Mild Dehalogenative Reduction of Tri- and Di-halogenomethyl Groups by Nickel Carbonyl

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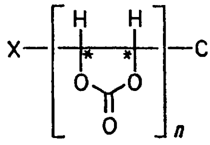
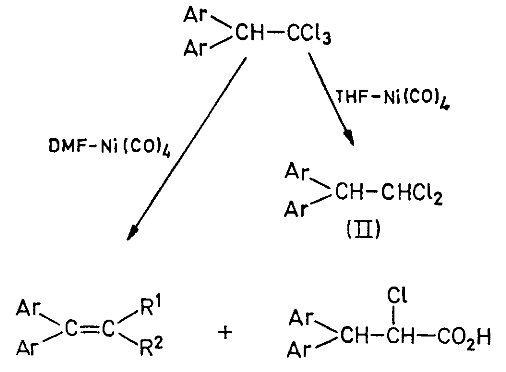
Summary Nickel carbonyl in tetrahydrofuran reductively converts polyhalogenomethyl groups into di- or mono-halogenomethyls under quite mild conditions which permit the stereoselective synthesis of 5-bromo-lyxose and -xylose.

In connection with the stereoselective synthesis of carbohydrates by telomerization,[1] we describe the first reductive dehalogenation of polyhalogenomethyl groups by nickel carbonyl, which is mild and selective enough to permit the reduction of such labile compounds as halogenated telomers of vinylene carbonate (I). Previously reported methods,[2] including use of the iron pentacarbonyl reagent, are unsatisfactory for the present purpose, principally on account of the drastic conditions employed.



(I) R = H, Cl, Br
X = Cl, Br, (H)

Reduction proceeds smoothly under neutral conditions in tetrahydrofuran, the most effective solvent examined so far, at room temperature or at 40°, under nitrogen. Thus, bis-(p-chlorophenyl)trichloroethane (DDT) (10 mmol) was reduced selectively in tetrahydrofuran (40 ml) with an excess of nickel carbonyl (23 mmol) at 40° (for 48 h) to dichloromethyl compounds (DDD) (II) in 92% yield. In more polar solvents such as dimethylformamide (and hexamethylphosphoric triamide) the major products were the unsaturated halogeno-compounds (III) (*ca.* 9%) and (IV) (16%), and the carboxylated derivatives (V) (12%) and (VI) (21%, m.p. 189°), in addition to a trace of (II).



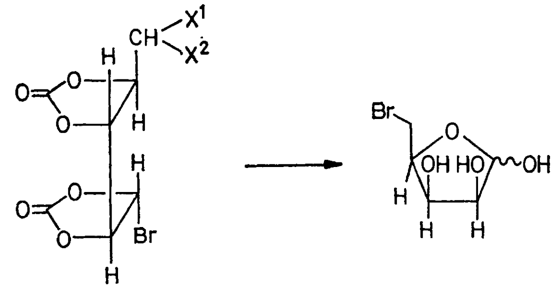
(II)

(III) $R^1 = R^2 = Cl$
(IV) $R^1 = H$, $R^2 = Cl$
(V) $R^1 = H$, $R^2 = CO_2H$

(VI)

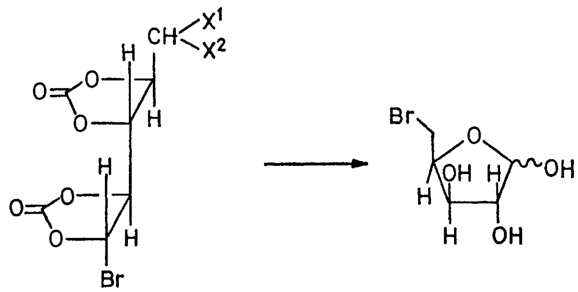
($Ar = C_6H_4{-}Cl{-}p$)

Solvents such as dioxan, isopropyl alcohol, cyclohexane, and benzene were practically ineffective in the reduction although a reaction carried out in tetrahydrothiophen afforded (II) in 35% yield.



(VII) $X^1 = X^2 = Br$
(VIII) $X^1 = Br$, $X^2 = H$

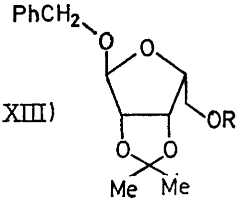
(IX)



(X) $X^1 = X^2 = Br$
(XI) $X^1 = Br$, $X^2 = H$

(XII)

(XIII)



Benzotrichloride underwent dehalogenative dimerization on treatment with nickel carbonyl in tetrahydrofuran to give 1,1,2,2-tetrachloro-1,2-diphenylethane (73%), and no benzal chloride was detectable. As might be expected, the tribromomethyl compound 1,1,1,3-tetrabromo-5-phenylpentane was more easily converted into the corresponding dibromomethyl derivative (b.p. 122°/0·1 mm) in 60% yield.

This method has been applied successfully to halogenated telomers of vinylene carbonate (I), which are quite sensitive both to acids and bases because of the presence of the carbonate group and active halogens, and di- and mono-halogenomethyl compounds were obtained in satisfactory yields (Table).†

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† No incorporation of deuterium to the product was observed in the reduction using tetrahydrofuran containing D_2O as a solvent.

TABLE

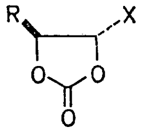
Reduction (at 40°) *of polyhalogenomethyl groups by* $Ni(CO)_4$ *in tetrahydrofuran*

Compound	Mole ratio [$Ni(CO)_4$/substrate]	Time (h)	Product	Yield (%)
(XIV) $R = CCl_3$, $X = Br$	2	48	(XIV) $R = CHCl_2$, $X = Br$	62
(XIV) $R = CBr_3$, $X = Br$	3	5	(XIV) $R = CHBr_2$, $X = Br$[a]	69
(XIV) $R = CCl_3$, $X = OMe$	2	48	(XIV) $R = CHCl_2$, $X = OMe$	59
(XV) $R = Br$	6	3	(XV) $R = H$	71

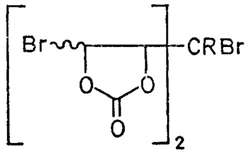
[a] The monobromomethyl compound ($R = CH_2Br$) was also isolated, in 3% yield.

Tribromomethyl compounds are reduced stepwise *via* the dibromomethyl to the monobromomethyl compounds. Thus, among eight possible $n = 2$ telomers, two isomers (VII) and (X), stereoselectively formed on telomerization of vinylene carbonate with methylene bromide,[1] were converted into the corresponding monobromomethyl compounds (VIII) (m.p. 171°) and (XI) (m.p. 128°), mild hydrolysis of which with acid gave 5-bromo-5-deoxy-DL-lyxose (IX) and 5-bromo-5-deoxy-DL-xylose (XII), respectively.

Treatment of the trichloroethyl carbonate (XIII; $R = Cl_3C{\cdot}CH_2{\cdot}O{\cdot}CO$, m.p. 61·5°) with nickel carbonyl in dimethylformamide–methanol at 40° gave a high yield of the alcohol (XIII; $R = H$, 90%), though the cleavage proceeded slower than with zinc–acetic acid agents.[3]



(XIV)



(XV)

All new compounds reported had elemental analyses and spectroscopic properties in full agreement with the assigned structures.

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[1] T. Tamura, T. Kunieda, and T. Takizawa, *Tetrahedron Letters*, in the press.

[2] C. A. Buehler and D. E. Pearson, 'Survey of Organic Syntheses,' Wiley-Interscience, New York, 1970, p. 408; E. Ts. Chukovskaya, A. A. Kamyshova, and R. Kh. Freidlina, *Zhur. org. Khim.*, 1967, 3, 1358; I. M. Downie and J. B. Lee, *Tetrahedron Letters*, 1968, 4951; R. G. Petrova and R. Kh. Freidlina, *Izvest. Akad. Nauk S.S.S.R., Ser. khim.*, 1970, 1574; E. Ts. Chukovskaya, N. A. Kuz'mina, and R. Kh. Freidlina, *ibid.*, p. 2343.

[3] T. B. Windholz and D. B. R. Johnston, *Tetrahedron Letters*, 1967, 2555.