on silica gel. Elution with $CHCl_3$–ether (1:1 v/v) gave **9c** (430 mg, 43%) and successive elution with the same solvent yielded **12c** (427 mg, 40%, 70.2% based on the recovery of the starting material): ^1H NMR δ 1.43–1.77 (2 H, m), 1.90–2.32 (2 H, m), 3.77 (8 H, s), 3.86–4.02 (4 H, m), 4.09–4.26 (4 H, m), 4.86–5.16 (2 H, m), 5.04 (1 H, s), 5.33 (1 H, s), 5.59–6.05 (1 H, m), 6.92 (3 H, m).

4a,6-*cis*,4a,8a-*cis*-4a-Aryldecahydroisoquinoline 6-Formate 13a. A mixture of **12a** (319 mg, 1 mmol) and formic acid (1 mL) was stirred at room temperature for 2 h. The mixture was made basic with 5% $NaHCO_3$ and extracted with $CHCl_3$. The extract was washed with water, dried (Na_2SO_4), and evaporated, and the remaining residue was chromatographed on silica gel (10 g). Elution with hexane–EtOAc (3:1, v/v) gave **13a** (271 mg, 72%): MS, m/z 347 (M^+); ^1H NMR δ 1.23–2.43 (11 H, m), 2.73 (1 H, d with small splitting, J = 12 Hz), 3.00 (1 H, dd, J = 2, 12 Hz), 3.66 (3 H, s), 3.80 (3 H, s), 5.10 (1 H, m, $W_{1/2}$ = 25 Hz), 6.92 (2 H, d, J = 9 Hz), 7.33 (2 H, d, J = 9 Hz), 7.97 (1 H, s).

4a,6-*cis*,4a,8a-*cis*-4a-Aryldecahydroisoquinoline 6-Formate 13b. A mixture of **12b** (349 mg, 1 mmol) and formic acid (1 mL) was stirred at room temperature for 2 h and worked up as above. The product was chromatographed on silica gel (10 g). Elution with hexane–AcOEt (2:1) gave **13b** (277 mg, 73.6%) as an oil: MS, m/z 377 (M^+); exact mass m/z 377.1807 (calcd for $C_{20}H_{27}NO_6$ m/z 377.1824); ^1H NMR δ 1.14–2.48 (11 H, m), 2.78 (1 H, d with small splitting, J = 12 Hz), 3.04 (1 H, dd, J = 3, 12 Hz), 3.68 (3 H, s), 3.90 (6 H, s), 5.11 (1 H, m, $W_{1/2}$ = 30 Hz), 6.94 (3 H, s), 7.93 (1 H, s).

4a,6-*cis*,4a,8a-*cis*-4a-Aryldecahydroisoquinoline 6-Formate 13c. A mixture of **12c** (479 mg, 1 mmol) and formic acid (1 mL) was stirred and worked up as above. The product was chromatographed on silica gel (10 g). Elution with $CHCl_3$–ether–AcOEt (5:5:1, v/v) gave **13c** (355 mg, 70%): mp 132–134 °C (MeOH–ether); MS, m/z 507 (M^+); ^1H NMR δ 1.20–2.40 (11 H, m), 2.70 (1 H, br d, J = 13 Hz), 2.99 (1 H, dd, J = 2, 13 Hz), 3.59 (3 H, s), 3.70 (8 H, s), 3.78–3.97 (4 H, m), 4.03–4.20 (4 H, m), 5.07 (1 H, m, $W_{1/2}$ = 30 Hz), 6.86 (3 H, br s), 7.91 (1 H, s). Anal. Calcd for $C_{26}H_{37}NO_9$: C, 61.52; H, 7.35; N, 2.76. Found: C, 61.56; H, 7.41; N, 2.74.

General Procedure for a Synthesis of 4a,6-*cis*,4a,8a-*cis*-4a-Aryl-6-hydroxy-2-methyldecahydroisoquinoline 14. To a stirred solution of $LiAlH_4$ (4 mL of 1 M solution in THF) was added a solution of **13** (1 Mmol) in THF (15 mL) under ice cooling. After the stirring had been continued at room temperature for 14 h, the mixture was worked up as usual.

14a: 82% yield; mp 74–76 °C (ether–hexan); IR ($CHCl_3$) 3600, 3590 cm^{-1}; MS, m/z 275 (M^+); ^1H NMR δ 2.10 (3 H, s), 3.82 (3 H, s), 3.60–4.12 (1 H, m), 6.93 (2 H, d, J = 9 Hz), 7.35 (2 H, d, J = 9 Hz). Anal. Calcd for $C_{17}H_{25}NO_2 \cdot H_2O$: C, 65.59; H, 9.28; N, 4.77. Found: C, 69.64; H, 9.26; N, 4.78.

14b: 64% yield; mp 104–107 °C (MeOH–ether); IR ($CHCl_3$) 3660, 3600 cm^{-1}; MS, m/z 305 (M^+); ^1H NMR δ 2.09 (3 H, s), 3.57–3.97 (1 H, m), 3.86 (6 H, s), 6.90 (3 H, br s). Anal. Calcd for $C_{18}H_{27}NO_3 \cdot H_2O$: C, 66.84; H, 9.04; N, 4.33. Found: C, 66.63; H, 8.91; N, 4.21.

14c: 94% yield; mp 79–82 °C (ether); MS, m/z 435 (M^+); ^1H NMR δ 2.06 (3 H, s), 3.78 (8 H, s), 3.80–4.00 (4 H, m), 4.00–4.23 (4 H, m), 6.73–7.00 (3 H, m). Anal. Calcd for $C_{24}H_{37}NO_6 \cdot H_2O$: C, 63.55; H, 8.67; N, 3.10. Found: C, 63.89; H, 8.69; N, 3.19.

Registry No. 4, 41757-95-3; **5a**, 7706-82-3; **5b**, 7706-60-7; (*E*)-**5c**, 99809-84-4; (*Z*)-**5c**, 99828-80-5; **6a**, 97580-22-8; **6b**, 97580-23-9; **6c**, 97580-24-0; **7a**, 97580-26-2; **7b**, 97580-27-3; **7c**, 97580-28-4; **8a**, 97580-30-8; **8b**, 97580-31-9; **8c**, 99809-85-5; **9a**, 97580-35-3; **9b**, 97580-36-4; **9c**, 97580-37-5; **10**, 97580-33-1; **11**, 97580-34-2; **12a**, 97580-38-6; **12b**, 97580-39-7; **12c**, 97579-65-2; **13a**, 99809-86-6; **13b**, 99809-87-7; **13c**, 99809-88-8; **14a**, 99809-89-9; **14b**, 99809-90-2; **14c**, 99809-91-3; $(MeCH_2O)_2P(O)CH_2CO_2CH_2Me$, 867-13-0; $H_2C{=}CH(CH_2)_2I$, 7766-51-0.

Polar Substituent Effects in the Bicyclo[2.2.2]octane Ring System: Polarography of 4-Substituted Bicyclo[2.2.2]oct-1-yl Iodides

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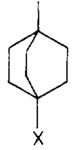
Polarographic half-wave potentials ($E_{1/2}$ values) have been reported recently for reduction of a limited number of 4-substituted bicyclo[2.2.2]oct-1-yl iodides **1**.[1] Unlike the effects of substituents monitored by chemical reactivity probes (energy monitors) in this classical saturated model system,[2] the $E_{1/2}$ values were found to correlate poorly against polar field parameters (σ_F).[3] Electroreduction of haloalkanes[4-7] is known to be irreversible, and the overall two-electron process involves a rate-determining dissociative electron transfer in the first step followed by rapid reduction of the radical to form a carbanion (eq 1). The



1

$R\cdot X^- \longleftrightarrow R^-\cdot X$

2 **3**

$$RX \xrightarrow{e} R\cdot + X^- \xrightarrow{e} R^- \xrightarrow{SH} RH \qquad (1)$$

transition state for the process is probably a radical anion ($[RX]^-\cdot$)[8] possessing partial radical character ($[RX]^-\cdot$ is usefully denoted by canonical structures **2** and **3** with the former being considered dominant) which leads to radical stability being manifested in the potential-determining first step.[9] From this viewpoint, destabilization of the transition state as a result of unfavorable substituent-induced structural constraints on bridgehead radical stability was

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[1] Abeywickrema, R. S.; Della, E. W. *Aust. J. Chem.* **1981**, *34*, 2331.

[2] (a) Stock, L. M. *J. Chem. Educ.* **1972**, *49*, 400 and references cited therein. (b) Grob, C. A.; Rich, R. *Tetrahedron Lett.* **1978**, 663. Grob, C. A.; Rich, R. *Helv. Chim. Acta* **1979**, *62*, 2793. (c) Charton, M. *Prog. Phys. Org. Chem.* **1981**, *13*, 119 and references cited therein.

[3] (a) The symbol σ_F is employed in place of σ_I in view of the overwhelming evidence that σ_I is a manifestation of polar field effects.[3b] (b) Reynolds, W. F. *Prog. Phys. Org. Chem.* **1983**, *14*, 165 and references cited therein.

[4] Rifi, M. R. In "Organic Electrochemistry"; Baizer, M. M., Ed.; Marcel Dekker: New York, 1973; pp 279–314.

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[6] Tanner, D. D.; Plambeck, J. A.; Reed, D. W.; Mojelsky, T. W. *J. Org. Chem.* **1980**, *45*, 5177 and references cited therein.

[7] For a recent review on organic halide reductions, see: Hawley, M. D. In "Encyclopedia of Electrochemistry of the Elements"; Bard, A. J., Lund, H, Ed.; Marcel Dekker: New York, 1980; Vol. XIV, Chapters 1–5.

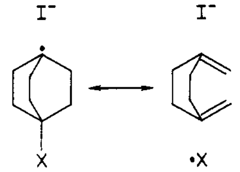
[8] (a) It has been shown by ESR spectroscopy in matrices[8b] that electron capture by alkyl halides leads to the formation of alkyl radical–halide ion adducts ($R\text{---}X^-$) as intermediates rather than true σ* radical anions ($[RX]^-\cdot$). (b) Symons, M. C. R. *Pure Appl. Chem.* **1981**, *53*, 223 and references cited therein.

[9] Abeywickrema, R. S.; Della, E. W. *J. Org. Chem.* **1981**, *46*, 2352 and references cited therein.

0022-3263/86/1951-0564$01.50/0

invoked to explain the deviations from linearity of the $E_{1/2}$ values vs. σ_F.[1]

Recently, we [10] have shown from the trends in the one-bond carbon–fluorine spin–spin coupling constants ($^1J_{CF}$)[11] for an extensive series of 4-substituted bicyclo[2.2.2]oct-1-yl fluorines (4) that structural effects of the kind mentioned above appear to be unimportant in the bicyclo[2.2.2]octane (BCO) ring system for most substituents. In addition, reminiscent of the situation for 1, the ^{19}F substituent chemical shifts (SCS; σ-electron-density monitors) of 4 were found to correlate poorly against σ_F alone.[10] This result has been ascribed to the strong regulation of the ^{19}F SCS by an electronegativity-dependent σ-electron-delocalization mechanism[10,12,16c] ("through-three-bond" or TB-3 effect). Thus, an alternative reason for the poor correlation of the $E_{1/2}$ values of 1 against σ_F parameters focuses on the possibility of a TB-3 effect (or σ-resonance influence) impinging on the radical character of the transition state, i.e., stabilization or destabilization of the transition state by odd-electron delocalization. In valence-bond terms, the delocalization effect on the electroreduction of 1 may be denoted by structures 5 and 6



5 6

(depicted for only one of the three ethano bonds). An encouraging piece of evidence in this regard is that odd-electron delocalization onto the remote bridgehead C–H bond in the bicyclo[2.2.2]octan-1-yl radical has been observed by means of ESR techniques.[13]

Although there is a paucity of information concerning the effects of σ-conjugating substituents on the stability of saturated free radicals, ESR studies of β-substituted ethyl radicals[14,15] strongly suggest that hyperconjugative delocalization of the odd electron to the C–X bond *increases* with *decreasing* electronegativity of the substituent. In particular, electropositive groups such as the metalloidal series (MMe_3; M = Si, Ge, and Sn) appear to be very effective in this regard.[14c,15] In order to ascertain whether or not the electroreduction of 1 is regulated, in part, by a σ-electron-delocalization mechanism, we decided to measure $E_{1/2}$ values very accurately for an extensive series of 1. By covering a diverse range of substituent electronic behavior in the model system, we were hopeful that a discernible trend might be revealed.

Results and Discussion

Conventional dc polarograms for 1 mM solutions of each of the derivatives of 1 in dimethylformamide containing 0.1 M tetra-*n*-butylammonium perchlorate exhibit well-defined waves with similar diffusion currents; a small current maximum appears at the top of the polarographic wave. Pulse polarograms for reduction of all the compounds consist of single waves (except for X = CN) with easily measurable half-wave potentials ($E_{1/2}$ values). The latter electrochemical parameters are assembled in Table I together with the appropriate polar field constants (σ_F).[16] In order to facilitate the discussion, the $E_{1/2}$ values are ranked according to a decrease in ease of reduction going down the table. It is noteworthy that the effect of the methoxy group is *opposite* to what was previously reported (values listed in parentheses in the table).[1] A cursory examination of the data reveals that, in general, the groups with fairly large σ_F values (>0.20) occur above H, which indicates an overriding stabilization influence by the polar-field effect of a *negatively* charged transition state in the potential-determining step. However, in accord with the previous findings for a less extensive data base,[1] the $E_{1/2}$ values (data for H omitted) correlate poorly against the σ_F parameters ($\rho_F = 0.47 \pm 0.08$, $c = -2.29$, $n = 21$, $r = 0.81$). Thus, besides electrostatic field effects, another factor (or factors) must be operating to influence the $E_{1/2}$ values. In this regard, it is significant that inclusion of an electronegativity parameter[3b,17] in the correlation does not lead to an improvement in the precision of the statistical fits.

Table I. Polarographic Reduction Potentials ($E_{1/2}$) in DMF of 4-Substituted Bicyclo[2.2.2]oct-1-yl Iodides and Polar Field Parameters (σ_F)

substituent, X	$E_{1/2}$, V, vs. SCE[a,b]	σ_F[c]
I	−1.95	0.40
Br	−2.00	0.44
CN[d]	−2.04 (−1.99)	0.48
Cl	−2.10	0.43
$OCOCH_3$	−2.11	0.34
F	−2.13 (−2.11)	0.40
CF_3	−2.18	0.42
$C\equiv CSi(CH_3)_3$	−2.19	0.24
$COCH_3$	−2.19	0.25
$COOCH_3$	−2.20	0.26
OCH_3	−2.21 (−2.15)	0.22
$Sn(CH_3)_3$	−2.22	0.00
p-FC_6H_4	−2.23	0.20
C_6H_5	−2.23	0.16
H	−2.23 (−2.12)	0.00
$NHCOCH_3$	−2.23 (−2.12)	0.18
p-$CH_3OC_6H_4$	−2.23	0.15
$CON(CH_3)_2$	−2.24 (−2.15)	0.19
$Si(CH_3)_3$	−2.24	0.00
CH_3	−2.25 (−2.16)	0.00
$N(CH_3)_2$	−2.26 (−2.17)	0.12
$C(CH_3)_3$	−2.29	0.00

[a] *n*-Bu_4NClO_4. Accurate to ±0.01 V. [b] Values in parentheses are taken from ref 1. [c] See ref 16. [d] This compound exhibited a small second wave with a half-wave potential of −2.39 V. Although the compound was an analytically pure sample, a minor impurity is possibly implicated.

However, with respect to the possibility of an electronegativity-dependent TB-3 effect and, as well, in an attempt to qualitatively define other possible factors, a scrutiny of the data (Table I) for specific groups of substituents is revealing. It can be seen that replacement of

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(11) (a) $^1J_{CF}$ is known to reflect structural changes at the bridgehead carbon atoms.[11b,c] (b) Della, E. W.; Cotsaris, E.; Hine, P. T. *J. Am. Chem. Soc.* **1981**, *103*, 4131. (c) Adcock, W.; Abeywickrema, A. N. *J. Org. Chem.* **1982**, *47*, 2945.

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(16) (a) The σ_F values were, in the main, derived from the ^{19}F SCS (DMF) of 1-X-4-(*p*-fluorophenyl)bicyclo[2.2.2]octanes[10b,16b,c] except for $C\equiv CSiMe_3$, *p*-FC_6H_4, and *p*-$CH_3OC_6H_4$. The value for $C\equiv CSiMe_3$ was determined from the ^{13}C SCS of the para carbon center of 1-(trimethylsilyl)-2-(4-phenylbicyclo[2.2.2]oct-1-yl)ethyne.[16d] ^{19}F SCS of 1-fluoro-4-(*p*-substituted phenyl)bicyclo[2.2.2]octanes were employed for determining the σ_F values for the latter two substituents.[11c] (b) Adcock, W.; Aldous, G. L.; Kitching, W. *J. Organomet. Chem.* **1980**, *202*, 385. (c) Adcock, W.; Iyer, V. S. *J. Org. Chem.* **1985**, *50*, 1538. (d) See ref 24 in Adcock, W.; Kok, G. B. *J. Org. Chem.* **1985**, *50*, 1079.

(17) Inamoto, N.; Masuda, S. *Tetrahedron Lett.* **1977**, *3287*.

H by the nonpolar ($\sigma_F \simeq 0$) group 14 type substituents (CH_3, $C(CH_3)_3$, $Si(CH_3)_3$, and $Sn(CH_3)_3$) presents a puzzling and confusing pattern of results. On the basis of radical character in the transition state being important,[1,9,18] it was expected that the electropositive substituents ($Si(CH_3)$ and $Sn(CH_3)_3$) would markedly facilitate reduction whereas the electronegative groups (CH_3) and $C(CH_3)_3$) would have an opposing but smaller effect by a TB-3 influence[16c] (see introduction). Clearly, these expectations are not borne out by the results. Note that the $E_{1/2}$ values for $Si(CH_3)_3$ and $Sn(CH_3)_3$ barely differ from the result for H by more than the experimental error of measurement. The unexpectedly large retarding influence on reduction by the sterically considerable $C(CH_3)_3$ group suggests that steric effects on the orientation of the carbon–iodine bond with respect to the electrode (cathode) surface,[4-7,9] as suggested by Lambert,[19] appears to be implicated as an important factor. This substituent factor may be responsible for masking the intrinsic electrostatic field and electronegativity influences of many of the groups since the pattern displayed by the $E_{1/2}$ values of the halogens, which have fairly similar σ_F values, is clearly in line with the operation of an electronegativity effect. The exact nature of the orbital interactions responsible for the apparent TB-3 effect of the halogens is not known.

Finally, it should be stressed that, although our discussion is limited and tentative due to obvious problems of interpretation and reconciliation of discordant observations, we have provided in this paper very accurate $E_{1/2}$ for an extraordinarily wide range of substituents. Thus, this data base provides a demanding test for any valid theory of electrochemical reduction of alkyl–halogen bonds. Unfortunately, the interpretative difficulties associated with the $E_{1/2}$ values of **1** preclude the assumption that the reactivity pattern displayed by these parameters is representative of electron-transfer reactions in general. Thus, for the time being, the use of **1** as a mechanistic probe for possibly distinguishing mechanistic alternatives (electron transfer vs. direct halogen abstraction)[20] of some haloalkane reactions (e.g., oxidative additions)[20] must await further study.

Note Added in Proof: The $E_{1/2}$ values of **1** have been remeasured in DMF with Me_4NClO_4 as the supporting electrolyte rather than n-Bu_4NClO_4. Compared to those listed in Table I, there is a relatively constant shift (ca. 0.2–0.4 V) to more positive $E_{1/2}$ values. However, a significant feature is that there is a serious dislocation of the relative trends in some instances. In particular, the new $E_{1/2}$ values for several compounds ($X = C(CH_3)_3$, $Si(CH_3)_3$, and $Sn(CH_3)_3$) are now all significantly more *positive* (ca. 0.08–0.13 V) than the value for the parent system ($X = H$, $E_{1/2} = -1.97$ V). These observations obviously raise serious questions about the mechanism of electrolytic reduction and, as well, the influence of the electrolyte. We are currently extending our studies in an attempt to shed some light on this conundrum.

Experimental Section

General Methods. Melting points are uncorrected. Broadband proton-decoupled ^{13}C NMR spectra (22.53 MHz) were recorded in the pulse Fourier-transform mode on a JEOL FX-90Q spectrometer. Routine ^1H NMR spectra were measured with a Varian EM-360 (60 MHz) instrument. All spectra were obtained on $CDCl_3$ solutions.

A three-electrode cell of conventional design[21] was employed for all polarographic experiments. Regular and pulse polarograms were obtained with the aid of a Princeton Applied Research Corporation (PARC) Model 174 polarographic analyzer and a Houston Instruments Model 2000 X–Y recorder; a mercury drop time of 0.5 s was used for pulse polarography. We utilized a reference electrode consisting of a saturated cadmium amalgam in contact with dimethylformamide saturated with both cadmium chloride and sodium chloride;[22,23] the potential of this electrode was measured immediately after each set of polarographic experiments and was found to be −0.758 ± 0.005 V vs. the aqueous saturated calomel electrode (SCE).

Dimethylformamide (distilled-in-glass reagent) was purchased from Burdick and Jackson Laboratories, Inc.; it was distilled at reduced pressure (12–14 torr) and stored under nitrogen in the dark. Tetra-*n*-butylammonium perchlorate, used as a supporting electrolyte, was obtained from the G. Frederick Smith Chemical Co. and was used without further purification. Mercury (Ventron, triply distilled) was used as received. Sample solutions were deoxygenated with prepurified (99.99%) nitrogen. All the various derivatives of **1** were stored in a desiccator over Drierite prior to use. Except for the compounds described below (**1**, $X = Si(CH_3)_3$ and $Sn(CH_3)_3$), all the iodides were available from previous studies.[16d,24-27]

1-Iodo-4-(trimethylsilyl)bicyclo[2.2.2]octane (1, X = Si(CH_3)$_3$). By use of the procedure of Olah et al.,[28] a solution of 1-fluoro-4-trimethylsilyl)bicyclo[2.2.2]octane (**4**, $X = Si(CH_3)_3$;[16c] 0.15 g, 0.79 mmol) in dry dichloromethane (2 mL) was treated with iodotrimethylsilane (0.2 g, 0.001 mol). After the solution was stirred in the dark at ambient temperature under nitrogen for 8 h a further amount of iodotrimethylsilane (0.2 g, 0.001 mol) was added and the reaction mixture was then stirred (ca. 16 h) until VPC analysis indicated complete consumption of the starting fluoro derivative (**4**, $X = Si(CH_3)_3$). A standard workup, followed by sublimation and recrystallization from a hexane–ethanol mixture (1:1), gave the desired iodo compound in a microcrystalline form (110 mg, 45.5%), mp 110–112 °C; ^{13}C NMR ($CDCl_3$, relative to Me_4Si) δ 48.74 (Cl), 40.33 (C2), 29.93 (C3), 14.19 (C4), −4.92 ($Si(CH_3)_3$). Anal. Calcd for $C_{11}H_{21}ISi$:C, 42.86; H, 6.80. Found: C, 42.96; H, 6.83.

1-Iodo-4-(trimethylstannyl)bicyclo[2.2.2]octane, (1, X = Sn(CH_3)$_3$). This compound was prepared from a solution of 1-fluoro-4-(trimethylstannyl)bicyclo[2.2.2]octane (**4**, $X = Sn(CH_3)_3$;[29] 1.0 g, 0.0017 mol) in anhydrous dichloromethane (3 mL) by treatment with iodotrimethylsilane (0.4 g in anhydrous dichloromethane, 0.002 mol) in a manner similar to that outlined above for the corresponding silicon compound. After this solution was stirred in the dark at room temperature for 16 h, an ethereal solution of methyllithium (8 mL, 1 M solution) was added to the reaction mixture in order to remove excess iodotrimethylsilane and, in addition, to methylate any tin iodides ($X = Sn(CH_3)_2I$ and $Sn(CH_3)I_2$) formed in the reaction. After the solution was stirred for an additional 1 h, the reaction was quenched with a saturated ammonium chloride solution. A standard workup, followed by sublimation and recrystallization from a hexane–ethanol mixture (1:1), afforded the iodo compound as fine crystals (0.2 g, 30%): mp 88–89 °C; ^{13}C NMR ($CDCl_3$, relative to Me_4Si) δ 48.74 (Cl), 41.43 [$J_{^{13}C-^{117,119}Sn} = 51.76, 53.71$ Hz; C2], 33.81 (C3), 19.29 $J_{^{13}C-^{117,119}Sn} = 424, 444$ Hz; C4], −12.55 [$J_{^{13}C-^{117,119}Sn} = 293.94, 308.59$ Hz; $Sn(CH_3)_3$]. Anal. Calcd for $C_{11}H_{21}ISn$: C, 33.12; H, 5.30. Found: C, 33.28; H, 5.35.

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Registry No. 1 (x = I), 10364-05-3; 1 (x = Br), 89566-55-2; 1 (x = CN), 80745-57-9; 1 (x = Cl), 89566-54-1; 1 (x = $OCOCH_3$), 74467-16-6; 1 (x = F), 78385-89-4; 1 (x = CF_3), 94994-04-4; 1 (x = $C{\equiv}CSi(CH_3)_3$), 94994-11-3; 1 (x = $COCH_3$), 99631-72-8; 1 (x = $COOCH_3$), 94994-00-0; 1 (x = OCH_3), 74467-18-8; 1 (x = $Sn(CH_3)_3$), 84010-82-2; 1 (x = p-FC_6H_4), 61541-35-3; 1 (x = C_6H_5), 55044-15-0; 1 (x = H), 931-98-6; 1 (x = $NHCOCH_3$), 80745-58-0; 1 (x = p-$CH_3OC_6H_4$), 99631-73-9; 1 (x = $CON(CH_3)_2$), 80745-59-1; 1 (x = $Si(CH_3)_3$), 99631-74-0; 1 (x = CH_3), 55044-63-8; 1 (x = $N(CH_3)_2$), 80745-60-4; 1 (x = $C(CH_3)_3$), 94994-05-5; 4 (x = $Si(CH_3)_3$), 95552-61-7; 4 (x = $Sn(CH_3)_3$), 78385-88-3.

Selective Oxidation of Aldehydes to Carboxylic Acids with Sodium Chlorite–Hydrogen Peroxide

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Several methods for the oxidation of aldehydes to the corresponding carboxylic acids are known.[1,2] However, no one seems to be completely satisfactory, the major drawbacks being high costs, low selectivities, and complex operating conditions. Their application to large-scale preparations is therefore difficult.

We thus addressed our attention to the use of the inexpensive sodium chlorite,[3] which reacts with aldehydes under very mild conditions to give carboxylic acids (eq 1).

$$RCHO + HClO_2 \rightarrow RCOOH + HOCl \qquad (1)$$

However, hypochlorite ion must be removed in order to avoid side reactions, since the redox pair $HOCl/Cl^-$ is a more powerful oxidant than $ClO_2^-/HOCl$.[4] Another drawback is the oxidation of ClO_2^- to ClO_2 according to eq 2.[3a,5]

$$HOCl + 2ClO_2^- \rightarrow 2ClO_2 + Cl^- + OH^- \qquad (2)$$

2-Methyl-2-butene,[7a,8] resorcinol,[3a,7] and sulfamic acid[3a,9] have been tested as HOCl scavengers. 2-Methyl-2-butene must be used in a very large excess. Resorcinol is converted into 4-chloro-1,3-dihydroxybenzene, which must be removed from the reaction mixture. Sulfamic acid works well in the oxidation of hydroxylated aromatic aldehydes, but it gave poor results in the case of α,β-unsaturated aldehydes (see below).

Our HOCl scavenger was 35% H_2O_2, which reduces HOCl according to eq 3,[5] without formation of organic side products.

$$HOCl + H_2O_2 \rightarrow HCl + O_2 + H_2O \qquad (3)$$

Best reaction conditions were achieved by working in a weakly acidic medium, where oxidation was rapid with no competitive reduction of $HClO_2$ to HOCl (eq 4).[5]

$$HClO_2 + H_2O_2 \rightarrow HOCl + H_2O + O_2 \qquad (4)$$

$$2ClO_2 + H_2O_2 \rightarrow 2HClO_2 + O_2 \qquad (5)$$

Under these conditions, any chlorine dioxide is reduced to chlorous acid (eq 5).[6,10]

Reactions were carried out by addition of 1.1–1.4 mol equiv of aqueous $NaClO_2$ to a solution of aldehyde and 1.04 mol equiv of 35% H_2O_2 in aqueous acetonitrile, at 20 °C, buffered with NaH_2PO_4 at pH 4.3. The addition of $NaClO_2$ required 1–2 h, and the reaction was complete after another 1–5 h depending on the aldehyde (procedure A). With the most sensitive substrates more H_2O_2 (up to 5 mol equiv) and a lower pH (~2) were required, in order to speed up HOCl reduction by H_2O_2. In a few instances carboxylic acids quantitatively precipitated and were directly filtered from the reaction medium. In most cases isolated yields were very high for satisfactorily pure products (Table I).

Following this procedure β-aryl-substituted α,β-unsaturated aldehydes are oxidized to the corresponding carboxylic acids without affecting the olefinic double bond (entries 1–5). Yields are lower with aliphatic α,β-unsaturated and/or more hydrophilic aldehydes (entries 19, 20). In the presence of an electron donor group in β-position (entry 21), chlorination of the double bond becomes predominant. The same occurs in the presence of isolated double bonds (entry 22). Triple bonds directly linked to the aldehyde group are substantially stable under these conditions. For example, phenylpropargylic aldehyde is converted into the corresponding carboxylic acid, together with only small amounts of benzoic acid (entry 6).

The method reported here is of general application to aromatic aldehydes, including those which are incompatible[2b] with HOCl (entries 7–9). Heterocyclic aldehydes are good substrates (entries 14–16), except for those which are sensitive to the acidic medium like pyrroles (entry 18). Furfural gives mainly 2-furoic acid with small quantities of maleic acid as a side product (entry 17).[11] p-Aminobenzaldehyde affords only tars (entry 12). In p-methylthiobenzaldehyde, oxidation of the aldehyde group is accompanied by the concomitant oxidation of sulfide to a mixture of sulfoxide and sulfone (entry 13).

The effect of various organic solvents was checked with cinnamaldehyde as substrate. Results are summarized in Table II.

The yield was increased using less hydrophilic alcohols (entries 1–4). Toluene (entry 5) greatly reduced the reaction rate, requiring 24 h for complete conversion of the substrate.

For aldehydes in which reaction of HOCl with the substrate is faster than reaction with H_2O_2 (Table I, entries 10, 11), dimethyl sulfoxide (Me_2SO) proved to be an effective HOCl scavenger when used as solvent, since it is

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