1 (R = H) is considerably more long-lived ($t_{1/2}$ > 5 min at −100 °C) than its higher homologues.

Finally, the course of the reactions of acid anhydrides and chlorides with organolithium reagents is not noticeably altered by the presence of Me_3SiCl. The increased rate of collapse of the adduct analogous to 1 generated upon nucleophilic addition to these carbonyl systems apparently precludes their interception by Me_3SiCl. In the case of diethyl carbonate (entries 21 and 22) some adduct trapping is observed in both steps involving carbonyl addition, but trapping efficiency in the crucial first addition step to give a secure ortho ester is not high.

In summary, we have demonstrated that the intermediate formed in the reaction of esters with nucleophiles (1) in some cases may be intercepted with good efficiency through an intermolecular reaction by conducting the reaction in the presence of chlorotrimethylsilane. Other reactions where this might be advantageous are under investigation.

Experimental Section

Gas chromatographic analyses were performed with a Hewlett-Packard 5790A gas chromatograph and a 3390A integrator using a 12-m cross-linked methyl silicone capillary column. Quantitations were done with the aid of an added internal hydrocarbon standard and calibration factors obtained from mixtures of known composition. Products were identified by comparisons with authentic samples. *n*-BuLi in hexane, *s*-BuLi in cyclohexane, PhLi in cyclohexane–diethyl ether, MeLi in diethyl ether, and *n*-butylmagnesium chloride in diethyl ether were obtained from Aldrich Chemical Co. Organolithium solutions were titrated prior to use.[12] Chlorotrimethylsilane was distilled from CaH_2 prior to use. Tetrahydrofuran (THF) was distilled from sodium benzophenone ketyl. Esters were freshly distilled and stored over 4A molecular sieves. Reactions conducted at −100 °C were cooled with a freezing MeOH bath (MeOH–liquid N_2), and those conducted at −78 °C were cooled with a dry ice–acetone bath. All reactions were conducted under an atmosphere of argon.

Acylation of *n*-BuLi with Ethyl Valerate. Typical Procedure. A solution containing 149 μL (1.0 mmol) of ethyl valerate in 6 mL of THF was cooled to −100 °C, and 630 μL (5.0 mmol) of Me_3SiCl was added. With vigorous stirring, 0.95 mL (1.25 mmol) of −78 °C 1.32 M *n*-BuLi was added dropwise over 3 min and the mixture was stirred 10 min at −100 °C. The mixture was stirred at −78 °C for 10 min and then brought to 0 °C where 300 μL of EtOH was added. At 20 °C, 1 mL of water was added and after stirring briefly 2 mL of 4 N HCl was added over 1 min. Vigorous stirring was continued for 2 min. Water (15 mL), NaCl (3 g), pentane (6 mL), and 100 μL of internal standard (tridecane in this case) were added, and the mixiture was vigorously stirred for 4 min. GC analysis of the pentane layer showed the presence of 116 mg (82%) of 5-nonanone and 32 mg (16%) of 5-butyl-5-nonanol. The remaining results shown in Table I were obtained in a similar manner with the variations noted in the table.

In a preparative scale run, 1.50 mL (0.01 mol) of ester and 6.3 mL of Me_3SiCl in 35 mL of THF was treated as above at −100 °C with 13.5 mmol of *n*-BuLi. After 10 min at −100 °C and 10 min at −78 °C, the mixiture was allowed to warm to 20 °C whereupon excess Me_3SiCl and most of the THF were removed under reduced pressure. The residue was stirred with 3 mL of EtOH for 1 min, treated with 3 mL of H_2O, and stirred for 3 min. The mixture was made acidic by the addition of a small amount of 4 N HCl followed by the addition of 10 mL of Et_2O. After stirring for 5 min, the mixture was diluted with water (25 mL) and extracted with pentane. Concentration and simple bulb-to-bulb distillation of the residue (150 °C, 30 mm) gave 5-nonanone (84%), which contained a small amount (6%) of 5-butyl-5-nonanol. When the crude reaction product was first chromatographed (SiO_2, CH_2Cl_2), distillation gave pure 5-nonanone in 77% yield.

Acknowledgment. We thank the National Science Foundation for support of this work.

(12) Watson, S. C.; Eastham, J. F. *J. Organomet. Chem.* **1967**, *9*, 165.

Reductive Dehalogenation of Electron-Poor Heterocycles:[1a] Nicotinic Acid Derivatives

George R. Newkome,* Charles N. Moorfield, and Bahman Sabbaghian[1b]

Department of Chemistry, Louisiana State University, Baton Rouge, Louisiana 70803-1804

Received September 30, 1985

Recently, we reported the convenient synthesis of 2,6-diiodopyridine[2] by the chloro → iodo exchange of the corresponding commerically available dichloropyridine. This rarely used procedure[3-5] employed the prolonged treatment of chloro substituted electron-poor heterocycle with a high concentration of iodide ion, derived from concentrated HI and NaI. We herein report the specific reductive dehalogenation of 2-chloronicotinic acids under these reaction conditions.

Selective dechlorination was discovered during the attempted transformation of 2,6-dichloro- to 2,6-diiodonicotinic acid, from which 6-iodonicotinic acid was isolated, as the major product. An attempt to obtain 2-iodonicotinic acid under the classical Finkelstein conditions using 2-butanone, as a solvent,[6] was unsuccessful in that only unchanged starting 2-chloronicotinic acid was isolated. Although Hirshberg and Spoerri[7] reported the preparation of iodopyrazines via this method, when Graft and coworkers[8,9] and Hoffman and Behrmann[10] applied a similar procedure to chloro*iso*nicotinic acids, the major side reaction was, however, dechlorination; whereas, Sell and Dootson[11] obtained 2,6-diiodo*iso*nicotinic acid upon repetition of the reaction in an open vessel. Fischer[12] reported an analogous reduction when chloropurines were treated with hydriodic acid and a phosphonium iodide.

The selective reduction was herein proven by characterization of the products obtained by transforming 2-chloro-, 6-chloro-, and 2,6-dichloronicotinic acid to either unsubstituted or 6-iodonicotinic acids. In all of these transformations, the chemical shift of the position 4 ($\Delta\delta$ 0.4 upfield) and 5 ($\Delta\delta$ 0.4 downfield) protons is indicative of the desired halogen–halogen exchange. This general chemical shift trend for iodo substitution is realized in all of the series including the trifluoromethyl derivatives.

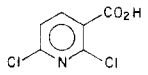
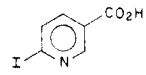
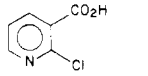
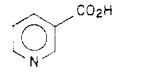
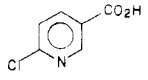
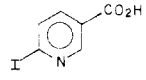
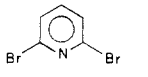
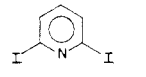
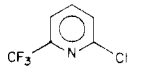
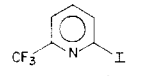
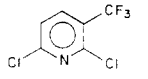
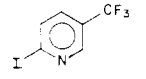
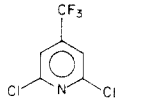
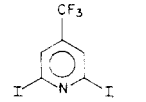
3,5-Dichloro-, 2-chloro-3-hydroxy-, and 2-chloro-5-hydroxypyridine did not undergo Cl → I exchange but afforded unchanged starting materials. Diazines, such as, 3,6-dichloropyridazine, 2,6-dichloropyrazine, and 2,4-dichloropyrimidine yielded only tars with no distinguishable NMR pattern. 2-Chloroquinoline solidified after 1 h under the reaction conditions and gave a grayish tarlike solid, which was insoluble in $CHCl_3$, ether, and water. In the reactions reported in Table I, no other characterizable products were isolated.

The results indicate that electron-deficient heterocycles with electron-withdrawing substituents can undergo a re-

(1) (a) Chemistry of Heterocyclic Compounds Series. Part 108. (b) Undergraduate Researcher.
(2) Newkome, G. R.; Roper, J. M. *J. Organomet. Chem.* **1980**, *186*, 147.
(3) Baker, B. R.; McEvoy, F. J. *J. Org. Chem.* **1955**, *20*, 118.
(4) Bruce, W. F.; Perez-Medina, L. A. *J. Am. Chem. Soc.* **1947**, *69*, 2571.
(5) Baker, W.; Curtis, R. F.; Edwards, M. G. *J. Chem. Soc.* **1951**, 83.
(6) Klingsberg, E. *J. Am. Chem. Soc.* **1950**, *72*, 1031.
(7) Hirshberg, A.; Spoerri, P. E. *J. Org. Chem.* **1961**, *26*, 1907.
(8) Graf, R. *J. Prakt. Chem.* **1932**, *133*, 37
(9) Graf, R. *J. Prakt. Chem.* **1937**, *148*, 13.
(10) Hofmann, A. W.; Behrmann, A. *Chem. Ber.* **1884**, *17*, 2681.
(11) Sell, W. J.; Dootson, F. W. *J. Chem. Soc.* **1900**, *77*, 233.
(12) Fischer, E. *Chem. Ber.* **1898**, *31*, 2550.

0022-3263/86/1951-0953$01.50/0

Table I

reac	starting material	product[a]	yield, %	mp [lit. mp], °C	^{1}H NMR,[b] δ H2	H3	H4	H5
1			51	190–193[h] [189–190][d]	8.80[c]		7.88	8.02
2			32	234–238 [236–237][f]	9.07[e]		8.25	7.51
3			45	187–192				
4			55	184–188 [185–186][h]		7.68[g]	6.93	7.68
5			43	83–85[j]		7.92[i]	7.50	7.65
6			39	77–80[j]	8.63[k]		7.52	7.89
7			37[l]	*j*		7.89[m]		7.98

[a] All products gave a mass spectrum with an M^+ (100%) as determined on an HP 5985 GC/mass spectrometer. New products gave satisfactory microanalysis, except where noted. [b] ^{1}H NMR spectra were determined on an IBM NR-80 spectgrometer using $CDCl_3$ for H4, 6-, and -7 and Me_2SO-d_6 for H1–3. [c] H2: dd, J = 2.2, 1.1 Hz. H4: dd, J = 8.2, 2.2 Hz. H5: dd, J = 8.2, 1.1 Hz. [d] Reference 4. [e] H2: s (br). H4: dt, J = 8.0, 1.8 Hz. H5: dd, J = 8.0, 4.8 Hz. H6: δ 8.77; dd, J = 4.8, 1.8 Hz. [f] Paraskewas, S. *Synthesis* **1974**, 819. [g] H3: d, J = 8.1 Hz. H4: t, J = 8.1 Hz. H5: d, J = 8.1 Hz. [h] Reference 2. [i] H3: d, J = 7.8 Hz. H4: t, J = 7.8 Hz. H5: d, J = 7.8 Hz. [j] Products were too thermally unsatable for full analytical analysis. [k] H2: s (br). H4: dd, J = 7.9, 2.6 Hz. H5: d, J = 7.9 Hz. [l] Isolated product was a mixture of mono- and diiodinate species (see text). [m] H3: H5, s.

ductive halogen → hydrogen exchange. Reduction at the position meta to an electron-withdrawing substituent was observed only in reaction 7 from which a mixture of mono- and diiodinated products were recovered; this was an exception to the normal ortho (para) to N-substitution pattern. The isolation of these two products may be indicative of an iodinated intermediate. In no other reaction, where the reduction was observed, was an iodinated species isolated.

Experimental Section

General Procedure for the Preparation of Iodonicotinic Acids. The chloro heterocycle (3.4 mmol) was added to a stirred mixture of NaI (4.4 mmol) and concentrated HI (2.7 mL, sp gr 1.5) and then refluxed for 24 h. The solution was cooled to 5 °C and acetone (10–15 mL) was added. The resulting precipitate was filtered, washed with cold aqueous $NaHSO_3$ solution, recrystallized from diethyl ether, and dried in vacuo for 5 h. The results are summarized in Table I.

General Procedure for the Preparation of Iodo(trifluoromethyl)pyridines. The reaction conditions were similar to the above except the mixture was cooled to 25 °C, and then H_2O (3–5 mL) and solid $Na_2S_2O_3$ were added sequentially. The clear solution is adjusted to pH 8–9 and extracted with Et_2O (3 × 15 mL). The combined organic fraction was dried over anhydrous Na_2SO_4, filtered, and concentrated in vacuo. The crude product is purified by thick layer chromatography (silica gel) using EtOAc, as the eluent.

Acknowledgment. We gratefully acknowledge the Ishihara Sanygo Kaisha Corporation for providing us with the trifluoropyridines.

Registry No. 2,6-Dichloronicotinic acid, 38496-18-3; 2-chloronicotinic acid, 2942-59-8; 6-chloronicotinic acid, 5326-23-8; 2,6-dibromopyridine, 626-05-1; 2-chloro-6-(trifluoromethyl)-pyridine, 39890-95-4; 2,6-dichloro-3-(trifluoromethyl)pyridine, 55304-75-1; 2,6-dichloro-4-(trifluoromethyl)pyridine, 39890-98-7; 6-iodonicotinic acid, 13054-02-9; nicotinic acid, 59-67-6; 2,6-diiodopyridine, 53710-17-1; 2-iodo-6-(trifluoromethyl)pyridine, 100366-74-3; 2-iodo-5-(trifluoromethyl)pyridine, 100366-75-4; 2,6-diiodo-4-(trifluoromethyl)pyridine, 100366-76-5.