$H_2)_{17}CH_3$, 112-92-5; $HOCH_2CF_3$, 75-89-8; $HOCH_2C(Me)_3$, 75-84-3; HOPh, 108-95-2; $FCO_2C(Me)_3$, 18595-34-1; $FCO_2C(Me)_2CH_2CH_3$, 104483-21-8; FCO_2Ad, 62087-82-5; FCO_2CH_2Ph, 93942-41-7; $FCO_2(CH_2)_6OCOF$, 119448-11-2; $FCO_2(CH_2)_7CH_3$, 104483-19-4; $FCO_2(CH_2)_{17}CH_3$, 104483-24-1; $FCO_2CH_2CF_3$, 112915-23-8; $FCO_2CH_2C(Me)_3$, 63934-51-0; FCO_2Ph, 351-80-4; $Cl_3CCHClOCO_2CH_2C(Me)_3$, 105595-28-6; $MeCHClOCO_2CH(Me)_2$, 98298-66-9; $MeCHClOCO_2Me$, 80196-03-8; FCO_2Et, 461-64-3; $FCO_2CH(Me)_2$, 461-71-2; $HOCH(Me)_2$, 67-63-0; HOMe, 67-56-1; $ClCH_2OCO_2Bu$-*t*, 35180-02-0; cholesteryl fluoroformate, 65928-85-0; *p*-MeObenzyl chloride, 824-94-2; cholesterol, 57-88-5.

Supplementary Material Available: Spectral (IR, ^1H NMR, and high-resolution MS) and analytical data for carbonates and new fluoroformates (4 pages). Ordering information is given on any current masthead page.

Advantages of Fluoroformates as Carboalkoxylating Reagents for Polar Reactants[1]

Vu Anh Dang and R. A. Olofson*,[2]

Department of Chemistry, The Pennsylvania State University, University Park, Pennsylvania 16802

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While chloroformates react explosively with DMSO and exothermically with DMF and other tertiary amides, we have found that fluoroformates are stable in these solvents below 100 °C. Several important classes of hydroxyl- and amine-containing organic compounds are insoluble in aprotic solvents less polar than DMSO and DMF and thus cannot be carboalkoxylated in inert media with chloroformates. In this paper, we show that such compounds can be easily and efficiently carboalkoxylated with fluoroformates in DMSO or DMF (NMP). Examples include the *per*-carboalkoxylation of glucose, salicin, adonitol, sucrose, and thymidine in 77–89% yield. KF, or preferably triethylamine, is used as the proton scavenger. While cellulose is only partly carboalkoxylated under these conditions, essentially all of the OH functions in polyvinyl alcohol of average MW 12000 are converted to carbethoxy groups.

Fluoroformates are easily available either by direct exchange of the corresponding chloroformates with KF[3] or by the methodology outlined in the preceding paper.[4] In this latter work, fluoroformates were generated in solvents such as DMF and *N*-methylpyrrolidinone (NMP) and were inert to the reaction medium[5] when made in DMSO.

The stability of fluoroformates in tertiary amide solvents and in DMSO contrasts sharply with the behavior of chloroformates in the same media. Chloroformates acylate DMF and other tertiary amides to give adduct salts **1**,

1 **2**

which mimic and fragment to Vilsmeier reagents.[6] N-Dealkylation, C-deprotonation (of R′), and displacement at R in **1** also occur.[6] Similar adducts **2** are formed in the highly exothermic reaction of DMSO with chloroformates. Ordinarily **2** rearranges to Pummerer type products.[7] When a weak base is included in the medium, Moffatt–Pfitzner–Barton type oxidation products also may be found.[8] Thus, unlike chloroformates, fluoroformates should be effective acylating agents in very polar solvents like DMF and DMSO. The evaluation of fluoroformates in this role is the subject of this paper.

Important classes of organic compounds which often are insoluble in aprotic media less polar than DMSO include amino acids, peptides, carbohydrates, nucleotides, and certain organic salts. It is frequently desirable to carboalkoxylate such compounds either to modify their properties as materials or as part of a synthetic scheme (e.g., introduction of protecting groups). Such acylations ordinarily have been accomplished by one of two classical methodologies. Often the polar reactant in a protic solvent such as water is treated with the chloroformate under conditions which selectively enhance the activity of the required reaction site at the expense of the solvent (e.g., Schotten–Bauman acylations). If the polar reactant contains labile protons, a mild, semipolar, aprotic base such as pyridine may be utilized both as solvent and acid scavenger. Then the medium is an equilibrium mixture including an organic salt in its conjugate base. Also, as the acid produced in the acylation step is converted to its salt, the medium becomes increasingly polar. Because some if not most of the chloroformate reacts with the solvent, both methods often are impractical.

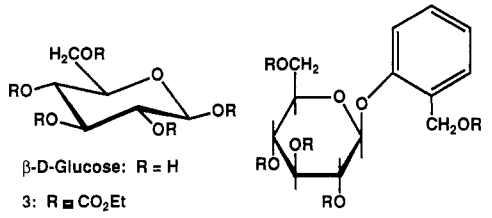
In most experiments used to determine the value of fluoroformates as carboalkoxylating reagents, carbohydrates were chosen as test systems because extensive literature is available to demonstrate the importance of the process in synthetic chemistry and for the modification of materials.[9] Moreover, many specialized techniques and clever tricks are described in published acylation procedures[10] which indicates a continuing need to consider the acylation of each carbohydrate as a special problem and suggests a lack of generally useful methodology. Carbohydrates can also provide a stringent test of reaction efficiency: for a pentol, 90% reaction at each site translates to only a 59% yield of product. Finally, intramolecular

(1) Adapted and condensed from the Ph.D. Dissertation of V. A. Dang, The Pennsylvania State University, University Park, PA, 1986.
(2) Dedicated to the memory of Professor Emil Thomas Kaiser of Rockefeller University, deceased July 18, 1988.
(3) Cuomo, J.; Olofson, R. A. *J. Org. Chem.* **1979**, *44*, 1016.
(4) Dang, V. A.; Olofson, R. A.; Wolf, P. R.; Piteau, M. D.; Senet, J.-P. G. *J. Org. Chem.*, preceding paper in this issue.
(5) Although not cleanly formed.[4]
(6) Zabicky, Z. *The Chemistry of Amides*; Interscience: London, 1970. Dorofeenko, G. N.; Minkin, V. I. *Russ. Chem. Rev.* **1960**, *29*, 599.
(7) Epstein, W. W.; Sweat, F. W. *Chem. Rev.* **1967**, *67*, 247. Yagihara, T.; Oae, S. *Tetrahedron* **1972**, *28*, 2765.
(8) Mancuso, A. J.; Swern, D. *Synthesis* **1981**, 165.
(9) Hough, L.; Priddle, J. E.; Theobald, R. S. *Adv. Carbohydr. Chem.* **1960**, *15*, 91. For example, fatty acid esters of sucrose are sold as lubricants, emulsifiers, foaming agents, and wetting agents: Hickson, J. L. *Sucrochemistry*, ACS Symposium Series 41, American Chemical Society: Washington, DC, 1977.
(10) Pigman, W.; Horton, D. *The Carbohydrates, Chemistry and Biochemistry*, 2nd ed.; *Academic Press*: London, 1972; Vol. 1A.

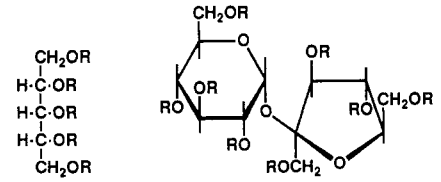
0022-3263/90/1955-1851$02.50/0

acylation to give cyclic carbonates is a major side reaction in the treatment of carbohydrates with chloroformates under Schotten–Bauman conditions.[10] Avoidance of this process is a good measure of the mildness of the carboalkoxylation conditions.

When Et_3N was added to a solution of β-D-glucose and ethyl fluoroformate (20% excess) in DMSO, the known pentacarbonate **3**[11a] was obtained as a crystalline solid in 82% yield. In the workup, the DMSO was removed along with the $Et_3NH^+ F^-$ by extraction into water from CH_2Cl_2.[11b] Similar treatment of the analgesic salicin with isopropyl fluoroformate afforded the crystalline pentacarbonate **5** in 80% yield. However, glucose was converted to a tricarbonate **4** (85% yield, IR 3590 and 1750 cm^{-1}) when treated with 1-adamantyl fluoroformate. The reaction sites were not determined, but the crystalline **4** seemed to be a single isomer. Presumably, the steric problems encountered in attaching bulky adamantyl groups to adjacent OH prevented the further acylation of **4**.

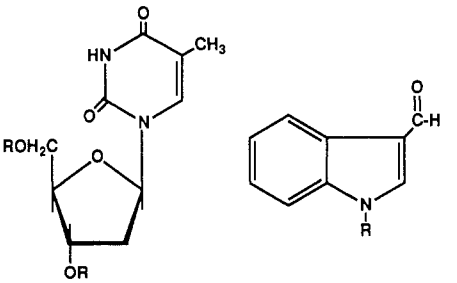


When EtOCOF was added to a mixture of β-D-glucose and KF, a uniquely complementary acid scavenger ($\rightarrow KHF_2$),[12] in DMSO, the pentacarbonate **3** was isolated in 89% yield (vs 82% with Et_3N). However, complete reaction only was achieved after heating at 60 °C for 10 h. Similarly, when adonitol was treated with EtOCOF and KF in DMSO, the yield of the pentacarbonate **6** was 91%, but only after heating the mixture for several hours at 60–90 °C. This low rate of reaction may be a consequence of the near insolubility of KF in DMSO or of a reduced basicity of F^- in the presence of adjacent OH's. Fluoride is known to form strong hydrogen bonds which greatly lower its basicity.[13]



Reaction of sucrose in DMSO with EtOCOF and with octyl fluoroformate using Et_3N as the added base afforded the octacarbonates **7** and **8** in 82% and 83% yields, respectively. While the yield of **7** was 88% with DMF in place of the DMSO, the reaction was not as satisfactory. Sucrose is not very soluble in DMF, harsher conditions were required, the crude product was darker, and several water extractions were required to remove all the DMF. While the carbonates **6–8** were oils, they were easily purified by a standard extraction workup and were characterized by IR (C=O stretch at 1760, no OH stretch at 3500–3700 cm^{-1}), ^1H NMR, and combustion analyses. When a product oil was obtained by two methods, both samples were submitted for combustion analysis.

In related experiments, thymidine in DMSO was converted to the biscarbonate **9** in 77% yield and reaction of the sensitive indole-3-carboxaldehyde with isopropenyl fluoroformate[14] in DMF afforded the carbamate **10** in 79% yield.



In recognition of the importance of acetate rayon and other modified cellulose polymers,[15] a few attempts were made to carboalkoxylate cellulose. In one experiment, cotton was swelled in DMSO at 120 °C. Then a 3-fold excess of isopropyl fluoroformate and Et_3N was added, and the reaction was continued for another day. After workup, the polymer was analyzed for alkoxycarbonyl content by mild saponification (modified Eberstadt method[16]). The calculated degree of substitution[17] (DS) was only 0.49 out of a possible 3.0 (3 HO's per anhydroglucose unit), presumably because of the low solubility of cotton in DMSO.

Cellulose dissolves at 100 °C in *N,N*-dimethylacetamide (DMA) and *N*-methylpyrrolidinone (MPN) containing 3–15% by weight of dried LiCl (recovered intact after workup).[18] Thus, in a pair of experiments, microcrystalline cellulose was dissolved in hot DMA–LiCl and MPN–LiCl, and the cooled solutions were treated consecutively with Et_3N and EtOCOF (ca. 1.4 equiv per OH). After standard workup, the observed DS of the ethoxycarbonyl cellulose was 1.0 in the DMA reaction and 1.1 in the MPN process. With octyl fluoroformate in DMA–LiCl, the DS of the recovered octyloxycarbonyl cellulose was 0.57. These cellulose carbonates swelled in acetone and were insoluble in water, ether, methanol, and CH_2Cl_2. Since there was no IR C=O stretch at 1820–1850 cm^{-1}, very little if any intramolecular reaction to give a cyclic 5-membered ring carbonate occurred.

Although DMSO is a poor solvent for cellulose, it is a good solvent for lower molecular weight (MW) polyols. Thus, treatment of polyvinyl alcohol of average MW 14000 in DMSO with EtOCOF and Et_3N gave a yellow rubberlike material with 85% of the OH's acylated. From a comparison of the NMR integrations of the polymer CH_2CH framework with the ethyl signals, it was found that very little if any cyclic carbonate had formed. The estimated

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DS may be low since no IR OH stretch was observed.

From the results presented here, it is evident that the combination of a fluoroformate with DMSO or DMF and Et_3N provides an excellent environment for the carboalkoxylation of polar compounds including small polymers. More work is necessary to determine whether fluoroformates also have value in the carboalkoxylation of cellulose. There is some evidence that the reactivity profile of fluoroformates can be extended to include acyl fluorides.[19]

Experimental Section[20]

Penta-*O*-(ethoxycarbonyl)-D-glucose (3). Ethyl fluoroformate[3] (8.34 g, 0.091 mol) was added to a mixture of dried KF (4.0 g, 0.069 mol) and β-D-glucose (1.95 g, 0.011 mol) in 60 mL of DMSO. After 10 h at 60 °C, the cooled mixture was diluted with CH_2Cl_2 (50 mL), washed with water (3 × 50 mL), dried (Na_2SO_4), and concentrated in vacuo to a brown syrup at 75 °C: 5.2 g (89% yield), crystallized from EtOH, white solid of mp 99–100 °C (lit.[11] mp 100–102 °C). Anal. Calcd for $C_{21}H_{32}O_{16}$: C, 46.67; H, 5.97. Found: C, 46.61; H, 5.95.

In another experiment, Et_3N (3.0 g, 0.030 mol) in 15 mL of CH_2Cl_2 was added to a stirred mixture of β-D-glucose (1.00 g, 0.0056 mol) and EtOCOF (3.00 g, 0.033 mol) in 20 mL of DMSO. After 1 day at room temperature and another 4 h at 60 °C, the cooled mixture was diluted with CH_2Cl_2 and worked up as above; mp 98–99 °C, 2.5 g (82% yield).

Tri-*O*-(1-adamantyloxycarbonyl)-D-glucose (4). Et_3N (2.8 g, 0.028 mol) in CH_2Cl_2 (10 mL) was added to a mixture of β-D-glucose (0.90 g, 0.005 mol) and adamantyl fluoroformate[4] (5.54 g, 0.028 mol) in DMSO–CH_2Cl_2 (50 mL, 4:1), which was stirred at 25 °C for 1 day, diluted with CH_2Cl_2 (50 mL), washed with water (3 × 75 mL), dried (Na_2SO_4), and concentrated to a white solid. This was washed with hot pentane (3 × 75 mL) and crystallized from EtOH: mp 155–158 °C, 3.0 g (85% yield); IR (CCl_4) 3590 (w), 1750 cm^{-1} (s). Anal. Calcd for $C_{39}H_{54}O_{12}$: C, 65.72; H, 7.61. Found: C, 65.72; H, 7.95.

Penta-*O*-(isopropoxycarbonyl)salicin (5). A mixture of Et_3N (3.5 g, 0.034 mol), isopropyl fluoroformate[3] (3.5 g, 0.033 mol), salicin (1.10 g, 0.0038 mol), and DMSO–CH_2Cl_2 (35 mL, 5:2) was stirred at 25 °C for 17 h, diluted with CH_2Cl_2 (100 mL), washed with water (3 × 100 mL), dried (Na_2SO_4), and concentrated in vacuo at 70 °C to a white solid, 2.2 g (80% yield); the solid was crystallized from EtOH: mp 144–145 °C; IR ($CDCl_3$) 1750, 1740 cm^{-1} (s); ^1H NMR ($CDCl_3$) δ 6.8–7.3 (m, 4 H), 3.7–5.3 (m, 14 H), 1.28 (d, 30 H, J = 6 Hz). Anal. Calcd for $C_{33}H_{48}O_{17}$: C, 55.30; H, 6.57. Found: C, 55.10; H, 6.69.

Penta-*O*-(ethoxycarbonyl)adonitol (6). A mixture of EtOCOF (4.90 g, 0.053 mol), dried KF (4.1 g, 0.071 mol), and adonitol (0.95 g, 0.0062 mol) in 40 mL of DMSO was heated at 60 °C for 10 h and then at 90 °C for 10 h. The cooled mixture was diluted with CH_2Cl_2 (100 mL), washed with water (3 × 100 mL), passed through charcoal, dried (Na_2SO_4), and concentrated in vacuo at 70 °C to afford **6** as a colorless syrup: 2.9 g (91% yield); IR ($CDCl_3$) 1755 cm^{-1} (s); ^1H NMR ($CDCl_3$) δ 5.30 (center of broad s, 3 H), 4.0–4.7 (m, 14 H), 1.32 (t, 15 H, J = 6 Hz). Anal. Calcd for $C_{20}H_{32}O_{15}$: C, 46.74; H, 6.35. Found: C, 48.87; H, 6.29.

Octa-*O*-(ethoxycarbonyl)sucrose (7). Et_3N (2.9 g, 0.029 mol) in 10 mL of CH_2Cl_2 was added to a stirred mixture of EtOCOF (2.60 g, 0.0283 mol) and sucrose (1.00 g, 0.0029 mol) in 20 mL of DMF. After 17 h at 50 °C, the cooled mixture was diluted with CH_2Cl_2 (100 mL), washed with water (7 × 100 mL), passed through charcoal, dried (Na_2SO_4), and concentrated in vacuo at 70 °C to obtain **7** as a light yellow syrup: 2.3 g (88% yield); IR ($CDCl_3$) 1755 cm^{-1} (s); ^1H NMR ($CDCl_3$) δ 4.0–5.9 (m, 30 H), 1.32 (t, 24 H, J = 6 Hz). Anal. Calcd for $C_{36}H_{54}O_{27}$: C, 47.06; H, 5.92. Found: C, 47.06; H, 5.87.

In another experiment, a mixture of Et_3N (4.4 g, 0.044 mol), sucrose (1.00 g, 0.0029 mol), EtOCOF (2.68 g, 0.029 mol), CH_2Cl_2 (20 mL), and DMSO (20 mL) was stirred at 25 °C for 1 day and at 50 °C for 4 h, diluted with CH_2Cl_2 (50 mL), washed with water (3 × 100 mL), dried (Na_2SO_4), and concentrated as above: 2.2 g (82% yield). Anal. Found: C, 46.87; H, 5.95.

Octa-*O*-(octyloxycarbonyl)sucrose (8). Octyl fluoroformate[4] (4.10 g, 0.023 mol) in 10 mL of CH_2Cl_2 and then Et_3N (2.35 g, 0.023 mol) were added to sucrose (1.00 g, 0.0029 mol) in 25 mL of DMSO. The mixture was stirred at room temperature for 2 days and at 70 °C for 3 h, cooled, and worked up as above: colorless syrup; 3.8 g (83% yield); IR ($CDCl_3$) 1755 cm^{-1} (s). Anal. Calcd for $C_{84}H_{150}O_{27}$: C, 63.37; H, 9.80. Found: C, 63.08; H, 9.63.

Di-*O*-(ethoxycarbonyl)thymidine (9). Et_3N (1.7 g, 0.017 mol) in 10 mL of CH_2Cl_2 was added to a mixture of thymidine (0.80 g, 0.0033 mol) and EtOCOF (1.52 g, 0.016 mol) in 40 mL of DMSO–CH_2Cl_2 (3:1). The mixture was stirred at room temperature for 1 day, diluted with CH_2Cl_2 (50 mL), washed with water (3 × 50 mL), dried (Na_2SO_4), and concentrated to a brown solid: crystallized from EtOH; mp 119–120 °C, 1.0 g (77% yield); IR ($CDCl_3$) 3495 (m), 1750 (s), 1710 (s), 1685 cm^{-1} (s); ^1H NMR ($CDCl_3$) δ 7.43 (s, 1 H), 6.38 (t, 1 H, J = 6 Hz), 5.0–5.4 (m, 1 H), 3.9–4.6 (m, 7 H), 2.1–2.6 (m, 2 H), 1.93 (s, 3 H), 1.32 (t, 6 H, J = 7 Hz). Anal. Calcd for $C_{16}H_{22}N_2O_9$: C, 49.74; H, 5.73. Found: C, 49.83; H, 5.78.

***N*-(Isopropenyloxycarbonyl)indole-3-carboxaldehyde (10).** Et_3N (2.8 g, 0.028 mol) in 20 mL of CH_2Cl_2 was added to a stirred mixture of indole-3-carboxaldehyde (3.00 g, 0.021 mol) and isopropenyl fluoroformate (from the chloroformate[14] by halide exchange,[3] 2.36 g, 0.023 mol) in 20 mL of DMF. After 6 h, the mixture was diluted with CH_2Cl_2, washed with water (2 × 100 mL), dried (Na_2SO_4), and concentrated to a brown solid: crystallized from hexane, mp 98–99 °C, 3.6 g (79% yield); IR ($CDCl_3$) 1755 (s), 1670 cm^{-1} (m); ^1H NMR ($CDCl_3$) δ 9.93 (s, 1 H), 7.1–8.3 (m, 5 H), 4.93 (d, 2 H, J = 6 Hz), 2.10 (s, 3 H). Anal. Calcd for $C_{13}H_{11}NO_3$: C, 68.11; H, 4.80; N, 6.11. Found: C, 68.05; H, 4.81; N, 6.00.

(Ethoxycarbonyl)cellulose. Microcrystalline cellulose powder (Fluka, DS-0) (dried under vacuum at 25 °C over P_2O_5 for 4 days, 1.00 g, 0.00704 mol of anhydroglucose unit) in DMA (15 g) was mechanically stirred at 165 °C for 30 min. The mixture was cooled to 100 °C, and LiCl (dried at 170 °C, 2.0 g) was added. The mixture then was stirred at room temperature for 15 h. Et_3N (3.0 g, 0.03 mol) in 5 mL of DMA and EtOCOF (3.00 g, 0.033 mol) in 5 mL of DMA were added. This mixture was stirred at 50 °C for 5 h and at 25 °C for 1 day. Addition of MeOH precipitated a white powder, which was collected by filtration, washed with MeOH and CH_2Cl_2, and dried overnight at 60 °C at 1 mm: 2.0 g (32% CO_2Et content by mild saponification,[16] DS = 1.0[17]); IR (KBr) 3480 (s), 1750 cm^{-1} (s).

Similarly, cellulose (1.00 g) in MPN (60 mL) and LiCl (5.6 g) made as above were stirred with Et_3N (2.8 g, 0.028 mol) and EtOCOF (2.60 g, 0.028 mol) for 1.5 days at 25 °C. Addition of ether precipitated a white solid, which was collected by filtration, washed with water and ether, and dried overnight at 60 °C (1 mm): 2.3 g (33% CO_2Et content, 1.1 DS).

(Octyloxycarbonyl)cellulose. A mixture of cellulose powder (0.70 g, 0.0049 mol of anhydroglucose unit), DMA (15 g), and LiCl (2.1 g) made as above was stirred with Et_3N (1.5 g, 0.015 mol) in 5 mL of DMA and octyl fluoroformate (2.52 g, 0.014 mol) in 5 mL of DMA at 60 °C for 16 h and at room temperature for 1 day. Addition of MeOH precipitated a white powder, which was collected by filtration, washed with MeOH and CH_2Cl_2, and dried overnight at 60 °C (1 mm): 2.7 g (33% CO_2octyl, 0.57 DS).

(Isopropoxycarbonyl)cellulose. After stirring cotton (1.00 g) in DMSO for 1 day at 120 °C, isopropyl fluoroformate (4.75 g, 0.045 mol) and Et_3N (5.25 g, 0.052 mol) were added. The next day, the heterogeneous mixture was cooled and filtered; the residue was washed with water and CH_2Cl_2 and then dried overnight at 60 °C at 1 mm: 1.8 g (21% CO_2iPr, 0.49 DS).

Poly(vinyl ethyl carbonate). Poly(vinyl alcohol) (av MW 14000, Aldrich) (1.00 g, 0.023 mol CH_2CHOH unit), EtOCOF (3.50 g, 0.038 mol), and Et_3N (4.0 g, 0.040 mol) in 25 mL of DMSO was stirred at 50 °C for 2 h and at 25 °C for 10 h, diluted with CH_2Cl_2

(19) As this investigation was completed, Lang and Shreeve, reporting the COF_2 induced Pummerer rearrangement of DMSO, noted that "... DMSO is unreactive with $CH_3C(O)F$ or $C_6H_5C(O)F$...". Lange, H. G.; Shreeve, J. M. *J. Fluor. Chem.* **1984**, *25*, 91. They did not mention the consequences of their observation in synthetic chemistry. Because of the availability of anhydrides as alternative acylating agents, such a reaction may not be as useful as carboalkoxylation with fluoroformates.

(20) For a list of apparatus used in physical and spectral measurements, see ref. 4.

(100 mL), washed with water (2 × 50 mL), dried (Na_2SO_4), and concentrated at 60 °C (1 mm) for 16 h to give a yellow rubberlike product: 2.2 g; IR ($CDCl_3$) 1760 cm^{-1} (s); ^1H NMR ($CDCl_3$) δ 4.8 (broad s, 1 H), 4.28 (q, 2 H, J = 6 Hz), 1.9 (broad s, 2 H), 1.35 (t, 3 H, J = 6 Hz); 0.85 DS.

Acknowledgment. We are grateful to Dr. J.-P. Senet for useful discussions. We also thank SNPE of France for the funds used to perform this investigation.

Registry No. **3**, 124820-66-2; **3** (R = H), 492-61-5; **4**, 125333-92-8; **5**, 124781-64-2; **5** (R = H), 138-52-3; **6**, 124781-65-3; **6** (R = H), 488-81-3; **7**, 106766-23-8; **7** (R = H), 57-50-1; **8**, 124820-67-3; **9**, 102198-10-7; **9** (R = H), 50-89-5; **10**, 124781-66-4; ethyl fluoroformate, 461-64-3; 1-adamantyl fluoroformate, 62087-82-5; isopropyl fluoroformate, 461-71-2; octyl fluoroformate, 104483-19-4; indole-3-carboxaldehyde, 487-89-8; isopropenyl fluoroformate, 74601-07-3; cellulose, 9004-34-6; poly(vinyl alcohol), 9002-89-5; poly(vinyl ethyl carbonate), 113150-73-5.

Regioselective Hydrogenation of Conjugated Dienes Catalyzed by Hydridopentacyanocobaltate Anion Using β-Cyclodextrin as the Phase-Transfer Agent and Lanthanide Halides as Promoters

Jong-Tae Lee and Howard Alper*

Ottawa-Carleton Chemistry Institute, Department of Chemistry, University of Ottawa, Ottawa, Ontario, Canada K1N 6N5

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β-Cyclodextrin is a useful phase-transfer agent for the hydrogenation of conjugated dienes to monoolefins catalyzed by the in situ generated hydridopentacyanocobaltate anion. This reaction, which usually proceeds by 1,2-addition to the diene, is promoted by cerium or lanthanum chloride. Polyethylene glycol (PEG-400), with or without added lanthanide, can also be used as the phase-transfer agent for the reduction process.

β-Cyclodextrin, a cyclic oligomer of D-glucose, has been employed as a phase-transfer agent in several nucleophilic substitution reactions.[1,2] This cycloamylose has also been useful in metal-catalyzed oxidation and reduction reactions. In particular, β-cyclodextrin is an effective phase-transfer catalyst for the palladium chloride catalyzed oxidation of both terminal and internal olefins (eq 1).[3] A subsequent publication has confirmed these findings.[4] Aryl alkyl ketones and aromatic aldehydes can be converted to hydrocarbons in high yields using hydrogen and catalytic amounts of the dimer of chloro(1,5-hexadiene)-rhodium (I) and β-cyclodextrin.[5] The heterogeneous hydrogenation of acylpyridines catalyzed by 10% palladium on carbon has also been investigated in the presence of stoichiometric quantities of β-cyclodextrin.[6]

$$RCH{=}CH_2 + O_2 \xrightarrow[\beta\text{-cyclodextrin, 65 °C}]{PdCl_2,\ CuCl_2,\ H_2O} RCOCH_3 \quad (1)$$

One of the useful phase-transfer reduction processes is the hydrogenation of conjugated dienes catalyzed by the hydridopentacyanocobaltate anion, generated in situ by treatment of cobalt chloride with potassium cyanide, potassium chloride, and a quaternary ammonium salt in aqueous base. It is believed that $[R_4N]_3HCo(CN)_5$ is transferred to the organic phase where it usually catalyzes 1,4-addition of hydrogen to a diene.[7] In contrast, use of neutral surfactants which function as micelles instead of quaternary ammonium salts can result in selective 1,2-addition in some cases with reaction here occurring in the aqueous phase.[8]

Table I. Phase Transfer Catalyzed Hydrogenation of 1 Using β-Cyclodextrin[a]

NaOH, N	$LnCl_3 \cdot 7H_2O$, Ln[a]	yield,[b] %	product distribution 2	3
0.055		87	24	76
0.25		91	44	56
0.50		85	64	36
1.0		71	70	30
3.0		59	90	10
5.0		55	91	9
0.25	La	95	44	56
0.5	La	100	64	36
1.0	La	100	75	25
1.0	Ce	100	79	21
5.0	Ce	95	98	2
5.0	Yb	69	90	10
2.0[c]	Ce	90	97	3

[a] Reaction conditions: 1 [5.0 mmol], base [10 mL], C_6H_6 [5 mL], β-cyclodextrin [0.55 mol], $LnCl_3 \cdot 7H_2O$ [0.55 mmol, if used], $CoCl_2$ [0.55 mmol], KCN [2.85 mmol], KCl [1.2 mmol]; H_2, room temperature, 1 atm., 24 h. [b] Yields and product ratios were determined by gas chromatography and by ^1H NMR. Products were identified by comparison of GC and NMR data with those of authentic materials. [c] Using a 7/1 ratio of $KCN/CoCl_2$.

Since it is known that β-cyclodextrin can bind a conjugated diene such as cyclopentadiene,[9] it seemed conceivable that the bound diene could be transferred to the aqueous phase where it would be hydrogenated in the presence of $HCo(CN)_5^{3-}$. It is also possible that β-cyclodextrin can serve as a second-sphere ligand[10] for HCo-

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