

101. The Synthesis and Application of Novel Nitrating and Nitrosating Agents¹⁾

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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-(CH₃)₂C₅H₃N→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(NO₃)) and thionyl nitrate (SO(NO₃)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 *Kt*OBu in THF.

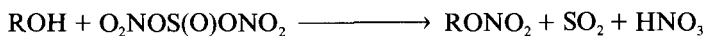
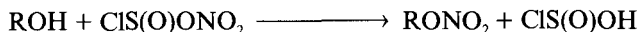
Nitration of OH-Groups in Aromatic Compounds. – Reaction of SOCl₂ with AgNO₃ may afford SOCl(NO₃) or SO(NO₃)₂, which as a result of a *S_N2* displacement at their NO₂-function by OH-groups may yield nitric esters (nitrates). Indeed, when 1 equiv. of

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AgNO₃ was allowed to react with 1 equiv. of SOCl₂ in dry THF, SOCl(NO₃) was obtained in excellent yield as evidenced by quantitative precipitation of AgCl; addition of 2 equiv. of AgNO₃ to SOCl₂/THF afforded SO(NO₃)₂³.

Although the reaction of appropriate substrates with SOCl(NO₃) at 20° did not proceed with evolution of SO₂ gas, the reactions with SO(NO₃)₂ were accompanied by liberation of SO₂ gas suggesting the following events:



It should be noted that when SOCl(NO₃) was heated at 40°, the evolution of SO₂ gas was observed.

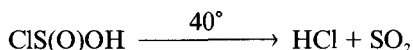
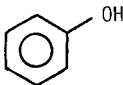
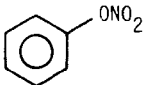
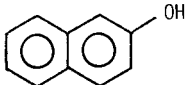
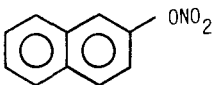
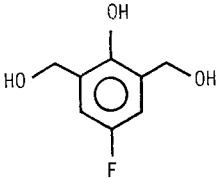
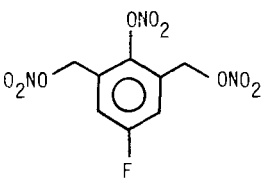
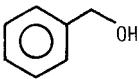
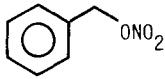
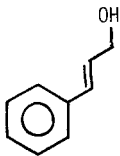
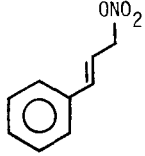
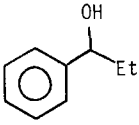
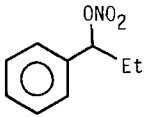
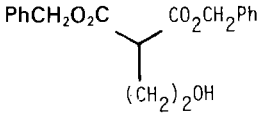
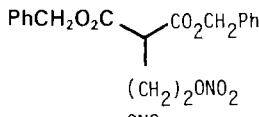
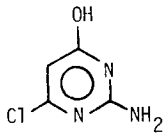
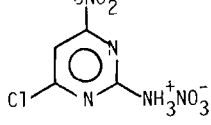
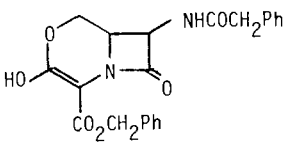
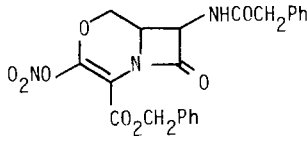
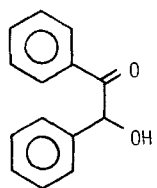
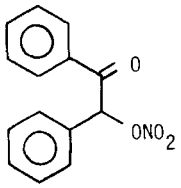


Table 1. Nitration of OH-Groups in Aromatic Compounds with SOCl(NO₃) or SO(NO₃)₂³)

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(NO₃) (0.1M) is intense yellow and can be kept under N₂ at 0° for a few months. The THF solution of SO(NO₃)₂ (0.1M) is intense orange and stable under N₂ 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 $\text{SOCl}(\text{NO}_3)$.

^{e)} Obtained with $\text{SO}(\text{NO}_3)_2$.

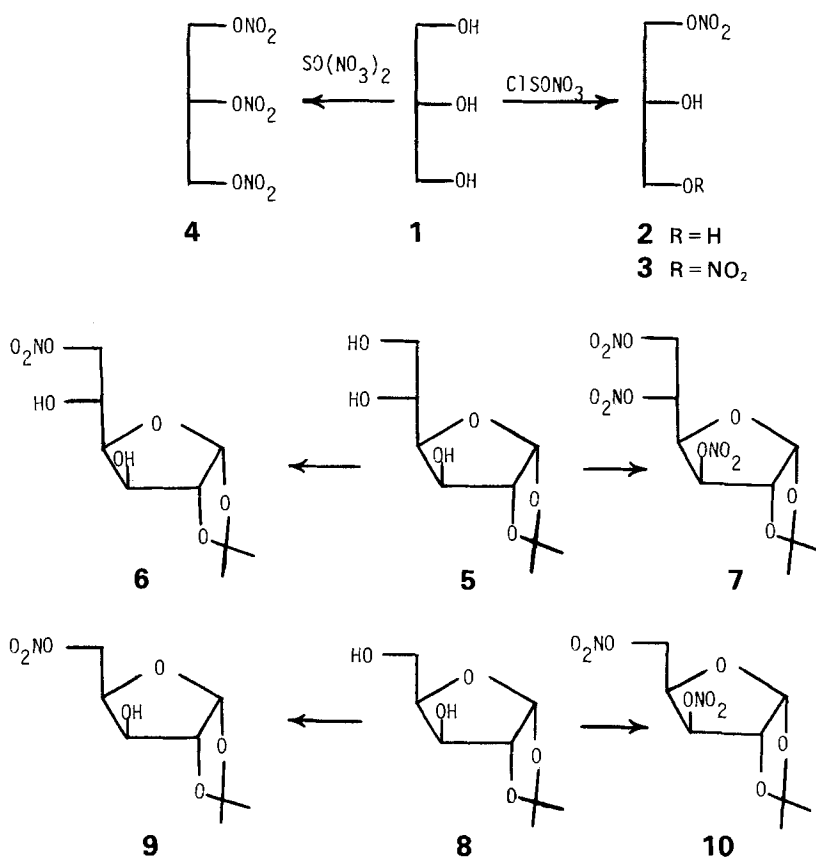
A series of aromatic compounds possessing OH-groups was treated with $\text{SOCl}(\text{NO}_3)$ or $\text{SO}(\text{NO}_3)_2$ in THF. The results are summarized in *Table 1* and show that OH-functions are nitrated in excellent yields. Other aromatic compounds such as benzene, toluene, anisol, aniline, 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]).



Compound **5** was selectively nitrated using $\text{SOCl}_2/\text{AgNO}_3$ in THF at $0-6^\circ$ 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 $\text{SOCl}_2/2\text{AgNO}_3$ was used. Table 2 summarizes these results. Thus, $\text{SOCl}(\text{NO}_3)$ and $\text{SO}(\text{NO}_3)_2$ 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 whether 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, $\text{SOCl}(\text{NO}_3)$ and $\text{SO}(\text{NO}_3)_2$ 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**

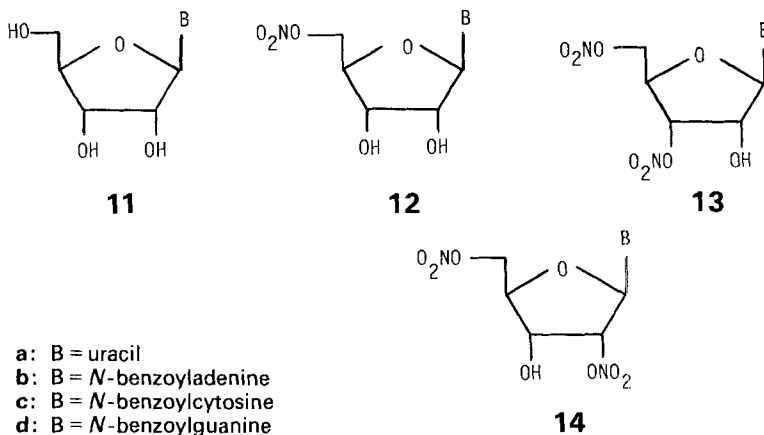


Table 3. Selective Nitration of Ribonucleosides^{a)}

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 ₂ Cl ₂ (2.2)	3	–	–	–
U (11a)	4.4	2.2/CF ₃ CO ₂ H(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 ⁶ A (11b)	2.2	1.3	3	95 (12b)	–	–
bz ⁶ A (11b) ^{c)}	4.4	2.6	2	–	60 (13b)	35 (14b)
bz ⁶ A (11b)	1.2	2.8	3	98 (12b)	–	–
bz ⁴ C (11c)	1.2	5	2	96 (12c)	–	–
bz ⁴ C (11c)	2.2	1.3	3	90 (12c)	–	–
bz ⁴ C (11c) ^{c)}	4.4	2.8	3	–	69 (13c)	25 (14c)
bz ² G (11d)	1.2	3	2	95 (12d)	–	–
bz ² G (11d)	2.2	2.2	2	80 (12d)	10 (13d)	3 (14d)
bz ² G (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-di-methylpyridine.

^{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.

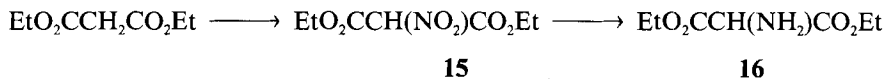
^{b)} Two developments in AcOEt.

by means of $\text{SOCl}_2/\text{AgNO}_3$ in THF. When the reaction was carried out with $\text{SOCl}_2/2\text{AgNO}_3$ 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*).

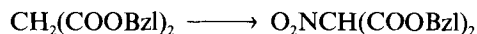
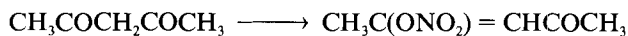
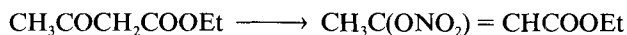
The selective protection of the 2',5'-positions in ribonucleosides was a more difficult task. After trying several alternatives, three procedures for the preparation of **14a–d** have been developed, *i.e.* nitration with $\text{SO}(\text{NO}_3)_2$ in the presence of 1,4-diazabicyclo[2.2.2]octane (DABCO), nitration with $\text{SO}(\text{NO}_3)_2/\text{pyridine}$, and nitration with $\text{SO}(\text{NO}_3)_2/\text{lutidine } N\text{-oxide}$ ($2,6\text{-(CH}_3)_2\text{C}_6\text{H}_3\text{N}\rightarrow\text{O}$; 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 $\text{SO}(\text{NO}_3)_2$ and $\text{SOCl}(\text{NO}_3)_2$ 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 ($\text{CF}_3\text{SO}_2\text{Cl}$) is a chlorinating agent transforming dialkyl malonates to their dichloro derivatives. Therefore, reaction of $\text{CF}_3\text{SO}_2\text{Cl}$ with AgNO_3 may give $\text{CF}_3\text{SO}_2\text{NO}_3$ 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 $\text{CF}_3\text{SO}_2\text{Cl}$ in THF, AgCl precipitated; addition of Et_2O resulted in quantitative precipitation of AgCl . To the THF solution of $\text{CF}_3\text{SO}_2\text{NO}_3$ was added diethyl malonate and KO^tBu , and the *C*-nitro derivative **15** was obtained in 40% yield. Catalytic hydrogenation of **15** gave diethyl 2-aminomalonnate (**16**) which was in every aspect identical with the authentic sample.



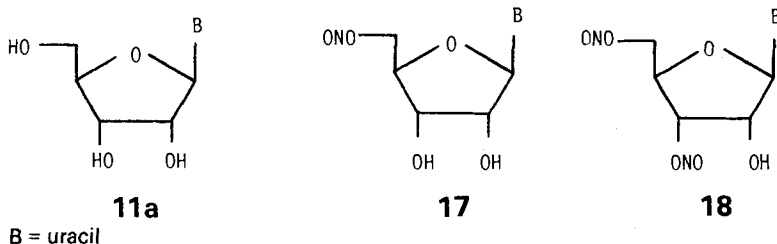
In order to establish the usefulness of the reagent $\text{CF}_3\text{SO}_2\text{NO}_3$, ethyl acetoacetate, 2,4-pentanedione, and dibenzyl malonate were subjected to it. Surprisingly, in the case of the compounds possessing keto groups, nitration of the OH-function of their enol form occurred in good yield affording nitrates. Reduction of the latter afforded the corresponding starting ketones in high yields.



It should be noted that reaction of $\text{CF}_3\text{SO}_2\text{NO}_3$ with nucleosides failed and resulted in recovery of the starting materials.

Nitrosations. – Having established the capacity and utility of $\text{SOCl}(\text{NO}_3)$ and $\text{SO}(\text{NO}_3)_2$, it was decided to prepare thionyl chloride nitrite ($\text{SOCl}(\text{NO}_2)$) and thionyl nitrite ($\text{SO}(\text{NO}_2)_2$) and to examine their nitrosating ability. Thus, treatment of 1 equiv.

of AgNO_2 with 1 equiv. of SOCl_2 in dry THF gave $\text{SOCl}(\text{NO}_2)$ 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 $\text{SO}(\text{NO}_2)_2$ was prepared in excellent yield. Both reagents are stable in THF under N_2 for months at -10° .



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'- $(\text{NO}_2)_2$	2',5'- $(\text{NO}_2)_2$
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 ₂ ONO)	
1-Phenylpropanol	2	1	3	82	(PhCH(Et)ONO)	
<i>N</i> -Benzylaniline	2	2	3	60	(PhCHN(NO)Ph)	
Acetophenone	3	3	24	40	(PhCOCH ₂ NO)	
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, ¹H-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, ¹H-NMR, MS(Cl), 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 $\text{SOCl}(\text{NO}_2)$ or $\text{SO}(\text{NO}_2)_2$, (*n* = number of alcoholic or phenolic H-atoms of substrate). After 1 h, Et₂O was

added, and the solution was washed with H₂O, 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 AgNO₃ (1.70 g, 10 mmol) was added at once. After dropwise addition of SOCl₂ (1.19 g, 10 mmol), the mixture was stirred for 10 h at 25°. H₂O 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 (I₂ stain); IR (neat): 1680 (ONO₂). ¹H-NMR (CDCl₃): 3.10–3.35 (br., 2H, 2OH, exchangeable with D₂O); 3.62 (br., 5H, CH₂CHCH₂). Anal. calc. for C₃H₇NO₅ (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 SOCl₂ and AgNO₃ were used. IR and ¹H-NMR of **2** and **3** were similar. Anal. calc. for C₃H₆N₂O₇ (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 SOCl₂ and 60 mmol of AgNO₃ 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 (CHCl₃): R_f 0.10 (I₂ stain). IR (neat): 1679 (ONO₂). Anal. calc. for C₉H₁₅NO₈ (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/AgNO₃/SOCl₂ was 1:6:3, and isolated by silica gel chromatography (AcOEt/Et₂O 2:11) in 95% yield. TLC(CHCl₃): R_f 0.4 (I₂ stain). IR (neat): 1679 (ONO₂). Anal. calc. for C₉H₁₃N₃O₁₂ (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 (CHCl₃) 0.3. IR (neat): 1677 (ONO₂). Anal. calc. for C₈H₁₃NO₇ (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 (CHCl₃) 0.60. IR (neat): 1678 (ONO₂). Anal. calc. for C₈H₁₂N₂O₉ (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), AgNO₃ (0.85 g, 5 mmol) was added followed by dropwise addition of SOCl₂ (0.9 g, 8 mmol). The mixture was stirred for 3 h at 25°. The solution was then filtered into H₂O (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 N⁶-benzoyl-5'-O-nitroadenosine, N⁴-benzoyl-5'-O-nitrocytidine, and N²-benzoyl-5'-O-nitroguanosine see Table 4. IR of **12a-d**: 1690s (ONO₂).

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 AgNO₃ and 2.8 mmol of SOCl₂ 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, N⁶-benzoyl-3',5'-di-O-nitroadenosine, N⁴-benzoyl-3',5'-di-O-nitrocytidine, and N²-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, N⁶-benzoyl-2',5'-di-O-nitroadenosine, N⁴-benzoyl-2',5'-di-O-nitrocytidine, and N²-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, ¹H-NMR, and MS (CI). Representative procedure: To a suspension of AgNO₃ (1.1 mmol) in THF (20 ml), CF₃SO₂Cl (1.0 mmol) was added. After 8 min, a THF solution of 1 mmol of diethyl malonate and 1 mmol of KO^tBu was added dropwise (exothermic reaction). After 3 h, Et₂O was added, the solution filtered, the filtrate washed with H₂O, dried over MgSO₄, and evaporated. The product was purified by column chromatography on silica gel (CH₂Cl₂): 40% yield of **15**.

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

Ethyl acetoacetate, 2,4-pentanedione, and dibenzyl malonnate 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 (AgNO₂ instead of AgNO₃), 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, AgNO₂ (4 mmol) was added. After dropwise addition of SOCl₂ (4 mmol) in dry THF (1 ml), the mixture was stirred for 24 h at 25°. After filtration into H₂O (20 ml), the solution was extracted with Et₂O, dried and evaporated. Chromatography on silica gel (CH₂Cl₂) 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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