

## Short Communications

## Effect of Crown Ethers on the Racemization of 2-Phenylpropionitrile in Methanol and Ethanol

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In a previous investigation of the racemization of 2-phenylpropionitrile in methanol<sup>1</sup> a small increase in the second-order rate constant (obtained by dividing the observed rate constant by the corresponding base concentration) with the base (sodium methoxide) concentration was found over the investigated interval (2.8–10.8 mM at 25 °C). It was suggested that this increase in the rate constant could be due to the existence of sodium methoxide ion pairs more efficient as catalysts than the non-ionpaired methoxide ions. We now wish to report some experimental facts which contradict the suggested explanation.

Our intention was to use a complexing agent for the sodium ions to decrease the concentration of possible sodium methoxide ion pairs. The most powerful complexing agents for alkali cations known are the cryptates.<sup>2</sup> The complex constant for formation of the sodium complex with 2,2,1-cryptate (4,7,13,16,21-pentaoxa-1,10-diazabicyclo[8,8,5]tricosane) is  $10^{5.4}$  M<sup>-1</sup> in methanol at 25 °C.<sup>2</sup> Unfortunately, this compound racemized 2-phenylpropionitrile in methanol<sup>3</sup> and could not be used as a complexing agent in the sodium methoxide solutions.

However, it turned out that it was possible to use another type of complexing agents, namely some macrocyclic polyethers, the crown ethers. Since the first investigation by Pedersen<sup>4</sup> crown ethers have been used to clarify the role of ion pairs in mechanisms of organic reactions as well as in synthetic applications. Two recent reviews on the properties and applications of crown ethers have been published recently.<sup>5,6</sup>

The properties of the crown ethers can be changed by altering the size of the macrocyclic ring and also by introducing different side groups on it.<sup>5</sup> We have used two different crown ethers: 18-crown-6 (1,4,7,10,13,16-hexaoxacyclooctadecane) and 15-crown-5 (1,4,7,10,13-pentaoxacyclopentadecane). The equilibrium con-

stant for the formation of the sodium complex with 18-crown-6 in methanol is  $10^{4.32}$  M<sup>-1</sup>.<sup>7</sup> The corresponding equilibrium constant for 15-crown-5 has not been measured as far as we know.

The magnitude of the complex constant has previously been assumed to be correlated to the similarity between the ionic diameter of the cation and the hole size in the crown ether.<sup>7</sup> In such a case 15-crown-5 should be somewhat better for sodium than 18-crown-6. Such a correlation is somewhat doubtful, however, but in any case it is plausible that the complex constant for 15-crown-5 should be of the same order of magnitude as for 18-crown-6. In a methanolic solution of sodium methoxide and an excess of crown ether the fraction of non-complexed sodium ions should thus be negligible.

Table 1 gives the results of the racemization of 2-phenylpropionitrile in methanol with added 18-crown-6. As can be seen, no difference exists in the observed rate before and after 18-crown-6 has been added. The crown ether has been added in excess and the result is the same irrespective of the degree of excess (last row in Table 1).

Table 1. Racemization rates for 2-phenylpropionitrile in methanol with sodium methoxide as base with and without the presence of 18-crown-6. Concentration of substrate 0.12 M. Temperature  $24.93 \pm 0.05$  °C.

[Base]/mM <sup>a</sup>	[18-crown-6]/mM	$k_{\text{obs}}/10^{-4}$ s <sup>-1</sup> <sup>b</sup>
2.70	—	5.11
2.70 <sup>c</sup>	37.8	5.18
5.61	—	12.2
5.61 <sup>c</sup>	60.5	12.4
34.8	—	85
34.8 <sup>c</sup>	41.6–87.0	85

<sup>a</sup> The estimated error in the base concentration is less than 5%. <sup>b</sup> Mean value obtained from two or three runs. Maximum deviation from the mean value is less than 1.7%. <sup>c</sup> The run with crown ether present was done using base solution from the same batch as for the one without crown ether.

Table 2. Effect of added 15-crown-5 on the alkoxide-catalysed racemization rate of 2-phenylpropionitrile in methanol and ethanol. Concentration of substrate 0.12 M. Temperature  $25.00 \pm 0.05$  °C.

[Base]/mM <sup>a</sup>	[15-crown-5]/mM	$k_{\text{obs}}/10^{-4} \text{ s}^{-1}$
Methanol/methoxide		
4.10	—	8.23 <sup>b</sup>
4.10 <sup>c</sup>	6.5	8.54 <sup>b</sup>
24.5	—	58.2 <sup>b</sup>
24.5 <sup>c</sup>	35.1	62.5 <sup>b</sup>
Ethanol/ethoxide		
3.1	—	153 <sup>d</sup>
3.1 <sup>c</sup>	5	168 <sup>d</sup>

<sup>a</sup> The estimated error in the base concentration is less than 5%. <sup>b</sup> Each value is obtained from only one run. <sup>c</sup> The run with crown ether present was done using base solution from the same batch as for the one without crown ether. <sup>d</sup> Mean value from two runs. Maximum deviation from the mean value is 2%.

The results obtained with 15-crown-5 (Table 2) are similar although a slight increase in  $k_{\text{obs}}$  was observed upon addition of 15-crown-5 at least at the highest base concentration in methanol. In no case was a decrease in  $k_{\text{obs}}$  observed upon addition of crown ethers which ought to be the case if the sodium methoxide ion pairs were more reactive than the non-ionpaired methoxide ions. Thus there is no evidence supporting the idea that the change in the second-order rate constant with base concentration should be due to a more reactive sodium methoxide ion pair.

The very small effect (if any) on  $k_{\text{obs}}$  upon addition of crown ethers could be due to a very low concentration of sodium methoxide ion pairs at these rather low base concentrations. The association constant for sodium methoxide in methanol is not known with any high accuracy but some conductometric measurements at very low sodium methoxide concentrations ( $3-13 \times 10^{-4}$  M) indicate that it should be close to zero or rather small ( $7.5 \pm 7.9 \text{ M}^{-1}$ ).<sup>8</sup>

Sodium ethoxide in ethanol has a much larger association constant ( $102 \pm 8 \text{ M}^{-1}$ ).<sup>8</sup> It is therefore interesting to see that the rate of proton abstraction from 2-phenylpropionitrile is increased by about 10% when 15-crown-5 is added to a 3.1 mM sodium ethoxide solution (Table 2). This indicates that the free ethoxide ions are more effective as catalysts in the abstraction than are the ion pairs.

*Experimental.* The experimental procedure has been described before.<sup>1</sup> The crown ethers were commercial samples from FLUKA AG and were used without any purification. Commercial 99.5% spectrographic ethanol was dried over  $\text{CaH}_2$  and distilled and handled in the same way as methanol.<sup>1</sup>

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