

intermediates, concerted reactions involving no intermediates cannot be excluded.

Preliminary experiments in our laboratory indicate that the fragmentation involved in the conversion of **5** to **3** may be quite general. Results of these and other related studies will be reported soon.

**Acknowledgment.** This work was supported by U.S. Department of Energy, Office of Basic Energy Sciences, Chemical Sciences Division, under Contract W-7405-ENG-82. We thank Leslie Campbell Hanson for assistance with the early experimental work.

**Registry No.** **2**, 4026-23-7; **3**, 120-12-7; **5**, 1460-59-9; **6**, 32277-35-3; **7**, 53-70-3; **8**, 224-41-9; **9**, 69978-58-1; **9** (carbomethoxy derivative), 96394-19-3; **10**, 69978-57-0; **10** (carbomethoxy derivative), 96411-82-4; **11**, 782-23-0; **12**, 613-26-3; 4-carbomethoxybenzocyclobutene, 93185-60-5.

### High Lithium Selectivity in Competitive Alkali-Metal Solvent Extraction by Lipophilic Crown Carboxylic Acids

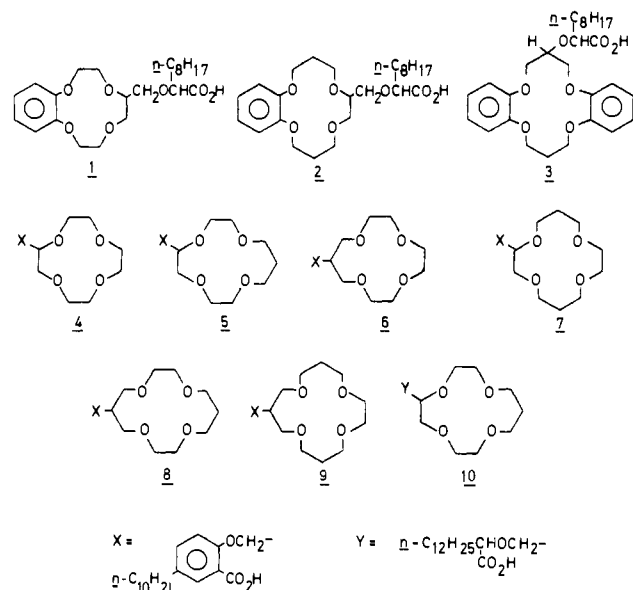
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Received October 26, 1984

Selectivity for lithium complexation by 13-crown-4,<sup>1</sup> benzo-13-crown-4,<sup>2</sup> 14-crown-4,<sup>1,3</sup> and dibenzo-14-crown-4<sup>4</sup> compounds has recently been reported for extractions of alkali-metal picrates from aqueous solutions into organic media<sup>1,2</sup> and for responses of polymeric membrane electrodes to alkali-metal cations.<sup>3,4</sup> These findings suggest that incorporation of such crown ether units into lipophilic crown ether carboxylic acids<sup>5</sup> might provide novel reagents for the solvent extraction of lithium from aqueous solutions. For solvent extraction, such ionizable crown ethers would have the special advantage that concomitant transfer of an aqueous phase anion is not required for extraction of a lithium cation into the organic solvent.<sup>6</sup>

The lipophilic crown ether carboxylic acids **1-10** with 12-, 13-



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**Table I.** Competitive Extraction Selectivity Orders and  $\text{Li}^+/\text{Na}^+$  Ratios

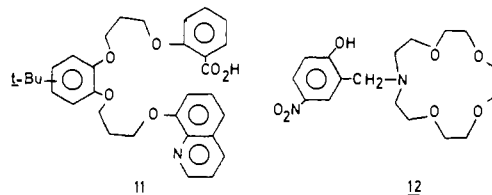
compd	ring type	selectivity order	max $\text{Li}^+/\text{Na}^+$ ratio
<b>1</b>	B12C4	$\text{Li}^+ > \text{Na}^+ > \text{K}^+ > \text{Rb}^+ > \text{Cs}^+$	1.8
<b>2</b>	B14C4	$\text{Li}^+ > \text{Na}^+ > \text{K}^+ > \text{Rb}^+$ (no $\text{Cs}^+$ )	4.7
<b>3</b>	DB14C4	$\text{Na}^+ > \text{Li}^+ > \text{K}^+ > \text{Rb}^+ > \text{Cs}^+$	0.6
<b>4</b>	12C4	$\text{Li}^+ > \text{Na}^+ > \text{K}^+ > \text{Rb}^+, \text{Cs}^+$	1.7
<b>5</b>	13C4	$\text{Li}^+ > \text{Na}^+ > \text{K}^+ > \text{Rb}^+ > \text{Cs}^+$	2.3
<b>6</b>	13C4	$\text{Li}^+ > \text{Na}^+ > \text{K}^+ > \text{Rb}^+, \text{Cs}^+$	2.5
<b>7</b>	14C4	$\text{Li}^+ \gg \text{Na}^+$ (no $\text{K}^+, \text{Rb}^+, \text{Cs}^+$ )	20
<b>8</b>	14C4	$\text{Li}^+ \gg \text{Na}^+$ (no $\text{K}^+, \text{Rb}^+, \text{Cs}^+$ )	19
<b>9</b>	15C4	$\text{Li}^+ > \text{Na}^+ > \text{K}^+, \text{Cs}^+ > \text{Rb}^+$	3.5
<b>10</b>	13C4	$\text{Li}^+ > \text{Na}^+ > \text{K}^+ > \text{Rb}^+ > \text{Cs}^+$	1.6

<sup>a</sup> B = benzo, DB = dibenzo. <sup>b</sup> Reproducibility is  $\pm 5\%$  of the listed value.

14-, and 15-membered macrocyclic rings and four ring oxygens were synthesized<sup>7-9</sup> from the corresponding crown ether alcohols.<sup>1,8</sup> Competitive solvent extractions of aqueous solutions of lithium, sodium, potassium, rubidium, and cesium chlorides (0.25 M in each) with 0.050 M solutions of the lipophilic crown ether carboxylic acids were conducted by the previously reported method.<sup>6</sup> Results are recorded in Table I.

For extractions conducted with **1-10**, metal loading of the chloroform phase was strongly influenced by the pH of the contacted aqueous phase. Acidic or neutral pH's gave little or no extraction, whereas maximal extraction efficiency (85% or greater loading) was observed at pH 10-11. All compounds except **3** exhibited lithium selectivity.

For the monobenzo-12-crown-4 and -14-crown-4 compounds **1** and **2**, respectively, the modest  $\text{Li}^+/\text{Na}^+$  ratio observed with the former is substantially enhanced for the latter. The  $\text{Li}^+/\text{Na}^+$  selectivity of 4.7 obtained with **2** surpasses the selectivity of 3.4 reported<sup>10</sup> for competitive transport of alkali-metal cations across a chloroform membrane by the acyclic polyether carboxylic acid **11** and a selectivity of 4.1 calculated from single ion extraction



constants for extractions of lithium and sodium cations from water into 1,2-dichloroethane by the chromogenic azacrown **12**.<sup>11</sup> Surprisingly the lithium selectivity noted with **2** is completely lost with the dibenzo-14-crown-4 derivative **3**.

Compounds **4-9** are a series which possesses a common lipophilic carboxylic acid unit but has systematic variation of the crown ether ring size. All are lithium selective, but the degree of selectivity is a function of ring size. Thus the low  $\text{Li}^+/\text{Na}^+$  ratio noted for the 12-crown-4 compound **4** is increased with the 13-crown-4 compounds **5** and **6**. Compared with **5**, compound **10** has the same crown ether ring system but a different lipophilic carboxylic acid group. The lower  $\text{Li}^+/\text{Na}^+$  ratio observed with **10** indicates that the less rigid lipophilic carboxylic acid group in **10** diminishes selectivity. With the 14-crown-4 derivatives **7** and **8**, only  $\text{Li}^+$  and  $\text{Na}^+$  are extracted into the chloroform phase and the lithium selectivity is very high. *The  $\text{Li}^+/\text{Na}^+$  ratios of 19-20 observed with **7** and **8** are the highest yet achieved in*

(7) Structures of **1**, **2**, and **5-10** were verified by elemental analysis and <sup>1</sup>H NMR and IR spectra. Full details of the syntheses of **1**, **2**, and **5-10** will be reported separately.

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competitive alkali-metal cation solvent extractions. A further increase in ring size to the 15-crown-4 derivative **9** produced a much lower selectivity for lithium extraction.

The outstanding lithium selectivity obtained with the lipophilic 14-crown-4 carboxylic acids **7** and **8** encourages the application of these and closely related complexing agents for the recovery of lithium from natural sources and waste streams.

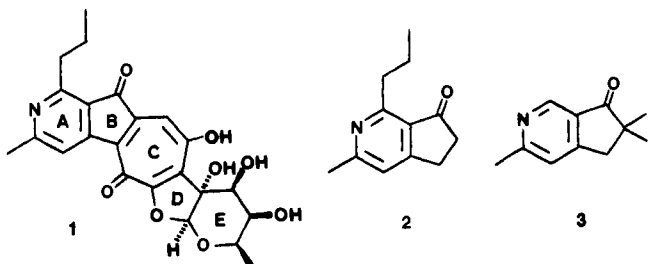
**Acknowledgment.** This research was supported by the Office of Basic Chemical Sciences of the U. S. Department of Energy and by the Texas Tech University Center for Energy Research (stipends for W.A.C. and L.E.S.).

## A New Pyridine Synthesis

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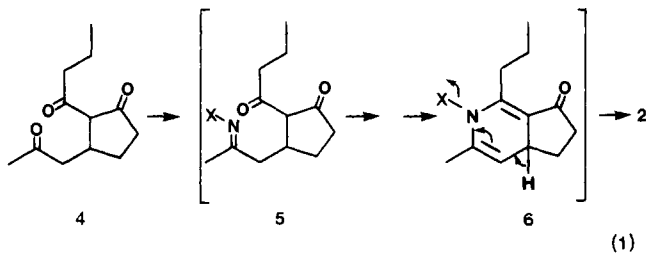
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In conjunction with a projected synthesis of the unusual red pigment rubrolone (**1**),<sup>1</sup> we had need of an expeditious route to



the AB unit **2**. Examination of the literature<sup>2</sup> revealed that available methods would require a lengthy synthesis: the reported<sup>3</sup> synthesis of **3**, which was the compound most structurally related to **2** then known, requires seven<sup>4</sup> steps. We now describe a conceptually new, highly convergent method of pyridine synthesis which not only affords **2** in a *one-pot* operation but also provides general and simple access to a diverse spectrum of complex pyridines.

The method results from an amalgamation of classical pyridine synthesis with new enolate technologies. As applied to **2**, the classical Knoevenagel<sup>2,5</sup> route would first require construction of the triketone **4** followed by reaction with hydroxylamine and cyclization. Formation of the pyridine ring in this fashion would presumably<sup>6a</sup> proceed along the general mechanistic lines shown in eq 1 (X = OH), the driving force being elimination of water



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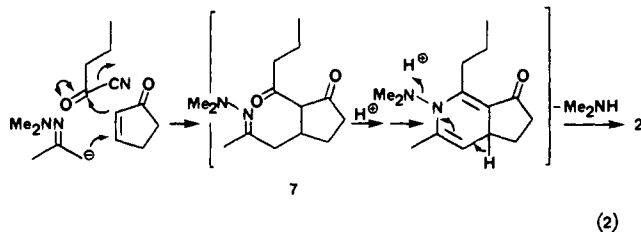
(6) See ref 2a: (a) p 279; (b) p 274.

Table I

Hydrazone <sup>15</sup>	Enone	Acyating Agent	Pyridine	Yield <sup>a</sup> (mp)
		—		82
		—		65
		—		38 (71-72 <sup>c</sup> )
		—		55
				31 (56-57 <sup>c</sup> )
				14
				14 (93-94 <sup>c</sup> )
				16
				45 (125-126 <sup>c</sup> )
				23 (189-190 <sup>c</sup> )

<sup>a</sup> Isolated overall yield (based on enone) of chromatographically pure material.

from **6** with generation of an aromatic system. Conventionally, X is an OH group, but in principle any moiety capable of functioning as a leaving group should suffice. Therefore, generation of any compound equivalent to **5** should serve to set the stage for pyridine ring formation. In practice, as illustrated for the preparation of **2**, this can be achieved as shown in eq 2.



Thus conjugate addition of the cuprate<sup>7</sup> derived from the anion of acetone dimethylhydrazone to cyclopentenone followed first

(7) The conjugate addition of dimethylhydrazone enolate derivatives to enones (including **11** + **12** and **14** + **15**) has been reported as part of a synthesis of 1,5-diketones: (a) Corey, E. J.; Enders, D. *Chem. Ber.* **1978**, *111*, 1362-1383. (b) Gawley, R. E.; Termine, E. J.; Aube, J. *Tetrahedron Lett.* **1980**, *21*, 3115-3119. (c) See also: Corey, E. J.; Boger, D. L. *Ibid.* **1978**, 4597-4600.