101. The Synthesis and Application of Novel Nitrating and Nitrosating Agents[1])

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(31.X.83)

Summary

Alcohols and phenols are efficiently nitrated with thionyl chloride nitrate or thionyl nitrate, even in the presence of an aromatic moiety. While thionyl chloride nitrate is suitable for nitration of primary OH-groups in carbohydrates, thionyl nitrate is reactive enough to react with secondary OH-groups as well. These reagents permit the highly selective nitration of the 5′-, 2′,5′- and 3′,5′-OH-groups of ribonucleosides to produce either mono- or diprotected nitro derivatives in high yields. Carbon acids and the enol form of some ketones are efficiently nitrated with trifluoromethanesulfonyl nitrate/potassium *tert*-butoxide. Lutidine *N*-oxide ($2,6\text{-}(CH_3)_2C_5H_3N\rightarrow O$) was found to have a marked effect on nitration reactions. Similarly, thionyl chloride nitrite and thionyl nitrite exhibit an excellent capacity for nitrosation of the aforementioned substrates.

Introduction. – The conditions effecting *O*-nitration with either mixed nitric-sulfuric acid [1–3], nitronium tetrafluoroborate [4], or acetyl nitrate [5] have been described. *Olah et al.* [6] reported a mild and effective procedure for the preparation of alkyl nitrates *via* transfer nitration of the corresponding alcohols with *N*-nitrocollidinium tetrafluoroborate.

We wish to introduce in this report two novel, very mild, and effective nitrating agents, namely thionyl chloride nitrate ($SOCl(NO_3)$) and thionyl nitrate ($SO(NO_3)_2$), for: (1) the rapid and efficient nitration of a OH-function in the presence of aromatic rings; (2) the highly selective nitration of primary OH-groups in carbohydrates and related compounds; (3) the selective nitration of 5′-, 2′,5′- and 3′,5′-OH-groups in ribonucleosides. We also report a mild, effective method of nitrating carbon acids in the pK_a range of dialkyl malonate or the OH-groups of the enol form of ketones such as ethyl acetoacetate, using trifluoromethanesulfonyl nitrate with K*t*OBu in THF.

Nitration of OH-Groups in Aromatic Compounds. – Reaction of $SOCl_2$ with $AgNO_3$ may afford $SOCl(NO_3)$ or $SO(NO_3)_2$, which as a result of a S_N2 displacement at their NO_2-function by OH-groups may yield nitric esters (nitrates). Indeed, when 1 equiv. of

[1]) Work supported by the Shiraz University Research Council.
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$AgNO_3$ was allowed to react with 1 equiv. of $SOCl_2$ in dry THF, $SOCl(NO_3)$ was obtained in excellent yield as evidenced by quantitative precipitation of AgCl; addition of 2 equiv. of $AgNO_3$ to $SOCl_2$/THF afforded $SO(NO_3)_2$[3]).

Although the reaction of appropriate substrates with $SOCl(NO_3)$ at 20° did not proceed with evolution of SO_2 gas, the reactions with $SO(NO_3)_2$ were accompanied by liberation of SO_2 gas suggesting the following events:

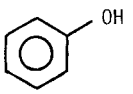
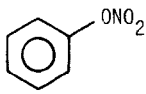
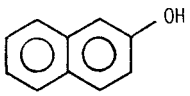
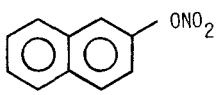
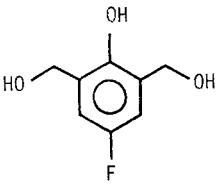
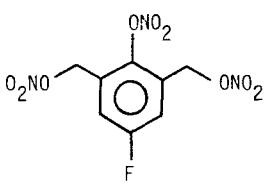
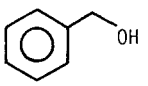
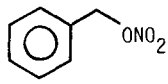
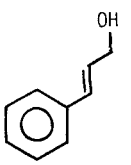
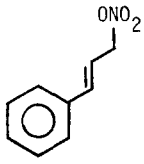
$$ROH + ClS(O)ONO_2 \longrightarrow RONO_2 + ClS(O)OH$$

$$ROH + O_2NOS(O)ONO_2 \longrightarrow RONO_2 + SO_2 + HNO_3$$

It should be noted that when $SOCl(NO_3)$ was heated at 40°, the evolution of SO_2 gas was observed.

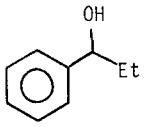
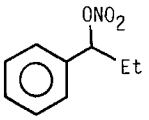
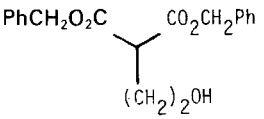
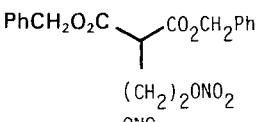
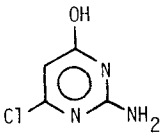
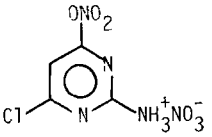
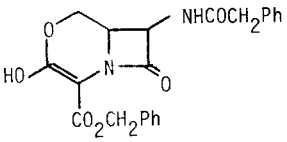
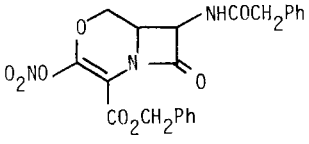
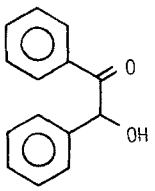
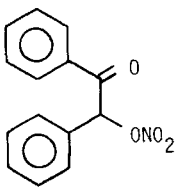
$$ClS(O)OH \xrightarrow{40°} HCl + SO_2$$

Table 1. *Nitration of OH-Groups in Aromatic Compounds with $SOCl(NO_3)$ or $SO(NO_3)_2$*[a])

Starting Material	Product[b])	Yield[c]) [%]
		90[d]) 95[e])
		96[d]) 97[e])
		85[d]) 76[e])
		98[d]) 95[e])
		96[d]) 95[e])

[3]) The THF solution of $SOCl(NO_3)$ (0.1M) is intense yellow and can be kept under N_2 at 0° for a few months. The THF solution of $SO(NO_3)_2$ (0.1M) is intense orange and stable under N_2 at 0° for only a few weeks.

Table 1 (continued)

Starting Material	Product[b])	Yield[c]) [%]
		95[d]) 90[e])
		85[d]) 89[e])
		65[e])
		70[d])
		70[d]) 60[e])

[a]) The solvent was dry THF in all cases.
[b]) The nitrates were characterized by spectroscopic and microanalysis data.
[c]) Yields are based on material isolated from column chromatography or TLC.
[d]) Obtained with $SOCl(NO_3)$.
[e]) Obtained with $SO(NO_3)_2$.

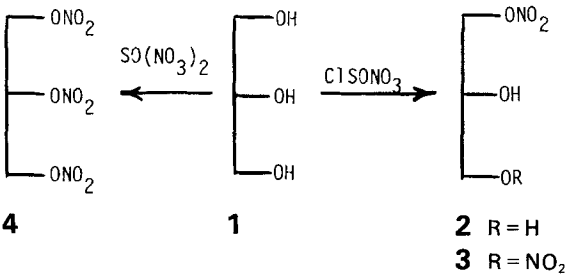
A series of aromatic compounds possessing OH-groups was treated with $SOCl(NO_3)$ or $SO(NO_3)_2$ in THF. The results are summerized in *Table 1* and show that OH-functions are nitrated in excellent yields. Other aromatic compounds such as benzene, toluene, anisol, aniline, naphthalene, anthracene, chlorobenzene, nitrobenzene, and benzoic acid did not react under the conditions employed.

Selective *O*-Nitrations in Carbohydrates. – Having established a method for the nitration of OH-groups in the presence of aromatic rings, it was decided to find a general procedure for the selective nitration of primary in the presence of secondary OH-groups. The selective protection of primary OH-groups is a useful synthetic reac-

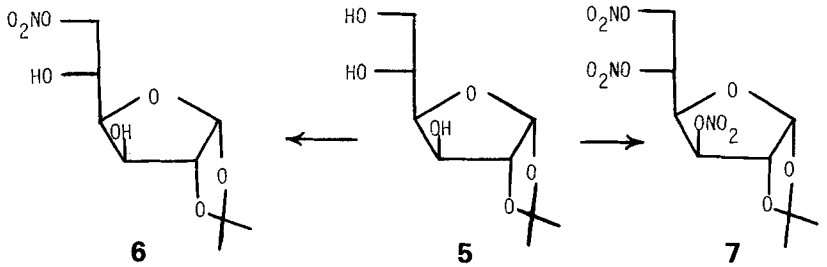
tion; numerous protecting groups have been evaluated in this regard, with varying degrees of success [7–9]. In particular, alkylsilyl protecting groups are widely used in synthetic chemistry [10–16]. Specific applications have arisen in the protection of glycerol for the preparation of phospholipids [17] [18], in the protection of carbohydrates [19], and in the protection of OH-groups in nucleosides [12–14] [20].

Owing to the propitious fact that nitrates possess a leaving group capacity comparable to that of sulfonyloxy groups and yet are readily cleaved by catalytic hydrogenation [21], they are of considerable synthetic utility for transformations in the aforementioned substrates. Thus, primary nitric ester groups readily undergo displacement reactions on treatment with nucleophiles [22].

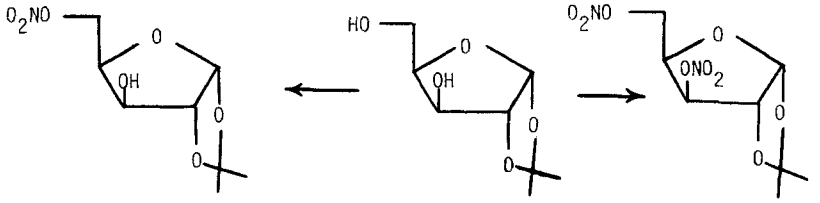
Glycerol (**1**), 1,2-*O*-isopropylidene-*a*-D-glucofuranose (**5**), and 1,2-*O*-isopropylidene-*a*-D-xylofuranose (**8**) were used as model compounds. Treatment of **1** with 1 equiv. each of $SOCl_2$ and $AgNO_3$ in THF gave a 65% yield of the mononitrated glycerol **2**, and treatment of **1** with 2 equiv. each of $SOCl_2$ and $AgNO_3$ in THF converted it in 70% yield into the 1,3-di-*O*-nitroglycerol (**3**). However, when **1** was reacted with 3 equiv. of $SOCl_2$ and 6 equiv. of $AgNO_3$ in THF, a quantitative yield of 1,2,3-tri-*O*-nitroglycerol (**4**) was obtained (trinitroglycerol produces headache on testing and explodes on rapid heating or on concussion [26]).



4 **1** **2** R = H
3 R = NO_2



6 **5** **7**



9 **8** **10**

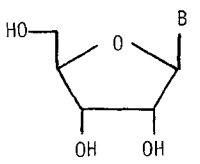
Compound **5** was selectively nitrated using $SOCl_2/AgNO_3$ in THF at 0–6° to give **6** in 55% yield. Under the same conditions, **8** was converted to its 5-nitrate **9** in 60% yield. Both **5** and **8** were fully nitrated to **7** and **10**, respectively, in quantitative yield when $SOCl_2/2AgNO_3$ was used. *Table 2* summerizes these results. Thus, $SOCl(NO_3)$ and $SO(NO_3)_2$ are useful reagents for the preparation of mono- and per-*O*-nitrated derivatives of carbohydrates and related compounds.

Table 2. *Nitration of* **1**, **5**, *and* **8** *under Different Reaction Conditions*[a])

Compound	$AgNO_3$ [mmol]	$SOCl_2$ [mmol]	time [h]	Products[b])
1	1	1	10	**2** (65%)
1	2	2	5	**3** (70%)
1	3	3	2	**3** (62%)
1	6	3	2	**4** (99%)
5	1	1	5	**6** (55%)
8	1	1	5	**9** (60%)
5	6	3	3	**7** (95%)
8	4	2	3	**10** (97%)

[a]) The solvent was dry THF in all cases.
[b]) Spectroscopic data and microanalysis of the products were consistent with the proposed structures.

Selective *O*-Nitrations in Ribonucleosides. – The manipulation of ribonucleosides wheather for coupling to form ribonucleotides or for the selective chemical modification of the carbohydrate portion of the structure, requires the availability of OH-protecting groups. The nonselective preparation of nitric esters of uridine by the aid of fuming nitric acid was already reported [2]. Several general procedures have been suggested [21] to improve either total yields or selectivity in nitration reactions. We have found that these procedures offer very little advantage in the selective nitration of ribonucleosides. However, $SOCl(NO_3)$ and $SO(NO_3)_2$ have offered excellent performance in rapid and selective nitration of 5′-, 2′,5′- and 3′,5′-OH-groups of ribonucleosides in high yields. As model, uridine (**11a**) was converted to its 5′-nitro derivative **12a**



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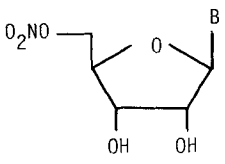

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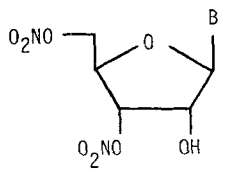

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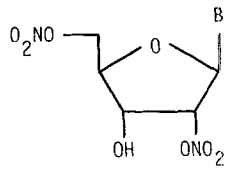

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a: B = uracil
b: B = *N*-benzoyladenine
c: B = *N*-benzoylcytosine
d: B = *N*-benzoylguanine

Table 3. *Selective Nitration of Ribonucleosides*[a])

Nucleoside	$AgNO_3$ [mmol]	$SOCl_2$[b]) [mmol]	Time [h]	Yields [%]		
				5′-NO_3	3′,5′-$(NO_3)_2$	2′,5′-$(NO_3)_2$
U (**11a**)	1.2	1.6	3	88 (**12a**)	–	–
U (**11a**)[c])	1.2	1.3	3	90 (**12a**)	5 (**13a**)	–
U (**11a**)	2.2	1.3	3	95 (**12a**)	–	–
U (**11a**)[c])	4.4	2.8	2	–	80 (**13a**)	15 (**14a**)
U (**11a**)	6	3/DABCO(5)	1	–	–	90 (**14a**)
U (**11a**)	6	3/py (5)	2	–	–	88 (**14a**)
U (**11a**)	4.4	SO_2Cl_2(2.2)	3	–	–	–
U (**11a**)	4.4	2.2/CF_3CO_2H(5)	5	50 (**12a**)	–	–
U (**11a**)	4.4	2.2/py→O(3)	5	90 (**12a**)	1 (**13a**)	3 (**14a**)
U (**11a**)	4.4	2.2/pic→O(3)	5	75 (**12a**)	2 (**13a**)	20 (**14a**)
U (**11a**)	4.4	2.2/lut→O(3)	5	3 (**12a**)	1 (**13a**)	90 (**14a**)
bz^6A (**11b**)	2.2	1.3	3	95 (**12b**)	–	–
bz^6A (**11b**)[c])	4.4	2.6	2	–	60 (**13b**)	35 (**14b**)
bz^6A (**11b**)	1.2	2.8	3	98 (**12b**)	–	–
bz^4C (**11c**)	1.2	5	2	96 (**12c**)	–	–
bz^4C (**11c**)	2.2	1.3	3	90 (**12c**)	–	–
bz^4C (**11c**)[c])	4.4	2.8	3	–	69 (**13c**)	25 (**14c**)
bz^2G (**11d**)	1.2	3	2	95 (**12d**)	–	–
bz^2G (**11d**)	2.2	2.2	2	80 (**12d**)	10 (**13d**)	3 (**14d**)
bz^2G (**11d**)	4.4	2.6	5	5 (**12d**)	60 (**13d**)	30 (**14d**)

[a]) Unless otherwise stated, the solvent was THF. Yields are based on materials isolated from short-column chromatography or TLC.

[b]) DABCO = 1,4-Diazabicyclo[2.2.2]octane; py = pyridine; pic = α-picoline = 2-methylpyridine; lut = 2,6-dimethylpyridine.

[c]) The solvent was THF/DMF 15:2.

Table 4. *Properties of Nitro and Nitroso Derivatives of Nucleosides*

Compound	m.p. [°C]	λ_{max} (EtOH) [nm]	IR (N=O) [cm^{-1}]	R_f (TLC)[a])
12a	143	264	1700	0.18
13a	182	264	1700	0.45
14a	167	264	1700	0.59
12b	129	280	1690	0.23
13b	102	280	1685	0.56
14b	88	280	1695	0.77
12c	169	247, 304	1700	0.16
13c	108	247, 304	1690	0.39
14c	98	247, 304	1690	0.58
12d	206	265, 295	1688	0.20[b])
13d	131	265, 295	1690	0.43[b])
14d	119	265, 295	1690	0.63[b])
17	123	265	1690	0.21
18	141	265	1690	0.48

[a]) The solvent in all cases was AcOEt.

[b]) Two developments in AcOEt.

by means of $SOCl_2/AgNO_3$ in THF. When the reaction was carried out with $SOCl_2/2AgNO_3$ in the presence of DMF, a high yield of 3',5'-dinitrouridine (**13a**) was obtained. These conditions were also applied to the ribonucleosides **11b–d**: Compounds **12b–d** and **13b–d** were obtained in high yields (see *Table 3*).

The selective protection of the 2',5'-positions in ribonucleosides was a more difficult task. After trying several alternatives, three procedures for the preparation of **14a–d** have been developed, *i.e.* nitration with $SO(NO_3)_2$ in the presence of 1,4-diazabicyclo[2.2.2]octane (DABCO), nitration with $SO(NO_3)_2$/pyridine, and nitration with $SO(NO_3)_2$/lutidine *N*-oxide (2,6-$(CH_3)_2C_6H_3N\rightarrow O$; see *Table 3*). In the absence of DABCO, pyridine, and lutidine *N*-oxide, only 5'-nitration occurs. All results are listed in *Table 3*, and the properties of the products are collected in *Table 4*.

The results described above clearly indicate that $SO(NO_3)_2$ and $SOCl(NO_3)_2$ are efficient nitrating agents and offer a new procedure for the selective protection of ribonucleosides in high yields.

Nitration of Carbon Acids and Enols. – We next attempted to find a general procedure for nitration of carbon acids. We already showed [23] that trifluoromethanesulfonyl chloride (CF_3SO_2Cl) is a chlorinating agent transforming dialkyl malonates to their dichloro derivatives. Therefore, reaction of CF_3SO_2Cl with $AgNO_3$ may give $CF_3SO_2NO_3$ which could convert dialkyl malonate to its nitro derivative (*e.g.* **15**). Indeed, when 1.1 equiv. of $AgNO_3$ was allowed to react with 1 equiv. of CF_3SO_2Cl in THF, AgCl precipitated; addition of Et_2O resulted in quantitative precipitation of AgCl. To the THF solution of $CF_3SO_2NO_3$ was added diethyl malonate and KO*t*Bu, and the *C*-nitro derivative **15** was obtained in 40% yield. Catalytic hydrogenation of **15** gave diethyl 2-aminomalonate (**16**) which was in every aspect identical with the authentic sample.

$$EtO_2CCH_2CO_2Et \longrightarrow \underset{\mathbf{15}}{EtO_2CCH(NO_2)CO_2Et} \longrightarrow \underset{\mathbf{16}}{EtO_2CCH(NH_2)CO_2Et}$$

In order to establish the usefulness of the reagent $CF_3SO_2NO_3$, ethyl acetoacetate, 2,4-pentanedione, and dibenzyl malonate were subjected to it. Surprisingly, in the case of the compounds possessing keto groups, nitration of the OH-function of their enol form occurred in good yield affording nitrates. Reduction of the latter afforded the corresponding starting ketones in high yields.

$$CH_3COCH_2COOEt \longrightarrow CH_3C(ONO_2) = CHCOOEt$$

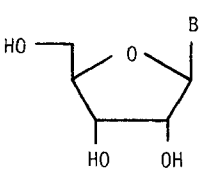
$$CH_3COCH_2COCH_3 \longrightarrow CH_3C(ONO_2) = CHCOCH_3$$

$$CH_2(COOBzl)_2 \longrightarrow O_2NCH(COOBzl)_2$$

It should be noted that reaction of $CF_3SO_2NO_3$ with nucleosides failed and resulted in recovery of the starting materials.

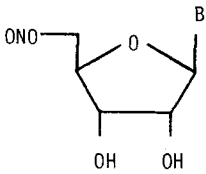
Nitrosations. – Having established the capacity and utility of $SOCl(NO_3)$ and $SO(NO_3)_2$, it was decided to prepare thionyl chloride nitrite ($SOCl(NO_2)$) and thionyl nitrite ($SO(NO_2)_2$) and to examine their nitrosating ability. Thus, treatment of 1 equiv.

of $AgNO_2$ with 1 equiv. of $SOCl_2$ in dry THF gave $SOCl(NO_2)$ as evidenced by quantitative precipitation of AgCl. Addition of a second equiv. of $AgNO_2$ to the system afforded 2 equiv. of AgCl, indicating that $SO(NO_2)_2$ was prepared in excellent yield. Both reagents are stable in THF under N_2 for months at $-10°$.



11a

B = uracil



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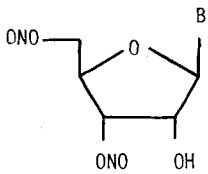

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A series of appropriate substrates of different types was reacted with these reagents in THF. The results are summarized in *Table 5*. The properties of new compounds are collected in *Table 4*.

Table 5. *Selective Nitrosation of Compounds Possessing OH-Groups and of Carbon Acids*[a])

Compound	$AgNO_2$ [mmol]	$SOCl_2$ [mmol]	time [h]	Yield [%]		
				5'-NO_2	3',5'-$(NO_2)_2$	2',5'-$(NO_2)_2$
U (**11a**)	3	3	3	90 (**17**)	–	–
U (**11a**)	6	3	3	92 (**17**)	–	–
U (**11a**)	3	3/py	3	–	58 (**18**)	–
U (**11a**)	3	3/lut→O	3	95 (**17**)	–	–
U (**11a**)[b])	3	3	3	–	95 (**18**)	–
U (**11a**)	6	3/py	3	–	90 (**18**)	–
U (**11a**)[b])	6	3	3	–	96 (**18**)	–
Phenol	3	3	3	80	(PhONO)	
Cinnamyl alcohol	1	1	3	90	($PhCH{=}CHCH_2ONO$)	
1-Phenylpropanol	2	1	3	82	(PhCH(Et)ONO)	
N-Benzylaniline	2	2	3	60	(PhCHN(NO)Ph)	
Acetophenone	3	3	24	40	($PhCOCH_2NO$)	
Dibenzyl malonate	4	4	24	90	$HON{=}C(COOBzl)_2$	
Ethyl acetoacetate	3	3	24	80	HON=C(Ac)COOEt	
2,4-Pentanedione	3	3	24	85	$HON{=}C(COCH_3)_2$	

[a]) Unless otherwise stated, the solvent was THF. Yields are based on material isolated from column chromatography. IR, ^{1}H-NMR and chemical-ionization mass spectra and microanalysis of all products were compatible with the proposed structures.

[b]) The solvent was THF/DMF 15:2.

Experimental Part

1. *General Remarks.* See [24].

2. *General Procedure for the Preparation of Nitric Esters.* All aromatic compounds *(Table 1)* possessing OH-groups were nitrated to the corresponding nitrates in the same manner. Their structures were proven by IR, ^{1}H-NMR, MS(CI), and microanalysis or by comparison with an authentic sample. The following is a representative procedure: To a solution of 1 mmol of substrate in 5 ml of dry THF at 25° were added *n*-mol-equiv. of $SOCl(NO_3)$[3]) or $SO(NO_3)_2$[3]), (*n* = number of alcoholic or phenolic H-atoms of substrate). After 1 h, Et_2O was

added, and the solution was washed with H_2O, dried, and evaporated. The product was purified by chromatography on silica gel. Catalytic hydrogenation of the nitrates afforded the starting substrates in high yields.

3. *Nitration of Carbohydrates and Related Compounds. 1-O-Nitroglycerol* (**2**). Glycerol (**1**; 0.92 g, 10 mmol) was suspended in THF (25 ml) and dried $AgNO_3$ (1.70 g, 10 mmol) was added at once. After dropwise addition of $SOCl_2$ (1.19 g, 10 mmol), the mixture was stirred for 10 h at 25°. H_2O was added and the mixture extracted with AcOEt. The AcOEt was dried and evaporated. The oil was purified by column chromatography (AcOEt): **2** in 65% yield. TLC (AcOEt): R_f 0.21 (I_2 stain); IR (neat): 1680 (ONO_2). ^{1}H-NMR ($CDCl_3$): 3.10–3.35 (br., 2H, 2OH, exchangeable with D_2O); 3.62 (br., 5H, CH_2CHCH_2). Anal. calc. for $C_3H_7NO_5$ (137.13): C 26.28, H 5.10, N 10.21; found: C 26.20, H 5.21, N 10.31.

1,3-Di-O-nitroglycerol (**3**) was synthesized like **2**, except that 20 mmol of each $SOCl_2$ and $AgNO_3$ were used. IR and ^{1}H-NMR of **2** and **3** were similar. Anal. calc. for $C_3H_6N_2O_7$ (182.04): C 19.78, H 3.29, N 15.38; found: C 19.89, H 3.20, N 15.41.

1,2,3-Tri-O-nitroglycerol (**4**) was prepared like **2**, except that 30 mmol of $SOCl_2$ and 60 mmol of $AgNO_3$ were used. Compound **4** was identical with an authentic sample.

1,2-O-Isopropylidene-6-O-nitro-α-D-glucofuranose (**6**) was prepared from 1,2-*O*-isopropylidene-α-D-glucofuranose (**5**) like **2** and isolated by silica gel chromatography (AcOEt): 55% yield. TLC ($CHCl_3$): R_f 0.10 (I_2 stain). IR (neat): 1679 (ONO_2). Anal. calc. for $C_9H_{15}NO_8$ (265.21): C 40.75, H 5.66, N 5.28; found: C 40.70, H 5.51, N 5.20.

1,2-O-Isopropylidene-3,5,6-tri-O-nitro-α-D-glucofuranose (**7**) was prepared like **2**, except that the ratio **5**/$AgNO_3$/$SOCl_2$ was 1:6:3, and isolated by silica gel chromatography (AcOEt/Et_2O 2:11) in 95% yield. TLC($CHCl_3$): R_f 0.4 (I_2 stain). IR (neat): 1679 (ONO_2). Anal. calc. for $C_9H_{13}N_3O_{12}$ (355.13): C 30.42, H 3.66, N 11.83; found: C 30.30, H 3.56, N 11.72.

1,2-O-Isopropylidene-5-O-nitro-α-D-xylofuranose (**9**) was prepared from 1,2-*O*-isopropylidene-α-D-xylofuranose (**8**) like **6**: oil in 60% yield; R_f ($CHCl_3$) 0.3. IR (neat): 1677 (ONO_2). Anal. calc. for $C_8H_{13}NO_7$ (235.03); C 40.85, H 5.53, N 5.96; found: C 40.90, H 5.42, N 5.99.

1,2-O-Isopropylidene-3,5-di-O-nitro-α-D-xylofuranose (**10**) was prepared from **8** like **7** and isolated as an oil in 97% yield. R_f ($CHCl_3$) 0.60. IR (neat): 1678 (ONO_2). Anal. calc. for $C_8H_{12}N_2O_9$ (280.32): C 34.28, H 4.28, N 10.00; found: C 34.30, H 4.29, N 10.01.

4. *Nitration of Ribonucleosides.* 4.1. *Selective 5'-Nitration.* Standardized procedure: Uridine (**11a**; 1.22 g, 5 mmol) was suspended in dry THF (50 ml). $AgNO_3$ (0.85 g, 5 mmol) was added followed by dropwise addition of $SOCl_2$ (0.9 g, 8 mmol). The mixture was stirred for 3 h at 25°. The solution was then filtered into H_2O (30 ml). This solution was extracted with AcOEt (50 ml), and the extracts were dried and evaporated. The residue was chromatographed on silica gel (AcOEt): *5'-O-nitrouridine* (**12a**) in 88% yield. Properties of **12a** as well as of N^6*-benzoyl-5'-O-nitroadenosine*, N^4*-benzoyl-5'-O-nitrocytidine, and* N^2*-benzoyl-5'-O-nitroguanosine* see *Table 4*. IR of **12a–d**: 1690*s* (ONO_2).

Catalytic hydrogenation of **12a–d** yielded the starting **11a–d**, resp., in about 90% yield.

4.2. *Selective 3',5'-Nitration.* General procedure as in *4.1*, except that 4.4 mmol of $AgNO_3$ and 2.8 mmol of $SOCl_2$ were used, and the solvent was THF/DMF 15:2 in all cases, except for **13d** *(Table 3)*. Properties of *3',5'-di-O-nitrouridine*, N^6*-benzoyl-3',5'-di-O-nitroadenosine*, N^4*-benzoyl-3',5'-di-O-nitrocytidine*, and N^2*-benzoyl-3',5'-di-O-nitroguanosine* (**13a–d**): see *Table 4*.

Catalytic hydrogenation of **13a–d** gave the starting **11a–d**, resp.

4.3. *Selective 2',5'-Nitration.* Procedure identical to *4.2*, except that pyridine, DABCO, or lutidine *N*-oxide were used in place of DMF. Ratio of reagents and results: see *Table 3*. Properties of *2',5'-di-O-nitrouridine*, N^6*-benzoyl-2',5'-di-O-nitroadenosine*, N^4*-benzoyl-2',5'-di-O-nitrocytidine*, and N^2*-benzoyl-2',5'-di-O-nitroguanosine* (**14a–d**) are listed in *Table 4*.

Catalytic hydrogenation of **14a–d** afforded the starting **11a–d** in excellent yield.

5. *Reaction with Trifluoromethanesulfonyl Nitrate.* All substrates were treated under the same conditions, and the structure of the products were proven by IR, ^{1}H-NMR, and MS (CI). Representative procedure: To a suspension of $AgNO_3$ (1.1 mmol) in THF (20 ml), CF_3SO_2Cl (1.0 mmol) was added. After 8 min, a THF solution of 1 mmol of diethyl malonate and 1 mmol of KO*t*Bu was added dropwise (exothermic reaction). After 3 h, Et_2O was added, the solution filtered, the filtrate washed with H_2O, dried over $MgSO_4$, and evaporated. The product was purified by column chromatography on silica gel (CH_2Cl_2): 40% yield of **15**.

Catalytic hydrogenation of **15** in EtOH (Pd/C) gave *diethyl 2-aminomalonate* (**16**) in 80% yield, identical with an authentic sample.

Ethyl acetoacetate, 2,4-pentanedione, and dibenzyl malonate were subjected to the same reaction conditions to afford the corresponding nitro derivatives (s. *General Section*).

6. *Nitrosation of Uridine* (**11a**). The general procedures for the preparation of *5'-O-nitroso-* and *3',5'-di-O-nitrosouridine* (**17** and **18**, resp.) are the same as described in *4.1* and *4.2* ($AgNO_2$ instead of $AgNO_3$), resp. Ratio of reagents, conditions, and results: see *Table 5*. Properties: see *Table 4*.

7. *Nitrosation Reaction.* Standardized procedure: To dibenzyl malonate (1 mmol) in dry THF, $AgNO_2$ (4 mmol) was added. After dropwise addition of $SOCl_2$ (4 mmol) in dry THF (1 ml), the mixture was stirred for 24 h at 25°. After filtration into H_2O (20 ml), the solution was extracted with Et_2O, dried and evaporated. Chromatography on silica gel (CH_2Cl_2) afforded the corresponding oxime in 90% yield (see *Table 5*), identical with an authentic sample prepared and characterized according to [25].

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