1,2′-Anhydro-6-deoxy-5-*C*-(2-hydroxy-5-methylphenyl)-α-DL-galactopyrranose (17). A mixture of **16** (0.07 g, 0.3 mmol), acetone (6 mL), water (1 mL), trimethylamine *N*-oxide (0.08 g, 0.7 mmol), and osmium tetroxide (1 mL) was stirred overnight at room temperature. The reaction was quenched with saturated sodium bisulfite (30 mL) and extracted with ethyl acetate (4 × 30 mL). The combined extracts were dried ($MgSO_4$), filtered, and evaporated under vacuum. The residue was purified by radial chromatography (Chromatotron, EtOAc as eluent) to furnish 0.06 g (72%) of pure **17** as a colorless solid: mp 159–160 °C; ^1H NMR (CD_3OD) δ 1.62 (s, 3 H), 2.28 (s, 3 H), 3.49 (dd, J = 10.1 Hz, J = 3.5 Hz, 1 H), 3.75 (d, J = 3.5 Hz, 1 H), 3.95 (dd, J = 10.1 Hz, J = 3.5 Hz, 1 H), 6.89 (m, 3 H).

Anal. Calcd for $C_{13}H_{16}O_5$: C, 61.89; H, 6.39. Found: C, 62.01, H, 6.54.

DL-2,3,6,7-Tetrahydro-7,9-dimethyl-2,7:3,6-diepoxy-5*H*-1,4-benzodioxonin-5-ol (18). To a mixture of **8** (255 mg, 1.01 mmol) in acetone (40 mL) and acetic acid (20 mL) was added a solution of sodium metaperiodate (410 mg, 1.9 mmol) in water (10 mL) and the mixture was stirred for two days. The reaction was diluted with water (40 mL) and enough sodium bicarbonate was added to neutralize the mixture. The layers were separated and the aqueous phase was extracted several times with ethyl acetate. The combined organic extracts were dried ($MgSO_4$), filtered, and evaporated to give a semisolid. Chromatography of the residue (silica gel, 30 g, CH_2Cl_2 to 5% EtOAc/CH_2Cl_2) followed by recrystallization of the eluate ($CHCl_3$–hexane) gave 130 mg (55%) of pure **19**: mp 140–158 °C; ^1H NMR ($CDCl_3$) δ 1.62 (s, 3 H), 2.29 (s, 3 H), 2.93 (d, J = 9.9 Hz, 1 H), 3.92 (d, J = 0.7 Hz, 1 H), 5.05 (dd, J = 0.7 Hz, J = 1.4 Hz, 1 H), 5.27 (d, J = 1.4 Hz, 1 H), 5.84 (d, J = 9.9 Hz, 1 H), 6.7–7.1 (m, 3 H); ^{13}C NMR ($CDCl_3$) 19.30, 20.71, 73.09, 86.75, 92.22, 95.09, 100.78, 115.35, 123.80, 124.99, 129.71, 129.87, 149.81.

The acetate derivative was prepared by acetylating **18** (65 mg, 0.26 mmol) with acetic anhydride (5 mL) and pyridine (1 mL) for 15 min at room temperature. Workup and then chromatography (silica gel, CH_2Cl_2) furnished an oil which slowly crystallized. Recrystallization (hexane–benzene) of this material furnished 69 mg (91%) of the acetate derivative of **19**: mp 113.5–115 °C; ^1H NMR ($CDCl_3$) δ 1.66 (s, 3 H), 2.10 (s, 3 H), 2.28 (s, 3 H), 4.10 (d, J = 0.9 Hz, 1 H), 5.10 (dd, J = 0.9 Hz, J = 1.4 Hz, 1 H), 5.60 (d, J = 1.4 Hz, 1 H), 6.64 (s, 1 H), 6.7–7.1 (m, 3 H); ^{13}C NMR ($CDCl_3$) 19.35, 20.71, 20.98, 73.37, 85.77, 91.95, 94.17, 101.64, 115.40, 123.86, 124.72, 129.76, 129.98, 149.75, 170.12.

Anal. Calcd for $C_{15}H_{16}O_6$: C, 61.63; H, 5.51. Found: C, 61.71; H, 5.40.

Synthesis and CuCN-Promoted Cyanation of Iodoformic Esters[1]

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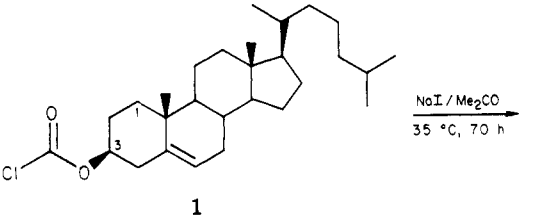
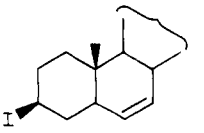
A number of iodoformic esters have been prepared, isolated, and identified for the first time. Phenyl iodoformate has been converted into phenyl cyanoformate under mild conditions. Decarboxylative iodination of iodoformates ROCOI to give RI and CO_2 can be slowed down by the choice of the group R.

Iodoformic esters[2] have hardly been described, although chloroformic esters[3,4] are well-known. Several years ago Kevill suggested that the "preparation of the more stable members of the iodoformate family may well be feasible".[3] Kevill and Weitl[5] had shown earlier that the reaction of cholesteryl chloroformate (**1**) and sodium iodide in acetone, at 35 °C, led to cholesteryl iodide (**2**) in 50% yield. The iodoformate of cholesterol was postulated as a reactive intermediate. Because of double bond participation, retention of configuration at C-3 is the expected steric course for the conversion of **1** into **2**. Goosen and his co-workers[6] prepared 9-triptycyl iodoformate (**4**) by irradiation of 9-triptycyl hydrogen oxalate (**3**) in the presence of mercuric oxide/iodine. Formation of 9-iodotriptycene (**5**) from iodoformate precursor **4** required extreme conditions, as expected for an ionic reaction at the triptycyl bridgehead. **4** appears to be the only iodoformate which has been described in the literature hitherto.



1



2 50%

We have recently prepared a series of iodocarbonyl compounds including acyl iodides[1d,7] and iodoglyoxalates.[1a] We now show that selected iodoformic esters **7a–d** can be prepared from chloroformic esters **6a–d** by Cl/I exchange

(1) Reactive Iodine Compounds 8. Part 7: (a) Geschwinder, P. M.; Preftitsi, S.; Hoffmann, H. M. R. *Chem. Ber.* **1984**, *117*, 408. Part 6: (b) Hoffmann, H. M. R.; Haase, K.; Ismail, Z. M.; Preftitsi, S.; Weber, A. *Chem. Ber.* **1982**, *115*, 3880. Part 5: (c) Belsner, K.; Hoffmann, H. M. R. *Synthesis* **1982**, 239. Part 4: (d) Hoffmann, H. M. R.; Haase, K.; Geschwinder, P. M. *Synthesis* **1982**, 237. Part 3: (e) Grundke, G.; Hoffmann, H. M. R. *J. Org. Chem.* **1981**, *46*, 5428. Part 2: (f) Haase, K.; Hoffmann, H. M. R. *Angew. Chem., Int. Ed. Engl.* **1982**, *21*, 83. Part 1: ref 7.

(2) Other names: iodocarbonic acid esters (iodo carbonates) or alkoxy- or (aryloxy)carbonyl iodides.

(3) Review: Kevill, D. N. "The Chemistry of Acyl Halides"; Patai, S., Ed.; Wiley-Interscience: New York, 1972; Chapter 12. See in particular p 439 for iodoformates.

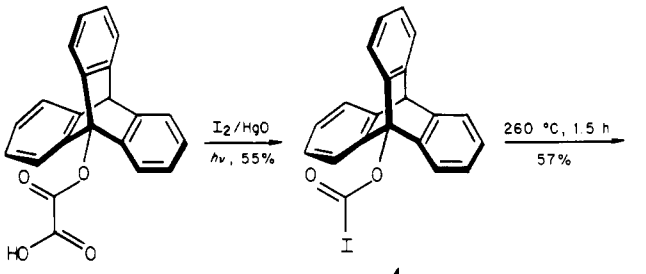
(4) For silver-assisted reactions of chloroformates see: Beak, P. *Acc. Chem. Res.* **1976**, *9*, 230.

(5) Kevill, D. N.; Weitl, F. L. *J. Org. Chem.* **1967**, *32*, 2633.

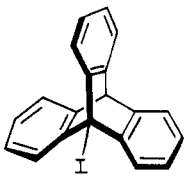
(6) Bartel, K.; Goosen, A.; Scheffer, A. *J. Chem. Soc. C* **1971**, 3766. For the free radical pathway to 9-iodotriptycene cf. Bartlett, P. D.; Greene, F. D. *J. Am. Chem. Soc.* **1954**, *76*, 1088.

(7) Hoffmann, H. M. R.; Haase, K. *Synthesis* **1981**, 715.

0022-3263/84/1949-1174$01.50/0

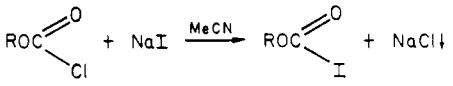


3 4



5

with NaI in acetonitrile. The acetonitrile mother liquor



6a-d 7a-d

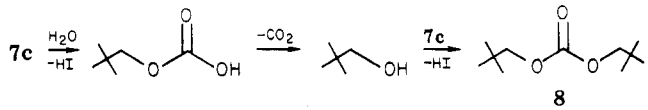
was extracted with pentane in our low-temperature reactor–extractor,[7] giving the desired iodoformic esters after evaporation of pentane (Table I).

^{13}C NMR spectroscopy was very helpful for characterizing the new iodoformates (Table II). The heavy atom effect of iodine[1a,7] causes an upfield shift ($\Delta\ \delta_1$ negative) of the iodocarbonyl carbon compared with the chlorocarbonyl carbon. In fact, for iodoformates the upfield shift ($\Delta\ \delta_1 = -34.2$ to -36.4) is greater than the corresponding shift for iodoglyoxalates ($\Delta\ \delta_1 = -6$ to -8.5)[1a] and for acyl iodides ($\Delta\ \delta_1 = -2.5$ to -16)[7]. As expected, the chemical shift difference $\Delta\ \delta_2$ for the more remote carbon C-2 was small. IR and ^1H NMR spectra of the chloroformates and corresponding iodoformates were very similar.

With regard to the reactivity of the chloroformates **6** toward NaI and the kinetic stability of the resulting iodoformates **7** it was noticeable that vinyl chloroformate[8] (**6a**) was very reactive towards NaI:Cl/I exchange proceeded efficiently at room temperature giving **7a** without difficulty. The reaction of chloroformates **6b** with NaI was less spontaneous and required heating to 70 °C. The resulting phenyl iodoformate (**7b**) could be redistilled in vacuo and gave accurate microanalyses. Since a phenyl group is a better π-donor than a vinyl group,[9] the chlorocarbonyl carbon in **6b** is probably deactivated electronically relative to **6a**. Greater steric hindrance in **6b** than in **6a** could contribute toward the relative deactivation of **6b**.

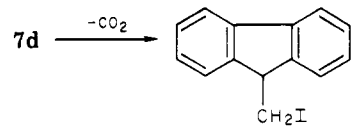
The reaction of **6c** and NaI gave neopentyl iodoformate (**7c**) accompanied by traces (<10%) of a product showing ^{13}C peaks at 26.3, 31.4, 76.9, and 155.5 ppm.

Presumably, dineopentyl carbonate (**8**) was formed due to unavoidable traces of moisture.



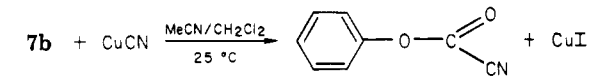
8

7d is thermally labile and the reaction of **6d** with NaI had to be carried out at room temperature. Even under these conditions, **7d** was partially (ca. 20%) decarboxylated to **9**, while some starting **6d** remained. Independently, **9** was prepared from **6d** under more forcing conditions (excess of NaI in acetonitrile, refluxing). Attempts to isolate iodoformates **7** with ordinary primary alkyl groups (R = n-C_8H_{15}, $PhCH_2$) and with a secondary alkyl group (R = i-Pr) were not successful. Note that the relative stability of the chloroformates as a function of R is C_6H_5 > primary alkyl > secondary alkyl > tertiary alkyl group. Benzyloxycarbonyl chloride (BOC–chloride in peptide chemistry) is decarboxylated readily to benzyl chloride.[3]



9

Reaction Mechanism. Kinetic studies of Kevill have shown the possibility of S_N2 (≡ $B_{AL}2$) attack on the alkyl carbon and of $B_{AC}2$ attack on the acyl carbon of chloroformates.[10] In the case of chloroformates **6a–c**, S_N2 attack is impossible or very slow. More specifically, for **6a,b** a vinylic carbon would have to be attacked; in **6c** S_N2 attack with formation of neopentyl iodide is hindered sterically. As a consequence, attack on acyl carbon is preferred. The resulting iodoformates cannot easily undergo a S_N1 like decarboxylation, because the derived cation is unstable. 9-Triptycyl iodoformate (**4**) which only decarboxylates at 260 °C (see above) is an extreme example in this respect. Finally, iodoformates could be converted readily into cyanoformates, a little studied class of compounds.[11]



10

Whereas phenyl chloroformate (**6b**) reacted with CuCN only after refluxing for several hours, phenyl iodoformate (**7b**) was found to react at room temperature.

Experimental Section

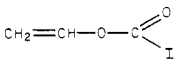
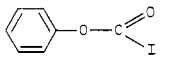
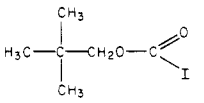
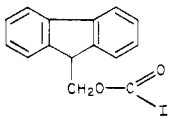
Procedure for the Preparation of Chloroformic Esters 6 from Alcohols.[12] Absolute pyridine (8.85 g, 110 mmol) is slowly dropped at 0 °C into phosgene (19.8 g, 14.2 mL, 200 mmol), a white solid being precipitated. After addition of freshly distilled alcohol (100 mmol) in absolute ether (30 mL), the resulting mixture is stirred for 1 h at 0 °C and 8 h at 25 °C. Hydrogen chloride and the excess of phosgene are removed under reduced pressure, and the residue is taken up in ether. After filtration and removal of ether the resulting colorless liquid is distilled in a Kugelrohr apparatus.

2,2-Dimethylpropyl chloroformate (6c): Colorless liquid; 12.2 g (80%); 90 MHz ^1H NMR ($CDCl_3$) δ 1.00 (s, 9 H, 3 CH_3), 4.06 (s, 2 H, CH_2); ^{13}C NMR ($CDCl_3$) δ 150.5 (CO), 81.2 (C-1), 31.8 (C-2), 26.1 (3 CH_3); IR (CCl_4) 2964 (s), 1775 (vs), 1368 (s), 1150 (vs), 685 (s) cm^{-1}.

Standard Procedure for the Preparation of Iodoformic Esters. The reaction is carried out in the low-temperature reactor–extractor as described in ref 7. Powdered NaI (18 g, 120 mmol) is dissolved in absolute acetonitrile (120 mL) and chloroformic ester (50 mmol of **7a**, **7b**, and **7c**; 25 mmol of **7d**). The product is isolated by extraction into pentane. After evaporation of the pentane the resulting product is stored over copper powder under an atmosphere of nitrogen at −20 °C.

(8) *Kontakte* **1982**, *3*, 32.
(9) Exner, O. "Correlation Analysis in Chemistry"; Chapman, N. B., Shorter, J., Eds.; Plenum Press: New York, 1978; p 439 ff.
(10) Kevill, D. N. Ref 3, p 408.
(11) See also: McCulloch, A. W.; McInnes, A. G.; Smith, D. G. *Can. J. Chem.* **1981**, *59*, 1395. Mander, L. N.; Sethi, S. P. *Tetrahedron Lett.* **1983**, *24*, 5425.
(12) Kharash, M. S.; Liu, Y. C.; Nudenberg, W. *J. Org. Chem.* **1954**, *19*, 1150.

Table I. Preparation of Iodoformic Esters 7a-d from Chloroformic Esters 6a-d

compd	iodoformic ester	react time, h	react temp, °C	extraction time, h	yield, %
7a		0.5	25	3	80
7b		1	70	3	85
7c		1	70	3	82[a]
7d		2	25	5	80[b]

[a] Contains 91% of 7c; see text. [b] Total yield. 20% of 9-fluorenylmethyl iodide plus 6d also present.

Table II. ^{13}C NMR Data (δ) for Chloroformates 6a-d and Iodoformates 7a-d[a]

compd	X	δ_1, $-C(=O)X$	δ_2, $>COC(=O)X$	$\Delta\delta_1$	$\Delta\delta_2$
6a	Cl	148.6	143.2		
7a	I	112.2	142.8	-36.4	-0.4
6b	Cl	149.4	151.8		
7b	I	113.4	152.3	-36.0	0.5
6c	Cl	150.5	81.2		
7c	I	116.3	81.6	-34.2	0.4
6d	Cl	150.5	73.3		
7d	I	115.7	73.4	-34.8	0.1

[a] X = halide.

Vinyl iodoformate (7a): Yield 7.2 g (80%); ^1H NMR ($CDCl_3$) δ 7.25 (dd, J_{cis} = 6 Hz, J_{trans} = 14 Hz, 1 H, =CHO), 5.05 (dd, ^2J = 3 Hz, J_{trans} = 14 Hz, 1 H in CH_2), 4.68 (dd, ^2J = 3 Hz, J_{cis} = 6 Hz, 1 H in CH_2); ^{13}C NMR ($CDCl_3$) δ 112.2 (CO), 142.8 (C-1), 100.4 (C-2) (Figure 1 in supplementary material); IR (CCl_4) 1772 (vs), 1645 (s), 1120 (vs), 1100 (vs) cm^{-1}.

Phenyl iodoformate (7b): Yield 10.5 g (85%); light yellow oil. After being distiled twice in a Kugelrohr apparatus (68 °C (1 mmHg)) a colorless oil is obtained: ^1H NMR ($CDCl_3$) δ 6.7-7.7 (aromatic H); ^{13}C NMR ($CDCl_3$) δ 113.4 (COI), 152.3 (CO COI), 129.6, 126.9, 120.5; IR (CCl_4) 1774 (vs), 1490 (s), 1175 (s), 1150 (vs), 1075 (vs), 1005 (s), 835 (s), 685 (s) cm^{-1}. Anal. Calcd for $C_7H_5IO_2$: C, 33.90; H, 2.02. Found: C, 33.64; H, 1.98.

2,2-Dimethylpropyl iodoformate (7c): Yield 9.92 g (82%), containing less than 10% of a byproduct with ^{13}C NMR signals at 26.3, 31.4, 76.9 and 155.5 ppm; ^1H NMR ($CDCl_3$) δ 1.00 (s, 9 H, 3 CH_3), 4.06 (s, 2 H, CH_2); ^{13}C NMR ($CDCl_3$) δ 116.3 (CO), 81.6 (C-1), 31.7 (C-2), 26.1 (3 CH_3); IR (CCl_4) 2960 (s), 1764 (vs), 1365 (m), 1110 (vs), 610 (m) cm^{-1}.

9-Fluorenylmethyl iodoformate (7d): Yield 7.0 g (80%); light yellow crystals which are not uniform and are estimated by NMR to be 78% pure; ^{13}C NMR ($CDCl_3$) δ 155.7 (CO), 73.4 (CH_2), 46.0 (C-9), 142.2, 141.0, 128.0, 127.1, 124.8, 120.0 (aromatic).

9-Fluorenylmethyl Iodide (9). A sample of 9 was obtained by refluxing **6d** with an excess of NaI in acetonitrile for 2 h and extracting the product with pentane. ^{13}C NMR ($CDCl_3$) δ 8.4 (CH_2), 47.9 (C-9), 119.8, 124.1, 127.0, 127.8, 140.8, 145.4 (aromatic).

Phenyl Cyanoformate (10). CuCN (1.79 g, 20 mmol) is suspended under an atmosphere of nitrogen in absolute acetonitrile (100 mL) and dichloromethane (30 mL). **7b** (2.48 g, 10 mmol) is added and the mixture is stirred for 2 h at 25 °C until an almost clear solution results. The solution is filtered and the solvent is removed on a rotavap to leave an oil, which is taken up in dichloromethane and filtered. The solvent is removed and the residue is distilled in a Kugelrohr apparatus to leave a colorless oil, which crystallizes on standing in a refrigerator, yield 1.11 g (75%). The analytical sample is obtained by recrystallizing twice from light petroleum: mp 51 °C; ^1H NMR ($CDCl_3$) δ 7.10-7.60 (m, 5 H, aromatic); ^{13}C NMR ($CDCl_3$) δ 109.2 (CN), 142.5 (CO), 149.2 (q aromatic), 130.0, 127.7, 120.5 (aromatic); IR (CCl_4) 2245 (s), 1765 (vs), 1490 (s), 1240 (vs), 1210 (vs), 1118 (s), 686 (s) cm^{-1}.[13] Anal. Calcd for $C_8H_5NO_2$: C, 65.30; H, 3.43; N, 9.52. Found: C, 65.13; H, 3.52; N, 9.22.

Acknowledgment. We thank the Deutsche Forschungsgemeinschaft and the Fonds der Chemischen Industrie for support of our work.

Registry No. **6a**, 5130-24-5; **6b**, 1885-14-9; **6c**, 20412-38-8; **6d**, 28920-43-6; **7a**, 88842-50-6; **7b**, 88842-51-7; **7c**, 88842-52-8; **7d**, 88842-53-9; **9**, 73283-56-4; **10**, 5532-82-1; phosgene, 75-44-5; 2,2-dimethyl-1-propanol, 75-84-3; 9*H*-fluorene-9-methanol, 24324-17-2; CuCN, 544-92-3.

Supplementary Material Available: ^{13}C NMR spectra of **6a** and **7a** (1 page). Ordering information is given on any current masthead page.

(13) Childs, M. E.; Weber, W. P. *J. Org. Chem.* **1976**, 41, 3486.