novel hydroxy crown ether **2a**. Further experiments revealed a similar propensity for ring closure with epibromohydrin. However, with 1,3-dichloro-2-propanol, no **2a** was formed. These observations suggest that the ring closure of **1a** involves an initial nucleophilic attack of a phenoxide oxygen on the epoxide ring of the halohydrin.

Extension of the reaction to the synthesis of hydroxy crown ethers with larger (**2b**) and smaller (**2c**, **2d**) macrocyclic cavities also resulted in 39–51% yields of cyclized products (Table I). In these reactions, the cation was varied to take advantage of the template effect.[15]

Reaction of **3** with diphenol **1e** produced a 55% yield of the previously reported[9] dihydroxy crown ether **2e**. It is interesting to note that the reaction of 1,3-dichloro-2-propanol and diphenol **1e** also forms **2e**, albeit in substantially lower yield[9] than when **3** is employed.

The synthesis of **2a** has also been conducted with 25 times the amounts of reagents and solvents listed in the typical procedure (Table I) with no apparent reduction in yield. Thus the potential of this ring closure method for the synthesis of hydroxy crown ethers on a much larger scale is demonstrated.[16]

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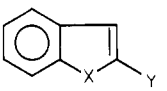
Oxidative Conversions of Sulfene Cycloadducts from Azaheptafulvenes and from Tropone to 1,2-Disubstituted Indoles and 2-Arylbenzofurans, Respectively

Summary: The cycloadducts from azaheptafulvenes and sulfenes as well as from tropone and arylsulfenes rearrange upon oxidation of their corresponding α-sulfonyl anions to give 1,2-disubstituted indoles and 2-arylbenzofurans.

Sir: The cycloadducts from 8-azaheptafulvenes and sulfenes,[1] as well as those from tropone and arylsulfenes,[2] readily undergo metalation (*n*-BuLi/THF, −78 °C) α to the sulfonyl unit. Subsequent treatment at low temperature with a solution of MoO_5·HMPA[3]–LDA (3 equiv), followed by warming to room temperature, quenching with water, and warming to 45 °C, gives in good yields the corresponding 1,2-disubstituted indoles or the 2-arylbenzofurans, respectively (Table I).

This is a one-pot procedure involving the oxidation of the α-sulfonyl anion,[4-6] rearrangement (presumably proceeding through the norcaradiene tautomer)[1,2,7,8] and ring closure to the indole or benzofuran system (Scheme I). The intermediate compound, **2** (X = CH_3N, Y = CH_3), was isolated under nonacidic, low-temperature workup con-

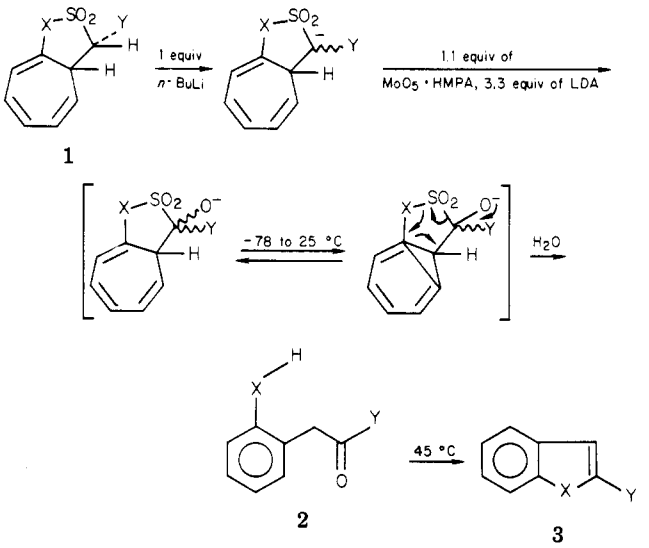
Table I[a,d]



X	Y	% yield[b,c]	mp or bp, °C
CH_3N	H	79	83 (2.5 mm)[e,f] (lit.[9] 133/26 mm)
CH_3N	CH_3	81	55.5-57.5[f] (lit.[10] 55.5-58.0)
$(CH_3)_3CN$	CH_3	52	78.0-79.5
p-$CH_3C_6H_4N$	CH_3	75	113.0-115.0
CH_3N	C_6H_5	72	101.0-103.0[f] (lit.[11] 101.5-102.5)
p-$CH_3C_6H_4N$	CH_3CH_2	78	111.0-113.0
p-$CH_3C_6H_4N$	*p*-ClC_6H_4	72	oil
p-$CH_3OC_6H_4N$	$(CH_3)_2CH$	78	104.5-105.5
p-BrC_6H_4N	$(CH_3)_2CH$	76	89.5-90.5
p-$CH_3C_6H_4N$	CH_3SO_2	64	oil
O	C_6H_5	75	118.0-119.5[f] (lit.[12] 118.0-119.5)
O	*p*-$CH_3C_6H_4$	77	126.5-127.5[f] (lit.[13] 127.0-128.0

[a] Reactions carried out in THF. [b] Yields are actual isolated yields. [c] All products were purified by column chromatography. [d] Products were characterized by NMR, IR, and mass spectroscopic data. [e] Picrate derivative of 1-methylindole, mp 149.0–150.0 °C (lit.[14] mp 150 °C). [f] Spectral data matched the NMR and IR data cited in the literature.

Scheme I



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ditions. The NMR and IR were consistent with the assigned structure.

The established requirement of 3 equiv of LDA/equiv of MoO_5·HMPA seems to indicate that lithium diisopropylamide is serving in a ligand capacity with molybdenum complex. The utilization of 1 or 2 equiv of LDA/equiv of MoO_5·HMPA results in recovered starting material while 4 equiv of LDA gives indole (benzofuran) in reduced yields.

The general procedure for the synthesis of an indole or benzofuran was as follows: A 50-mL, three-necked round-bottomed flask equipped with a nitrogen inlet tube and a Teflon magnetic stirring bar was charged with γ-sultam 1 (1–5 mmol). The γ-sultam was dissolved in anhydrous THF (8–15 mL) and cooled to −78 °C with the aid of a dry ice/acetone bath. *n*-Butyllithium (1 equiv) in hexane was added via syringe, and the solution was stirred at −78 °C for 1 h. In a second 50-mL flask equipped in the same manner was placed 1.1 mmole of MoO_5·HMPA (previously dried from MoO_5·HMPA·H_2O via P_2O_5/0.2 mm, 36 h) and dissolved in anhydrous THF (5–10 mL). The solution was cooled to −78 °C prior to the addition of LDA (3.3 mmol). The MoO_5·HMPA–LDA solution was added to the γ-sultam solution via a double-ended needle. The reaction was stirred at −78 °C for 2 h. The solution was allowed to warm to room temperature, quenched with water (10 mL), and brought to 45 °C for 1 h. Saturated sodium sulfite (10 mL) was added and the reaction diluted with water (40 mL). The reaction mixture was extracted with diethyl ether (2 × 50 mL) and dried ($MgSO_4$), and the diethyl ether was removed in vacuo. The crude product was purified by column chromatography (silica gel eluted with petroleum ether).

Registry No. 1 (X = CH_3N; Y = H), 64825-94-1; 1 (X = CH_3N; Y = CH_3), 64825-96-3; 1 (X = CH_3)$_3$CN; Y = CH_3), 78307-50-3; 1 (X = *p*-$CH_3C_6H_4N$; Y = CH_3), 78307-51-4; 1 (X = CH_3N; Y = C_6H_5), 64826-00-2; 1 (X = *p*-$CH_3C_6H_4N$; Y = CH_3CH_2), 78307-52-5; 1 (X = *p*-$CH_3C_6H_4N$; Y = *p*-ClC_6H_4), 78307-53-6; 1 (X = *p*-$CH_3OC_6H_4N$; Y = $(CH_3)_2CH$, 78307-54-7; 1 (X = *p*-BrC_6H_4N; Y = $(CH_3)_2CH$), 78307-55-8; 1 (X = *p*-$CH_3C_6H_4N$; Y = CH_3SO_2), 78307-56-9; 1 (X = O; Y = C_6H_5), 42224-35-1; 1 (X = O; Y = *p*-$CH_3C_6H_4$), 78307-57-0; 2 (X = CH_3N; Y = CH_3), 78307-58-1; 3 (X = CH_3N; Y = H), 603-76-9; 3 (X = CH_3N; Y = H) picrate, 29052-34-4; 3 (X = CH_3N; Y = CH_3), 875-79-6; 3 (X = $(CH_3)_3CN$; Y = CH_3), 46250-15-1; 3 (X = *p*-$CH_3C_6H_4N$; Y = CH_3), 78307-59-2; 3 (X = CH_3N; Y = C_6H_5), 3558-24-5; 3 (X = *p*-$CH_3C_6H_4N$; Y = CH_3CH_2), 78307-60-5; 3 (X = *p*-$CH_3C_6H_4N$; Y = *p*-Cl_6H_4), 78307-61-6; 3 (X = *p*-$CH_3OC_6H_4N$; Y = $(CH_3)_2CH$), 78307-62-7; 3 (X = *p*-BrC_6H_4N; Y = $(CH_3)_2CH$), 78307-63-8; 3 (X = *p*-$CH_3C_6H_4N$; Y = CH_3SO_2), 78307-64-9; 3 (X = O; Y = C_6H_5), 1839-72-1; 3 (X = O; Y = *p*-$CH_3C_6H_4$), 25664-48-6.

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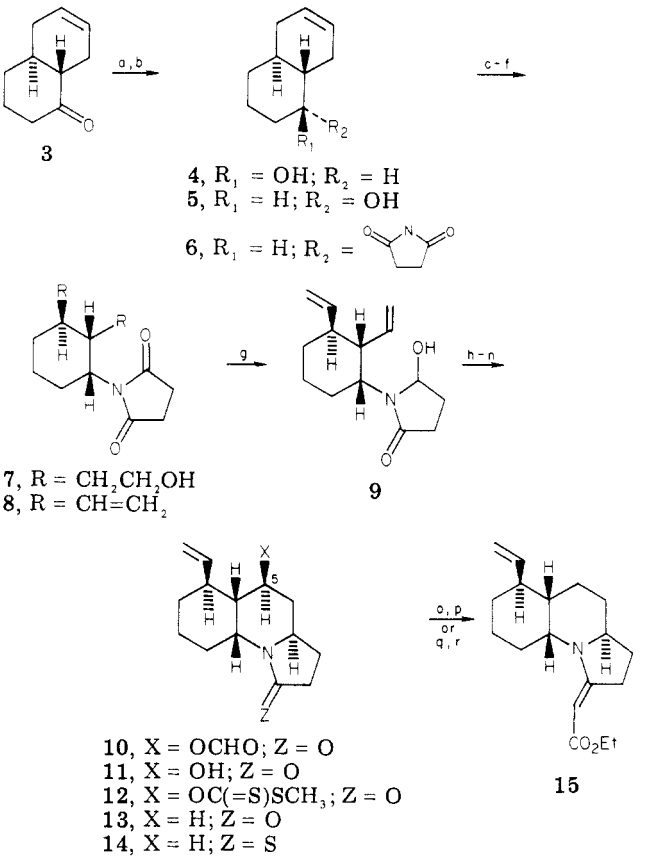
A Synthesis of (±)-Gephyrotoxin

Summary: A formal total synthesis of the Dendrobatid alkaloid gephyrotoxin (1) is described.

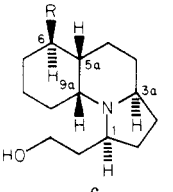
Sir: Gephyrotoxin (1), a component of a skin secretion produced by the poison-dart frog, *Dendrobates histrionicus*,[1] has been the objective of several synthetic studies.[2-5]

Scheme I[a]



[a] (a) $LiAlH_4$, THF, −70 °C; (b) PPh_3, $EtO_2CN{=}NCO_2Et$, $C_4H_5NO_2$; (c) O_3, CH_3OH, −70 °C; (d) $NaBH_4$, CH_3OH, −70 °C → 25 °C; (e) *o*-$NO_2PhSeCN$, *n*-Bu_3P, THF; (f) H_2O_2, 25 °C; (g) *i*-Bu_2AlH, $PhCH_3$, −65 °C; (h) HCOOH, 25 °C, 30 min; (i) 1.5 equiv of NaOH, CH_3OH-H_2O; (j) NaH, imidazole, THF, 60 °C; (k) CS_2; (l) CH_3I; (m) *n*-Bu_3SnH, toluene, reflux, 16 h; (n) $(pMeOPhPS_2)_2$, toluene, 100 °C, 10 min; (o) $BrCH_2CO_2Et$, Et_2O; (p) Ph_3P, Et_3N, CH_2Cl_2; (q) CH_3I, Et_2O; (r) $EtO_2CCHCOOMg$, DMF, 60 °C, 2 h.

Most notably, the groups of Kishi[4] and Overman[2] have reported syntheses of (±)-1 and perhydrogephyrotoxin (2), respectively. We have now completed a formal synthesis of (±)-1, the details of which are outlined herein.



1, R = $CH_2CH{=}^{c}CHC{\equiv}CH$
2, R = $CH_2CH_2CH_2CH_2CH_3$

Our approach to the stereochemical problems presented by gephyrotoxin focused on (i) establishing the relative stereochemistry at the three contiguous asymmetric centers (C-6, C-5a, C-9a), (ii) transmitting the proper stereochemistry to C-3a using an *N*-acyliminium ion cyclization,[6,7] and

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