followed by rearrangement of the [4.4] to the [3.5] bicycles.[9]

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[9] *Cf.* calathene ("basketene") to rhynchene ("snoutene"): W. G. Dauben, M. G. Buzzolini, C. H. Schallhorn, D. L. Whalen, and K. J. Palmer, *Tetrahedron Lett.*, 787 (1970).

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Selective Removal of Protecting Groups Using Controlled Potential Electrolysis

Sir:

The 2,2,2-trichloroethoxy moiety has been used recently to modify the reactivity of carboxylic acids,[1] and, similarly, the 2,2,2-trichloroethoxycarbonyl group has been shown to be useful for protection of hydroxy and amino units.[2] The unique feature of the 2,2,2-trichloroethoxy derivatives is easy disassembling *via* reduction with zinc metal in acetic acid or hot ethyl alcohol.[1,2]

We wish to report that controlled potential electrolysis in conjunction with a variety of 2-haloethyl moieties expands the versatility of and introduces selectivity into this technique. Controlled potential electrolysis at a mercury electrode allows removal of 2-haloethoxy groups in neutral media (protic or aprotic) at temperatures ranging from ambient or higher to well below 0°. Most importantly, the electrolytic technique makes possible selective removal of very similar protecting groups by careful choice of electrode potential.

A central feature of this method is the availability of 2-iodoethyl,[3] 2,2,2-tribromoethyl,[4] and 2,2-dichloroethyl chloroformates[5] in addition to the commercially available 2,2,2-trichloroethyl chloroformate. The chloroformates interact with amino,[2a,b] hydroxyl,[2a,c] and thiol groups to afford the 2-haloethoxycarbonyl derivatives (*e.g.*, Table II).

Polarographic studies (Table I) indicate that the ease of reduction of 2-haloethoxy esters is very sensitive to the identity of the halogen atom and nearby substituents. Commercially available potentiostats[6] are capable of controlling the reduction potential to ±0.01 V, which, in practical terms, allows quantitative reduction of one compound in a mixture where the components differ in $E_{1/2}$ by 0.3 V. Thus reduction of a particular 2-haloethoxy group in the presence of a less easily reduced analog from Table I is simple and efficient.

Table I

Ester	$E_{1/2}{}^{a}$
$PhCO_2CH_2CH_2I$	$>-2.20^{b}$
$PhCO_2CH_2CHCl_2$	-1.91
$PhCO_2CH_2CCl_3$	-1.28
$PhCO_2CH_2CBr_3$	-0.60^{c}

[a] Half-wave potentials are in volts relative to the saturated calomel electrode. The polarographic studies were done in methyl alcohol containing 0.1 *M* lithium perchlorate. [b] A discrete wave was not observed for this derivative; at −2.2 V, the medium begins to show significant reduction. [c] The half-wave is partially obscured by a maximum which could not be suppressed.

Representative results of the electrolytic removal of 2-haloethoxy units from simple monofunctional compounds are displayed in Table II. The general experimental procedure involves a cylindrical vessel fitted with two side arms which are separated from the main compartment with coarse grade glass frits. A mercury pool electrode in the main compartment serves as the cathode (working electrode) while a saturated calomel reference electrode is placed in one side arm and a platinum sheet in the other side arm (anode, counter electrode). The cylinder is capped with a large ground-glass joint bearing a gas inlet tube and an exit stopcock; the lower portion of the apparatus is encased in a water jacket for cooling. The electrolyte solution (0.1 *M* lithium perchlorate in methyl alcohol) is added to the cell and the side arms. To the solution in the main compartment (*ca.* 20 ml)

Table II

Substrate	Product	V	Yield, %
1. $PhCO_2CH_2CCl_3$	$PhCO_2H$	−1.65	87 (91[a])
2. $PhCO_2CH_2CHCl_2$	$PhCO_2H$	−1.85	78
3. $PhCO_2CH_2CBr_3$	$PhCO_2H$	−0.70	85
4. p-$CH_3C_6H_4NHCO_2$-CH_2CCl_3	p-$CH_3C_6H_4NH_2$	−1.70	88
5. p-$CH_3C_6H_4NHCO_2$-CH_2CHCl_2	p-$CH_3C_6H_4NH_2$	−2.15	47
6. $PhCH_2OCO_2CH_2CCl_3$	$PhCH_2OH$	−1.50	70
7. $PhCH_2SCO_2CH_2CCl_3$	$PhCH_2SH$	−1.50	90[b]
8. $PhCH_2SCO_2CH_2CCl_3$	$PhCH_2SSCH_2Ph$	−1.50	90[c]
9. Cholesteryl 2,2,2-trichloroethyl carbonate	Cholesterol	−1.65	80
10. *N*-Acetyl-*S*-(2,2,2-trichloroethoxycarbonyl)-cysteine	*N*-Acetylcysteine	−1.60	100[d]
11. *N*-Acetyl-*S*-(2,2,2-trichloroethoxycarbonyl)-cysteine methyl ester	*N*-Acetylcysteine methyl ester	−1.50	88[b]

[a] This is the result of an experiment with a platinum gauze electrode in place of the mercury pool, and dimethylformamide in place of methyl alcohol. [b] The isolation procedure involved addition of a small molar excess of acetic acid immediately after electrolysis. [c] This experiment was done without purging with inert gas. [d] The crude product had mp 93–104° [mp 109–110° reported by T. A. Martin, J. R. Corrigan, and E. W. Waller, *J. Org. Chem.*, **30**, 2839 (1965)], and no impurities detectable by ^1H nmr. Purification by recrystallization was not efficient.

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[2] (a) T. B. Windholz and D. B. R. Johnson, *Tetrahedron Lett.*, 2555 (1967); (b) S. Karady, S. H. Pines, L. M. Weinstock, F. E. Roberts, G. S. Brenner, A. M. Hoinowski, T. Y. Chang, and M. Sletzinger, *J. Amer. Chem. Soc.*, **94**, 1411 (1972); (c) S. Rakhit, J. F. Bagli, and R. Deghenghi, *Can. J. Chem.*, 47, 2906 (1969).

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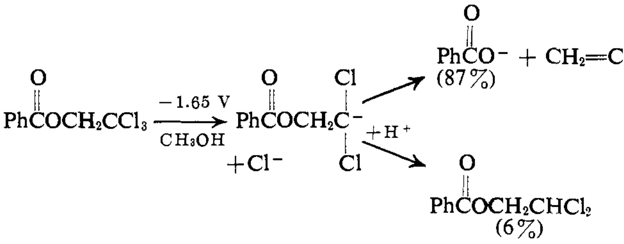
[5] Conversion of 2,2-dichloroethyl alcohol to the corresponding chloroformate has been achieved in 58% yield (bp 30–32° (0.10 Torr)) using pyridine and phosgene in benzene.

[6] The present work was done on a Wenking Model 68FR0.5 Potentiostat from Brinkman Instruments Inc.

is added 2,2,2-trichloroethyl benzoate (0.50 g, 1.97 mmol) and the mixture is degassed with an argon stream[7] for 15–30 min. Then the potentiostat is engaged to provide a potential difference of −1.65 V between the mercury pool and the reference electrode. The current, initially 145 mA, drops off slowly over 2 hr, reaching a steady value of *ca.* 3 mA. Water cooling is necessary to prevent local heating effects, especially at the glass frit separating the working and counter electrodes. The reaction mixture is separated from the mercury, concentrated at reduced pressure, and after protonation, the usual isolation *via* acidification, aqueous extraction, and one recrystallization, 0.21 g (87%) of benzoic acid is obtained, mp 120–121°.

Several entries in Table II require special mention. In most cases of electroremoval of the 2,2,2-trichloroethoxy unit, small and variable quantities of the corresponding 2,2-dichloroethoxy derivative are isolated. For example, this side reaction leads to 6% of 2,2-dichloroethyl benzoate from the electrolysis of 2,2,2-trichloroethyl benzoate (entry 1, Table II; eq 1). The amount of this substitution product is relatively insensitive to changes in solvent (dimethylformamide, acetonitrile), added proton source (acetic acid, trifluoroacetic acid), or the nature of the inert electrolyte. No parallel substitution products are observed during electroremoval of the 2,2-dichloroethoxy or 2,2,2-tribromoethoxy derivatives, and none is reported during zinc reduction of 2,2,2-trichloroethoxy units.[1,2]



$$PhCOCH_2CCl_3 \xrightarrow[CH_3OH]{-1.65\ V} PhCOCH_2\underset{Cl}{\overset{Cl}{C^-}} + Cl^- \longrightarrow PhCO^- + CH_2{=}CCl_2\ (87\%);\quad \xrightarrow{+H^+} PhCOCH_2CHCl_2\ (6\%) \qquad (1)$$

The electroremoval of the 2-haloethoxycarbonyl group from sulfhydryl units is directed in a simple way to high yields of either the free thiol or the disulfide-bonded dimer. Isolation of the thiol requires an inert atmosphere during reduction followed by addition of acetic acid before isolation. If air is not removed, the reduction proceeds smoothly to afford the disulfide (entries 7 and 8, Table II). As an example of deprotection of sulfhydryl groups and as a preliminary test of possible racemization during the reduction, *N*-acetyl-L-cysteine methyl ester ($[\alpha]^{25}D$ +20.91°, 2.31% solution in ethyl acetate) was converted to *N*-acetyl-*S*-(2,2,2-trichloroethoxycarbonyl)-L-cysteine methyl ester (mp 71–72.3°) in 92% yield after column chromatography. Electroremoval of the S-protecting group afforded *N*-acetyl-L-cysteine methyl ester in high purity and 88% yield with $[\alpha]^{25}D$ +19.85° (1.68% solution in ethyl acetate) after an isolation procedure involving addition of a small excess of acetic acid and simple aqueous extraction to remove lithium perchlorate. Overall for the two steps, the retention of configuration is 97.5%.

The selective removal of similar protecting groups is demonstrated by controlled potential reduction of two equimolar mixtures: (1) 2,2-dichloroethoxycarbonyl-*p*-toluidine with 2,2,2-trichloroethyl benzyl carbonate and (2) 2,2,2-trichloroethyl benzoate with 2,2,2-tribromoethyl benzoate. In each case, the appropriate choice of reduction potential (based on polarographic data) led to complete reaction of the more easily reduced species with negligible conversion of the other component.

$$p\text{-}CH_3C_6H_4NHCO_2CH_2CHCl_2 + C_6H_5CH_2OCO_2CH_2CCl_3 \xrightarrow[CH_3OH]{-1.70\ V} p\text{-}CH_3C_6H_4NHCO_2CH_2CHCl_2 + C_6H_5CH_2OH\ (72\%) + C_6H_5OCO_2CH_2CHCl_2\ (26\%)$$

$$C_6H_5CO_2CH_2CCl_3 + C_6H_5CO_2CH_2CBr_3 \xrightarrow[CH_3OH]{-0.70\ V} C_6H_5CO_2CH_2CCl_3\ (91\%) + C_6H_5CO_2H\ (85\%)$$

Further work is underway to increase the variety of electroremovable derivatives of the simple functional groups involved here, as well as extensions to new protecting groups for other functionality.

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[7] Nitrogen is equally effective for most applications.

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A Test of the Closed-Shell Overlap-Repulsion Model for the Ethane Barrier[1]

Sir:

The elusive nature of the origin of the internal rotation barrier in ethane has been stressed repeatedly.[2] In a recent paper,[3] it was suggested that a number of possible contributions to the barrier cannot play an essential role because they do not behave consistently in two minimum-basis-set, Slater-orbital, SCF–LCAO–MO calculations that yield equal values (3.3 kcal/mol) for the barrier but differ in their choice of geometries; in one,[4] the same bond lengths and bond angles ("fixed" geometry) are used for staggered and eclipsed ethane, while the other[5] employs minimum-energy "optimized" geometries for the individual conformations. In this communication we test the closed-shell overlap-repulsion model for the barrier proposed some years ago[6] by making a corresponding comparison. Since the original model calculation was based on the "fixed" geometry approximation, we have extended it to the "optimized" geometries[5] for the two conformers. Localized bond-orbital functions of the same form (eq 2 and 3 of ref 5) as employed previously are used, with the carbon hybrids directed along the bonds and the coefficient of the 1s orbital on hydrogen set equal to the optimum value found in the "fixed" geometry calculation.[6] The Hartree product formed from these nonorthogonal, localized bond functions gives a nega-

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[1] Supported in part by a grant from the Natural Science Foundation.

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[6] O. J. Sovers, C. W. Kern, R. M. Pitzer, and M. Karplus, *ibid.*, **49**, 2592 (1968).