Leaving Group Abilities for the Cathodic Cleavage of *p*-Methoxycarbonylbenzyl Carboxylates

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Summary Relative rates of cathodic cleavage of 11 *p*-methoxycarbonylbenzyl carboxylates have been measured by competitive electrolyses; of the carboxylate leaving groups studied naphthalene-1-carboxylate is the best, cyanoacetate the worst, and there is no obvious correlation between leaving group ability and structure.

CATHODIC cleavage reactions have been much used in electrosynthesis but to date there has been no systematic study of the factors determining leaving group ability. For intelligent design of electrosynthetic methods it is necessary to have this information. For certain examples, *e.g.* benzyl halide cleavage,[1] correlations between structure and reduction potential have been made but little is known about the ranking of anionic leaving groups. We report herein the results of competition experiments which, for cathodic cleavage from a series of benzyl carboxylates, allows a quantitative ordering of leaving group ability.

The probable mechanism of cleavage from benzylic systems[2] is given in the Scheme; relative rates of cleavage were measured by competition experiments and because it is found that such values are independent of potential it is probable that they reflect differences in k_1. In a typical experiment a solution of compounds (**1**) and (**3**) (see Table) [2 mM in each substrate, dimethylformamide (DMF)–$Bu_4NOAc{\cdot}HOAc$ (0·2 M)] was reduced at −1·7 V (*vs.* Ag/AgI) on a stirred mercury pool cathode. The initial current density was 2·3 mA cm^{-2} and the electrolysis was stopped at 0·7 F mol^{-1} [based on the combined amounts of (**1**) and (**3**)]. After aqueous work-up and isolation by ether extraction the ^1H n.m.r. spectrum of the product mixture was obtained and compared with that for a 1:1 mixture of (**1**) and (**3**). The singlet signals for the benzylic protons are separated by 0·15 p.p.m. and after the electrolysis are of unequal intensity; also after electrolysis a new singlet appears (δ 2·40, p-$MeO_2C{\cdot}C_6H_4{\cdot}Me$). The chemical shift for the methoxycarbonyl methyl protons is the same in (**1**), (**3**), and methyl *p*-toluate and consequently was used as an internal standard in the measurement of the relative consumption of (**1**) *vs.* (**3**) and the formation of methyl *p*-toluate. Under these conditions 48·6% of (**1**) and 21·8% of (**3**) were consumed, *i.e.* $k_1(\mathbf{1})/k_1(\mathbf{3}) = 2{\cdot}29$; similar electrolysis at −1·8 V gives a value of 2·21.

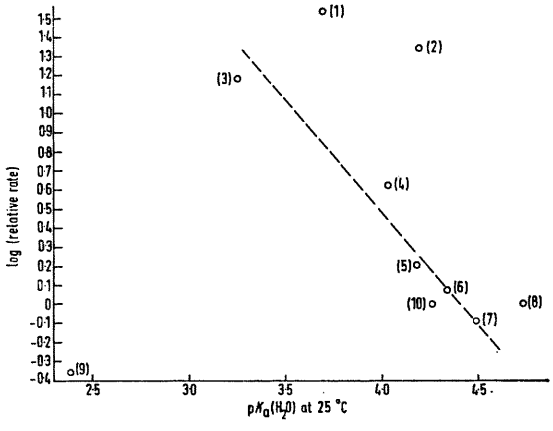
$$ArCH_2X \overset{e}{\rightleftharpoons} [ArCH_2X]^{\cdot-} \overset{k_1}{\rightarrow} X^- + ArCH_2^{\cdot}$$

$$ArCH_2^{\cdot} \overset{e}{\rightleftharpoons} ArCH_2^- \overset{H^+}{\rightarrow} ArCH_3$$

SCHEME

The assumption involved in this method and their justification are: (a) the diffusion coefficients of starting materials and products are similar throughout the series; and (b) initial electron transfer is to the common electrophore (p-$MeO_2C{\cdot}C_6H_4{\cdot}CH_2$–). The different carboxylate functions being compared as leaving groups will have similar polar effects on the corresponding p-methoxycarbonyl ester because there is no mesomeric interaction and polar effects transmitted through bonds or through space will be considerably attenuated. Consequently it is likely that the standard electrode potentials throughout the series will be similar. This assumption is supported by the observed independence of rates of cleavage on cathode potential. Pairs of substrates were chosen to cover, by overlap, the whole series and the rates of cleavage are related to that of the acetate (X = $MeCO_2$). In most cases each pair was electrolysed at three separate cathode potentials, within the range in which significant reaction took place, and the relative rates of cleavage were found to be independent of the cathode potential and reproducible to $\pm 5\%$ or better. This result is consistent with assumption (b).

The relatively large variation of peak potential with substrate structure (Table) is unlikely to be due to changes in the standard potential for the first electron transfer; the observed irreversible peak potential will be influenced by the rate of the chemical step (k_1) and the standard potential for the second electron transfer. The restriction to relatively low conversion also allows the assumption of a low, steady state, concentration of the radical-anion.



FIGURE

The detailed results of these experiments are summarised in the Table and in the Figure. The Figure is based on the simple expectation that leaving group abilities may be related to the pK_a of the conjugate acid of the leaving anion. In this case it is roughly true for a limited number of benzoates but even within that series the p-phenyl substituted benzoate is a very much better leaving group than expected. There is no general correlation however and it is particularly noteworthy that the anion of the strongest acid ($NCCH_2CO_2H$) is the poorest leaving group. A plot of the logarithms of the relative rates *vs.* cyclic voltammetric peak potentials for the esters similarly gave no recognisable correlation.

TABLE. Relative rates of cathodic cleavage from p-$MeO_2C{\cdot}C_6H_4{\cdot}CH_2X$[a]

X	$-Ep$[b]	Relative rate of cleavage
Naphthalene-1-carboxylate (**1**)	1·23	35
Biphenyl-4-carboxylate (**2**)	1·20	22
o-$EtO_2C{\cdot}C_6H_4{\cdot}CO_2$ (**3**)	1·10	15
p-$Cl{\cdot}C_6H_4{\cdot}CO_2$ (**4**)	1·24	4·2
$PhCO_2$ (**5**)	1·52	1·6
p-$Me{\cdot}C_6H_4{\cdot}CO_2$ (**6**)	1·50	1·2
p-$MeO{\cdot}C_6H_4{\cdot}CO_2$ (**7**)	1·45	1·0
$MeCO_2$ (**8**)	1·58	1·0
$NC{\cdot}CH_2CO_2$ (**9**)	1·88	0·43
$PhCH_2CO_2$ (**10**)	1·85	1·0
p-$Me_2N{\cdot}C_6H_4{\cdot}CO_2$ (**11**)	1·48	0·78

[a] Competitive electrolyses in DMF–$Bu_4NOAc{\cdot}HOAc$ (0·1 M), Hg cathode. [b] Irreversible reduction at vitreous carbon or Hg drop cathode, DMF–$Bu_4NOAc{\cdot}HOAc$ (0·1 M), scan rate in the range 100–200 mV s^{-1}, reference electrode Ag/AgI.

Because pK_a values for aqueous solution and cleavage rates for DMF solution were used, several pK_a values for DMF solution were measured using an indicator method.[3] Using the compound numbers given in the Table the values for pK$_a$ (DMF, 20 °C) are: (**1**), 9·20; (**4**), 9·90; (**5**) 11·2; and (**9**), 6·27. A plot of pK_a(DMF) *vs.* pK_a(H_2O) was strictly linear.

The finding that the best leaving anions are naphthalene-1-carboxylate and biphenyl-4-carboxylate suggests that assumption (b) is also correct. These bulky anions (and the related starting materials) would be expected to diffuse most slowly so it is unlikely that the rate of cleavage is controlled by a diffusion process. It is also convenient for synthetic purposes that these two groups are the most easily cleaved; for a range of alcohols the esters are easily formed and are easily purified crystalline derivatives.

The complete failure to relate leaving group abilities for anions with other properties has good precedent in recent work[4] on (Elcb)$_R$ mechanisms. In fact it would seem that there is a close analogy between that mechanism (with slow loss of anion from an intermediate carbanion) and the mechanism herein proposed for cathodic cleavage (Scheme).

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