Synthesis of anthracene ethers from anthracene methyl ethers *via* an acid-catalyzed exchange reaction†

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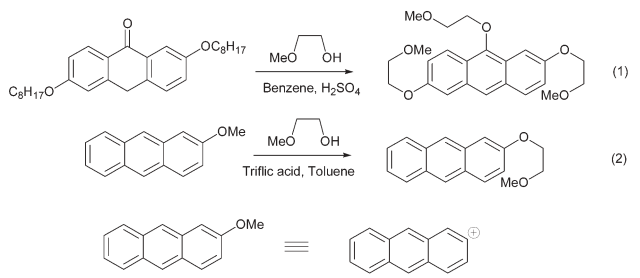
Selective synthesis of anthracene ethers was achieved under mild conditions *via* an acid-catalyzed ether–ether exchange reaction and its scope and limitations, as well as its potential in synthesizing anthracene-based crown ethers, tested.

Linearly fused aromatic hydrocarbons, commonly known as acenes, have very prominent positions in both computational chemistry[1] and organic material chemistry.[2] Theoretical studies have come to the consensus that the HOMO and LUMO of higher oligoacenes are nearly degenerate although the actual size of the band gap is still an ongoing controversy. Even as the simplest member of this distinguished family, anthracene and its derivatives have proved extremely versatile in material science. They have been used as the key component in light emitting diodes,[3] field-effect transistors,[4] sensors,[5] and organic gellators.[6]

Despite all the incentives provided by both theory and application, the synthesis of acenes remains a difficult problem.[7] We recently launched a project directed towards the synthesis, physical studies and potential application of acenes. In this Communication, we wish to report a new ether–ether exchange reaction on the anthracene core. We believe this reaction is a valuable addition to the hitherto-limited arsenal at synthetic chemists' disposal to tackle acene synthesis and derivatization.

The discovery of the exchange reaction is serendipitous. Our original goal was to aromatize 2,6-dialkoxy anthrone following a known procedure (eqn. (1) in Scheme 1).[8] However, after the reaction, we realized that not only the aromatization has taken place, but both octyloxy groups on the starting anthrone were also replaced by 2-methoxyethoxy groups, evidently from excess 2-methoxyethanol employed in the reaction. The progress of the reaction was monitored by TLC and no intermediate products can be detected. Further inquiry revealed that this reaction is not particular to 9-alkoxyanthracene; 2-methoxyanthracene also undergoes such a transformation to give 2-(2-methoxyethoxy)-anthracene under the same conditions. The net reaction conveys 2-methoxyanthracene as an anthryl cation synthon. In contrast, 2-methoxynaphthalene remains unchanged under the same conditions.

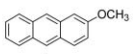
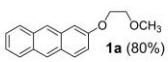
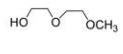
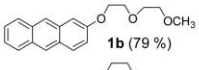
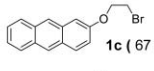
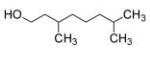
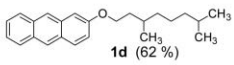
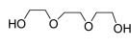
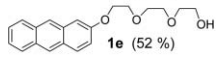
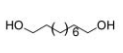
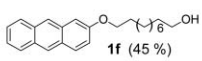
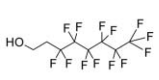
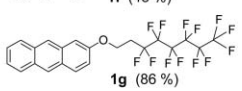


Scheme 1 Discovery and optimization of the exchange reaction.

We then set out to optimize the reaction conditions. It soon became clear that using a non-oxidative strong organic acid is crucial since the alkoxy-substituted anthracene products are prone to oxidative degradation. A high boiling aprotic solvent can facilitate the removal of methanol to make the exchange irreversible. The optimal combination for exchange reaction is one equivalent of trifluoromethanesulfonic acid (with respect to anthracene) and two equivalents of alcohol (relative to the number of –OMe to be replaced) in boiling toluene. The procedure was thus applied to all the reactions in the following studies unless otherwise mentioned.

Table 1 shows our results from reactions conducted with 2-methoxyanthracene. Oligoether, halogen, and polyfluorinated alkyl groups are all compatible with the reaction conditions. Compounds **1e** and **1f** are synthesized without employing protecting groups for the free hydroxy group. An alkylation pathway would require the use of less accessible ω-halogenated alcohols as the alkylating agent. The efficient incorporation of polyfluorinated chain (entry 7) is especially noteworthy.

Table 1 Simple ether–ether exchange reaction on 2-methoxyanthracene

Entry	Substrate	Alcohol	Product yield (%)
1	 **1**		 **1a** (80%)
2			 **1b** (79 %)
3			 **1c** (67 %)
4			 **1d** (62 %)
5			 **1e** (52 %)
6			 **1f** (45 %)
7			 **1g** (86 %)

† Electronic supplementary information (ESI) available: Detailed synthetic procedure and characterization for all new compounds. See http://www.rsc.org/suppdata/cc/b4/b412090f/

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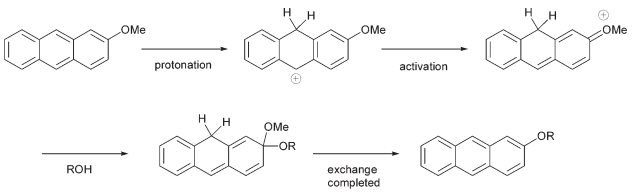
Previously, the only general entry into this class of (aryl–O–$CH_2CH_2R_f$) compounds is *via* the Mitsunobu reaction and the yield is far from satisfactory.[9] The limitations of this exchange protocol were also probed. Unfortunately, only primary alcohols are good substrates for this reaction. Attempts to use menthol, cholesterol, and cyclohexanol in the reaction produced complex mixtures. Alcohols that are easily ionized (allyl and benzyl alcohol) preferentially alkylate toluene under the reaction conditions. The reaction with 4-nitrobenzyl alcohol proceeded in low yield. The reaction with 1-adamantanol is also sluggish and complicated.

The mechanism of the reaction became obvious once the superb proton affinity of anthracene was recognized.[10] As shown in Scheme 2, protonation of anthracene at the 9 (or 1) position gives the intermediate cationic species. The activation of the carbon–oxygen bond was achieved through the strong electron-withdrawing nature of the cation which was trapped by the excess alcohol at the *ipso* position to produce the mixed-ketal intermediate. Elimination of the methanol molecule regenerated the aromaticity and furnished the desired exchange product.

As demonstrated in table 2, isomeric dimethoxyanthracene derivatives all underwent efficient double exchange reaction to furnish the expected products (table 2, entries 1–6). To react 2, 3-dimethoxyanthracene (**4**) and oligoethylene glycol seems to be an appealing route to anthracene annulated crown ethers. However, when **4** and 1.5 equivalents of triethylene glycol were put under the



Scheme 2 Postulated mechanism for the ether–ether exchange reaction.

Table 2 Double exchange reaction in dimethoxyanthracene derivatives

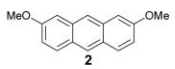
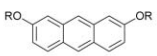
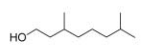
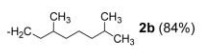
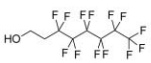
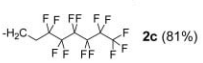
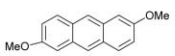
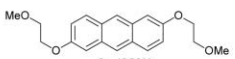
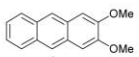
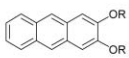
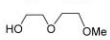
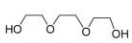
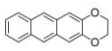
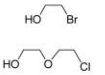
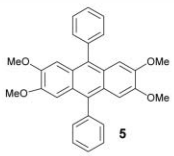
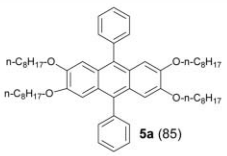
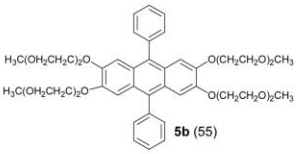
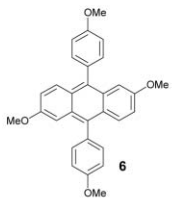
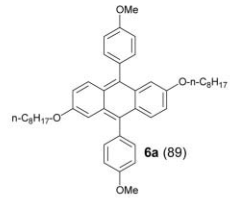
Entry	Substrate	Alcohol	Product yield (%)
			
	2		
1		$n\text{-}C_8H_{17}OH$	R = $n\text{-}C_8H_{17}$ **2a** (89%)
2			 **2b** (84%)
3			 **2c** (81%)
4			
	3		**3a** (92%)
			
	4		
5			R = CH_2CH_2OMe **4a** (69%)
6			R = $CH_2CH_2OCH_2CH_2OMe$ **4b** (81%)
7			 **4c** (76%)
8			R = CH_2CH_2Br **4d** (84%)
9			R = $CH_2CH_2OCH_2CH_2Cl$ **4e** (86%)

Table 3 Multiple and selective ether–ether exchange reactions

Entry	Substrate	Alcohol	Product yield (%)
1	 **5**	$n\text{-}C_8H_{17}OH$	 **5a** (85)
2		$HO(CH_2CH_2O)_2CH_3$	 **5b** (55)
3	 **6**	$n\text{-}C_8H_{17}OH$	 **6a** (89)

reaction conditions (entry 7), only **4c** was isolated. Evidently, the lone pair on the ether oxygen is nucleophilic enough to undergo intramolecular cyclization with the protonated anthracene. In fact, **4c** is also observed as the minor product in entry 5 and 6 (25 and 5%). Nevertheless, both **4d** and **4e** are now easily accessible and can be coverted into crown ethers in one simple step.

The exchange reaction can also be applied to the synthesis of multiple ether substituted anthracenes without noticeable deterioration of product yield. Our preliminary results into this venue are shown in Table 3. The efficiency of these multi-sited reactions might be due to the superior proton affinitiy of **5** and **6**. An interesting chemo-selectivity was observed in entry 3. Only the methoxy groups directly attached to the anthracene core can be replaced. Even when we use 8 equivalents of 1-octanol, the anisyl methoxy group remains intact. This disparity in reactivity is most likely due to the fact that the anthracene plane and anisyl groups are orthogonal to each other. As a result, the protonated anthracene is unable to activate the methoxy groups on the anisyl substituents.

In summary, we have developed a convenient protocol to make various anthracene ethers *via* exchange reaction. The reaction conditions are compatible with several common functional groups. Currently, we are trying to extend this reaction to higher acenes and other group VI elements.[11]

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