Tetrahedron Letters Vol. 21, pp 1425 - 1428 0040-4039/80/0408-1425$02.00/0

SELECTIVE DEACYLATION OF ENOL ESTERS WITH HYDROXYLAMINE[1)]

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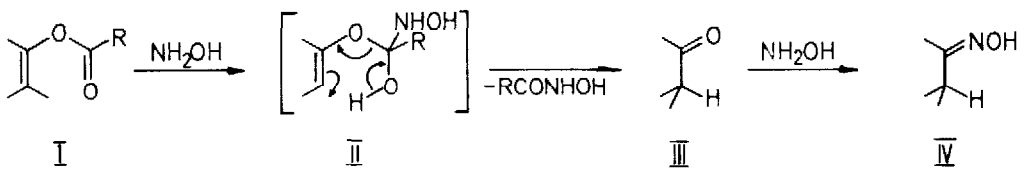
An effective procedure for selectively cleaving enol esters in the presence of normal ester functions has been developed, involving hydroxylaminolysis to the oxime of the parent ketone.

Hydroxylaminolysis of alkyl or acyl esters has commonly been used for the preparation of hydroxamic acids[2)]. Enol esters would be expected to react similarly, i.e. I → II → III, the liberated ketone being further transformed to the respective oxime IV, from which it may be regenerated by deoximation.

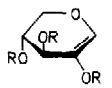
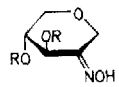
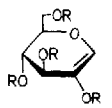
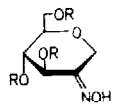
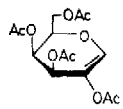
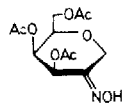
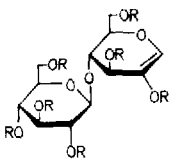
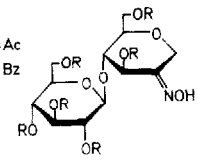
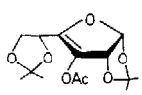
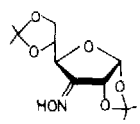
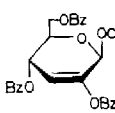
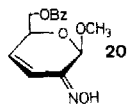
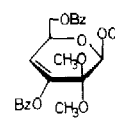
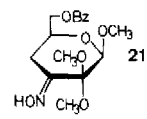
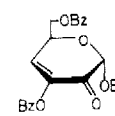
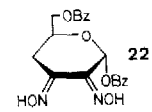


I II III IV

This essentially simple process does not seem to have been utilized preparatively[3)] despite its potential application for the liberation of the parent ketones from furanoid and pyranoid enol esters. Many of these are readily accessible[7)], but have consistently withstood attempts to prepare the desired ketoses via base-catalyzed deacylations[8)]. Our expectation proved to be correct, and, as a result, we now report on the ready utilization of the procedure I → IV for converting enolic ester groups into the respective ketoximes without affecting normal primary or secondary ester functions elsewhere in the molecule.

The results summarized in Table 1 amply illustrate the preparative feasibility and the apparent generality of the selective hydroxylaminolysis of enol esters. Enediol-derived ester groups, as e.g. in the 2-hydroxyglycal esters 1 - 7, and in particular, in the furanoid ester 8, react most readily, the latter being already hydroxylaminolysed after 45 min at ambient temperature. In the case of the hex-2-enopyranoside 9, removal of the enolic benzoyl group is accompanied by β-elimination, allowing the isolation of the major product, enone-oxime 20 in high yield. Enolone esters, such as 11, yield the respective dioximes, i.e. 22, whereby a monoxime is detectable as intermediate (TLC). Expectedly, 22 readily gives metal

Table 1. Hydroxylaminolysis of Enol Esters: Yields and physical Data of Ketoximes

Educt[a]	Product[b]	Procedure[c]	Yield	m.p. (°C)	$[\alpha]_D$ in $CHCl_3$ (c, °C)
 **1** R=Ac **2** R=Bz	 **12** R=Ac **13** R=Bz	A (20 h) B (5 d) C (12 h)	76 79 83	103 - 104 198 - 200	-58.3 (0.3, 21) -86.5 (0.6, 21)
 **3** R=Ac **4** R=Bz	 **14** R=Ac **15** R=Bz	D (12 h) B (3 d)	86 93	89 - 90 176 - 177	-39.0 (0.4, 21) -52.9 (0.3, 21)
 **5**	 **16**	D (15 h)	74	155	-41.2 (0.5, 22)
 **6** R=Ac **7** R=Bz	 **17** R=Ac **18** R=Bz	D (7 h) C (13 h)	89 76	125 - 127 amorph	-22.3 (0.3, 21) +12.3 (0.6, 22)
 **8**	 **19**	D (45 min)	63	103 - 104	+183 (0.6, 21)
 **9**	 **20**	D (3 d)	89	syrup	-148 (0.3, 22)
 **10**	 **21**	D (5 d)	76	83 - 85	-16.4 (1, 22)
 **11**	 **22**	E (2 h)	64	119 - 121	+15 (0.2, 22)

a) Origin of educts **1** - **4**: R.J. Ferrier and G.H. Sankey, *J. Chem. Soc. C* **1966**, 2339. — **5**: K. Maurer and A. Müller, *Ber. Dtsch. Chem. Ges.* **63**, 2069 (1930). — **6**: K. Maurer, *Ber. Dtsch. Chem. Ges.* **63**, 30 (1930). — **7**: m.p. 166-168°C, $[\alpha]_D^{22}$ = +15° (c = 1, chloroform), prepared in 70 % yield from octa-*O*-benzoyl-β-D-cellobiose by treatment with HBr/acetic acid and subsequent elimination of HBr with diethylamine, cf. A. Löhe, *Doctoral Dissertation*, Technische Hochschule Darmstadt, 1980. — **8**: W. Meyer zu Reckendorf, *Chem. Ber.* **102**, 1071 (1969). — **9**: R.J. Ferrier, N. Prasad, and G.H. Sankey, *J. Chem. Soc. C* **1969**, 587. — **10** and **11**: F.W. Lichtenthaler and U. Kraska, *Carbohydr. Res.* **58**, 363 (1977).

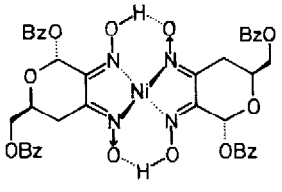
b) Values for combustion analysis, molecular weights (MS-FD spectra), ^1H- and ^{13}C-NMR data are in accord with the structures assigned. On the basis of a sizable downfield shift of H-1e (as compared with H-1e in the deoximated ketones), ketoximes **12** - **18** possess E-configuration.

c) Preparative procedure involved treatment of substrate with 3 - 3.5 molar equiv. of hydroxylamine hydrochloride in the following systems: A 1:1 tetrahydrofuran / acetate buffer (pH 4.5) at 25°C; B tetrahydrofuran / water (5:1) plus sodium acetate (4 molar equiv.) at 25°C; C pyridine at 70°C; D pyridine at 25°C; E $NaHCO_3$ in tetrahydrofuran / water (5:1).

complexes as, e.g. a carmine-red, needle-shaped nickel complex of m.p. 128-130°C and $[\alpha]_D^{21}$ = -70° (c = 0.4, chloroform), to which on the basis of analytical data structure 23 was tentatively assigned.

In the case of glycal esters 1 - 7 ketoxime formation is accompanied by the exclusive accumulation of acet- and benz-hydroxamic acid, respectively, as detected by TLC and evidenced by isolation. Conversion of the more reactive enolone ester 11 into dioxime 22, however, produced substantial amounts of benzoic acid, indicating that the enolic ester function in the intermediate monoxime of 11 may not only be cleaved via hydroxylaminolysis, but by hydrolysis as well due to the slightly alkaline conditions.

Enhanced reactivity towards enolic ester groups is similarly observed by such nucleophiles as *O*-benzylhydroxylamine and semicarbazide, the tetraacetyl-2-hydroxyglucal 3 being readily converted in pyridine solution into the *O*-benzyloxime 24 [81 %, m.p. 48°C, $[\alpha]_D^{21}$ = -39° (c = 0.5, chloroform)] and semicarbazone 25 [76 %, m.p. 110°C, $[\alpha]_D^{22}$ = -72° (c = 0.2, chloroform)], respectively. N-Methylhydroxylamine, however, when treated with 3 in the form of its hydrochloride in aqueous tetrahydrofuran/sodium acetate (2 d, 25°C), did not give the corresponding nitrone, but a product (m.p. 80-81°C, $[\alpha]_D^{21}$ = -209° (c = 1, chloroform), 55 %), to which structure 26 had to be assigned on the basis of MS- and ^{1}H-NMR-data. Thus, the more basic N-methylhydroxylamine obviously induced a 3,4-elimination of acetic acid in the intermediate tri-*O*-acetyl-1,5-anhydro-D-fructose prior to nitrone formation.



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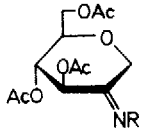
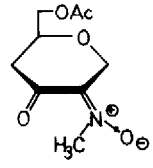


24 R=$OCH_2C_6H_5$
25 R=$NHCONH_2$



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Apart from their preparative utilization as chiral synthons, these ketoximes open up an efficient entry into the hitherto inaccessible series of 1,5-anhydroketoses[9] and — via N-halosuccinimide-induced refunctionalization at C-1 — also provide a ready access to 2-oximinoglycosyl halides[10] and, thus, to aminosugar-containing oligosaccharides.

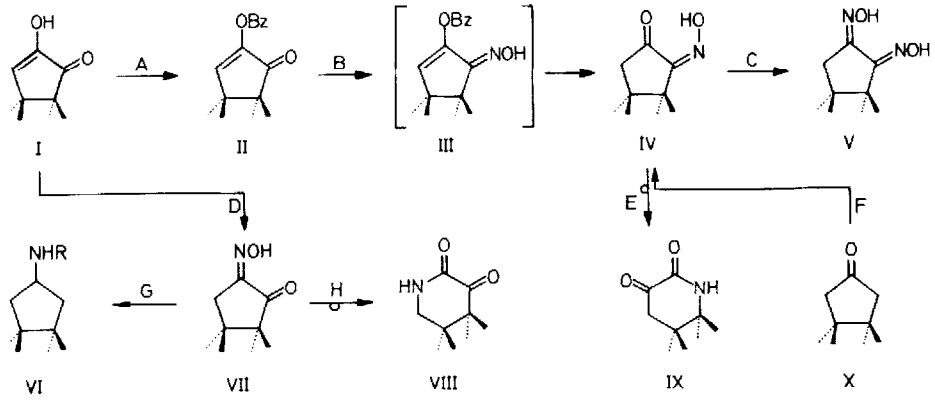
REFERENCES AND NOTES

1) Sugar Enolones, XIII. Grateful acknowledgement is made to the Fonds der Chemischen Industrie for their support of this research. — Part XII: F.W. Lichtenthaler and P. Jarglis, *Chem. Ber.* 113, 489 (1980).

2) S.R. Sandler and W. Karo, *Organic Functional Group Preparations*, Vol. III, 406 ff., Academic Press, New York, 1972.

3) There appears to be only one example of a hydroxylamine-induced enol ester hydrolysis in the literature, i.e. the incidentally observed conversion of cyclopent-enolone benzoate II into the monoxime IV with loss of the benzoyl group[4]. Related thereto is the selective removal of the phenol-type *O*-benzoyl group in di-*O*-benzoyl kojic acid by hydroxylamine[5], and, possibly, the preferential hydroxylamine-induced saponification of 2'-*O*-acyl groups in peracylated *ribo*-nucleosides[6].

4) C.K. Ingold and C.W. Shoppee, *J. Chem. Soc.* 1928, 365, 1868. — The somewhat complex experimental data reported therein may — under partial correction of the views then presented — be reinterpreted as follows: enolone benzoate II on treatment with molar amounts of hydroxylamine, yields the Z-monoxime IV, structure and configuration following from its independent formation via nitrosation of X, and from its Beckmann rearrangement to the lactam IX; in contrast, the free cyclopent-enolone I is converted into the isomeric Z-monoxime VII ("γ-oxime" of I. & S.) on molar oximation as evidenced by its rearrangement to the lactam VIII, clearly different from IX, and by its reductive conversion into VI (R = H, Ac).



Conditions: A, C_6H_5COCl/pyridine; B, $NH_2OH \cdot HCl$ (1 molar)/$NaHCO_3$ in EtOH, 18 h, room temp.; C, $NH_2OH \cdot HCl$/NaOAc in EtOH, 2 h, reflux; D, $NH_2OH \cdot HCl$ (1 molar equiv.)/NaOAc/10% NaOH, 40 h, 40°C; E, NOCl/$CHCl_3$, 30 min, 100°C; F, isoamyl nitrite/NaOMe in MeOH, 30 min, 35°C; G, NaHg/HOAc in EtOH, 50-60°C or Na/EtOH, reflux; H, HCl/ether, reflux.

Since direct enol ester cleavage in II would yield I and, thus, VII on oximation, the hydroxylamine-induced removal of the benzoyl group II → IV must proceed via enolone oxime III as the intermediate, oximation of the carbonyl group being obviously faster than hydroxylaminolysis (or hydrolysis) of the ester function. This conclusion is sustained by the obtention of enolone oximes of type III in pyranoid systems[9].

That benzoic acid (in unreported yield though) was obtained in the conversion II → IV indicates that III may not only undergo hydroxylaminolysis but hydrolysis as well under the slightly alkaline conditions.

5) A. Beélik and C.B. Purves, *Can. J. Chem.* 33, 1361 (1955).

6) Y. Ishido and N. Sakairi, *Nucleic Acids Res., Spec. Publ.* 3, s13 (1977).

7) M.G. Blair, *Adv. Carbohydr. Chem.* 9, 97 (1954); R.J. Ferrier, *ibid.* 24, 219 (1969); F.W. Lichtenthaler, *Pure Appl. Chem.* 50, 1343 (1978).

8) Deacetylation of 3 and 5 with methanolic ammonia or with sodium methoxide/methanol gave yellowish amorphous products that contained nitrogen and sodium, respectively [K. Maurer and H. Mahn, *Ber. Dtsch. Chem. Ges.* 60, 1316 (1927); K. Maurer, *ibid.* 62, 332 (1929); K. Maurer and A. Müller, *ibid.* 63, 2069 (1930)].

9) F.W. Lichtenthaler, E.S.H. El Ashry, and V.H. Göckel, *Tetrahedron Lett.* 1980, ensuing paper.

10) P. Jarglis and F.W. Lichtenthaler, to be published.

(Received in Germany 9 January 1980)