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METAL-GRAPHITE REAGENTS IN CARBOHYDRATE CHEMISTRY, IX[1]

FRAGMENTATIONS OF 1-DEOXY-1-IODO-2,3;4,5-DI-O-ISOPROPYLIDENE PENTITOLS

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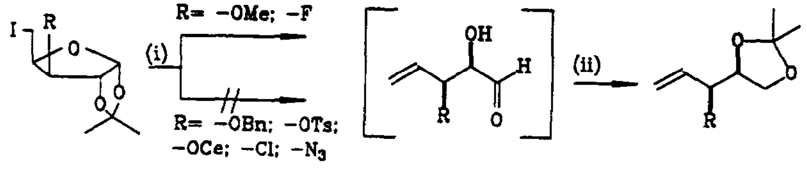
Summary: Compounds 1 and 3, each readily available in both enantiomeric forms smoothly fragment on treatment with zinc/silver-graphite or potassium-graphite laminate (C_8K), respectively, thus affording the full set of stereoisomeric 1,2-O-isopropylidene-pent-4-enitols.

The actual endeavour to relate the skeleton of carbohydrates to substructures of more complex natural products, generally referred to as "chiron approach",[3] has significantly contributed to the advancement of synthetic organic chemistry within the last decade. Unsaturated sugar derivatives, besides their chiral core open for further manipulation, are among the substrates most often used in this synthetic strategy.

The systematic application of metal-graphite reagents[4] to deoxy halo sugars has recently improved the availability of unsaturated cyclic and acyclic carbohydrate derived synthons,[5-9] partly inaccessable by other methods. Although highly reactive, these reagents turned out to be very tolerant as to the functional-, protecting- and leaving groups employed.[7,9] Among them, zinc/silver-graphite affords inter alia most valuable hex-5-enals not only in excellent yields by dealkoxyhalogenation of 6-deoxy-6-halo sugars,[7] but also in all configurations possible when complemented by a straightforward aldehyde/alkene interconversion sequence formally inverting the chirality of the respective building block.[8] This, as a result, largely extends the number of targets that can be related to well accessable carbohydrate precursors.

The major limitation of this reductive ring opening reaction presently known results most probably from sterical crowding in the substrate inhibiting a simultaneous attack of the graphite-supported zinc[10] onto the halo- as well as the endocyclic oxygen atom.[9] This arrangement is found e.g. in some 5-deoxy-5-halo-pentofuranose derivatives, the corresponding ring-opened products of which (pent-4-enals or, after reduction with borohydride, pent-4-enitols) can only be obtained in markedly reduced yield if at all (Scheme I).[9] This communication reports an alternative, metal-graphite based approach allowing the convenient preparation of the full set of these valuable 5-carbon building blocks.[11]



SCHEME I. (i) Zn/Ag-graphite (ii) (a) $NaBH_4$ (b) 2,2-dimethoxypropane; p-TsOH

The 2,3;4,5-di-O-isopropylidene derivatives of arabitol as well as of xylitol are each available in both enantiomeric forms,[12,13] which on treatment with iodine/triphenylphosphine/imidazole[9,14] readily afford the corresponding 1-deoxy-1-iodo derivatives 1 and 3 in almost quantitative yield. When reacted with either zinc/silver-graphite at ambient temperature or potassium-graphite laminate (C_8K) at 0°C in THF they smoothly fragment within a few minutes thus affording 1,2-O-isopropylidene-D (or L)-erythro (or threo)-pent-4-enitols respectively as the only products.[15-17] With C_8K as the reagent, the intermediate 3-O-potassium alkoxides may be trapped immediately on addition of electrophiles[6] such as iodomethane, benzyl bromide, ethyl chloroformate, acetic anhydride or chloro diphenylmethylsilane. Thus, all stereoisomeric and differently protected pent-4-enitols, inaccessable via furanoses (vide supra) are available by a simple one-pot procedure.

The zinc/silver-graphite induced dealkoxyhalogenations described above perfectly parallel those previously observed,[5,7-9] whereas the C_8K-promoted reactions are more ambiguous with respect to their mechanism. Although the fragmentations of substrates 1 and 3 are precedented by those of glycosyl halides[6] and 1-deoxy-1-halo sorbofuranose and -fructopyranose derivatives,[7b] the ready dehydrohalogenation of other deoxy halo sugars indicates a distinct Lewis-base character of this reagent.[7a] 1-Deoxy-1-halo pentitols, however, on treatment with a base (LDA in THF or Li in ammonia) are converted into 1-alkynes as outlined recently.[13] Thus, the reactivity of C_8K seems to be substrate dependent and can hardly be generalized at this moment.

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SCHEME II

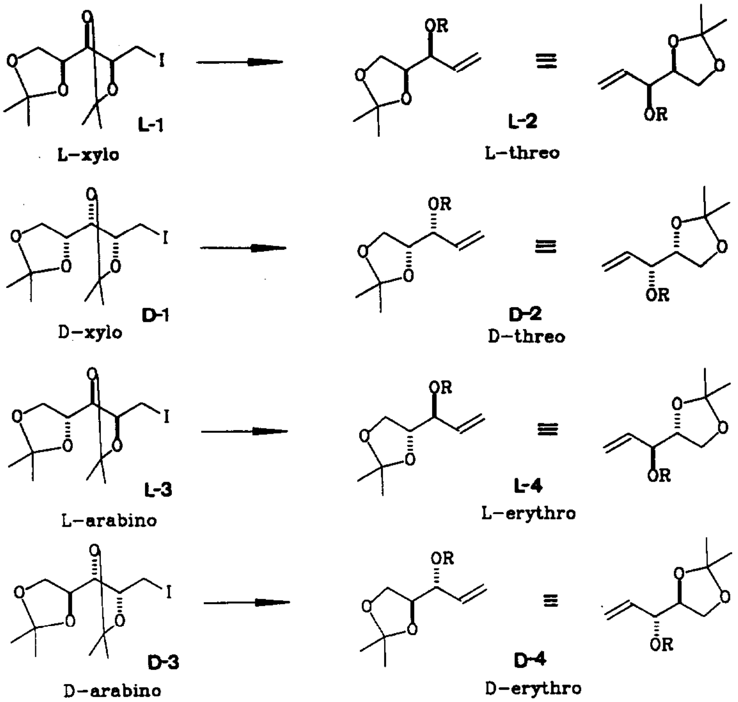

Table 1. Metal-Graphite induced Dealkoxyhalogenations of 1 and 3.

SUBSTRATE	REAGENT	ELECTROPHILE	R	PRODUCT (%)
L-1	Zn/Ag-graphite	---	-H	L-2a (90)
D-1	Zn/Ag-graphite	---	-H	D-2a (90)
D-1	C_8K	---	-H	D-2a (95)
D-1	C_8K	MeI	-Me	D-2b (91)
D-1	C_8K	ClCOOEt	-COOEt	D-2c (90)
D-3	C_8K	---	-H	D-4a (93)
D-3	C_8K	Ac_2O	-Ac	D-4b (81)
D-3	C_8K	BnBr	-Bn	D-4c (86)
L-3	Zn/Ag-graphite	---	-H	L-4a (92)
L-3	C_8K	---	-H	L-4a (87)
L-3	C_8K	$Ph_2MeSiCl$	$-SiMePh_2$	L-4d (50)[a]

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[a] diminished yield is due to the hydrolytic lability of 4c, thus affording 4a as by-product on column chromatography.

References and Notes

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15. *Typical Procedures*: (a) A solution of 1 or 3 in anhydr. THF is rapidly dropped into a suspension of Zn/Ag-graphite (2 equiv.)[ref. 7] in THF at ambient temperature under argon. After stirring for 5-10 min (TLC) the mixture is filtered, the filtrate evaporated and the residue subjected to flash chromatography. (b) A solution of 1 or 3 in anhydr. THF is dropped into a stirred suspension of C_8K (1.5 equiv.) [ref. 7] in THF under argon at 0°C, followed by addition of the respective electrophile (2 equiv.) after 5-10 min. The mixture is stirred at ambient temperature until the trapping is complete (TLC) and worked-up as described above.
16. 13 C-NMR ($CDCl_3$, 75MHz): 2a: 136.5(C-4), 117.6(C-5), 109.9(=C= isoprop.), 78.8 (C-3), 74.1(C-2), 65.9(C-1), 26.8, 25.4(Me-isoprop.); 2b: 134.2(C-4), 119.8 (C-5), 109.7(=C= isoprop.), 84.2(C-3), 77.5(C-2), 65.8(C-1), 56.5(-OMe), 26.6, 25.4(Me-isoprop.); 2c: 154.4(-OCOOR), 131.9(C-4), 119.9(C-5), 110.0(=C= isopr.), 78.7(C-3), 76.2(C-2), 65.4(C-1), 64.0(-CH_2O-), 26.3, 25.3(Me-isopr.), 14.1 (Me-); 4a: 136.2(C-4), 116.8(C-5), 109.5(=C= isopr.), 78.3(C-3), 72.1(C-2), 65.1(C-1), 26.5, 25.2(Me-isopr.); 4b: 170.8(-COOR), 132.6(C-4), 118.9(C-5), 109.9(=C= isopr.), 76.3(C-3), 74.0(C-2), 65.8(C-1), 26.4, 25.3(Me-isopr.), 21.1 (CH_3CO-); 4c: 135.6(C-4), 138.5, 128.6, 128.1, 127.9(-Ph), 119.7(C-5), 109.8(=C= isopr.), 81.3(-CH_2O-), 78.0(C-3), 70.9(C-2), 67.1(C-1), 26.8, 25.6 (Me-isopr.); 4d: 135.0(C-4), 138.0, 137.7, 129.3, 129.0, 128.8, 128.4, 128.0 (Ph-), 119.2(C-5), 109.7(=C= isopr.), 77.3(C-3), 73.0(C-2), 67.2(C-1), 26.8, 25.4(Me-isopr.), 0.8(MeSi-);
17. PMR ($CDCl_3$, 300 MHz): 2a: 5.73(H-4), 5.30(H-5a), 5.16(H-5b), 3.68(H-3), 2.91(-OH); 2b: 5.51(H-4), 5.21(H-5a), 5.19(H-5b), 3.79(H-3), 3.21(-OMe); 2c: 5.70(H-4), 5.34(H-5a), 5.23(H-5b), 5.03(H-3), 4.09(-OCH_2), 1.18(Me-); 4a: 5.81(H-4), 5.33(H-5a), 5.19(H-5b), 4.21(H-3), 2.68(-OH); 4b: 5.79(H-4), 5.24-5.30(H-5a, H-5b, H-3); 2.05(CH_3CO-); 4c: 5.87(H-4), 5.43(H-5a), 5.31(H-5b), 4.68 and 4.43(AB, -CH_2Ph); 4d: 5.78(H-4), 5.33(H-5a), 5.26(H-5b), 0.48(MeSi-);

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