

Alkylation of the Sulfur- and Nitrogen-containing Compounds Analogous to Thiazoline Systems

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(Received November 26, 1982)

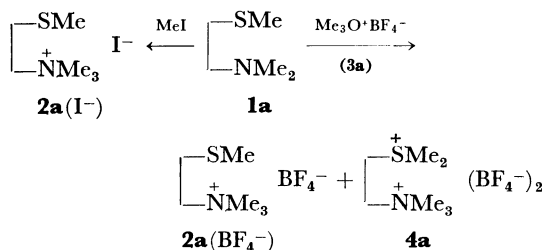
N,N-Dimethyl-2-(alkylthio)ethylamines and 3-methylthiazolidines underwent *N*-methylation both with trimethyloxonium tetrafluoroborate (**3a**) and with methyl iodide. In the methylation of *N,N*-dimethyl-*o*-(methylthio)aniline, the main reaction was *S*-methylation. On the other hand, in the *o*-ethylthio derivative, *S*-methylated product was major with methyl iodide, while *N*-methylated product was major with **3a**. In the *N*-ethyl or *N*-benzyl derivative, only *S*-methylation occurred with both reagents. 3-Methyl-2, 2-diphenyl-2,3-dihydrobenzothiazole gave *S*-methylated product with **3a**, suggesting that *S*-methylation becomes major when the 2-substituent is bulkier. 4-Methyl-3,4-dihydro-2*H*-benzo[*b*][1,4]thiazine was methylated on the nitrogen with **3a**, while it gave *S*-methylated product with methyl iodide. Phenothiazines and 1-dialkylamino-8-(methylthio)naphthalenes gave only *S*-methylated products. The selective *S*-methylation in the case of *N*-methylation was carried out through protonation on the nitrogen atom followed by methylation with **3a**. Possibility of intramolecular interaction between sulfonio and amino groups has been discussed based on their NMR data.

In the alkylation of a compound containing both sulfur and nitrogen atoms, the position of alkylation depends on the structure of the compound and the kind of alkylating reagent.¹⁾ We previously reported that 3-alkyl-2,3-dihydrobenzothiazoles were selectively alkylated on the nitrogen with Meerwein reagents.¹⁾

Therefore, our work on alkylation was extended to the compounds containing both sulfur and nitrogen atoms analogous to thiazoline systems, in order to obtain an information on the relation between the structure of the compound and the alkylated position.

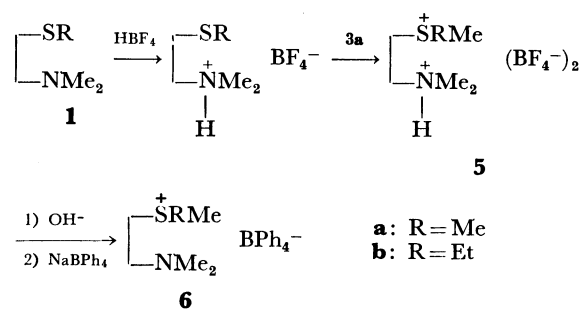
Results and Discussion

Methylation of *N,N*-Dimethyl-2-(alkylthio)ethylamines (**1**) and 3-Methylthiazolidines (**7**). *N,N*-Dimethyl-2-(methylthio)ethylamine (**1a**) reacted with methyl iodide to give trimethyl(2-methylthioethyl)ammonium iodide (**2a**(I⁻)), while with trimethyloxonium tetrafluoroborate (**3a**) it gave a mixture of *N*-methylated (**2a**(BF₄⁻)) and *N,S*-dimethylated salts (**4a**). These structures could be assigned by NMR.

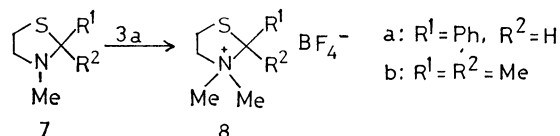


Accordingly, **1a** is methylated on nitrogen to give **2a** both with methyl iodide and with **3a**, but with a stronger alkylating reagent such as **3a**, **2a** is further methylated on the sulfur to give **4a**.

Based on the above result, we succeeded in preparation of the sulfonium salt (**6**) from **1**. The nitrogen atom in **1** was first protonated with tetrafluoroboric acid and then the ammonium salt was methylated with **3a** to give [2-(dialkylsulfonio)ethyl]dimethylammonium salt (**5**) which was deprotonated to give **6**.

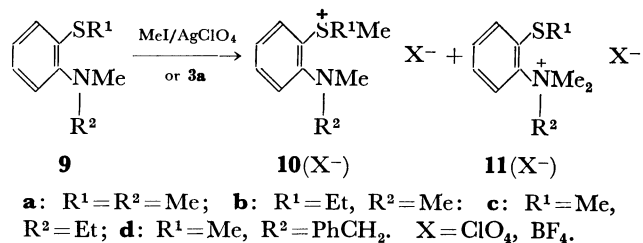


3-Methylthiazolidines (**7**) were methylated with **3a** to give cyclic ammonium salts (**8**) analogously to that of **1**. The NMR spectra of **8** were analogous to those of 3,3-dimethylbenzothiazolinium salts,¹⁾ confirming the structure (**8**).



Thus it is concluded that aliphatic or alicyclic compounds containing sulfur and nitrogen atoms are selectively alkylated on nitrogen both with methyl iodide and with **3a**.

Methylation of *o*-(Alkylthio)aniline Derivatives (**9**). Methylation of *N,N*-dimethyl-*o*-(methylthio)aniline (**9a**) with methyl iodide–silver perchlorate system gave a mixture of the sulfonium (**10a**(ClO₄⁻)) and the ammonium salts (**11a**(ClO₄⁻)) in a ratio of ca. 4:1 (by NMR), while methylation with **3a** gave a mixture of **10a**(BF₄⁻) and **11a**(BF₄⁻) in a ratio of ca. 1.5:1. The salts **10a** and **11a** were isolated in pure form by repeated recrystallization from ethanol.



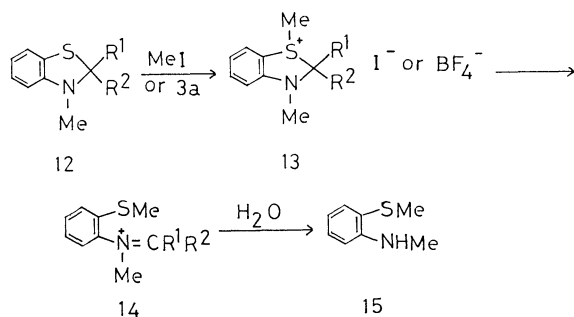
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The results are consistent with that methyl iodide is regarded as a soft reagent possessing a considerable affinity to sulfur atom and **3a** as a hard one possessing a considerable affinity to nitrogen.

Methylation of **9b** with methyl iodide-silver perchlorate gave a mixture of **10b**(ClO₄⁻) and **11b**(ClO₄⁻) in a ratio of 2:1, while that with **3a** gave a mixture of **10b**(BF₄⁻) and **11b**(BF₄⁻) in a ratio of 1:2, indicating to be more selective than in the case of **9a**. In the former, the ratio did not change after single recrystallization, but in the latter, only **11b** was isolated after single recrystallization. Both **9c** and **9d** gave only *S*-methylated products (**10c** and **10d**) with both reagents.

These results are attributed to the considerable decrease of the nucleophilicity of nitrogen atom due to conjugation with benzene ring as compared with that of sulfur atom, and suggest that a congestion around sulfur atom moderately decreases the *S*-methylation, while a congestion around the nitrogen drastically decreases *N*-methylation with **3a**.

Methylation of 3-Methyl-2,2-diphenyl-2,3-dihydrobenzothiazole (**12c**) and 4-Methyl-3,4-dihydro-2H-benzo[b][1,4]-thiazine (**16**).



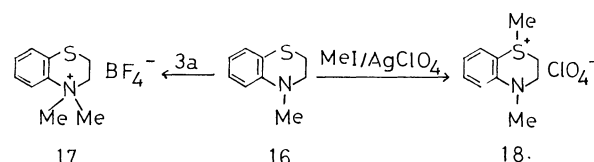
a: R¹=R²=Me; **b:** R¹=H, R²=Ph; **c:** R¹=R²=Ph;
d: R¹=H, R²=*t*-Bu.

3-Methyl-2,3-dihydrobenzothiazoles (**12**) are methylated on the nitrogen atom.¹⁾ However, considering the above results, it is expected that **12** would be methylated rather on the sulfur atom, if a bulky group exists at the 2-position, because of steric congestion around the nitrogen due to shorter C-N bond than C-S bond.

In fact, Hori *et al.*²⁾ have reported that methylation of 2,2,3-trimethyl-2,3-dihydrobenzothiazole (**12a**) with methyl iodide gave ring-opening immonium salt (**14a**) via *S*-methylated compound (**13a**). We also found that methylation of 3-methyl-2-phenyl-2,3-dihydrobenzothiazole (**12b**) with **3a** gave *N*-methyl-*o*-(methylthio)aniline (**15**) as by-product,¹⁾ which is decomposition product of *S*-methylated product (**13b**).²⁾

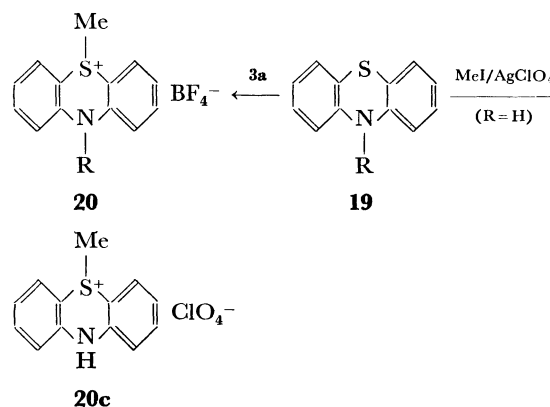
Therefore, **12c** was methylated with **3a** to expect *S*-methylation. Actually, the reaction gave *S*-methylated **13c** in 31% yield. Very recently, Hori *et al.*³⁾ have reported that methylation of **12d** with **3a** gave **15** through unstable **13d**.

On the other hand, methylation of **16** with **3a** selectively gave ammonium salt (**17**), while methylation with methyl iodide-silver perchlorate gave sulfonium salt (**18**).

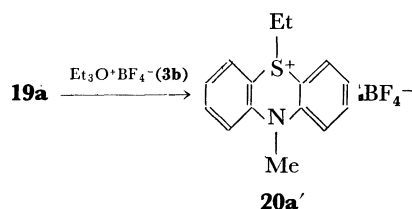


The difference in **12** and **16** may be ascribable to an effect of five-membered ring fused with benzene ring in **12**. Namely, it is considered that thiazoline ring makes the delocalization of the lone pair electrons of nitrogen conformationally unfavorable, while sulfur atom can resonate with benzene ring under such circumstances.⁴⁾ Thus the reactivity towards **3a** becomes larger on nitrogen than on sulfur analogously to the aliphatic systems.

Alkylation of Phenothiazines (**19**). 10-Methylphenothiazine (**19a**) was methylated on sulfur even with **3a** to give sulfonium salt (**20a**). The ethylated salt (**20a'**) from **19a** with triethyloxonium tetrafluoroborate (**3b**) was different from the methylated salt (**20b**) from **19b** with **3a**, indicating that these salts were sulfonium salts. Phenothiazine (**19c**) was also methylated on sulfur with methyl iodide-silver perchlorate to give sulfonium salt (**20c**).



a: R=Me; **b:** R=Et; **c:** R=H



These facts indicate that the reactivity on the nitrogen atom extremely decreases because of the large delocalization of lone pair electrons over two benzene rings. It may also be attributed to not only the steric hindrance due to two benzene rings but also the steric hindrance due to two *peri*-hydrogen atoms.

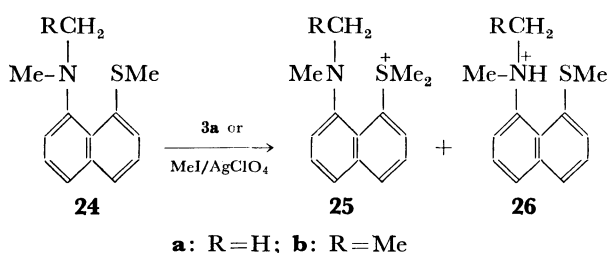
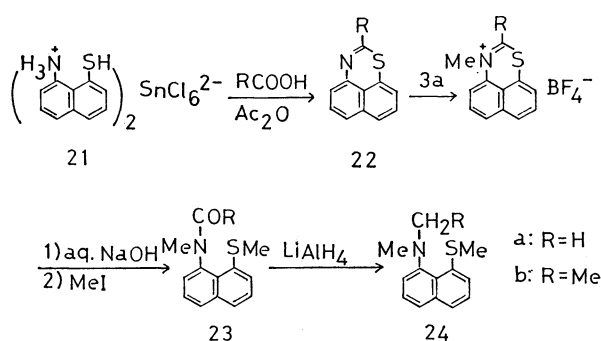
Methylation of 1-Dialkylamino-8-(methylthio)naphthalenes (**24**). 1-Dialkylamino-8-(methylthio)naphthalenes (**24**) were prepared from the reported hexachlorostannane (**21**)⁵⁾ as Scheme 1.

Methylation of **24** with methyl iodide-silver perchlorate gave sulfonium salt (**25**), while with **3a** it gave a mixture of *S*-methylated **25a** and ammonium tetrafluoroborate (**26a**) from **24a** and only **26b** from **24b**.

TABLE 1. CHEMICAL SHIFTS^{a)} OF *N*- OR *S*-METHYL PROTONS IN PARENT COMPOUNDS AND THE METHYLATED SALTS (δ , AT 34 °C)

Parent		In CDCl ₃ ^{b)}	Salt	In DMSO- <i>d</i> ₆ ^{b)}	
1a	SMe	2.12	6a (BPh ₄ ⁻)	⁺ SMe	2.48 (2.68)
	NMe	2.27		NMe	2.16 (2.71)
1b	SMe	—	6b (BPh ₄ ⁻)	⁺ SMe	2.31 (2.58)
	NMe	2.28		NMe	2.15 (2.65)
9a	SMe	2.41 (2.59)	10a (ClO ₄ ⁻)	⁺ SMe	3.21 (3.56)
	NMe	2.74 (3.46)		NMe	2.79 (3.45)
9b	SMe	—	10b (ClO ₄ ⁻)	⁺ SMe	3.23 (3.62)
	NMe	2.72		NMe	2.80 (3.51)
9c	SMe	2.39	10c (ClO ₄ ⁻)	⁺ SMe	3.21
	NMe	2.70		NMe	2.77
24a	SMe	2.40	25a (ClO ₄ ⁻)	⁺ SMe	3.23 (3.41)
	NMe	2.69		NMe	2.82 (3.34)
24b	SMe	2.40	25b (ClO ₄ ⁻)	⁺ SMe	3.21 (3.33)
					3.27 (3.37)
	NMe	2.67		NMe	2.84 (3.24)
29	PhSMe	2.48	30 (ClO ₄ ⁻)	⁺ SMe	3.33 (3.28)
31	PhNMe ₂	2.90	32 (ClO ₄ ⁻)	⁺ NMe	3.69 (3.68)
33	<i>o</i> -C ₆ H ₄ (NMe ₂) ₂	2.77	34 (BF ₄ ⁻)	⁺ NMe	3.82 (3.88)
				NMe	2.72 (3.09)
35	1-NaPh-SMe ^{c)}	2.53	36 (ClO ₄ ⁻)	⁺ SMe	3.43
37	1-Naph-NEt-Me ^{c)}	2.83	38 (BF ₄ ⁻)	⁺ NMe	3.91

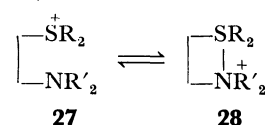
a) Accuracy is within ± 0.02 ppm. b) Values in parenthesis are those in CF₃COOH. c) Naph denotes naphthalene ring.



Apparently **26** is derived from the protonation of **24** in the course of the decomposition of **3a** by ethanol. Methylation on the nitrogen atom did not take place even with Meerwein reagent, because of an extremely large steric congestion around the nitrogen atom.

Possibility of Intramolecular Interaction Between Sulfonio

and Amino Groups. It would be expected that the sulfonio salts (**27**) containing amino group such as **6**, **10**, and **25** may be in an equilibrium with ammonio-sulfuranes (**28**) or exist in the form of **28**, which have both an ammonium part and a σ -sulfurane part (hypervalent I-type⁶⁾).



Although many stable σ -sulfuranes have recently been synthesized by Martin *et al.*,⁷⁾ there is no example of the σ -sulfurane such as **28**, which has alkyl groups on sulfur atom. Therefore, it is quite interesting to examine whether there is any possibility of contribution of **28** in **27**.

In order to characterize the structures of **6**, **10**, and **25**, several reference compounds and their methylated compounds were prepared. In Table 1 were shown chemical shifts of methyl protons in both parent and their methylated compounds. The accuracy for these data was estimated to be ± 0.01 ppm for the solvent effect (checked by changing the ratio of DMSO-*d*₆ to CDCl₃), -0.02 ppm for *S*⁺-Me, $+0.02$ ppm for *N*-Me in methanol-*d*₄ vs. DMSO-*d*₆, and the concentration effect was essentially negligible.

The *N*-methyl protons in **6** (δ 2.15) are in rather higher field than those in parent compound (**1**) (δ

2.28), probably because of anisotropy effect due to tetraphenylborate anion (cf. **10d**(BPh₄⁻): δ 2.61 (NMe), 2.91 (SMe) vs. **10d**(BF₄⁻): δ 2.63 (NMe), 3.12 (SMe)).

Both in **10** and **25**, the *N*-methyl protons are in lower field than those in parent compounds (**9** and **24**). The *S*-methyl protons in **10** and **25** are not so low as for those of reference compounds (**30** and **36**). This may be attributed to **28**. It is considered that **28** is decomposed by protonation in trifluoroacetic acid, so that the *S*-methyl chemical shifts in **10** and **25** are in lower field by the release of lone pair electrons on nitrogen. However, these phenomena can be interpreted as the inductive effect due to additional cationic center by protonation of the amino group.

In **34**, the methyl protons of dimethylamino group are in rather higher field than those in parent **33**, while that in **10** is rather lower than that in parent **9**. This phenomenon may be interpreted by the contribution of **28**. However, the inductive effect by the sulfonio group is slightly stronger than that by the ammonio group.⁸⁾ Therefore, the above fact can also be attributed to the difference of inductive effect.

From the above discussion based on NMR, no definite conclusion to support the structure **28** could be obtained. However, since the amino and sulfonio groups in **25a** are fixed closely (0.22–0.25 nm) in the peri position, there may be a possibility of strong interaction between nitrogen and sulfur atoms. The related works are in progress.

Experimental

All the boiling and melting points are not corrected. ¹H NMR spectra were measured with Hitachi R-24B and R-20B spectrometers using TMS as an internal standard.

Materials. *N,N*-Dimethyl-2-(methylthio)ethylamine (**1a**),^{9,10)} 3-methyl-2,2-diphenyl-2,3-dihydrobenzothiazole (**12c**),¹¹⁾ 4-methyl-3,4-dihydro-2*H*-benzo[*b*][1,4]thiazine (**16**),¹²⁾ *N*-methyl- (**19a**) and *N*-ethylphenothiazines (**19b**),¹³⁾ and *N,N,N',N'*-tetramethyl-*o*-phenylenediamine (**33**)¹⁴⁾ were prepared by the reported methods. *N,N*-Dimethyl-2-(ethylthio)ethylamine (**1b**) was prepared by a similar method to that of **1a**, bp 90 °C/60 mmHg (1 mmHg $\approx$ 133.322 Pa) (lit.¹⁵⁾ 61 °C/16 mmHg). 3-Methyl-2-phenyl- (**7a**)¹⁶⁾ and 2,2,3-trimethylthiazolidines (**7b**)¹⁶⁾ were prepared by the reported method.¹⁷⁾

N,N-Dimethyl-*o*-(methylthio)aniline (**9a**). *o*-(Methylthio)aniline (5.05 g, 36.3 mmol) was methylated with Me₂SO₄ (8.9 ml, 94 mmol) and K₂CO₃ (7 g) in C₆H₆ (20 ml) to give **9a** (4.18 g, 69%), bp 92 °C/0.2 mmHg (lit.¹⁸⁾ 130 °C/20 mmHg).

N,N-Dimethyl-*o*-(ethylthio)aniline (**9b**). This compd was prepared by a similar methylation of *o*-(ethylthio)aniline in 56% yield, bp 95 °C/0.3 mmHg; ¹H NMR (CDCl₃): δ = 1.32 (t, *J* = 7 Hz, 3H), 2.72 (s, 6H), 2.90 (q, *J* = 7 Hz, 2H), and 7.0–7.2 (br s, 4H). Found: C, 66.02; H, 8.49; N, 7.95%. Calcd for C₁₀H₁₅NS: C, 66.25; H, 8.34; N, 7.73%.

N-Ethyl-*N*-methyl-*o*-(methylthio)aniline (**9c**). Bis[*o*-ethylamino)phenyl] disulfide,¹⁹⁾ prepared from 3-ethylbenzothiazolium iodide (9.62 g, 33.0 mmol), was methylated with **3a** (3.16 g, 21.4 mmol) in CH₂Cl₂ (20 ml) and then treated with aq NaOH. After dry column chromatography (DCC) (SiO₂, CCl₄) the methylated product was reduced with sodium (0.5 g, 22 mmol) in liq NH₃ (50 ml) and ether (20 ml). To the residue, after evaporation, were added

EtOH (20 ml) and MeI (1.5 ml). Extraction with ether after addition of water and distillation gave **9c** (1.19 g, 20%), bp 80 °C/0.3 mmHg; ¹H NMR (CDCl₃): δ = 1.10 (t, *J* = 7 Hz, 3H), 2.39 (s, 3H), 2.70 (s, 3H), 2.97 (q, *J* = 7 Hz, 2H), and 7.04 (br s, 4H). Found: C, 66.05; H, 8.51; N, 7.56%. Calcd for C₁₀H₁₅NS: C, 66.25; H, 8.34; N, 7.73%.

N-Benzyl-*N*-methyl-*o*-(methylthio)aniline (**9d**). To a mixture of *o*-(methylthio)aniline (17.3 g, 124 mmol), benzaldehyde (60 g, 590 mmol), NaOAc (20 g, 240 mmol), and AcOH (100 ml) in EtOH (250 ml) was added NaBH₄ (25 g, 660 mmol) portionwise. After stirring for 4 h and usual work-up, distillation gave *N*-benzyl-*o*-(methylthio)aniline (21.4 g, 75%), bp 142 °C/0.25 mmHg. The aniline (16.1 g, 70 mmol) was treated with the Me₂SO₄ (8.0 ml, 85 mmol) and Na₂CO₃ (8 g, 76 mmol) in C₆H₆ (60 ml) to give **9d** (6.44 g, 38%), bp 142 °C/0.2 mmHg; ¹H NMR (CDCl₃): δ = 2.41 (s, 3H), 2.60 (s, 3H), 4.07 (s, 2H), and 7.0–7.6 (m, 9H). Found: C, 74.00; H, 7.15; N, 5.89%. Calcd for C₁₅H₁₇NS: C, 74.03; H, 7.04; N, 5.76%.

Preparation of 24. 1) **24a**: Naphtho[1,8-*de*][1,3]-thiazine (**22a**) was prepared by a modified method of preparation of **22b**.^{5b)} To anhyd NaOAc (19 g) in boiling HCOOH (160 ml) were added tin (8.0 g, 68 mmol) and **21** (18.9 g, 30.5 mmol) under nitrogen. To this soln was added Ac₂O (26 ml) portionwise, and the mixture was neutralized with aq NH₃. From the ethereal extract of the resulting ppt, **22a** was isolated by DCC (SiO₂, CH₂Cl₂-CCl₄ (1:2)), 4.73 (42%), mp 95–110 °C; ¹H NMR (CDCl₃): δ = 6.6–7.4 (m, 6H) and 7.97 (s, 1H). Found: C, 71.61; H, 3.63; N, 7.60; S, 17.20%. Calcd for C₁₇H₇NS: C, 71.32; H, 3.81; N, 7.56; S, 17.31%.

22a (2.16 g, 11.7 mmol) was methylated with **3a** (3.09 g, 20.9 mmol) in refluxing CH₂Cl₂ (70 ml) for 1.5 h. After addition of ether, the resulting ppt was suspended in EtOH (60 ml), aq NaOH (6 g, 70 ml H₂O) was added under nitrogen, and refluxing was kept for 1 h. MeI (3.5 ml, 56 mmol) was added, and the mixture was heated for 0.5 h. After usual work-up, DCC (Al₂O₃, CH₂Cl₂) gave **23a** (1.29 g, 48%), bp 165 °C/0.5 mmHg; ¹H NMR (CDCl₃): δ = 2.40 (s, 3H), 3.23 (s, 3H), 6.9–7.8 (m, 6H), and 8.00 (s, 1H). Found: C, 67.35; H, 5.60; N, 5.92%. Calcd for C₁₃H₁₃NOS: C, 67.50; H, 5.66; N, 6.06%.

To **23a** (1.29 g, 5.6 mmol) in ether (30 ml) at 0 °C was added dropwise LiAlH₄ (450 mg, 12 mmol) in ether (40 ml), and the mixture was stirred for 1 h. After usual work-up, distillation gave **24a** (1.03 g, 85%), bp 110 °C/0.15 mmHg; ¹H NMR (CDCl₃): δ = 2.40 (s, 3H), 2.69 (s, 6H), and 7.0–7.7 (m, 6H). Found: C, 71.61; H, 7.09; N, 6.57; S, 14.27%. Calcd for C₁₃H₁₅NS: C, 71.84; H, 6.96; N, 6.44; S, 14.75%.

2) **24b**: **23b** was prepared in the same manner as that of **23a** from **22b**^{5b)} in 52% yield; ¹H NMR (CDCl₃): δ = 1.71 (s, 3H), 2.45 (s, 3H), 3.19 (s, 3H), and 6.9–7.9 (m, 6H).

24b was prepared in the same manner as that of **24a** in 57% yield, bp 125 °C/0.25 mmHg; ¹H NMR (CDCl₃): δ = 1.07 (t, *J* = 7 Hz, 3H), 2.40 (s, 3H), 2.67 (s, 3H), 3.04 (dq, *J* = 7 Hz and 2 Hz, 2H), and 7.0–7.8 (m, 6H). Found: C, 72.44; H, 7.42; N, 5.97; S, 13.51%. Calcd for C₁₄H₁₇NS: C, 72.68; H, 7.41; N, 6.05; S, 13.86%.

Methyl 1-Naphthyl Sulfide (35). 1-Naphthalenethiol was prepared from 1-naphthalenesulfonyl chloride (6.05 g, 26.7 mmol) and zinc (12.2 g, 186 mmol) in concd H₂SO₄ (13 ml) by a similar method to Org. Synth.,²⁰⁾ and methylated with MeI (3 ml) and NaOH (2 g) in EtOH (30 ml). Usual work-up gave **35** (1.20 g, 26%), bp 90 °C/0.25

mmHg (lit.²¹) 104 °C/1 mmHg).

N-Ethyl-*N*-methyl-1-naphthylamine (**37**). 1-Naphthylamine (6.83 g, 47.7 mmol) was treated with triethyl orthoformate (10.6 g, 71.2 mmol) and concd H₂SO₄ (0.3 g) by a similar method to Org. Synth.²² to give *N*-ethyl-*N*-naphthylformamide (71.4 g, 78%), bp 153 °C/0.1 mmHg. This amide (4.19 g, 21.0 mmol) was reduced with LiAlH₄ (600 mg, 16 mmol) in ether (90 ml). After usual work-up, DCC (Al₂O₃, hexane) gave **37** (2.85 g, 73%), bp 90 °C/0.3 mmHg; ¹H NMR (CDCl₃): δ=1.19 (t, *J*=7 Hz, 3H), 2.83 (s, 3H), 3.13 (q, *J*=7 Hz, 2H), and 6.9–8.4 (m, 7H). Found: C, 84.43; H, 8.21; N, 7.43%. Calcd for C₁₃H₁₅N: C, 84.28; H, 8.16; N, 7.56%.

General Procedure of Alkylation.

1) With **3** (Method I): A mixture of a compd (5 mmol) and **3a** or **3b** (5.5–7 mmol) in CH₂Cl₂ (10–15 ml) was stirred at room temp for several hours. The soln was evaporated to a few ml, to which abs ether was added. The resulting ppt was washed with ether followed by addition of a few ml of EtOH to decompose **3**, washed with ether, and dried *in vacuo*. NMR spectrum of a portion of the crude ppt in DMSO-*d*₆ was measured to determine the ratio of sulfonium and ammonium salts. The yield was determined after recrystallization.

2) With Methyl Iodide in the Presence of Silver Perchlorate (Method II): To a compd (5 mmol) and MeI (5.5–7.5 mmol) in CH₂Cl₂ (10–20 ml) was added AgClO₄ (5 mmol) with MeNO₂ (5 ml). The mixture was stirred at room temp for several hours. The filtrate was treated by the same method as in Method I.

2a(I[−]): 94% yield (Method II but without AgClO₄), mp 226–227.5 °C (decomp) (from EtOH); ¹H NMR: δ=2.17 (s, 3H), 2.6–2.9 (m, 4H), and 3.22 (s, 9H).

2a(BF₄[−]): 28% yield from filtrate by Method I, mp 166–170 °C (from MeOH-Et₂O); ¹H NMR: δ=2.18 (s, 3H), 2.6–3.8 (m, 4H), and 3.14 (s, 9H). Found: C, 32.76; H, 7.38; N, 6.45%. Calcd for C₆H₁₈BF₄NS: C, 32.60; H, 7.30; N, 6.34%.

4a: 25% yield from ppt by Method I, mp 239–242 °C (from MeOH-MeCN); ¹H NMR: δ=2.99 (s, 6H), 3.17 (s, 9H), and 3.81 (br s, 4H). Found: C, 25.76; H, 5.72; N, 4.20%. Calcd for C₇H₁₉B₂F₈NS: C, 26.04; H, 5.93; N, 4.34%.

8a(BF₄[−]): not crystallize; 60% yield (Method I); ¹H NMR: δ=2.93 (s, 3H), 3.21 (s, 3H), 3.3–4.5 (m, 4H), 6.20 (s, 1H), and 7.4–8.0 (m, 5H). Found: C, 47.13; H, 5.62; N, 4.79%. Calcd for C₁₁H₁₆BF₄NS: C, 47.00; H, 5.74; N, 4.98%.

8b(BF₄[−]): 50% yield (Method I), mp 190–192 °C (decomp) (from EtOH-Et₂O); ¹H NMR: δ=1.80 (s, 6H), 3.21 (s, 6H), 3.25 (br t, *J*=6 Hz, 2H), and 4.08 (br t, *J*=6 Hz, 2H). Found: C, 35.78; H, 7.15; N, 5.75%. Calcd for C₇H₁₆BF₄NS: C, 36.07; H, 6.92; N, 6.01%.

10a(ClO₄[−]): 65% yield (Method II), mp 143–145 °C (from EtOH); ¹H NMR: δ=2.79 (s, 6H), 3.21 (s, 6H), and 7.3–8.1 (m, 4H). Found: C, 42.78; H, 5.86; N, 5.04%. Calcd for C₁₀H₁₆ClNO₄S: C, 42.63; H, 5.72; N, 4.97%. The ¹H NMR spectrum of the crude salt showed methyl peaks of **11a**(ClO₄[−]) at δ=2.69 (SMe) and 3.87 (Me₃N⁺), indicating formation of a mixture of **10a** and **11a** in a ratio of ca. 4:1.

Mixture of **10a**(BF₄[−]) and **11a**(BF₄[−]): ca. 1.5:1 in crude (Method I); 81% yield after recrystd from EtOH. **10a**(BF₄[−]): from soluble part to CH₂Cl₂; mp 127–128 °C (from EtOH-Et₂O); ¹H NMR: δ=2.81 (s, 6H), 3.21 (s, 6H), and 7.3–8.0 (m, 4H). Found: C, 44.62; H, 6.22; N, 5.22%. Calcd for C₁₀H₁₆BF₄NS: C, 44.63; H, 5.99;

N, 5.20%. **11a**(BF₄[−]): from the insoluble part; mp 186–186.5 °C (from EtOH); ¹H NMR: δ=2.67 (s, 3H), 3.83 (s, 9H), and 7.2–8.0 (m, 4H). Found: C, 44.49; H, 6.03; N, 5.20%. Calcd for C₁₀H₁₆BF₄NS: C, 44.63; H, 5.99; N, 5.20%.

Crude mixture of **10b**(ClO₄[−]) and **11b**(ClO₄[−]): ca. 2:1 (Method II); 99% yield. Recrystallization from EtOH gave the mixture of the same ratio, 69% yield, mp 100–101 °C. **10b**(ClO₄[−]): ¹H NMR: δ=1.30 (t, *J*=7 Hz, 3H), 2.80 (s, 6H), 3.23 (s, 3H), ca. 3.6 (q, *J*=7 Hz, 2H), and 7.1–7.9 (m, 4H). **11b**(ClO₄[−]): ¹H NMR: δ=1.38 (t, *J*=7 Hz, 3H), ca. 3.2 (q, *J*=7 Hz, 2H), 3.89 (s, 9H), and 7.1–7.9 (m, 4H). Found (mixture): C, 44.59; H, 6.27; N, 5.03%. Calcd for C₁₁H₁₈ClNO₄S: C, 44.67; H, 6.13; N, 4.74%.

Crude mixture of **10b**(BF₄[−]) and **11b**(BF₄[−]): ca. 1:2 (Method I), 96% yield. Pure **11b**(BF₄[−]): 46% yield; ¹H NMR: δ=1.32 (t, *J*=7 Hz, 3H), 3.16 (q, *J*=7 Hz, 2H), 3.81 (s, 9H), and 7.2–7.9 (m, 4H). **10b**(BF₄[−]): ¹H NMR: δ=1.21 (t, *J*=7 Hz, 3H), 2.78 (s, 3H), 3.19 (s, 3H), ca. 3.6 (t, *J*=7 Hz, 2H), and 7.2–7.9 (m, 4H).

Crude mixture of **10c**(ClO₄[−]) and **11c**(ClO₄[−]) (δ=3.69, *N*-Me): >10:1 (Method II), 89% yield. Pure **10c**(ClO₄[−]): 33% yield, mp 107–108 °C (from EtOH); ¹H NMR: δ=1.14 (t, *J*=7 Hz, 3H), 2.77 (s, 3H), 3.06 (q, *J*=7 Hz, 2H), 3.21 (s, 6H), and 7.3–8.0 (m, 4H). Found: C, 44.59; H, 6.08; N, 4.85%. Calcd for C₁₁H₁₈ClNO₄S: C, 44.67; H, 6.13; N, 4.74%.

Crude mixture of **10c**(BF₄[−]) and **11c**(BF₄[−]): >10:1 (Method I), ca. 100% yield. Pure **10c**(BF₄[−]): 42% yield, mp 95–96 °C (from EtOH); ¹H NMR: δ=1.11 (t, *J*=7 Hz, 3H), 2.73 (s, 3H), 3.03 (q, *J*=7 Hz, 2H), 3.17 (s, 6H), and 7.3–8.0 (m, 4H). Found: C, 46.71; H, 6.50; N, 4.82%. Calcd for C₁₁H₁₈BF₄NS: C, 46.66; H, 6.41; N, 4.95%.

10d(ClO₄[−]): 99% yield (Method II), mp 104–105 °C (from EtOH-Et₂O); ¹H NMR: δ=2.67 (s, 3H), 3.19 (s, 6H), 4.16 (s, 2H), and 7.3–8.1 (m, 9H). Found: C, 53.40; H, 5.73; N, 3.86%. Calcd for C₁₆H₂₀ClNO₄S: C, 53.70; H, 5.63; N, 3.91%.

10d(BF₄[−]): by Method I; ¹H NMR: δ=2.63 (s, 3H), 3.12 (s, 6H), 4.09 (s, 2H), and 7.0–8.0 (m, 9H). Because of difficulty of purification, BF₄[−] was exchanged with Ph₄B[−] to give **10d**(BPh₄[−]): 37% yield, mp 135–136.5 °C; ¹H NMR: δ=2.61 (s, 3H), 2.91 (s, 6H), 4.05 (s, 2H), and 6.6–7.8 (m, 29H). Found: C, 83.33; H, 6.77; N, 2.36%. Calcd for C₄₀H₄₀BNS: C, 83.17; H, 6.98; N, 2.42%.

13c(BF₄[−]): 31% yield (Method I), mp 178.5–179.5 °C (from EtOH); ¹H NMR: δ=2.36 (s, 3H), 2.88 (s, 3H), and 6.6–7.9 (m, 14H). Found: C, 62.10; H, 5.05; N, 3.60%. Calcd for C₂₁H₂₀BF₄NS: C, 62.24; H, 4.97; N, 3.46%.

17: 38% yield (Method I), mp 90–93 °C (from EtOH-Et₂O); ¹H NMR: δ=3.60 (s, 6H), 3.3–3.8 (m, 2H), 4.0–4.3 (m, 2H), and 6.5–8.0 (m, 4H). Found: C, 45.06; H, 5.49; N, 5.34%. Calcd for C₁₀H₁₄BF₄NS: C, 44.97; H, 5.28; N, 5.24%.

18(BPh₄[−]): 43% yield by Method II followed by anion exchange, mp 226–227.5 °C (decomp); ¹H NMR: δ=2.96 (s, 3H), 3.49 (s, 3H), 3.62 (br s, 4H), and 6.5–7.5 (m, 24H). Found: C, 81.90; H, 7.05; N, 2.89%. Calcd for C₃₄H₃₄BNS: C, 81.75; H, 6.86; N, 2.80%.

20a: 79% yield (Method I), mp 264.5–265.5 °C (decomp) (from EtOH); ¹H NMR: δ=2.92 (s, 3H), 3.72 (s, 3H), and 7.1–8.0 (m, 8H). Found: C, 53.15; H, 4.52; N, 4.73%. Calcd for C₁₄H₁₄BF₄NS: C, 53.36; H, 4.48; N, 4.44.

20a': 82% yield (Method I), mp 158.5–160 °C (from EtOH); $^1\text{H NMR}$: δ =1.08 (t, J =7 Hz, 3H), 3.33 (q, J =7 Hz, 2H), 3.69 (s, 3H), and 7.1–8.0 (m, 8H). Found: C, 54.67; H, 5.04; N, 4.56%. Calcd for $\text{C}_{15}\text{H}_{16}\text{BF}_4\text{NS}$: C, 54.73; H, 4.90; N, 4.26%.

20b: 81% yield (Method I), mp 241–242.5 °C (decomp) (from EtOH); $^1\text{H NMR}$: δ =1.47 (t, J =7 Hz, 3H), 2.89 (s, 3H), 4.33 (q, J =7 Hz, 2H), and 7.1–8.1 (m, 8H). Found: C, 54.59; H, 4.86; N, 4.31%. Calcd for $\text{C}_{15}\text{H}_{16}\text{BF}_4\text{NS}$: C, 54.73; H, 4.90; N, 4.26%.

20c: 59% yield (Method II), mp 184.5–187 °C (decomp) (from EtOH); $^1\text{H NMR}$: δ =2.88 (s, 3H), 7.0–8.0 (m, 8H), and 11.1 (br s, 1H); IR (KBr): 3300 cm^{-1} (NH). Found: C, 49.96; H, 3.98; N, 4.70%. Calcd for $\text{C}_{13}\text{H}_{12}\text{ClNO}_4\text{S}$: C, 49.77; H, 3.86; N, 4.46%.

25a(ClO_4^-): 85% yield (Method II), mp 196–197.5 °C (from EtOH); $^1\text{H NMR}$: δ =2.82 (s, 6H), 3.23 (s, 6H), and 7.5–8.4 (m, 6H). Found: C, 50.80; H, 5.38; N, 4.46%. Calcd for $\text{C}_{14}\text{H}_{18}\text{ClNO}_4\text{S}$: C, 50.68; H, 5.47; N, 4.22%.

Crude mixture of **25a**(BF_4^-) and **26a**(BF_4^-): 2:3 (Method I); 93% yield; $^1\text{H NMR}$: **25a**, δ =2.79 (s, 6H) and 3.19 (s, 6H); **26a**, δ =2.48 (s, 3H) and 2.98 (s, 6H).

25b(ClO_4^-): 36% yield (Method II), mp 107.5–109 °C; $^1\text{H NMR}$: δ =1.17 (t, J =7 Hz, 3H), 2.84 (s, 3H), 3.24 (d, J =3.6 Hz, 6H), 3.3–3.8 (m, 2H), and 7.6–8.4 (m, 6H). Found: C, 52.21; H, 5.92; N, 3.81%. Calcd for $\text{C}_{15}\text{H}_{20}\text{ClNO}_4\text{S}$: C, 52.09; H, 5.83; N, 4.05%.

26b(BF_4^-): 87% yield (Method I), mp 148–150 °C (from EtOH); $^1\text{H NMR}$: δ =1.09 (t, J =7 Hz, 3H), 2.50 (s, 3H), 3.00 (br s, 6H), 3.40 (br q, J =7 Hz, 2H), and 7.3–8.1 (m, 6H). Found: C, 53.20; H, 5.84; N, 5.04%. Calcd for $\text{C}_{14}\text{H}_{18}\text{BF}_4\text{NS}$: C, 52.68; H, 5.68; N, 4.39%.

30: 57% yield (Method II), mp 162–163 °C (from EtOH); $^1\text{H NMR}$: δ =3.33 (s, 6H) and 7.6–8.2 (m, 5H).

32: 93% yield (Method II), mp 183–186 °C (from EtOH); $^1\text{H NMR}$: δ =3.69 (s, 9H) and 7.5–8.1 (m, 5H).

34: 78% yield (Method I), mp 142–143 °C (from EtOH); $^1\text{H NMR}$: δ =2.72 (s, 6H), 3.82 (s, 9H), and 7.3–8.0 (m, 4H).

36: 97% yield (Method II), mp 157–158 °C (from EtOH); $^1\text{H NMR}$: δ =3.43 (s, 6H) and 7.7–8.6 (m, 7H).

38: 48% yield (Method I), mp 165–166 °C (from EtOH); $^1\text{H NMR}$: δ =0.99 (t, J =7 Hz, 3H), 3.91 (s, 6H), 4.45 (q, J =7 Hz, 2H), and 7.5–8.7 (m, 7H).

Preparation of 6. 1) **6a**: **1a** (222 mg, 1.87 mmol) was protonated with 42% aq HBF_4 (2 ml) in CH_2Cl_2 (8 ml). The resulting material was dissolved in CH_2Cl_2 (10 ml), to which was added **3a** (431 mg, 2.91 mmol). After usual work-up, recrystallization from EtOH–MeCN gave **5a** (487 mg, 85%). A suspension of **5a** (342 mg, 1.11 mmol) in CH_2Cl_2 (15 ml) was deprotonated with aq NaOH and the aqueous layer was separated, to which was added aq NaBPh_4 . The resulting ppt was recrystd from EtOH–MeCN to give colorless crystals of **6a**, 297 mg (59% yield based on **5a**), mp 160 °C (decomp); $^1\text{H NMR}$ ($\text{DMSO}-d_6$): δ =2.16 (s, 6H), 2.48 (s, 6H), 2.3–2.6 (br t, J =6 Hz, 2H), 3.16 (br t, J =6 Hz, 2H), and 6.6–7.5 (m, 20H). Found: C, 79.72; H, 8.25; N, 3.09%. Calcd for $\text{C}_{30}\text{H}_{36}\text{BNS}$: C, 79.46; H, 8.00; N, 3.09%.

2) **6b**: **5b** was prepared from **1b** by the same method as

that of **5a**, ca. 100% yield; $^1\text{H NMR}$ ($\text{DMSO}-d_6$): δ =1.39 (t, J =7 Hz, 3H), 2.86 (s, 6H), 2.93 (s, 3H), 3.40 (q, J =7 Hz, 2H), and 3.58 (br s, 4H). Similarly **6b** was obtained in 64% yield, mp 143–147 °C (decomp) (from EtOH– Me_2CO); $^1\text{H NMR}$ ($\text{DMSO}-d_6$): δ =1.12 (t, J =7 Hz, 3H), 2.15 (s, 6H), 2.31 (s, 3H), 2.4–3.2 (m, 6H), and 6.7–7.6 (m, 20H). Found: C, 79.81; H, 8.44; N, 3.25%. Calcd for $\text{C}_{31}\text{H}_{38}\text{BNS}$: C, 79.64; H, 8.19; N, 3.00%.

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