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SYNTHETIC UTILIZATION OF ELECTROGENERATED BASES, I — MICHAEL REACTIONS

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Electrochemical reduction of organic compounds often affords strongly basic and/or nucleophilic species (carbanions, radical anions, dianions, etc.). While their nucleophilic character has been extensively exploited in many coupling,[1(a)] polymerization[1(b)] and displacement[2] reactions, their basicity has been used in synthesis only to a limited extent.[3,4] In previous work, the stoichiometric reaction of electrogenerated bases (EGB^-) with phosphonium salts has been observed, the EGB^- being derived from azobenzene[3] (which functions solely as a base precursor) or from the phosphonium salt itself.[5] In such a reaction, use of a reactant as a base precursor is wasteful since half of it is consumed in base formation. However, in a catalytic reaction only a small portion should have to be reduced and sufficient EGB^- might be generated without having a marked effect on the yield. We now report the use of such bases in a typical base catalyzed reaction - the Michael reaction.[6]

In the Michael reaction, the acceptor (activated olefin) is often readily reducible, whereas in most cases the donor is only reducible at a more negative potential or not reducible at all. This allows the generation of a base by reduction of a small portion of the acceptor in a mixture of the two. As indicated (Table 1; reactions 1-5) only 1-10% of the acceptor need be reduced in order to initiate the catalytic reaction. The mechanism involved is presumably the usual one[6] in which the added base is replaced by EGB^-, as exemplified below. The nature of EGB^- depends on the nature of the acceptor and the mechanism of its electrochemical reduction; it may be an initially formed radical anion or the product of subsequent reactions of that species, e.g., a dimer dianion, formed via dimerization.

$$EGB^- + CH_2X_2 \rightleftharpoons EGBH + \bar{C}HX_2$$

$$\bar{C}HX_2 + CH_2{=}CHZ \rightarrow X_2CHCH_2\bar{C}HZ$$

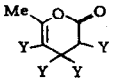
$$X_2CHCH_2\bar{C}HZ + CH_2X_2 \rightleftharpoons X_2CHCH_2CH_2Z + \bar{C}HX_2$$

The previously reported 1:1 adducts result from reactions 1,[6] 2,[6] 3,[7] and 5.[6] The cyclic product from reaction 4 is evidently formed via base catalyzed cyclization of the 1:1 adduct [$MeCOCH_2COOEt + EtOCH{=}C(COOEt)_2$ gives a similar product[8]]. The EGB^- from azobenzene is also effective, either in situ (Table 1; reaction 6) or after transfer from the cell to a separate reaction vessel.

Table 1. Electro-promoted Michael reactions [a]

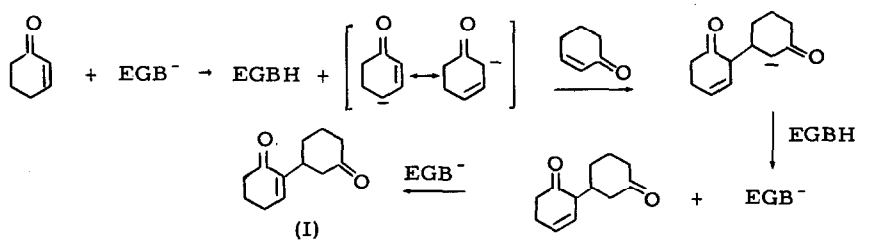
Acceptor [b] ($E_{\frac{1}{2}}$) [c]	Donor [b] ($E_{\frac{1}{2}}$) [c]	Base Precursor	E_{cath} [c]	Electricity Passed [d]	1:1 Adduct Yield [e]
1. CH_2=CHZ (-2.15)	XCH_2X (nr)	CH_2=CHZ	-2.08	0.024	18.5 [f]
2. CH_2=CHZ (-2.15)	XCHΦX (nr)	CH_2=CHZ	-2.04	0.016	15
3. X_2C=CX_2 (-0.88) (-1.07)	XCH_2X (nr)	X_2C=CX_2	-1.10	0.10	93
4. Y_2C=CY_2 (-0.82) (-0.98)	WCH_2Y (-2.08) (-2.60)	Y_2C=CY_2	-1.00	0.039	60 [g]
5. CH_2=CHX (-2.12)	XCH_2X (nr)	CH_2=CHX	-1.88	0.055	77
6. CH_2=CHX (-2.12)	XCH_2X (nr)	ΦN=NΦ [h]	-1.65	--	75

(a) Carried out in a divided cell with Hg cathode, Me_2NCHO solvent and $[Pr_4N]BF_4$ background electrolyte. The catholyte (ca 125 ml) usually contained 0.1 mole of donor and 0.1 or 0.2 mole of acceptor.
(b) W = MeCO. X = COOEt. Y = COOMe. Z = CN.
(c) $E_{\frac{1}{2}}$ = polarographic half wave potential, E_{cath} = reduction potential used, both in volts with respect to sce. nr = not reducible.
(d) Faradays per mole of acceptor.
(e) Based on acceptor consumed.
(f) 8% 2:1 adduct also isolated.
(g) Product is:



(h) ΦN=NΦ (0.0025 mole/mole donor) was completely reduced in the presence of donor before acceptor was added.

An application of the EGB^- catalyzed Michael reaction of some electrochemical interest is the dimerization of compounds containing both donor and acceptor functions in the same molecule, e.g., cyclohexenone:



The dimer (I) [9] and analogous dimers of crotononitrile [10] (formed <u>in situ</u> by isomerization of but-3-enonitrile) and aconitate ester [11] are obtained by initiation with EGB^- formed by reduction of <u>ca.</u> 1% of the monomer (Table 2). Glutaconate ester also gives a similar dimer [11] but a considerable portion of the monomer must be reduced to achieve this. Although this latter reaction is not catalytically efficient, it does give some indication of the

Table 2. Electro-promoted dimerizations [a]

Monomer [a] ($E_{\frac{1}{2}}$) [a]	E_{cath} [a]	% of Monomer Reduced	Dimer Yield
1. $CH_2CH_2CH_2CH{=}CHC{=}O$ (-2.06)	-1.90	0.13	65
2. $CH_2{=}CHCH_2Z$ [b] (-2.31)	-2.16	1.0	35
3. $YCH_2C(Y){=}CHY$ (-1.35)	-1.37	1.5	88
4. $XCH_2CH{=}CHX$ (-2.08)	-2.10	20	50

(a) See footnotes (a)-(c), Table 1.
(b) Rapidly isomerized to $CH_3CH{=}CHZ$ upon passage of current.

nature of EGB^- in these systems. Thus, glutarate ester is produced in amounts comparable with the current passed suggesting the sequence of reactions (1-4).

$$X\,CH_2CH{=}CHX + e^- \rightarrow [X\,CH_2\bar{C}H\bar{C}H\bar{X}]^{-\cdot} \quad (1)$$

$$[X\,CH_2\bar{C}H\bar{C}H\bar{X}]^{-\cdot} + X\,CH_2CH{=}CHX \rightarrow X\,CH_2\dot{C}H\,CH_2X + [X\,\bar{C}H\,\bar{C}H\,\bar{C}HX]^- \quad (2)$$

$$X\,CH_2\dot{C}H\,CH_2X + e^- \rightarrow X\,CH_2\bar{C}H\,CH_2X \quad (3)$$

$$X\,CH_2\bar{C}H\,CH_2X + X\,CH_2CH{=}CHX \rightarrow X\,CH_2CH_2CH_2X + [X\,\bar{C}H\,\bar{C}H\,\bar{C}HX]^- \quad (4)$$

$$[X\,\bar{C}H\,\bar{C}H\,\bar{C}HX]^- + X\,CH_2CH{=}CHX \rightarrow X\,CH{=}CH\,\underset{\displaystyle XCH_2CH\,\bar{C}HX}{\underset{|}{C}}HX \quad (5)$$

$$X\,CH{=}CH\,\underset{\displaystyle XCH_2CH\,\bar{C}HX}{\underset{|}{C}}HX + X\,CH_2CH{=}CHX \longrightarrow \text{dimer} + [X\,\bar{C}H\,\bar{C}H\,\bar{C}HX]^- \quad (6)$$

$$X\,CH{=}CH\,\underset{\displaystyle XCH_2CH\,\bar{C}HX}{\underset{|}{C}}HX \longrightarrow \left[\begin{array}{c} X\,CH_2CH\,CH_2X \\ | \\ X\,\underline{C}H\,\underline{C}H\,\underline{C}X \end{array}\right]^- \quad (7)$$

$$4\,X\,CH_2CH{=}CHX + 2e^- \rightarrow [X\,\bar{C}H\,\bar{C}H\,\bar{C}HX]^- + \left[\begin{array}{c} X\,CH_2CH\,CH_2X \\ | \\ X\,\underline{C}H\,\underline{C}H\,\underline{C}X \end{array}\right]^- + X\,CH_2CH_2CH_2X \quad (8)$$

These steps also produce the allylic anion which is the active species in the catalytic cycle (5, 6). Our interpretation of the low efficiency of the catalysis in this reaction is that there is a competing isomerization (7) of the dimer anion to an allylic dimer anion, whose rate of proton abstraction from the monomer is too slow to sustain the catalytic reaction. Evidence for this comes from examination of the reduction of glutaconate ester under coulometric

conditions. When a dilute (ca. 10^{-2} molar vs. ca. 1 molar for the macro experiments) solution of the ester is exhaustively reduced the uptake of electrons (n_{app}) is 0.51 e^-/mole, indicative of the process (8). Evidence for the formation of the allylic anions comes from the recovery of glutaconate and of glutaconate dimer [$X CH_2C{=}C(X)CH(CH_2X)_2$] after quenching with water (both of these compounds would have been reduced if they were present as neutral molecules). Equation (8) is simply a summation of equations (1)-(4), (5) and (7) in which only half of the allylic monomer anion formed is converted to allylic dimer anion. This is plausible since these anions should be comparable in stability. The absence of appreciable catalytic dimerization in dilute solution (coulometric conditions) is a reasonable effect of concentration on the competition between reactions (6) and (7), the latter presumably being independent of glutaconate concentration.

If our reasoning is correct, it is surprising that aconitate is dimerized so efficiently. Although the difference is simply one of degree, the reasons for it are evidently quite subtle. We find that fractional values of n_{app} are the general rule for compounds having both carbon acid and activated double bond functions in the same molecule and suggest that they may be generally explained by processes similar to (1)-(8). Similar fractional values have been observed and similar interpretations made in the reduction of some β-diketones.[12]

Reaction of malonate and ethenetetracarboxylate ethyl esters (Table 1; reaction 3)

A mixture of $CX_2{=}CX_2$[13] (3.16 g; 10 mmoles) and CH_2X_2 (2.00 g; 12.5 mmoles) in Me_2NCHO containing $[Pr_4N]BF_4$ (0.1 molar) was reduced at -1.10 v vs. sce in a cell previously described.[2] After 1 mF of current had passed the electrolysis was stopped and after 2 h the catholyte was poured into ice/water. Ether extraction afforded an oil. Glc analysis showed the presence of $CX_2{=}CX_2$ (0.3 mmole), CHX_2CHX_2 (0.7 mmole), CH_2X_2 (2.7 mmole) and $CHX_2CX_2CHX_2$ (8.9 mmole; 97% based on $CX_2{=}CX_2$ not reduced and not recovered). Distillation afforded the latter, hexaethyl propane-1,1,2,2,3,3-hexacarboxylate as a viscous oil [3.1 g; 71%; b 171° (0.05 mm)]. Found: C, 52.6; H, 6.8 Calc. for $C_{21}H_{32}O_{12}$: C, 52.9; H, 6.8%.

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