (50 mL) was added, the layers were separated, and the aqueous layer was extracted with four 50-mL portions of chloroform. The organic extracts were combined, washed with dilute hydrochloric acid and saturated brine solution, and dried over Drierite. Filtration followed by evaporation of the solvent gave 80% of starting material and 20% of N-methyl-N-phenyl-2-methylthiopropionamide as determined by NMR analysis.

N-Methyl-N-phenyl-2-methylthiopropionamide Utilizing Methanethiol p-Toluenesulfonate. According to the general procedure, 0.8 g (5 mmol) of N-methyl-N-phenylpropionamide was treated with 2 equiv each of LDA and methanethiol p-toluenesulfonate. Workup gave a crude product which on analysis by NMR spectroscopy showed only monosulfenylation of the starting amide.

A similar experiment utilizing N-methylthiosuccinimide gave 85% monosulfenylation and 15% disulfenylation as determined by NMR spectroscopic analysis.

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Registry No.—Dimethyl disulfide, 624-92-0; methanethiol p-toluenesulfonate, 4973-66-4; N-methylthiosuccinimide, 2043-24-5.

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Use of [2,3] Sigmatropic Rearrangements for the Specific Ortho-Substitution of Polycyclic Aromatic Amines. The Methylation of Naphthylamines and the Synthesis of 1*H*-Benz[*g*]indoles and 3*H*-Benz[*e*]indoles

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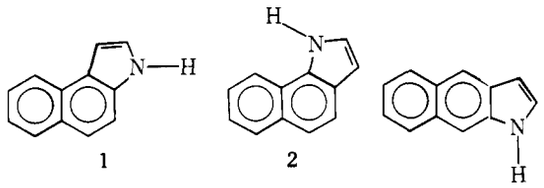
Procedures have been developed for the specific ortho-alkylation of polycyclic aromatic amines. Both α- and β-naphthylamine have been ortho-methylated by a procedure involving sequential treatment of the amine with (a) *tert*-butyl hypochlorite, (b) dimethyl sulfide, (c) sodium methoxide, and (d) Raney nickel. This procedure, which uses a [2,3] sigmatropic rearrangement of an ylide in the key ring functionalization step, gave only ortho-substitution. Replacement of the dimethyl sulfide by sulfides having a carbonyl group in the β position permitted the synthesis of 1*H*-benz[*g*]indoles and 3*H*-benz[*e*]indoles from the appropriate naphthylamine precursors.

Recently, the need for general methods for the specific ortho-substitution of polycyclic aromatic amines has been discussed in connection with oncological studies of related nonsubstituted aromatic amines.[1] Being fully aware of the need for such selective procedures for ortho-alkylation and also of the lack of good general methods for the synthesis of 1*H*-benz[*g*]indoles and 3*H*-benz[*e*]indoles, we decided to attempt to apply our general procedures for ortho-alkylation[2-6] and for the synthesis of indoles[6-9] to the polycyclic aromatic amines. We now wish to report in detail the specific ortho-substitution of α- and β-naphthylamine.

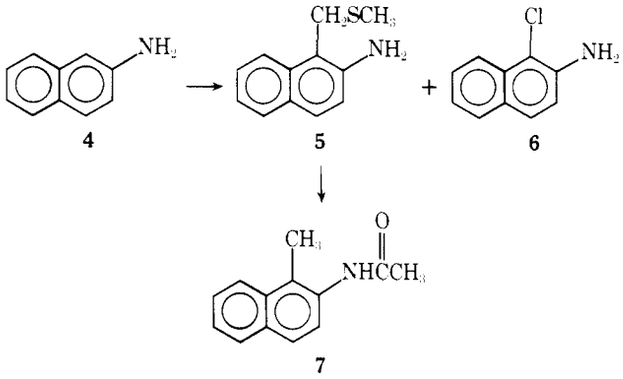
Benzindoles, although first reported in the literature in the late 19th century,[10,11] have not been extensively studied. 3*H*-Benz[*e*]indole (**1**) was first described in 1886,[10] while 1*H*-benz[*g*]indole (**2**) was reported the following year.[11] Both were prepared through application of the Fischer indole synthesis.[12] Subsequently, a variety of methods appeared in the literature for the preparation of **1** and **2** and for derivatives of these two systems.[13] It is interesting to note at this point that sound chemical evidence for the structure of **1** has never been provided. Instead, the structure of **1** was postulated on the basis of its nonidentity with 1*H*-benz[*f*]indole (**3**). As part



1 **2** **3**

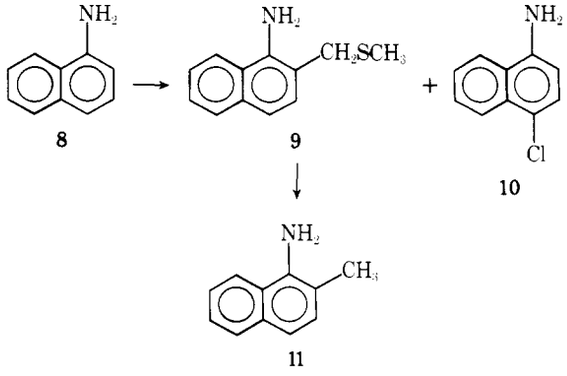
of the present study, we have provided what we believe to be a definitive structure proof of the 3*H*-benz[*e*]indole nucleus.

We first examined the simple ortho-alkylation of 2-aminonaphthalene (**4**) according to our standard process. In a sequential series of reactions, 1 equiv of *tert*-butyl hypochlorite, 1 equiv of dimethyl sulfide, and 1.5 equiv of sodium methoxide were added to 1 equiv of **4** at −78 °C. Workup gave a 95% yield of a 3:1 mixture of **5** and **6**. Separation of the mixture followed by Raney nickel desulfurization of **5** and



4 **5** **6** **7**

acetylation with acetyl chloride gave a 70% overall yield of the recrystallized acetamide **7**. A similar study was carried out with α-naphthylamine (**8**) as the starting material. Under our standard reaction conditions **8** gave 40% yields of **9** and **10**. Raney nickel desulfurization of **9** gave a 90% yield of **11**. Overall, the preparation of **7** and **11** illustrate the utility of our general process for ortho-alkylation of polycyclic aromatic



8 **9** **10** **11**