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Reductive Removal of Sulfonyl Groups: Cleavage of Sulfonamides and Sulfonates by Alkali Metal combined with Crown Ether[1)]

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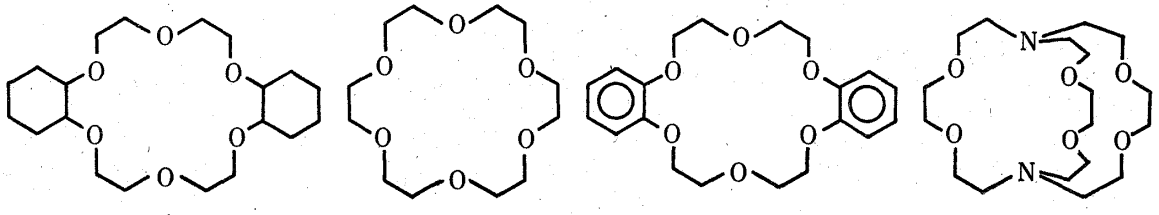
A system of potassium metal-crown ether-diglyme has been proved to be highly effective for reductive removal of the sulfonyl group from *O*-sulfonates or sulfonamides. The reaction proceeds even with mesylamides of dialkyl amines, which resist reductive cleavage by naphthalene radical anion. It has also been found that a simple combination of potassium metal or sodium–potassium alloy with isopropanol in diglyme or toluene is effective for the cleavage of dialkylamine sulfonamides which are relatively susceptible to reduction. In particular, the use of sodium–potassium alloy gave satisfactory results.

Keywords——dissolving metal reduction; potassium; sodium–potassium alloy; dicyclohexyl-18-crown-6; isopropanol; diglyme; toluene; tosylamide; mesylamide; *O*-tosylate

Enhancement of the solubility of an alkali metal in aprotic organic solvents by crown ether has been reported.[2–4)] In this system, a metal anion is believed to be generated in the form of a contact ion pair with a metal cation complexed with a crown ether.[3,4)] Since, in hitherto known dissolving metal reductions,[5,6)] a solvated electron[6,7)] is considered to be the active species, the present system was expected to reveal novel aspects of dissolving metal reduction. In fact, a combination of potassium (K) metal with dicyclohexyl-18-crown-6 (**1**)[2)] in toluene or diglyme was found to be quite effective for reductive defluorination of unactivated alkyl fluorides.[1a,8,9)]



1 **2** **3** **4**

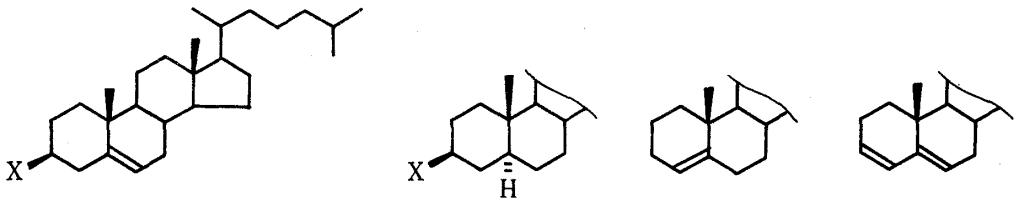
Chart 1

In this paper, a reductive cleavage of various sulfonamides and *O*-sulfonates by the present system using crown ether is described.

Cleavage of *O*-*p*-Toluenesulfonates with K-Dicyclohexyl-18-crown-6-Diglyme

Initially, cholesteryl *p*-toluenesulfonate (**5**) and cholestanyl *p*-toluenesulfonate (**7**) were treated with K-dicyclohexyl-18-crown-6 in diglyme[10)] under a nitrogen atmosphere at ambient temperature for 3 h. In the former case, a simple sulfur–oxygen bond cleavage occurred to regenerate cholesterol (**6**) in 50% yield, furthermore, cholest-4-ene (**9**) and cholest-3,5-diene (**10**) were also obtained in a combined yield of 41%, suggesting the occurrence of elimination of the tosyl group and successive reduction of the resulting conjugated diene.[11)] Replacement of the above crown ether (**1**) by cryptand 2,2,2 (**4**)[12)] resulted in the formation of the alcohol (**6**) and the olefin (**10**) in 33 and 50% yields, respectively. In the latter case, however, cho-

lestanyl *p*-toluenesulfonate (**7**), a saturated sulfonate, was smoothly cleaved under the above conditions to yield cholestanol (**8**) in 74% yield, using crown ether (**1**).[13]



5 : X=OTs
6 : X=OH

7 : X=OTs
8 : X=OH

9

10

Chart 2

Cleavage of Sulfonamides with K-Dicyclohexyl-18-crown-6-Diglyme

Sulfonyl groups have been widely used as masking groups for amines or alcohols.[14] In contrast to the easiness of sulfonylation, removal of the sulfonyl group from sulfonamide is not so straightforward as from *O*-sulfonates and attempts are still being made to solve this problem.[15] Hydrolytic cleavages tend to require drastic conditions and are often unsuccessful. Among various types of reactions used for cleavage, the most commonly used method is dissolving metal reduction or analogous procedures.[16–18] The radical anion method using sodium naphthalene[17] seems to be the most practical. Closson reported that this reducing system cleanly cleaves *p*-toluenesulfonamides (tosylamides) and also methanesulfonamides (mesylamides) of secondary aryl amines, but totally fails with mesylamides of primary amines and aliphatic amines. The use of alkali metal in hexamethylphosphoric triamide (HMPT) containing *tert*-butanol (*t*BuOH) may be complementary to the radical anion method, as suggested by Cuvigny and Larchevêque.[18] However, the use of HMPT as a solvent is rather limited by its potential carcinogenicity.[19] Thus, we decided to examine whether the alkali metal-crown ether system is applicable to the cleavage of sulfonamides, particularly to the removal of the *N*-mesyl protecting group, with the aim of providing a new procedure to complement the naphthalene radical anion method.

$\begin{matrix} R \\ R' \end{matrix}\!\!>\!NX$ Ts=*p*-toluenesulfonyl
Ms=methanesulfonyl

11: R,R′=CH_2<$\begin{matrix} CH_2\text{–}CH_2\text{–} \\ CH_2\text{–}CH_2\text{–} \end{matrix}$>, X=Ts
12: R,R′=CH_2<$\begin{matrix} CH_2\text{–}CH_2\text{–} \\ CH_2\text{–}CH_2\text{–} \end{matrix}$>, X=Ms
13: R,R′=CH_2<$\begin{matrix} CH_2\text{–}CH_2\text{–} \\ CH_2\text{–}CH_2\text{–} \end{matrix}$>, X=H·HCl
14: R=C_8H_{17}, R′=H, X=Ts
15: R=C_8H_{17}, R′=H, X=H·HCl
16: R=C_6H_{11}, R=$C_{12}H_{25}$, X=Ts
17: R=C_6H_{11}, R=$C_{12}H_{25}$, X=Ms
18: R=C_6H_{11}, R=$C_{12}H_{25}$, X=Ac
19: R=C_6H_{11}, R=$C_{12}H_{25}$, X=CHO

20: R=C_6H_{11}, R′=$C_{10}H_{21}$, X=Ts
21: R=C_6H_{11}, R′=$C_{10}H_{21}$, X=Ms
22: R=C_6H_{11}, R′=$C_{10}H_{21}$, X=Ac
23: R=C_6H_{11}, R′=$C_{10}H_{21}$, X=CHO
24: R=C_6H_{11}, R′=$C_{16}H_{33}$, X=Ms
25: R=C_6H_{11}, R′=$C_{16}H_{33}$, X=Ac
26: R=C_6H_{11}, R′=$C_{16}H_{33}$, X=CHO
27: R=C_6H_{11}, R′=$C_{16}H_{33}$, X=H·HCl
28: R=C_8H_{17}, R′=$C_{16}H_{33}$, X=Ts
29: R=C_8H_{17}, R′=$C_{16}H_{33}$, X=Ms
30: R=C_8H_{17}, R′=$C_{16}H_{33}$, X=Ac
31: R=C_8H_{17}, R′=$C_{16}H_{33}$, X=CHO
32: R=C_8H_{17}, R′=$C_{16}H_{33}$, X=H·HCl
33: R=C_8H_{17}, R′=$C_{12}H_{25}$, X=Ms
34: R=C_8H_{17}, R′=$C_{12}H_{25}$, X=Ac

Chart 3

The *p*-toluenesulfonamide (**11**) and methanesulfonamide (**12**) of piperidine were first tested as an example of regeneration of volatile amines from sulfonamides. After reduction in the same manner as in the case of *O*-sulfonates, the generated amine was distilled directly from the reaction mixture into a liquid nitrogen trap. Upon acidification with conc. hydro-

chloric acid, piperidine was obtained as the hydrochloride (**13**) in 82% and 76% yields, respectively.

N-Octyl-*p*-toluenesulfonamide (**14**), a tosylamide of a primary amine, could also be cleaved in 66% yield.[20]

Next, *N*-cyclohexyl-*N*-dodecyl-*p*-toluenesulfonamide (**16**) and *N*-cyclohexyl-*N*-decyl-*p*-toluenesulfonamide (**20**), both with a bulky branched alkyl group, were reduced with the K-dicyclohexyl-18-crown-6-diglyme system at ambient temperature for 3 h, followed by acetylation with acetic anhydride–pyridine. The former gave the corresponding acetamide (**18**) and the formamide (**19**) in 58 and 29% yields, respectively. Similarly, the latter afforded **22** in 57% yield and **23** in 21% yield. Formation of the formamides was completely unexpected.

Mesylamides of dialkylamines with a branched alkyl group, **24**, **17**, and **21**, could also be cleaved by the same system to give acetamides, **25**, **18** and **22**, as major products, and formamides, **26**, **19** and **23**, respectively, as shown in Table I. As the above formamides can be hydrolyzed almost quantitatively to the corresponding amine hydrochloride by refluxing them in ethanol containing hydrochloric acid, the yields of amines obtainable from the mesylamides can be estimated as the sum of the acetamide and the formamide.

Table I. Reductive Cleavage of Sulfonamides with K Metal combined with Dicyclohexyl-18-crown-6 in Diglyme or Toluene[a]

Entry	Substrate RR'NX				Yield %[b]	
	R	R'	X		RR'NAc	RR'NCHO
1	C_8H_{17}	$C_{16}H_{33}$	Tosyl	**28**	35—50	—
2	C_6H_{11}	$C_{12}H_{25}$	Tosyl	**16**	58	29
3	C_6H_{11}	$C_{10}H_{11}$	Tosyl	**20**	57	21
4	C_6H_{11}	$C_{16}H_{33}$	Mesyl	**24**	82	11
5	C_6H_{11}	$C_{12}H_{25}$	Mesyl	**17**	74	23
6	C_6H_{11}	$C_{10}H_{21}$	Mesyl	**21**	70	20

a) Sulfonamide (0.5 mmol) was treated with excess K metal in diglyme containing dicyclohexyl-18-crown-6 (1.0 mmol) at ambient temperature under a nitrogen atmosphere for 3 h, followed by quenching with isopropanol. The reduction in entry 1 was carried out in toluene.
b) Isolated yields from silica gel TLC after acetylation with acetic anhydride–pyridine.

The structures of the formamides were deduced from the physical data (see Table VIII) and were confirmed by chemical interconversion between the formamide and the corresponding acetamide obtained directly from the reductive cleavage of a sulfonamide. Although the origin and the mechanism of formation of the *N*-formyl group is not clear yet, this phenomenon seems to be general for the reduction by the K-crown ether-diglyme system. This strongly suggests that the species actually involved in the formylation is liberated by cleavage of the C–O bond of crown ether and/or diglyme.[21]

As shown in Table I, toluene gave poorer results than diglyme, contrary to our expectation based on the successful reductive defluorination in this solvent.[8] However, during the course of experiments using toluene as a solvent at 0°C, it was found that the yields were greatly affected by the presence of moisture. Therefore, the effect of a proton source[6] on the reductive cleavage reaction in the absence of a crown ether was examined.

Cleavage of Sulfonamides in the Presence of a Proton Source without Crown Ether

N-Octyl-*N*-hexadecyl-*p*-toluenesulfonamide (**28**) (0.5 mmol), which gave only 30% of the corresponding amine on hydrolysis by heating in acetic acid containing hydrochloric acid or by refluxing in isopropanol (iPrOH) with iPrOK, was treated with K in toluene containing iPrOH as a proton source at ambient temperature for 3 h. In a control experiment without

iPrOH, 86% of the starting material was recovered along with 7% of the acetamide after acetylation with acetic anhydride–pyridine and isolation by TLC on silica gel. Nevertheless, the yield of the acetamide (**30**) rose in parallel with the amount of the added iPrOH. When 2.6, 5.2 and 13.0 mol equivalents of iPrOH was added, the acetamide was obtained in 36, 66 and 83% yields, respectively (Table II). No other product could be detected on TLC except for the starting material, and in the last case, even the starting material was hardly detectable.

Table II. Reductive Cleavage of Sulfonamides (**28**) and (**29**) with K Metal in Toluene; Effect of iPrOH[a]

Sulfonamides C_8H_{17} >NX $C_{16}H_{33}$	iPrOH (ml)	(mol eq)	Yield %[b]	
			Acetamide (**30**)	Sulfonamide
X=Ts (**28**)	0.0		7	86
	0.1	(2.6)	36	19
	0.2	(5.2)	66	9
	0.5	(13.0)	83	—
X=Ms (**29**)	0.5	(13.0)	51	38
	1.0[c]	(26.0)	52	31

a) Sulfonamide (0.5 mmol) was treated with excess K metal in toluene (20 ml) containing a specified amount of iPrOH at ambient temperature for 3 h.
b) Isolated yield (by TLC on silica gel) after acetylation with acetic anhydride (3 ml)–pyridine (3 ml).
c) Another portion of 0.5 ml was added one hour after the initial addition of 0.5 ml.

On the other hand, the corresponding mesylamide (**29**) of the same amine gave the acetamide (**30**) in only 51% yield, and 38% of the mesylamide (**29**) was recovered unchanged. With more iPrOH, the results was no better (Table II). This sluggishness of reactivity of mesylamide could be successfully overcome by changing the solvent from toluene to diglyme, and the acetamide was obtained in 83% yield (Table III). Homologous mesylamide (**33**) was also cleaved to give **34** in 78% yield under the same reaction conditions.

Table III. Solvent Effect on the Reductive Cleavage of Mesylamide (**29**) with K Metal-iPrOH; Toluene *vs.* Diglyme[a]

Solvent	Yield %[b]	
	RR'NAc (**30**)	RR'NMs (**29**)
Toluene	51	38
Diglyme	83	7

a) Sulfonamide (0.5 mmol) was treated with K metal in 20 ml of the solvent containing iPrOH (0.5 ml) at ambient temperature for 3 h.
b) Isolated yield (by TLC on silica gel) after acetylation with acetic anhydride (3 ml)–pyridine (3 ml).

For comparison the above tosylamide (**28**) and mesylamide (**29**) were subjected to reduction, by A) Na-naphthalene[17] and B) K-HMPT-*t*BuOH[18], followed by acetylation with acetic anhydride in pyridine (Table IV).

System "A" cleaved the tosylamide (**28**) in 66% yield, but totally failed with the mesylamide (**29**), and system "B" cleaved the tosylamide (**28**) in 46% yield and the mesylamide (**29**) in 75% yield. On the other hand, the present simple system succeeded in demasking both the tosylamide (**28**) and the mesylamide (**29**) in 83% yield in each case, proving the effectiveness of this method.

Mesylamides with a branched alkyl group, such as *N*-cyclohexyl-*N*-hexadecylmesylamide (**24**), appear to resist the reductive cleavage reaction, and even under the optimal conditions for the mesylamides of amines with straight alkyl chains stated above, the acetamide (**25**)

Table IV. Reductive Cleavage of Tosylamide (28) and Mesylamide (29); Comparison of Metal-iPrOH Method with Others

C_8H_{17} $C_{16}H_{33}$>NX Sulfonamide	Yield of acetamide %[a] Methods: Na–Naphthalene[b]	K-*t*BuOH HMPT[d]	K-iPrOH[f] (Solvent)	
X=Ts (28)	66	46[e]	83	(Toluene)
X=Ms (29)	0[c]	75	83	(Diglyme)

a) Isolated yield (by TLC on silica gel) after acetylation with acetic anhydride (3 ml)–pyridine (3 ml) for 0.5 mmol of **28** or **29**.
b) See reference 17).
c) Starting material was recovered in 67% yield.
d) See reference 18).
e) Starting material was recovered in 36% yield.
f) See Table II and III.

Table V. Cleavage of Mesylamide with a Branched Alkyl Group (24) by K Metal-Toluene System; Effect of Alcohol[a]

$C_{16}H_{33}$–N(Ms)–⬡ (24)

Alcohol	Yield %[b] RR'NAc	RR'NMs
*n*PrOH	15	73
iPrOH	32	51
*t*BuOH	11	77

a) Mesylamide (0.5 mmol) was treated with K metal in toluene (20 ml) containing alcohol (0.5 ml) at ambient temperature for 3 h.
b) Isolated by TLC on silica gel after acetylation with acetic anhydride (3 ml)–pyridine (3 ml).

Table VI. Cleavage of Mesylamides with a Branched Alkyl Group by Alkali Metal-iPrOH System; Effect of Metal Source[a]

Mesylamide		Metal	Solvent	Yield %[b] RR'NAc	RR'NMs
$C_{16}H_{33}NC_6H_{11}$ Ms	(24)	K	Toluene	32	51
		Na-K[c]	Toluene	86	—
$C_{12}H_{25}NC_6H_{11}$ Ms	(17)	K	Diglyme	69	12
		Na-K[c]	Toluene	84	—

a) Mesylamide (0.5 ml) was treated with excess metal in each solvent (20 ml) containing iPrOH (0.5 ml) at ambient temperature for 3 h.
b) Isolated yield (by TLC on silica gel) after acetylation with acetic anhydride (3 ml)–pyridine (3 ml).
c) Na–K (44: 56 w/w) alloy.

was obtained in only 32% yield from **24**. Thus, the alcohol added as a proton source was changed from iPrOH to *n*PrOH or *t*BuOH. As shown in Table V, primary and tertiary alcohols gave no better results, affording the acetamide (**25**) in 15 and 11% yields, respectively.

Secondly, K metal was replaced by Na–K (44: 56 w/w) liquid alloy.[23] Table VI shows that Na–K alloy in toluene containing iPrOH successfully cleaved mesylamide (**24**) to give (**25**) in 86% yield as a sole product. Analogously, *N*-cyclohexyl-*N*-dodecylmesylamide (**17**) was cleaved to give **18** in 84% yield.

Thus, Na–K alloy–iPrOH–toluene system has been proved to be essentially as effective as that of K-dicyclohexyl-18-crown-6-diglyme (Table I), although the use of Na–K alloy involves a possible risk of explosion.[24]

We have demonstrated that a system of K metal–crown ether–diglyme or toluene is very effective for the reductive cleavage of *O*-sulfonates and dialkylamine sulfonamides. Furthermore, the effectiveness of Na–K alloy for the same purpose, and that of a simple combination of K metal with iPrOH in diglyme or toluene for the cleavage of dialkylamine sulfonamides which are susceptible to reduction were demonstrated. The application of the present system to the reduction of other functional groups, including conjugated dienes and sulfur-containing groups, will be reported shortly.

Experimental

Melting points were recorded on a Kofler-type block and are uncorrected. Thin layer chromatography (TLC) for preparative purposes was carried out on Merck Kieselgel 60 PF_{254}. Infrared (IR) spectra were measured in CCl_4 or $CHCl_3$. Nuclear (proton) magnetic resonance (NMR) spectra were measured in $CDCl_3$ at 60 MHz *vs.* tetramethylsilane as an internal standard. The formyl proton of **19**, **23** and **26** appears as two signals with relative intensities of 1 : 2 at higher and lower field, respectively. Mass spectra were obtained with a single focus instrument with an electron impact ionization (EI) system, unless otherwise stated, usually at 160—180°C and at 20 eV. High-resolution mass spectra were provided by a double-focusing instrument with EI at 20 eV. Commercial reagent grade dicyclohexyl-18-crown-6 from Merck was used after being dried with a rotary pump at ambient temperature for 0.5—1.0 h. Diglyme or toluene was distilled from sodium wire or lithium aluminum hydride. Commercial reagent grade potassium metal was cut into small pieces in dry *n*-hexane in nitrogen and washed with 10% isopropanol/*n*-hexane just before use. Nitrogen gas refers to nitrogen (99.9995%<) dried over molecular sieves (3 Å) and by means of a liquid nitrogen trap.

Preparation of Sulfonamides of Dialkyl Amines——The general procedure for the preparation of sulfonamides of dialkyl amines is shown in the following example of the preparation of *N*-octyl-*N*-hexadecyl-*p*-

Table VII. Yields and Properties of Sulfonamides

	Sulfonamide RR′NX			Yield %	mp °C	Formula	Analysis (%) Calcd (Found)				(Others) IR $CHCl_3$ cm^{-1} NMR $CDCl_3$ δ ppm unless otherwise specified
	R	R′	X				C	H	N	S	
16	C_6H_{11}	$C_{12}H_{25}$	Ts	81	Oil	$C_{25}H_{43}NO_2S$	71.21 (71.24	10.28 10.47	3.32 3.34	7.60 7.60)	MS 421 (M^+); IR 1330, 1150; NMR 0.86 (CH_3), 1.27 (CH_2), 2.39 (PhC<u>H</u>$_3$), 7.12 (Ph<u>H</u>), 7.58 (Ph<u>H</u>)
17	C_6H_{11}	$C_{12}H_{25}$	Ms	58	35.5—38	$C_{19}H_{39}NO_2S$	66.03 (66.29	11.38 11.48	4.05 4.03	9.28 9.22)	MS 345 (M^+); IR 1330, 1142 NMR 0.84 (CH_3), 1.25 (CH_2), 2.80 (SO_2CH_3)
20	C_6H_{11}	$C_{10}H_{21}$	Ts	85	Oil	$C_{23}H_{39}NO_2S$	70.18 (69.89	9.99 10.15	3.56 3.54	8.15 8.05)	MS 393 (M^+); IR 1330, 1150; NMR 0.87 (CH_3), 1.27 (CH_2), 2.40 (PhC<u>H</u>$_3$), 7.18 (Ph<u>H</u>), 7.62 (Ph<u>H</u>)
21	C_6H_{11}	$C_{10}H_{21}$	Ms	68	34—35	$C_{17}H_{35}NO_2S$	64.30 (64.61	11.11 11.23	4.41 4.37	10.10 10.04)	MS 317 (M^+); IR 1320, 1140 NMR 0.88 (CH_3), 1.26 (CH_2), 2.83 (SO_2CH_3)
24	C_6H_{11}	$C_{16}H_{33}$	Ms	81	55—55.5	$C_{23}H_{47}NO_2S$	68.77 (69.03	11.79 11.89	3.49 3.46	7.98 7.97)	MS 401 (M^+); IR 1340, 1150; NMR 0.88 (CH_3), 1.25 (CH_2), 2.84 (SO_2CH_3)
28	C_8H_{17}	$C_{16}H_{33}$	Ts	86	34.5—35	$C_{31}H_{57}NO_2S$	73.31 (73.51	11.31 11.43	2.76 2.65	6.31 6.22)	MS 507 (M^+); IR 1345, 1150 NMR 0.88 (CH_3), 1.26 (CH_2), 2.42 (PhC<u>H</u>$_3$), 7.62 (Ph<u>H</u>), 7.22 (Ph<u>H</u>)
29	C_8H_{17}	$C_{16}H_{33}$	Ms	73	Oil	$C_{25}H_{53}NO_2S$	69.54 (69.78	12.37 12.59	3.24 3.32	7.43 7.46)	MS 431 (M^+); IR 1345, 1150 NMR 0.88 (CH_3), 1.82 (CH_2), 2.68 (SO_2CH_3)

Ts=*p*-toluenesulfonyl, Ms=methanesulfonyl.

toluenesulfonamide (**28**). In case of insufficient dissolution of the starting material in dimethylformamide, diethyl ether was added until a homogeneous solution was obtained. All the IR, NMR, elemental analysis or MS data support the indicated structures of the sulfonamides of dialkyl amines, as summarized in Table VII.

Preparation of *N*-Octyl-*N*-hexadecyl-*p*-toluenesulfonamide (28)——Octylamine *p*-toluenesulfonamide (1.70 g, 6.0 mmol) in dimethylformamide (30 ml) was treated with 60% oil dispersion of sodium hydride (960 mg) on an ice-water bath for 30 min. Hexadecyl bromide (2.75 g, 9.0 mmol) was added to it and the mixture was stirred at ambient temperature for 38 h, followed by warming at 60°C for 1 h. After decomposition with water and extraction with ether, 3.4 g of a colorless oil was obtained. Chromatography on a silica gel column (300 mesh, 200 g) with hexane and then with benzene gave 2.61 g of tosylamide (**28**) (68% yield) from the benzene eluate.

General Procedure for the Reductive Cleavage of *O*-Sulfonates and Sulfonamides——A solution of *O*-sulfonate or sulfonamide (0.5 mmol), with or without dicyclohexyl-18-crown-6 (1.0 mmol), in dry diglyme or toluene (20 ml) was degassed by means of a rotary pump for 1—3 min in a two-necked cylindrical vessel (35 $\phi \times 100$ mm) connected to a vacuum line and a nitrogen gas line and equipped with a septum. Dry nitrogen gas was introduced at 1 atm through a molecular sieves drying tube and a liquid nitrogen trap. Then a lump of K metal (*ca.* 7 mm cube), previously washed with 10% iPrOH in *n*-hexane, or Na–K (44: 56 w/w) alloy, was added under a stream of nitrogen gas through the side arm by removing the septum. Once again, degassing and the introduction of nitrogen gas at 1 atm were repeated. Alcohol (0.5 ml) was injected through the septum, if required. The reaction mixture was magnetically stirred at ambient temperature for 3 h under a nitrogen atmosphere, and then the reaction mixture was transferred by means of a long syringe needle into a round-bottomed flask containing iPrOH (0.5 ml) for quenching. After removal of the solvent, the residue was treated with acetic anhydride (3 ml) and pyridine (3 ml) at ambient temperature in the usual manner. The products were isolated by TLC on silica gel developing with *n*-hexane/ethyl acetate (6: 1—4: 1).

Table VIII. Properties of Acetamides, Formamides and Hydrochloride

	Compound RR′NX R	R′	X	Formula	High-resolution mass or elemental analysis	(Others) IR CCl_4 cm^{-1} NMR $CDCl_3$ δ ppm unless otherwise specified
					H-MS observed M^+ (error, mmu)	
18	C_6H_{11}	$C_{12}H_{25}$	CH_3CO	$C_{20}H_{39}NO$	309.30407 (1.1)	Oil; IR 1650; NMR 0.89 (CH_3), 1.30 (CH_2), 1.98 (CH_2CO)
19	C_6H_{11}	$C_{12}H_{25}$	CHO	$C_{19}H_{37}NO$	295.28779 (0.5)	Oil; IR 1670; NMR 0.88 (CH_3), 1.26 (CH_2), 8.05 and 8.14 (1 : 2, CHO)
22	C_6H_{11}	$C_{10}H_{21}$	CH_3CO	$C_{18}H_{35}NO$	281.26968 (−2.0)	Oil; IR 1640; NMR 0.88 (CH_3), 1.26 (CH_2), 2.08 (CH_3CO)
23	C_6H_{11}	$C_{10}H_{21}$	CHO	$C_{17}H_{33}NO$	267.25548 (−0.5)	Oil; IR 1670; NMR 0.90 (CH_3), 1.26 (CH_2), 8.04 and 8.14 (1 : 2, CHO)
					Analysis (%) Calcd (Found) C H N	
25	C_6H_{11}	$C_{16}H_{33}$	CH_3CO	$C_{24}H_{47}NO$	78.84 12.96 3.83 (78.54 13.19 3.65)	Oil; MS 365 (M^+); IR 1650; NMR 0.88 (CH_3), 1.26 (CH_2), 2.08 (CH_3CO)
26	C_6H_{11}	$C_{16}H_{33}$	CHO	$C_{23}H_{45}NO$	78.56 12.90 3.98 (78.39 12.82 3.86)	Oil; MS 351 (M^+); IR 1675; NMR 0.88 (CH_3), 1.25 (CH_2), 8.04 and 8.13 (1 : 2, CHO)
30	C_8H_{17}	$C_{16}H_{33}$	CH_3CO	$C_{26}H_{53}NO$	78.91 13.50 3.54 (78.99 13.60 3.48)	Oil; MS 395 (M^+); IR 1650; NMR 0.88 (CH_3), 1.25 (CH_2), 2.07 (CH_3CO)
31	C_8H_{17}	$C_{16}H_{33}$	CHO	$C_{25}H_{51}NO$	78.67 13.47 3.67 (78.80 13.42 3.66)	Oil; MS 381 (M^+); IR 1680; NMR 0.88 (CH_3), 1.26 (CH_2), 8.03 (CHO)
32	C_8H_{17}	$C_{16}H_{33}$	H_2Cl	$C_{24}H_{52}NCl$	73.88 13.44 3.59 (74.16 13.58 3.63)	mp 205—213.5°C; IR (KBr) 2790, 2550, 2460

Acid Hydrolysis of the Formamide and Conversion to the Acetamide——i) *N*-Cyclohexyl-*N*-hexadecylamine Hydrochloride (**27**): A solution of formamide (**26**) (50 mg, 6.0 mmol) in MeOH (1 ml) containing conc. hydrochloric acid (1 ml) was heated under reflux for one day. As TLC analysis revealed incomplete hydrolysis, the solvent was removed and replaced by EtOH (2 ml) containing conc. hydrochloric acid (0.2 ml), and the reaction mixture was heated under reflux for 16 h. This time, only a trace of the starting formamide could be detected by TLC. Evaporation of the solvent yielded 47 mg of a white powder, which

was recrystallized from EtOH to give 39 mg of the amine hydrochloride (**27**) as a white powder. IR (KBr and $CHCl_3$) showed no absorption due to a formamide group.

ii) *N*-Cyclohexyl-*N*-hexadecylacetamide (**25**): The above amine hydrochloride (**27**) was treated with acetic anhydride–pyridine in the usual manner without further purification. After isolation by TLC, 34 mg of a colorless oil was obtained. This was indistinguishable from the acetamide (**25**) obtained directly from the reductive cleavage of **24** by TLC and by IR, NMR and MS.

Acid Hydrolysis of the Acetamide and Conversion to the Formamide——i) *N*-Octyl-*N*-hexadecylamine Hydrochloride (**32**): Hydrogen chloride gas was introduced for 30 min into a solution of the acetamide (**30**) (752 mg, 1.9 mmol) in acetic acid (30 ml) containing conc. hydrochloric acid (4 ml), and the mixture was heated under reflux for 18 d. Evaporation of the solvent under reduced pressure and recrystallization from EtOH gave 444 mg (60%) of **32** as an amorphous powder, mp 170—205°C, showing no absorption in the carbonyl region in the IR spectrum.

ii) *N*-Octyl-*N*-hexadecylformamide (**31**): A solution of the amine hydrochloride (**32**) (389 mg, 1 mmol) in formic acid (98—100%) (5 ml) was refluxed under an argon atmosphere for 39 h, followed by removal of the solvent under reduced pressure. The crude crystals obtained were subjected to TLC on silica gel to afford 56 mg of the formamide (**31**) as an oil. This was indistinguishable from the formamide (**31**) obtained directly from the reductive cleavage of **28** or **29** by IR, NMR and MS.

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In the absence of any reducible substrate, the above system is black-blue in color with excess metal under stirring even at ambient temperature, but in the presence of a substrate, the reaction mixture appears yellowish. The black-blue color of the K metal-crown ether complex liberated from the surface of the shiny metal is immediately discharged by the substrate.
11) 1,4-Reduction of a conjugated diene to a mono-olefin by the present system with a proton source will be reported separately.
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cryptand 2,2,2 is believed to yield in addition a substantial concentration of solvated electrons; see also 3) and 4).
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