nacolone (0.08 mL, 0.68 mmol), and KO^{t}Bu (76 mg, 0.68 mmol) in dry THF (5 mL) was stirred for 30 min at −35 °C. After the addition of water, the mixture was extracted with benzene under argon. The organic extract was concentrated, and the residue was purified by column chromatography on silica gel (benzene eluent) to give 3,6-dihydroazulene derivative **12** as a colorless oil: ^{1}H NMR (CCl_4) δ 1.11 (9 H, s, $C(CH_3)_3$), 2.26–2.48 (1 H, m, H6), 2.75 (2 H, d, J = 7, $COCH_2$), 3.50 (2 H, s, H2), 4.99 (1 H, dd, J = 4, 10, H5 or H7), 5.06 (1H, dd, J = 4, 10, H5 or H7), 6.22 (1 H, d, J = 10, H4), 6.73 (1 H, d, J = 10, H8). This dihydro compound (**12**) and the other fractions containing **12** were oxidized with chloranil and chromatographed on silica gel (benzene eluent) to give ethyl 2-chloro-6-(3,3-dimethyl-2-oxobutyl)azulene-1-carboxylate (**5a**) (54.6 mg, 73%) as red needles: mp 115–116 °C (hexane); IR (KBr) 1707, 1672 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 1.21 (9 H, s, $C(CH_3)_3$), 1.43 (3 H, t, J = 7, ethyl CH_3), 3.82 (2 H, s, $COCH_2$), 4.36 (2 H, q, J = 7, ethyl CH_2), 7.00 (1 H, s, H3), 6.95–7.30 (2 H, m, H4,5), 8.01 (1 H, d, J = 11, H7), 9.30 (1 H, d, J = 11, H8). Anal. Calcd for $C_{19}H_{21}ClO_3$: C, 68.56; H, 6.36; Cl, 10.65. Found: C, 68.37; H, 6.34; Cl, 10.64.

Reaction of 2-Chloroazulene (6) with Pinacolone Enolate. A mixture of **6** (105 mg, 0.65 mmol), pinacolone (0.26 mL, 2.1 mmol), and KO^{t}Bu (230 mg, 2.0 mmol) in dry THF (10 mL) was stirred for 2 h at 0 °C. After the addition of water, the mixture was extracted with benzene under argon atmosphere. The organic extract was concentrated, and the residue was purified by column chromatography on silica gel (50% benzene in hexane eluent) to give 1,4-dihydro derivative **13** as a colorless oil: ^{1}H NMR (CCl_4) δ 0.98 (9 H, s, $C(CH_3)_3$), 2.41 (2 H, d, J = 7, $COCH_2$), 3.20 (2 H, s, H1), 3.64 (1 H, br q, J = 7, H4), 5.45 (1 H, dd, J = 8, 10, H5), 5.9–6.3(2 H, m, H6, 7), 6.19 (1 H, br s, H3), 6.48 (1 H, d, J = 10, H8). Oxidation of **13** with chloranil gave 4-(3,3-dimethyl-2-oxobutyl)-2-chloroazulene (**8a**) as violet needles: mp 64–65 °C (hexane); IR (KBr) 1697 cm^{-1}; ^{1}H NMR (CCl_4) δ 1.26 (9 H, s, $C(CH_3)_3$), 4.22 (2 H, s, $COCH_2$), 6.9–7.5 (5 H, m, H1,3,5,6,7), 8.14 (1 H, d, J = 10, H8). Anal. Calcd for $C_{16}H_{17}ClO$: C, 73.70; H, 6.57; Cl, 13.60. Found: C, 73.70; H, 6.80; Cl, 13.50.

The other fractions containing dihydroazulenes were oxidized with chloranil and chromatographed on silica gel (10% ethyl acetate in hexane eluent) to give **8a** and 6-(3,3-dimethyl-2-oxobutyl)-2-chloroazulene (**9a**) (125 mg, 74%, **8a**:**9a** = ca. 1:1 on the basis of ^{1}H NMR spectral data). Further purification using HPLC (SI60-5, 7.5 × 300 mm column, 5% acetone in hexane eluent) afforded the authentic samples. **9a** as violet needles: mp 165–167 °C (hexane); IR (KBr) 1697 cm^{-1}; ^{1}H NMR (CCl_4) δ 1.20 (9 H, s, $C(CH_3)_3$), 3.87 (2 H, s, $COCH_2$), 6.99 (2 H, d, J = 11, H5,7), 7.12 (2 H, s, H1,3), 8.04 (2 H, d, J =: 11, H4,8). Anal. Calcd for $C_{16}H_{17}ClO$: C, 73.70; H, 6.57; Cl, 13.60. Found: C, 73.73; H, 6.87; Cl, 13.65.

Reaction of 6 with 3-Methyl-3-phenyl-2-butanone Enolate. A mixture of **6** (50 mg, 0.31 mmol), 3-methyl-3-phenyl-2-butanone (150 mg, 0.93 mmol), and KO^{t}Bu (105 mg, 0.93 mmol) in dry THF (5 mL) was stirred for 8 h at room temperature. After the usual workup, the crude product was oxidized with chloranil and chromatographed on silica gel (benzene eluent) to give 1-(2-chloro-6-azulyl)-3-methyl-3-phenyl-2-butanone (**9d**) (41 mg, 41%) as blue prisms: mp 91–92 °C (hexane); IR (KBr) 1707 cm^{-1}; ^{1}H NMR (CCl_4) δ 1.51 (6 H, s, CH_3), 3.54 (2 H, s, $COCH_2$), 6.72 (2 H, d, J = 10, H5,7), 7.07 (2 H, s, H1,3), 7.28 (5 H, s, C_6H_5), 7.92 (2 H, d, J = 10, H4,8). Anal. Calcd for $C_{21}H_{19}ClO$: C, 78.13; H, 5.93; Cl, 10.98. Found: C, 78.05; H, 6.12; Cl, 10.95.

Reaction of Azulene (7) with Pinacolone Enolate. A mixture of **7** (75 mg, 0.59 mmol), pinacolone (0.22 mL, 1.76 mmol), and KO^{t}Bu (200 mg, 1.78 mmol) in dry THF (4 mL) was stirred for 2 h at 0 °C. After the usual workup, the crude product was oxidized with chloranil and chromatographed on silica gel (Waco gel 300, 40% hexane in benzene eluent) to give 1-(6-azulyl)-3,3-dimethyl-2-butanone (**11a**) (30.1 mg, 23%) as blue needles: mp 101–103 °C; IR (KBr) 1692 cm^{-1}; ^{1}H NMR (CCl_4) δ 1.19 (9 H, s, $C(CH_3)_3$), 3.89 (2 H, s, $COCH_2$), 6.92 (2 H, d, J = 10, H5,7), 7.24 (2 H, d, J = 4, H1,3), 7.74 (1 H, t, J = 4, H2), 8.16 (2 H, d, J = 10, H4,8). Anal. Calcd for $C_{16}H_{18}O$: C, 84.91; H, 8.02. Found: C, 84.70; H, 8.24.

Further elution afforded 1-(4-azulyl)-3,3-dimethyl-2-butanone (**10a**) (10.3 mg, 8%) as blue prisms: mp 115–119 °C (hexane); IR (KBr) 1705 cm^{-1}; ^{1}H NMR (CCl_4) δ 1.24 (9 H, s, $C(CH_3)_3$), 4.31 (2 H, s, $COCH_2$), 6.85–7.60 (5 H, m, H1,3,5,6,7), 7.73 (1 H, t, J = 4, H2), 8.26 (1 H, d, J = 10, H8). Anal. Calcd for $C_{16}H_{18}O$: C, 84.91; H, 8.02. Found: C, 84.67; H, 8.26.

Registry No. 1, 36044-40-3; **2a**, 120418-45-3; **2b**, 120418-47-5; **3a**, 120418-46-4; **3b**, 120418-48-6; **3c**, 120418-49-7; **4**, 54522-71-3; **5a**, 120418-50-0; **6**, 36044-31-2; **7**, 275-51-4; **8a**, 120418-51-1; **9a**, 120418-52-2; **9d**, 120418-53-3; **10a**, 120418-54-4; **11a**, 120418-55-5; **12**, 120418-43-1; **13**, 120418-44-2; ^{t}BuCOMe, 75-97-8; Me_2CO, 67-64-1; $MeCOCH_2CO_2Me$, 105-45-3; $PhCMe_2COMe$, 770-85-4; Et_2CO, 96-22-0; $^i\!Pr_2CO$, 565-80-0.

Alkylthio Aromatic Amines

Paul F. Ranken* and B. Gary McKinnie[1]

Ethyl Corporation, Ethyl Technical Center, P.O. Box 14799, Baton Rouge, Louisiana 70898

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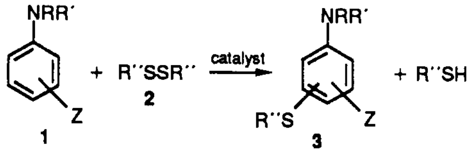
We recently reported that the aluminum phenoxide-catalyzed reaction of phenols with alkyl disulfides provides a superior synthesis of *o*-(alkylthio)phenols.[2] Our interests in ortho-alkylated phenols and ortho-alkylated aromatic amines prompted us to investigate whether alkylthio aromatic amines could be similarly prepared. Except for the preparation of sulfenamides,[3] the synthetic utility of the reaction of aromatic amines with alkyl disulfides has remained unexplored. We report that moderate to good yields of alkylthio aromatic amines can be achieved by reacting aromatic amines with aliphatic disulfides in the presence of Lewis acid catalysts, particularly aluminum chloride and copper iodide (Table I). Alkylthiation is accomplished either by heating a stirred mixture of catalyst, disulfide, and aromatic amine to a predetermined temperature (method A) or by slow addition of the disulfide to a heated mixture of aromatic amine and catalyst (method B). The latter procedure generally results in shorter reaction times while the former is somewhat more convenient. As with the alkylthiation of phenols, appropriate aromatic amines give ortho/para mixtures which are conveniently separated by fractional distillation, the ortho isomer being more volatile.



Z = H, alkyl, NH_2, Cl, OCH_3; R′, R = H, CH, CH_3; R′′ = CH_3, C_2H_5

A number of catalysts were evaluated for their efficacy in promoting the reaction of aniline with dimethyl disulfide (Table II). Certain metal halides and mild protonic acids catalyzed the formation of (methylthio)anilines. Copper iodide gave the best yield of 2-(methylthio)aniline, and aluminum chloride gave the best yield of 4-(methylthio)aniline. By contrast, phenol reacts with dimethyl disulfide in the presence of aluminum catalysts to give predominantly 2-(methylthio)phenol (ortho/para = 2.4).[2] Scoping experiments showed that indole, aromatic diamines, and aromatic monoamines containing alkyl, methoxy, or chlorine substituents underwent alkylthiation successfully. Sluggish reaction was achieved with *o*-nitroaniline while *p*-bromoaniline gave several side products. Reaction of

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[1] A portion of this work is described in U.S. Patent 4,594,453.

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0022-3263/89/1954-2985$01.50/0

Table I. Alkylthio Aromatic Amines

Z	R, R′	R″	catalyst	reaction time, h, method	convn, %	3 (yield, %)
H	H, H	methyl	CuI	20, A	76	**a**, 2-(methylthio)aniline (33) **b**, 4-(methylthio)aniline (32)
H	H, H	methyl	$AlCl_3$	25, A	71	**a**, 2-(methylthio)aniline (25) **b**, 4-(methylthio)aniline (48)
2-Me	H, H	methyl	$AlCl_3$	10, A	68	**c**, 2-methyl-6-(methylthio)aniline (21) **d**, 2-methyl-4-(methylthio)aniline (48)
2,6-$(Me)_2$	H, H	methyl	$AlCl_3$	4, A	78	**e**, 2,6-dimethyl-4-(methylthio)aniline (87)
4-Me	H, H	methyl	CuI	19, A	74	**f**, 2-(methylthio)-4-methylaniline (64)
4-Cl	H, H	methyl	$AlCl_3$	24, A	69	**g**, 2-(methylthio)-4-chloroaniline (54)
4-MeO	H, H	methyl	CuI	37, A	70	**h**, 2-(methylthio)-4-methoxyaniline (58)
2-CH	CH, H	methyl	CuI	3, B	86	**i**, 3-(methylthio)indole (41)
H	CH_3, CH_3	methyl	CuI	20, A	81	**j**, 4-(methylthio)-*N*,*N*-dimethylaniline (42)
H	H, H	ethyl	$AlCl_3$	9, B	68	**k**, 2-(ethylthio)aniline (27) **l**, 4-(ethylthio)aniline (38)
2-Me, 3-NH_2	H, H	methyl	$AlCl_3$	7, A	80	**m**, 2-methyl-3-amino-4-(methylthio)aniline (32)
H	H, H	methyl	$AlCl_3$	120, A	100	**n**, tris(methylthio)aniline (67)

Table II. Catalysts for the Preparation of (Methylthio)aniline (3a,b)

catalyst	reactn time,[a] h	aniline convn, %	yield,[b] %	ortho/para
CuI	20	76	65	1.1
$AlCl_3$	25	71	73	0.5
$AlCl_3/I_2$[c]	7	76	74	0.5
NH_4Br	116	44	77	1.0
$ZrCl_4$	19	68	59	0.6
$TiCl_4$	16	68	40	0.4
$FeCl_3$	48	<20	<20	–
$ZnCl_2$	48	<20	<20	–
NH_4I	15	72	70	0.8

[a] Time required for 0.2 mol of aniline, 0.2 mol of methyl disulfide, and 0.0134 mol of catalyst to achieve a reaction temperature of 170–175 °C. [b] Quantitative analysis by gas chromatography using a 30-m DB-1 column with undecane as internal standard. [c] $AlCl_3$ = 0.0134 mol; I_2 = 0.00167 mol.

aniline with excess dimethyl disulfide was found to give an excellent yield of tris(methylthio)aniline. The selectivity of the reaction was only modest, however, with 2,4,6-tris(methylthio)aniline being the predominant component of a 5.8:1.6:1.0 mixture of isomers.

The alkylthiation reaction conditions and the alkylthio aromatic amine product distribution are consistent with the concept of an aromatic amine/Lewis acid complex interacting with the disulfide to provide an electrophile for an aromatic substitution reaction. Similar alkylsulfonium electrophiles have been proposed for the boron trifluoride catalyzed addition of disulfides to alkenes[4] and the acid-catalyzed reaction of alkyl disulfides with phenols.[5] Additional indirect support for this type of mechanism is the observation that 2-(methylthio)aniline and 4-(methylthio)aniline are susceptible to a redistribution reaction. Heating each isomer with a catalytic amount of aluminum chloride at elevated temperature gave extensive rearrangement of the para isomer and modest rearrangement of the ortho isomer (Table III). Virtually no redistribution was found with 3-(methylthio)aniline. Fujisawa, Ohtsuka, and Tsuchihashi have observed that aryl disulfides undergo rearrangement when treated with aluminum chloride,[6] presumably by sulfonium ion formation, ring thiation, and subsequent proton loss.[7] The (methylthio)anilines probably form an anilino/aluminum chloride complex which can effect both reorientation and disproportionation of the methylthio group. The instability of the *m*-(methylthio)arenium ion accounts for the relative inertness of 3-(methylthio)aniline.

The volatile products from the redistribution experiments with 2-(methylthio)aniline and 4-(methylthio)aniline were examined by gas chromatography/mass spectroscopy and found to contain small amounts of *N*-methylaniline and *N*-methyl-X-(methylthio)anilines. We have conducted no investigation of this observation and can only speculate that the products of N-methylation arise from condensation with thioformaldehyde,[8] generated in situ from CH_3S^+, or by nitrogen interaction with the electrophile.

Experimental Section

Proton magnetic resonance spectra were measured on a Varian EM-390 spectrometer. Carbon spectra were recorded on a Nicolet 360 spectrometer. Chemical shifts are reported in parts per million relative to tetramethylsilane. Mass spectra were obtained on a Finnigan 4023 gas chromatograph/mass spectrometer equipped with a 50-m SE-52 fused silica capillary column.

All reactions were carried out in a nitrogen atmosphere in an efficient fume hood. Mercaptan byproduct was trapped in aqueous sodium hydroxide and oxidized with hypochlorite.

Typical Procedure A: 2-Methyl-6-(methylthio)aniline and 2-Methyl-4-(methylthio)aniline (3c,d). A solution of 1.79 g (0.0134 mol) of aluminum chloride and 21.4 g (0.2 mol) of 2-methylaniline was stirred at 150 °C for 30 min, cooled to 100 °C, and 18.8 g (0.2 mol) of dimethyl disulfide was added. The reaction was heated at reflux until a pot temperature of 170–175 °C was achieved, which took 10 h. The reaction was cooled to ambient temperature, diluted with 30 mL of ether, and treated with 60 mL of 1 N NaOH. The organic phase was separated, the aqueous phase was extracted twice with 20 mL of ether, and the organic layers were combined, treated with saturated aqueous NaCl, and concentrated with a rotary evaporator. Distillation through a 16 × 1.5 cm column packed with 1.27 × 2.54 × 2.54 mm Heli-Pak

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Table III. Aluminum Chloride Catalyzed Redistribution of (Methylthio)anilines[a]

(methylthio)aniline	product mixture, wt % MeSSMe	aniline	2MTA	3MTA	4MTA	2,4-diMTA	2,6-diMTA
4-(methylthio)aniline	2	17	26	0.3	13	18	7
2-(methylthio)aniline	2	15	39	0.1	6	12	6
3-(methylthio)aniline	–	trace	–	93	–	trace	–

[a] (Methylthio)aniline (0.1 mol) stirred at 175 °C under nitrogen with aluminum chloride (0.0067 mol) for 20 h.

Table IV. Physical and Spectral Properties

3	bp, °C/mmHg	(lit. bp)	^{1}H NMR (CCl_4); ^{13}C NMR ($CDCl_3$)
a	117–22/13	(124/14)[9]	2.30 (s, 3 H), 4.12 (s, 2 H), 6.60 (m, 2 H), 7.04 (m, 1 H), 7.28 (m, 1 H); 17.5, 114.8, 118.5, 120.1, 128.7, 133.2, 147.1
b	141–3/13	(139/15)[10]	2.31 (s, 3 H), 3.49 (s, 2 H), 6.45 (m, 2 H), 7.10 (m, 1 H); 18.4, 115.6, 125, 130.8, 145.4
c	131–3/12	(ref 11)	2.07 (s, 3 H), 2.27 (s, 3 H), 4.13 (s, 2 H), 6.50 (t, 1 H, *J* = 2.5), 6.86 (d, 1 H, *J* = 2.5), 7.12 (d, 1 H, *J* = 2.5); 17.8, 118, 119.6, 122, 130, 131.3, 145.3
d	150–1/10	(ref 12)	2.04 (s, 3 H), 2.31 (s, 3 H), 3.38 (s, 2 H), 6.40 (m, 1 H), 6.93 (m, 2 H); 17.1, 18.7, 115.4, 122.9, 125.3, 128.5, 132.0, 143.3
e	178–8/30	(ref 13)	2.08 (s, 3 H), 2.31 (s, 3 H), 3.38 (s, 2 H), 6.87 (s, 2 H); 17.4, 18.8, 122.2, 124.5, 129.8, 141.5
f	152–4/30	(139/5)[14]	2.15 (s, 3 H), 2.25 (s, 3 H), 4.00 (s, 2 H), 6.41 (d, 1 H, *J* = 2.5), 6.75 (dd, 1 H, *J* = 2.5), 7.15 (d, 1 H, *J* = 2.5); 17.6, 20.2, 114.9, 120.1, 127.9, 129.4, 133.5, 144.4
g	90–1/0.3	(ref 15)	2.31 (s, 3 H), 4.10 (s, 2 H), 6.49 (d, 1 H, *J* = 3), 6.96 (dd, 1 H), 7.27 (d, 1 H, *J* = 1); 17.2, 115.6, 121.8, 122.5, 128.2, 131.5, 145.1
h	96–103/0.3	(96/0.05)[16]	2.30 (s, 3 H), 3.70 (s, 3 H), 3.85 (s, 2 H), 6.51 (s, 1 H), 6.53 (d, 1 H, *J* = 1), 6.82 (d, 1 H, *J* = 1); 17.2, 55.6, 114.5, 115.9, 117.3, 121.6, 140.6, 152.4
i	136–40/1	(112/0.15)[17]	2.30 (s, 3 H), 6.91 (d, 1 H, *J* = 1), 7.10 (m, 3 H), 7.66 (m, 2 H); 19.8, 107.2, 111.5, 118.8, 120.0, 122.4, 127.6, 128.3, 135.9
j	97–98/0.8	(153/15)[10]	2.32 (s, 3 H), 2.90 (s, 3 H), 6.55 (d, 2 H, *J* = 3)8 7.14 (d, 2 H, *J* = 3); 18.6, 40.0, 112.7, 130.8, 131.1, 148.9
k	84–90/1.2	(97/10)[18]	1.19 (t, 3 H, *J* = 2.5), 2.67 (q, 2 H, *J* = 2.5), 4.20 (s, 2 H), 6.62 (m, 1 H), 7.07 (m, 1 H), 7.30 (m, 2 H); 14.7, 28.6, 114.6, 118.1, 129.3, 135.5, 148.1
l	96–8/0.7	(165/12)[19]	1.17 (t, 3 H, *J* = 2.5), 2.71 (q, 2 H, *J* = 2.5), 3.59 (s, 2 H), 6.48 (m, 2 H), 7.18 (m, 2 H); 14.1, 29.5, 114.6, 122, 133, 145.5
m	132–6/0.6	(ref 11)	1.80 (s, 3 H), 2.13 (s, 3 H), 3.41 (s, 1 H), 4.22 (s, 1 H), 5.90 (d, 1 H, *J* = 2.8), 7.00 (d, 1 H, *J* = 2.8); 10.7, 19.2, 106.1, 106.3, 108.6, 133.4, 145.9, 146.8
n	159–85/0.2	(ref 11)	2.29 (s, 6 H), 2.32 (s, 3 H), 4.82 (s, 2 H), 7.27 (s, 2 H); 16.6, 17.9, 120.2, 124.5, 132.3, 144.8

3011 Hastelloy B gave 1.6 g of dimethyl disulfide (bp 40 °C/30 mm), 6.4 g of 2-methylaniline (bp 103–109 °C/30 mm), 3.0 g (21% yield) of 2-methyl-6-(methylthio)aniline (bp 131–133 °C/12 mm), and 10.3 g (48% yield) of 2-methyl-4-(methylthio)aniline (bp 150–51 °C/10 mm).

Typical Procedure B: 3-(Methylthio)indole (3i). A mechanically stirred mixture of 121.7 g (1.04 mol) of indole and 12.75 g (0.067 mol) of copper iodide was heated in a nitrogen atmosphere at 150 °C for 30 min, and the tan slurry was cooled to 140–45 °C. Dimethyl disulfide (100 mL; 1.11 mol) was added at such a rate to keep the temperature above 132 °C. The reaction vigorously evolved methyl mercaptan, and the addition was complete in 35 min. After all of the disulfide had been added, the reaction was heated from 136 °C to 160 °C, which took 1 h. The reaction was cooled to 140 °C, 20 mL (1.31 mol total) of dimethyl disulfide was added, and the reaction reheated to 160 °C in about 70 min. The reaction was cooled, diluted with 100 mL of ether, and stirred with 40 mL of 2 N NaOH. The mixture was filtered through glass fiber filter paper, the solids were washed with 15 mL of ether, the organic layer was separated, and the solvent was removed with a rotary evaporator to give 145 g of dark brown oil. Distillation through a short path still to an overhead temperature of 180 °C (1 mm) gave 109 g of distillate. Redistillation through a 16 × 1.5 cm vacuum jacketed Vigreux column and then a 16 × 1.5 cm column packed with 1.27 × 2.54 × 2.54 mm Heli-Pak 3011 Hastelloy B gave 13 g of indole followed by 11 g of a mixture of indole and 3-(methylthio)indole (75–129 °C/0.8 mm) and 71.2 g (41% yield) of pure 3-(methylthio)indole (bp 136–140 °C/1–1.5 mm).

Redistribution of (Methylthio)aniline. A golden solution of 13.9 g (0.1 mol) of freshly distilled (methylthio)aniline and 0.89 g (0.0067 mol) of aluminum chloride was stirred under nitrogen for 20 h at 174 ± 3 °C. The reaction was cooled, diluted with ether, and treated with 30 mL of 1 N NaOH. The organic layer was separated, and the aqueous layer was extracted twice with 15 mL of ether. The combined organics were treated with 20 mL of saturated NaCl, dried (Na_2SO_4), and filtered, and the solvent was removed with a rotary evaporator to give a black liquid. Quantitative analysis by GC using undecane as an internal standard gave the results in Table III. Qualitative analysis of the redistribution of 2-(methylthio)aniline showed 2% dimethyl disulfide, 22% aniline, 1% *N*-methylaniline, 43% 2-(methylthio)aniline, 1% *N*-methyl-2-(methylthio)aniline, 7% 4-(methylthio)aniline, 8% 2,4-bis(methylthio)aniline, and 15% 2,6-bis(methylthio)aniline.

Table V

fraction	bp, °C	wt, g	composition
1	120–159	32.3	9, 11, and 6 area % bis(methylthio)aniline; 60, 13, and 1 area % tris(methylthio)aniline
2	159–173	73.7	0.3, 2, and 2 area % bis(methylthio)aniline; 70, 18 and 8 area % tris(methylthio)aniline
3	173–185	25.6	45, 18, and 31 area % tris(methylthio)aniline; 5 area % tetrakis(methylthio)aniline

Preparation of Tris(methylthio)aniline (3n). A yellow solution of 61.8 g (0.66 mol) of aniline and 5.94 g (0.0445 mol) of aluminum chloride was stirred at 150 °C for 1 h. The reaction was cooled, and 250 g (2.66 mol) of dimethyl disulfide was added. The reaction was stirred at reflux until a reaction temperature of 135 °C was achieved. This took 5 days. Analysis of an aliquot of the crude reaction mixture showed, after hydrolysis, 31% dimethyl disulfide, 6% bis(methylthio)anilines, 61% tris(methylthio)anilines, and 2% tetrakis(methylthio)aniline. The reaction was cooled, and 50.9 g of unreacted dimethyl disulfide was recovered under reduced pressure with a rotary evaporator. The dark blue reaction mixture was diluted with ether and treated with 100 mL of 1 N NaOH. The phases were separated, and the aqueous layer was extracted twice with ether. The combined organics were treated twice with 100 mL of saturated aqueous sodium chloride and distilled through a short path still at 0.2–0.3 mm to give the data in Table V. The proton NMR spectrum of fraction 2 indicated that 2,4,6-tris(methylthio)aniline was the predominant isomer. The yield based on the combination of fractions 2 and 3 was 67%.

Registry No. 1 (Z = R = R′ = H), 62-53-3; 1 (Z = 2-Me, R = R′ = H), 95-53-4; 1 (Z = 2,6-Me_2, R = R′ = H), 87-62-7; 1 (Z = 4-Me, R = R′ = H), 106-49-0; 1 (Z = 4-Cl, R = R′ = H), 106-47-8; 1 (Z = 4-MeO, R = R′ = H), 104-94-9; 1 (Z = 2-CH, R = CH, R′ = H), 120-72-9; 1 (Z = H, R = R′ = Me), 121-69-7; 1 (Z = 2-Me-3-NH_2, R = R′ = H), 823-40-5; **3a**, 2987-53-3; **3b**, 104-96-1; **3c**, 100305-95-1; **3d**, 75794-20-6; **3e**, 120578-20-3; **3f**, 29690-20-8; **3g**, 29690-21-9; **3h**, 1658-03-3; **3i**, 40015-10-9; **3j**, 2388-51-4; **3k**, 13920-91-7; **3l**, 3463-02-3; **3m**, 119361-05-6; **3n**, 102093-65-2; $AlCl_3$, 7446-70-0; NH_4Br, 41591-55-3; $ZrCl_4$, 10026-11-6; $TiCl_4$, 7550-45-0; $FeCl_3$, 7705-08-0; $ZnCl_2$, 7646-85-7; NH_4I, 59917-23-6.

New Type of Ionophores for Lithium Ion: N-Pivot Lariat Ethers Based on Monoaza-14-crown-4

Yohji Nakatsuji, Ryuhei Wakita, Yasuhiro Harada, and Mitsuo Okahara*

Department of Applied Chemistry, Faculty of Engineering, Osaka University, Yamada-oka, Suita, Osaka, Japan 565

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Liquid membrane transport is one of the important separation techniques for useful substances. Macrocyclic polyethers are successfully used as the carriers for alkali metal cations in such systems.[1] The efficiency and the selectivity in the transport are dominated by molecular recognition of the cation size by a carrier. Concerning lithium ion, 14-crown-4 ethers are known to show a high selectivity.[2] However, the efficiency of liquid membrane transport based on the complexing ability is expected to be insufficient because 14-crown-4 possesses only four coordination atoms. To compensate for the weak complexing ability, proton-ionizable crown ethers were developed and gave improved results.[3–6] In this case, however, the selectivity was not necessarily coincident with the selectivity expected from the structure of the macrocyclic ring used as the constituent.[6] The driving force for recognition seems to be rather dependent on the nature of the ionizable moiety. As another promising approach to raise the complexing ability, derivatization to lariat ether by introducing an electron-donating side arm to the crown ring should be considered.[7] Recently, the combination of lipophilic monoazacrown ether and picric acid was found to cooperatively work as an effective ionophore in the active transport system,[8] and the selectivity was attained by the discrimination of the cation size using the macrocyclic ring in this case. This transport system enabled the use of a carrier with a relatively lower complexing ability such as *N*-octylmonoaza-15-crown-5 (log $K(Na^+)$ = 3.08, in MeOH, at 25 °C).

Scheme I. Synthesis of Monoaza-crown Ethers

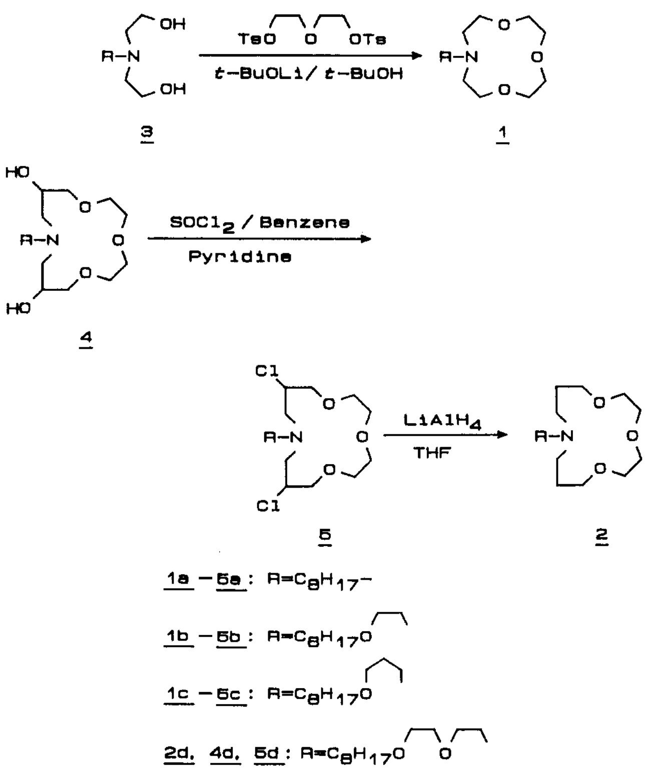

Table I. Competitive Passive Transport[a] Data toward Li^+, Na^+, and K^+

	transport velocity, 10^6 mol/h			selectivity	
ionophore no.	Li^+	Na^+	K^+	Li^+/Na^+	Li^+/K^+
1a	5.78	0.70	0.18	8.3	32
1b	5.44	6.71	1.78	0.8	3.1
1c	3.75	0.59	0.16	6.4	24
2a	1.35	0.21	0.030	6.3	45
2b	7.18	0.30	0.074	24	97
2c	2.77	0.14	0.020	20	136
2d	4.39	1.76	0.27	2.5	16

[a] Transport conditions: aqueous phase 1 (10 mL), [LiCl] = [NaCl] = [KCl] = [Me_4NOH] = 0.1 M; organic phase (CH_2Cl_2, 20 mL), ionophore and picric acid, 5 × 10^{-5} mol; aqueous phase 2 (10 mL), [HCl] = 0.1 M, 25 °C.

We now describe that novel N-pivot lariat ethers based on the 14-crown-4 ring are effective carriers for Li^+ in liquid membrane transport.

N-Substituted monoaza-12-crown-4 ethers **1** were prepared by the reaction of N-substituted diethanolamine **3** and diethylene glycol ditosylate according to a conventional procedure. On the other hand, N-substituted monoaza-14-crown-4 ethers **2** were synthesized by chlorination of the corresponding dihydroxy-14-crown-4[9] **4** with thionyl chloride, followed by reduction with $LiAlH_4$ in THF as shown in Scheme I. The structures were ascertained by IR, NMR, MS, and elemental analyses.

Transport experiments were carried out in a U-type cell under the conditions described in the footnotes in Table I. The results are also summarized in Table I.

As for **1a** and **2a**, the transport by **1a** is rather faster than that by **2a**, though the Li^+ selectivity is about the same. The introduction of the electron-donating side arm to the azacrown ethers, however, gave a different trend

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