Regioselectivity in Methylation and Phenylation of the Zwitterionic Pyrido[2,1-*f*]-*as*-triazinium-1- and 3-olates and thiolates [1]

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Substituted derivatives of the title ring system have been synthesized and the regioselectivity in methylation and phenylation of the zwitterionic pyrido[2,1-*f*]-*as*-triazinium 1- and 3-olates **4a-g** and **10** and thiolates **7a,b** and **12** has been studied by nmr techniques. Depending on the soft or hard nature of the used reagent (methyl iodide, trimethyloxonium hexafluorophosphate or diphenyliodonium tetrafluoroborate), the reaction yielded NMe **5** and/or OMe **6**, **11a** and NPh **14** or OPh **11b** products in the case of olates; while thiolates gave NMe **8** and/or SMe **9**, **13a** and SPh **13b**, **15** compounds. Mechanistic suggestions are given to rationalize the observed phenomena.

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Introduction and Synthesis.

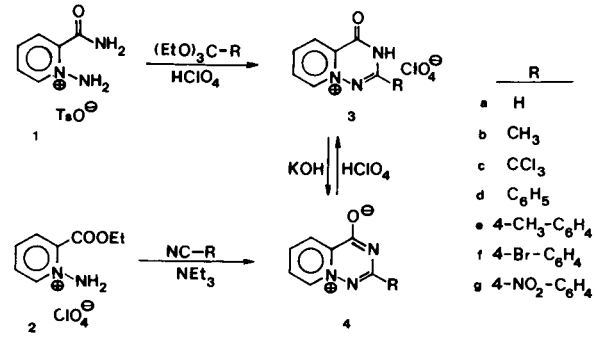
In an earlier paper [2] we reported a convenient novel synthesis of pyrido[2,1-*f*]-*as*-triazinium-1- and -3-olates. A remarkable regioselectivity has been found upon methylating these zwitterions: the reaction of 1-olates with soft methyl iodide resulted in the formation of the 2-NMe product only, with hard trimethyloxonium salt, however, it afforded the mixture of 2-NMe *and* 1-OMe derivatives. Finally, methylation of 3-olates led only to OMe products, regardless of the nature of the reagent.

In the present work we wish to provide further experimental and theoretical evidence for the nature and rationalization of the regioselectivity affording two different kinds (NMe and OMe) of products. For this reason 3-substituted 1-olates **4a-f** and -thiolates **6a,b** with different (electronic and steric) substituent effects have been synthesized.

We now describe a new route for the synthesis of unsubstituted pyrido[2,1-*f*]-*as*-triazin-5-ium-1-olate (**4a**): the reaction of picolinic acid amide *N*-aminium tosylate (**1**) with orthoformic acid ethyl ester in acetonitrile (80°) and with addition of perchloric acid gave a well-defined crystalline salt **3a** in about 70% yield (Scheme 1). In the presence of base, this salt could be easily converted into the zwitterion **4a**. In this way it is possible to avoid the formation of the dangerous hydrogen cyanide which was a by-product of our earlier method [2] (**2** + formamide + phosphoryl chloride). The same procedure could be adapted to the preparation of 3-methylpyrido[2,1-*f*]-*as*-triazin-5-ium-1-olate (**4b**) when orthoacetic (instead of formic) acid triethyl ester was used as the reagent.

Our earlier synthesis [2] of 3-phenyl-1-olate - without significant alteration - proved to be employable to obtain differently substituted 3-aryl-1-olates **4e,f,g**: in 40-70% yield. These zwitterions have been converted with perchloric acid to the corresponding 3-aryl-1(2*H*)-oxopyrido-[2,1-*f*]-*as*-triazinium perchlorates **5e,f,g** in excellent yield

Scheme 1



(Table II).

Use of trichloroacetonitrile instead of aryl cyanide gave 3-trichloromethylpyrido[2,1-*f*]-*as*-triazin-5-ium-1-olate (**4c**) and it could readily be transferred to the corresponding perchlorate **3c**.

The synthesis of 1-thiolates **7a,b** has been performed through the exchange of the O to an S atom with the application of the pentasulfide technique (pyridine, 100°, 1 hour). By this method Ning *et al.* [3] succeeded in O → S exchange in some fused zwitterions.

Thus, pyrido[2,1-*f*]-*as*-triazin-5-ium-1-thiolate (**7a**) has been produced in good yield from **4a** olate and 3-phenylpyrido[2,1-*f*]-*as*-triazin-5-ium-1-thiolate (**7b**) from compound **4d** (Scheme 2). Similarly, 1-phenylpyrido[2,1-*f*]-*as*-triazin-5-ium-3-thiolate (**12**) could be prepared from the earlier described [2] 3-olate compound **10**.

The methylation of 1-olates **4a-g** and of 1-thiolates **7a,b** with soft and hard reagents has been carried out under standard conditions, as follows: i) The substrate (1 mmole) in the mixture of acetonitrile (5 ml) and DMF (5 ml) was refluxed with methyl iodide (10 mmoles) for 1 hour. The crystals precipitated after mixing with ether have been investigated by nmr in trifluoroacetic acid + DMSO-d_6. ii) The suspension of substrate (1 mmole) and trimethyloxonium hexafluorophosphate (1 mmole) in dry dichloro-

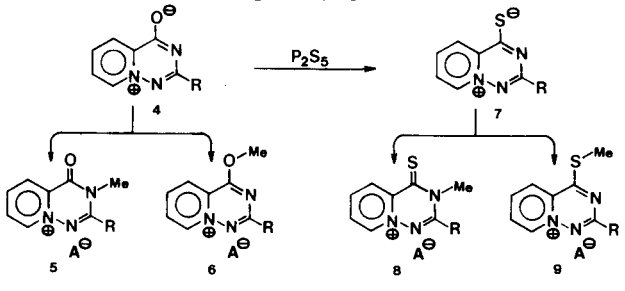
methane (10 ml) was stirred at room temperature for 24 hours. After addition of ether the precipitate has been investigated by nmr in trifluoroacetic acid-DMSO-d_6 solution.

The determination of the product ratios from the crude products was carried out by comparing the integral values of NMe (*ca.* δ 3.6) and OMe (*ca.* δ 4.6) singlets in the case of olates, and of SMe (*ca.* δ 3.0) and NMe (*ca.* δ 3.9) singlets, respectively, in the case of thiolates.

Results and Discussion.

The product ratios from the *methylation* of 1-olates and 1-thiolates are summarized in Table I.

Scheme 2



When the methylation was carried out with the *soft methyl iodide*, only a single type of product was formed, generally in good or excellent yields (78-99%). In the case of 1-olates **4a-g**, 2-methyl-1(2*H*)-oxopyrido[2,1-*f*]-*as*-triazinium iodides **5a-g**, *i.e.* the 2-NMe derivatives, were produced regardless of the nature of the R-substituent at the adjacent 3-C atom; the O atom in the exo-position is not methylated. The result was significantly different in the case of 1-thiolates **7a,b** where the only products of the methylation are 1-methylthiopyrido[2,1-*f*]-*as*-triazinium iodides **9a,b**, *i.e.* only the S atom in the exo-position has been methylated. It seems likely that the position of methylation with methyl iodide is determined by the heteroatom of smaller electronegativity (N *vs.* O and S *vs.* N) *i.e.* the easier availability of the lone electron pair of the atom in question.

When the methylation occurs with the *hard, positively charged trimethyloxonium salt*, it is expected that the greater negative charge of the heteroatom of greater electronegativity of the zwitterion will play a role.

The reaction of the unsubstituted 1-olate **4a** and of the 3-methyl derivative **4b** with the hard reagent afforded still exclusively NMe products **5a,b**. In the case of 3-trichloromethyl derivative **4c** the methylation yielded, however, two compounds, *viz.* the mixture of NMe **5c** and OMe **6c** derivatives with predominance of the latter (29:71). The trichloromethyl group in the zwitterion **4c** retards the attack of the reagent at N-2 not only by its steric demand but also with its electron-withdrawing property. This statement is supported by the determination of product components in the reaction mixture of the methylation of 3-aryl-1-olates **4d-g**: the different 3-aryl groups eclipse the N-2 atom nearly to the same degree, however, the relative amount of NMe (in favour of OMe) product decreases with greater electron-withdrawing aryl group gradually from 49% (R = C_6H_5) to 28% (R = *p*-NO_2-C_6H_4) (Table I).

The methylation of 1-thiolates **7a,b** with the hard reagent gave no more exclusively an SMe derivative **9a**: also NMe compound **8a** was formed in 20% if the unsubstituted 1-thiolate **7a** was the starting material, in accordance with the fact that the centre of the negative charge is the N atom, having a greater electronegativity than the S atom. The reaction of 3-phenyl-1-thiolate (**7b**) yielded, besides SMe compound **9b**, only 1% of NMe product **8b**, again in accordance with the greater shielding of N-2 atom and the greater steric demand of the hard reagent.

For the investigation of regioselectivity in methylation of 3-olates and 3-thiolates, 1-phenylpyrido[2,1-*f*]-*as*-triazin-

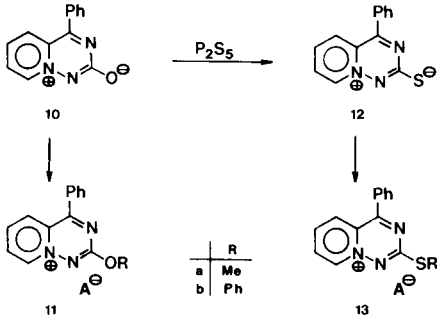
Table I

Methylation of Zwitterionic 1-Olates **4** and 1-Thiolates **7**

		With MeI			With $Me_3O^+PF_6^-$			
Compound	R	Product A = I	MP (°C)	Yield (%)	Products A = PF_6	Ratio	MP (°C)	Yield (%)
4a	H	**5a**	273-275	99	**5a**	100	174-176	92
4b	CH_3	**5b**	259-261	83	**5b**	100	238-240	87
4c	CCl_3	**5c**	164-168	78	**5c + 6c**	29:71	213-217	84
4d	C_6H_5	**5d**	288-290	88	**5d + 6d**	49:51	278-286	99
4e	4-Me-C_6H_4	**5e**	280-284	84	**5e + 6e**	47:53	272-276	95
4f	4-Br-C_6H_4	**5f**	283-287	88	**5f + 6f**	38:62	275-283	95
4g	4-NO_2-C_6H_4	**5g**	278-280	83	**5g + 6g**	28:72	267-277	69
7a	H	**9a**	241-242	90	**8a + 9a**	20:80	233-237	94
7b	C_6H_5	**9b**	241-244	98	**8b + 9b**	1:99	221-224	92

ium-3-olate (**10**) and 3-thiolate (**12**) have been used as model compounds. It turned out that both with soft and hard reagents only one product was formed, *viz.* the 3-OMe **11a** and 3-SMe **13a** derivatives, respectively. This experimental fact is in accordance with our earlier supposition [2]: *i.e.*, formation of 2-NMe derivative in the reaction of 3-olates and 3-thiolates would be concomitant with the loss of aromatic stability even in the fused pyridine moiety and, would therefore, not be probable.

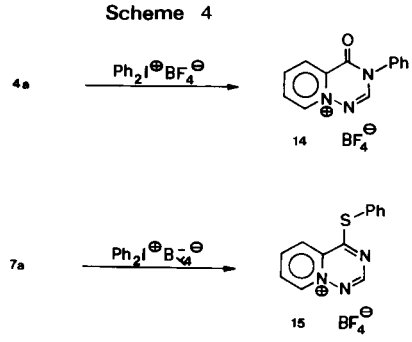
Scheme 3



The *phenylation* of 1- and 3-olates and thiolates has been carried out with the use of diphenyliodonium fluoroborate. This compound proved to be an excellent *N*-arylating agent for a number of neutral [4] and anionic [5,6] compounds. More recently [7] phenylation of tetrazolopyridine and its benzenologues *i.e.* bridgehead nitrogen containing fused heteroaromatics have been performed successfully with this reagent.

The phenylation of zwitterions **4**, **7**, **10**, and **12** (1 mole) has been carried out with diphenyliodonium tetrafluoroborate (2 moles), refluxing in phenyl cyanide solution for 40 minutes. In all cases only a single crystalline compound has been obtained in moderate (35-72%) yield.

Scheme 4



The phenylation of the unsubstituted pyrido[2,1-*f*]-*as*-triazin-5-ium-1-olate (**4a**) afforded 2-phenyl-1(2*H*)-oxopyrido[2,1-*f*]-*as*-triazinium fluoroborate (**14**), while the appropriate 1-thiolate **7a** led to 1-phenylthiopyrido[2,1-*f*]-*as*-triazinium fluoroborate (**15**) (Scheme 4). The structures of **14** and **15** are supported by ir and nmr spectra: *e.g.* the appearance of the carbonyl band shows that **14** is an NPh product; according to the ^{1}H-nmr spectrum, both rings of the fused system of **15** are aromatic, which is possible only in the case of the SPh structure. It is worth noting that the phenylation of 3-phenylpyrido[2,1-*f*]-*as*-triazin-5-ium-1-olate (**4d**) did not take place and the starting material could be recovered in about 70% yield. In contrast, the phenylation of the corresponding 1-thiolate (**7b**) led to 1-phenylthio-3-phenylpyrido[2,1-*f*]-*as*-triazinium fluoroborate (**9b**; SPh instead of SMe). In other words, *O*-phenylation did not, whereas *S*-phenylation did occur if the point of attack at N-2 was hindered by the 3-phenyl group.

The phenylation of 3-olate **10** and 3-thiolate **12** - similarly to the methylation - led to the appropriate 3-phenoxy **11b** and 3-thiophenoxy **13b** derivatives (Scheme 3). The structural assignments of these compounds were supported again by nmr and ir spectra; both rings of both derivatives proved to be of aromatic character.

Interpretation and Conclusion.

Considering the data of earlier publications [8,9], in our previous paper [2] we have already emphasized that the points of attack in the substrate molecule are controlled during the methylation - in addition to the nature of the reagent - by the availability of the lone pair of electrones of the hetero atoms of zwitterions which, in turn, depends mostly (i) on the electronegativity of the atom in question, (ii) on its partial negative charge, and (iii) on the steric hindrance at this site.

On the basis of the values of electronegativity of the hetero atoms, the expected order of the preferred point of attack is S > N-2 > O >> N-4. The availability of the lone pair at N-4 is strongly decreased by influence of the positive charge of neighbouring bridgehead nitrogen atom. The greater partial negative charge of the hetero atoms of greater electronegativity plays a role in the quaternization when (i) the methylating agent is positively charged, and (ii) the hetero atom of smaller electronegativity is hindered sterically.

The quaternization of the heteroaromatic N-atom with methyl iodide is generally regarded [9] as an S_N2 process. It is reasonable to suppose the same mechanism for this reaction when the trimethyloxonium salt is the reagent. For the phenylation with diphenyliodonium fluoroborate an Ar-S_N2 mechanism is proposed by McKillop [10].

As the lone pair of electrons of the heteroaromatic nitrogen atom is oriented outwards in the plane of the aromatic system, the successful collision of the reagent with the substrate could occur only when the approach of the reagent does take place more or less in the plane of the heteroaromatic molecule. So, it is easy to understand the great steric sensitivity of the quaternization reaction depending on both substrate and reagent. The reagents used in this study show - as a consequence of their struc-

ture - the following order of increasing steric demand:

$$Me\text{-}I < Me\text{-}\overset{+}{O}Me_2 < Ph\text{-}\overset{+}{I}Ph$$

On the basis of these statements it is possible to rationalize the different kinds and degrees of regioselectivity in the methylation reactions of 1-olates **4** and thiolates **7** both with methyl iodide and with trimethyloxonium salt (Table I).

While the quaternization of the unsubstituted 1-olate **4a** even with the charged reagents afforded only 2-NMe **5a** or 2-NPh **14** derivatives, respectively, a steric obstruction of the lone pair electron of N-2 directed the charged reagents at 1-O atom. Thus, reaction of 3-phenyl-1-olate **4d** with trimethyl oxonium salt led to 2-NMe **5d** and 1-OMe **6d** in a ratio of 49:51, with diphenyl iodonium fluoroborate, however, no reaction occurred and the starting material **4d** was recovered. The lack of the formation of 1-OPh derivative is possibly caused by the steric hindrance of the peri H-9 atom. A similar phenomenon has been reported [10] in phenylation of the anion of 4-hydroxybenzo-*v*-triazine that gives rise exclusively to 2-NPh derivative instead of the OPh isomer. Likewise a great steric sensitivity of diphenyl iodonium fluoroborate has been shown [7] recently in the phenylation of fused tetrazoles. The experimental finding that phenylation of 3-phenyl-1-thiolate **7b** takes place smoothly and is not hindered by the peri H-atom may well be accounted not only for the smaller electronegativity but also for the relatively great size of the S-atom compared to the oxygen.

The fact that reaction of 3-olate **10** and 3-thiolate **12** with alkylating and arylating reagents results in only *O*-and *S*-substituted products is, however, obviously due to the structural feature that these products conserve the heteroaromatic π-sextet of the pyridine moiety. We have shown earlier [1] that the separated π-sextets in fused heteroaromatics often play a role in orientation of regioselective reactions. From the above cases we can conclude that, in this respect, conservation of π-sextet of rather the

Table II

Characteristics for Compounds **3a-g** and **4a-g**

Compound	R	Mp (°C)	Yield (%)	Formula	Mw	Analysis (%) Calcd./Found C	H	N
3a	H [a]	242-244	65	$C_7H_6ClN_3O_4$	247.60	33.96 34.04	2.44 2.25	16.97 16.78
3b	CH_3	234-236	74	$C_8H_8ClN_3O_5$	261.62	36.73 36.87	3.08 3.17	16.06 16.02
3c	CCl_3	317-318	81	$C_8H_5Cl_4N_3O_5$	364.98	26.33 26.51	1.38 1.44	11.51 11.68
3d	C_6H_5 [a]	281-283	44	$C_{13}H_{10}ClN_3O_5$	323.69	48.24 48.62	3.11 3.15	12.98 12.90
3e	4-Me-C_6H_4	213-214	84	$C_{14}H_{12}ClN_3O_5$	337.73	49.80 50.01	3.58 3.52	12.44 12.45
3f	4-Br-C_6H_4	325	88	$C_{13}H_9BrClN_3O_5$	402.61	38.78 38.65	2.25 2.12	10.44 10.58
3g	4-NO_2-C_6H_4	293-294	86	$C_{13}H_9ClN_4O_7$	368.70	42.34 42.51	2.46 2.38	15.20 15.14
4a	H [a]	237-238	71	$C_7H_5N_3O$	147.13	57.14 56.86	3.43 3.58	28.56 28.32
4b	CH_3	189-191	73	$C_8H_7N_3O$	161.17	59.62 59.62	4.38 4.32	26.07 25.92
4c	CCl_3	243-244	49	$C_8H_4Cl_3N_3O$	264.52	36.33 36.18	1.52 1.63	15.89 15.81
4d	C_6H_5 [a]	224-227	59	$C_{13}H_9N_3O$	223.22	69.94 69.58	4.06 4.15	18.82 19.03
4e	4-Me-C_6H_4	272-274	39	$C_{14}H_{11}N_3O$	237.27	70.87 70.60	4.67 4.54	17.17 17.28
4f	4-Br-C_6H_4	283-284	43	$C_{13}H_8BrN_3O$	302.15	51.68 51.52	2.67 2.63	13.91 13.87
4g	4-$NO_2C_6H_4$	271-272	71	$C_{13}H_8N_4O_3$	268.24	58.21 58.13	3.01 3.22	20.89 20.71

[a] Obtained earlier by another method (ref [2]).

pyridine than the *as*-triazine ring seems to be more important.

Further studies on regioselectivity of alkylation and arylation of bridgehead nitrogen containing heteroaromatics are in progress.

EXPERIMENTAL

Melting points were determined on a Büchi capillary melting point apparatus and are uncorrected. The ir spectra were recorded with a Specord 75 IR apparatus and nmr spectra with a Varian EM 360-A spectrometer (TMS as internal standard).

3-Amino-2-carbamoylpyridinium Tosylate (**1**).

To a stirred solution of pyridine-2-carboxamide (3.66 g, 30 mmoles) in dichloromethane (30 ml), *O*-(*p*-toluenesulfonyl)hydroxylamine (5.62 g, 30 mmoles) in dichloromethane (120 ml) was added at room temperature. The mixture was stirred for 3 hours at 25°, the crystals were filtered and recrystallized from ethanol (20 ml) to give colourless needles (8.1 g, 87%), mp 135-137°; ir (potassium bromide): 3250, 3180, 3090, 3050, 2820, 1690, 1200 cm^{-1}; ^1H-nmr (trifluoroacetic acid): δ 9.00 (d, 1H, H-6), 8.45 (m, 2H, H-3,4), 8.10 (m, 1H, H-5), 7.90 (d, 2H, H-2',6'), 7.40 (d, 2H, H-3',5'), 2.45 (s, 3H, CH_3).

Anal. Calcd. for $C_{13}H_{15}N_3O_4S$: C, 50.45; H, 4.89; N, 13.58. Found: C, 50.22; H, 4.73; N, 13.62.

1(2*H*)-Oxopyrido[2,1-*f*]-*as*-triazinium Perchlorates **3a-g**.

A: A solution of **1** (3.09 g, 10 mmoles) and ortho ester (30 mmoles) in acetonitrile (15 ml) were refluxed for 3 hours. Perchloric acid (2 ml, 70% solution) and ethyl acetate (15 ml) were added. The mixture was cooled, the crystals were filtered and recrystallized from ethanol-water to give **3a,b** and **d** (Table II and III).

B: To a suspension of **4c-g** (1 mmole) in acetonitrile (5 ml) and water (0.5 ml), perchloric acid (0.2 ml, 70% solution) was added and warmed up to boiling. The solution was mixed with ethyl acetate (5 ml) and cooled. The crystals were filtered to give analytically pure **3c-g** (Table II and III).

3-Methylpyrido[2,1-*f*]-*as*-triazinium-1-olate (**4b**).

A suspension of **3b** (1.3 g, 5 mmoles) in ethanol (15 ml) was stirred at room temperature with a solution of potassium hydroxide (0.28 g, 5 mmoles) in water (1 ml) for 10 minutes. The solution was mixed with chloroform (25 ml), filtered and evaporated. The residue was recrystallized from acetonitrile to give white flakes (0.59 g, 73%), mp 188-191° (Table II and III).

3-Substituted pyrido[2,1-*f*]-*as*-triazinium-1-olates **4c-g**.

General Procedure.

Into a stirred solution of **2** (5.33 g, 20 mmoles) in 0.2 mole of aryl or alkyl cyanide [a], triethylamine (2.02 g, 2.68 ml, 20 mmoles) was dropped at 100° (30 minutes). The mixture was stirred for 10 minutes at 100°, ether (80 ml) was added to the hot solution, and the resulting solid was collected by filtration, washed with water and ethyl acetate, and recrystallized from dimethylformamide to give **4c-g**.

[a] In the case of 4-nitrophenyl derivative **4g** 0.1 mole of 4-nitrobenzonitrile and 30 ml of dimethylformamide were used (Table II and III).

Reaction of 1-Olates **4b-g** with Methyl Iodide. 2-Methyl-1(2*H*)-oxopyrido-[2,1-*f*]-*as*-triazinium Iodide Salts **5b-g**.

A suspension of 1-olate **4b-g** (1 mmole) in dimethylformamide (5 ml) and acetonitrile (5 ml) was refluxed with methyl iodide [a] (1.4 g, 0.6 ml, 10 mmoles) for 1 hour [b]. The mixture was cooled, ether (20 ml) was added to the suspension, the resulting crystals were filtered and recrystallized from aqueous acetonitrile to give **5b-g** (A = I) (Table I and IV).

[a] In the case of **4c**, the reaction gave a complex mixture, therefore it was carried out in acetonitrile (10 ml) with methyl tosylate (1 g, 5 mmoles) and was refluxed for 3 days. [b] In the case of **4g** it was refluxed for 10 hours.

Table III

Spectral Data for Compounds **3b-g** and **4b-g**

Compound	IR (potassium bromide) (cm^{-1})	^1H-NMR (δ ppm) [b]
3b	3100-2700, 1730, 1630, 1510, 1480, 1450, 1100	9.24 (d, 1H, H-6), 9.0 (m, 2H, H-8,9), 8.6 (m, 1H, H-7), 2.75 (s, 3H, CH_3)
3c	3200-2800, 1740, 1640, 1480, 1440, 1100	9.34 (d, 1H, H-6), 8.89 (m, 2H, H-8,9), 8.50 (m, 1H, H-7)
3d [a]		
3e	3200-2900, 1730, 1605, 1550, 1490, 1470, 1440, 1100	9.38 (d, 1H, H-6), 9.06 (m, 2H, H-8,9), 8.60 (m, 1H, H-7), 8.26 (d, 2H, H-2',6'), 7.57 (d, 2H, H-3',5'), 2.56 (s, 3H, CH_3)
3f	3250-2900, 1720, 1610, 1590, 1550, 1460, 1100	9.36 (d, 1H, H-6), 9.03 (m, 2H, H-8,9), 8.60 (m, 1H, H-7), 8.14 (d, 2H, H-3',5'), 7.90 (d, 2H, H-2', 6')
3g	3150-2800, 1725, 1620, 1590, 1520, 1470, 1440,	9.48 (d, 1H, H-6), 9.12 (m, 2H, H-8,9), 8.75 (m, 1H, H-7), 8.6 (m, 4H, 4-NO_2-Ph)
4b	3060, 3030, 2910, 1640, 1600, 1560, 1500, 1450, 1410	9.01 (d, 1H, H-6), 8.7-8.0 (m, 3H, H-7,8,9), 2.37 (s, 3H, CH_3)
4c	3100, 3060, 3050, 1640, 1605, 1560, 1510, 1460, 1430	9.23 (d, 1H, H-6), 8.6 (m, 2H, H-8,9), 8.2 (m, 1H, H-7)
4d [a]		
4e	3110, 3060, 3020, 1640, 1600, 1570, 1495, 1430, 1400	9.14 (d, 1H, H-6), 8.59 (d, 1H, H-9), 8.41 (m, 1H, H-8), 8.26 (m, 2H, H-2',6'), 8.18 (m, 1H, H-7), 7.38 (m, 2H, H-3',5'), 2.45 (s, 3H, CH_3)
4f	3110, 3060, 3020, 1640, 1600, 1570, 1495, 1430, 1400	9.13 (d, 1H, H-6), 8.61 (d, 1H, H-9), 8.43 (m, 1H, H-8), 8.30 (m, 2H, H-2',6'), 8.18 (m, 1H, H-7), 7.76 (m, 2H, H-3',5')
4g	3100, 3060, 1645, 1605, 1560, 1510, 1430, 1410	9.21 (d, 1H, H-6), 8.7-8.3 (m, 6H, H-8,9 and 4-NO_2-Ph), 8.22 (m, 1H, H-7)

[a] For characteristics see ref [2]. [b] Measured in trifluoroacetic acid, **3b,e,f,g**, DMSO-d_6,**4b,c,e,f,g** and DMSO-d_6 and trifluoroacetic acid, **3c**.

Reaction of 1-Olates **4b-g** with Trimethyloxonium Hexafluorophosphate.

General Procedure.

A suspension of 1-olate **4b-g** (1 mmole) and trimethyloxonium hexafluorophosphate (0.21 g, 1 mmole) in dry dichloromethane (10 ml) was stirred at room temperature for 24 hours, then ether (10 ml) was added to the mixture and the resulting suspension was filtered to give a mixture of crystals which contained 3-substituted 2-methyl-1(2*H*)-oxopyrido[2,1-*f*]-*as*-triazinium hexafluorophosphate (**5**) and 3-substituted 1-methoxypyrido-[2,1-*f*]-*as*-triazinium hexafluorophosphate **6** in different ratios. The product was investigated without recrystallization.

Table IV

Characteristics of Compounds **5b-g** (A = I)

Compound	Analyses (%) Calcd./Found	IR (cm^{-1})	^{1}H-NMR (δ ppm) [d]
5b [a]	$C_9H_{10}IN_3O$ C 35.66 H 3.33 N 13.86 C 35.32 H 3.49 N 13.61	3100, 3060, 3040, 2930, 2890, 1695, 1620, 1560, 1480, 1460	9.20 (d, 1H, H-6), 9.1-8.3 (m, 3H, H-7,8,9), 3.85 (s, 3H, N-CH_3), 2.85 (s, 3H, CH_3)
5c [b]	$C_{16}H_{14}Cl_3N_3O_4S$ C 42.63 H 3.13 N 9.32 C 42.84 H 3.26 N 9.18	3060, 3020, 2980, 1710, 1610, 1560, 1480, 1440, 1190	9.39 (d, 1H, H-6), 9.10 (m, 2H, H-8,9), 8.74 (m, 1H, H-7), 7.9-7.4 (m, 4H, tosyl), 4.22 (s, 3H, N-CH_3), 2.48 (s, 3H, CH_3)
5d [c]			
5e	$C_{15}H_{14}IN_3O$ C 47.51 H 3.72 N 11.08 C 47.63 H 3.85 N 10.87	3100, 3070, 3030, 2920, 1710, 1620, 1605, 1560, 1480, 1440	9.22 (d, 1H, H-6), 9.1-8.0 (m, 3H, H-7,8,9), 7.55 (m, 4H, 4-Me-Ph), 3.72 (s, 3H, N-CH_3), 2.53 (s, 3H, CH_3)
5f	$C_{14}H_{11}BrIN_3O$ C 37.86 H 2.50 N 9.46 C 37.82 H 2.38 N 9.35	3100, 3070, 3040, 2920, 2850, 1705, 1600, 1550, 1480, 1420	9.28 (d, 1H, H-6), 9.2-8.3 (m, 3H, H-7,8,9), 7.9 (m, 4H, 4-Br-Ph), 3.71 (s, 3H, N-CH_3)
5g	$C_{14}H_{11}IN_4O_3$ C 40.99 H 2.70 N 13.66 C 41.18 H 2.65 N 13.71	3100, 3060, 3040, 2910, 2850, 1710, 1615, 1590, 1565, 1475	9.24 (d, 1H, H-6), 9.0 (m, 2H, H-8,9), 8.60 (m, 3H, H-7 and 3',5'), 8.05 (m, 2H, H-2',6'), 3.65 (s, 3H, N-CH_3)

[a] This compound was converted to perchlorate salt **5b** (A = ClO_4) and was found to be identical with the 2,3-dimethyl-1-oxo derivative, synthesized earlier (ref [2]). [b] This compound is a tosylate salt. [c] This compound was synthesized earlier (ref [2]). [d] Measured in trifluoroacetic acid.

Compound **5b** (A = PF_6) had the following spectral properties; ir (potassium bromide): 3100, 3070, 3030, 2880, 1710, 1620, 1570, 1490, 1450, 1420, 840, 550, cm^{-1}; ^{1}H-nmr (trifluoroacetic acid-DMSO-d_6): δ 9.46 (d, 1H, H-6), 9.09 (m, 2H, H-8,9), 8.66 (m, 1H, H-7), 3.68 (s, 3H, N-CH_3), 2.75 (s, 3H, CH_3).

Anal. Calcd. for $C_9H_{10}F_6N_3OP$: C, 33.68; H, 3.14; N, 13.08. Found: C, 33.45; H, 3.12; N, 12.81.

The compound was converted to perchlorate salt (**5b**, A = ClO_4) and was found to be identical with the 2,3-dimethyl-1-oxo derivative synthesized earlier (ref [2]).

Compounds **5c** and **6c** had the following spectral properties; ir (potassium bromide): 3120, 3080, 3050, 2950, 1720, 1600, 1580, 1530, 1480, 1455, 840, 550 cm^{-1}; ^{1}H-nmr (trifluoroacetic acid): δ 9.58 and 9.31 (two doublets: 1H, H-6, ratio: 7:3), 9.0 (m, 2H, H-8,9), 8.66 (m, 1H, H-7), 4.64 and 4.15 (two singlets: 3H, O-CH_3 and N-CH_3, ratio: 71:29).

Anal. Calcd. for $C_9H_7Cl_3F_6N_3OP$: C, 25.46; H, 1.66, N, 9.90. Found: C, 25.71; H, 1.84; N, 9.72.

Compounds **5e** and **6e** had the following spectral properties; ir (potassium bromide): 3120, 3100, 3030, 2950, 1710, 1605, 1590, 1580, 1460, 1420, 840, 550 cm^{-1}; ^{1}H-nmr (trifluoroacetic acid): δ 9.65 and 9.45 (two doublets, 1H, H-6, ratio: 1:1), 8.90 (m, 2H, H-8,9), 8.7-7.3 (m, 5H, H-7 and 4-Me-Ph), 4.54 and 3.55 (two singlets, 3H, O-CH_3 and N-CH_3, ratio: 53:47), 2.47 (s, 3H, CH_3).

Anal. Calcd. for $C_{15}H_{14}F_6N_3OP$: C, 45.35; H, 3.55; N, 10.58. Found: C, 45.18; H, 3.64; N, 10.43.

Compounds **5f** and **6f** had the following spectral properties; ir (potassium bromide): 3105, 3080, 3050, 2910, 1710, 1610, 1580, 1555, 1510, 1460, 840, 550 cm^{-1}; ^{1}H-nmr (trifluoroacetic acid): δ 9.66 and 9.45 (two doublets, 1-H, H-6, ratio: 4:3), 8.92 (m, 2H, H-8,9), 8.8-8.3 (m, 3H, H-7 and 4-Br-Ph), 7.78 (m, 2H, 4-Br-Ph), 4.56 and 3.54 (two singlets, 3H, O-CH_3 and N-CH_3, ratio: 62:38).

Anal. Calcd. for $C_{14}H_{11}BrF_6N_3OP$: C, 36.38; H, 2.40; N, 9.09. Found: C, 36.45; H, 2.68; N, 8.87.

Compounds **5g** and **6g** had the following spectral properties; ir (potassium bromide): 3110, 3080, 2950, 1710, 1605, 1580, 1520, 1460, 840, 550 cm^{-1}; ^{1}H-nmr (DMSO-d_6): δ 9.63 and 9.30 (two doublets, 1H, H-6, ratio: 7:3), 9.1-8.1 (m, 7H, H-7,8,9 and 4-NO_2-Ph), 4.66 and 3.64 (two singlets, 3H, O-CH_3 and N-CH_3, ratio: 72:28).

Anal. Calcd. for $C_{14}H_{11}F_6N_4O_3P$: C, 39.26; H, 2.59; N, 13.08. Found: C, 39.21; H, 2.72; N, 12.84.

Pyrido[2,1-*f*]-*as*-triazinium-1-thiolates **7a-c**.

A suspension of **4a**, **4d** and **4g** (10 mmoles) and phosphorus pentasulfide (3.33 g, 15 mmoles) in dry pyridine (70 ml) was warmed at 100° for 1 hour (in the case of **4g** was warmed for 3 hours). The hot mixture was poured onto ice-water (200 ml), the crystals were fitered, washed with water and recrystallized from dimethylformamide to give yellow-brown prisms **7a-c**.

Compound **7a** had the following physical and spectral properties; 73%, mp 241-243°; ir (potassium bromide): 3120, 3090, 3070, 3050, 3030, 1610, 1555, 1410, 1440 cm^{-1}; ^{1}H-nmr (DMSO-d_6): δ 9.28 (d, 1H, H-9), 9.17 (d, 1H, H-6), 8.73 (m, 2H, H-3,8), 8.45 (m, 1H, H-7).

Anal. Calcd. for $C_7H_5N_3S$: C, 51.52; H, 3.07; S, 19.65. Found: C, 51.31; H, 3.29; S, 19.58.

Compound **7b** had the following physical and spectral properties; 61%, mp 211-213°; ir (potassium bromide): 3060, 3030, 1610, 1550, 1490, 1440, 1420 cm^{-1}; ^{1}H-nmr (DMSO-d_6): δ 9.23 (d, 1H, H-9), 9.10 (d, 1H, H-6), 8.6-7.8 (m, 4H, H-7,8 and 2',6'), 7.6 (m, 3H, H-3',4',5').

Anal. Calcd. for $C_{13}H_9N_3S$: C, 62.25; H, 3.79; S, 13.40. Found: C, 62.37; H, 3.52; S, 13.28.

Compound **7c** had the following physical and spectral properties; 67%, mp 259-261°; ir (potassium bromide): 3095, 3070, 3040, 1610, 1600, 1550, 1510, 1440, 1400 cm^{-1}; ^{1}H-nmr (DMSO-d_6): δ 9.22 (d, 1H, H-9), 9.16 (d, 1H, H-6), 8.7-8.4 (m, 5H, H-8 and 4-NO_2-Ph), 8.25 (m, 1H, H-7).

Anal. Calcd. for $C_{13}H_8N_4O_2S$: C, 54.92; H, 2.84; S, 11.28. Found: C, 54.63; H, 2.98; S, 11.28.

Reaction of 1-Thiolates **7a,b** with Methyl Iodide.

General Procedure.

A suspension of 1-thiolate **7a,b** (1 mmole) in dimethylformamide (5 ml) was stirred at room temperature with methyl iodide (1.4 g, 0.6 ml, 10 mmoles) for 6 hours. After addition of ether (15 ml), the suspension was filtered and recrystallized from aqueous acetonitrile to give 1-methylthiopyrido[2,1-*f*]-*as*-triazinium iodide salts **9a,b**, (A = I) (Table I).

Compound **9a** had the following spectral properties; ir (potassium bromide): 3100, 3070, 3055, 3030, 3000, 2950, 2920, 1610, 1580, 1545, 1470, 1450 cm^{-1}; ^{1}H-nmr (trifluoroacetic acid + DMSO-d_6): δ 9.44 (d, 1H, H-6), 9.18 (s, 1H, H-3), 8.86 (m, 2H, H-8,9), 8.57 (m, 1H, H-7), 2.93 (s, 3H, S-CH_3). In the spectrum of the crude product a singlet could be found at 3.95 ppm (integral ratio to the singlet at 2.93 was 1:99) which was assigned to the N-CH_3 group of 2-methyl-1(2*H*)-thionopyrido[2,1-*f*]-*as*-triazinium iodide **8a**, (A = I).

Anal. Calcd. for $C_8H_8IN_3S$: C, 31.49; H, 2.64; N, 13.77. Found: C, 31.68; H, 2.42; N, 13.55.

Compound **9b** had the following spectral properties; ir (potassium bromide): 3100, 3050, 3020, 2980, 1605, 1580, 1530, 1480, 1455; ^{1}H-nmr (perdeuterionitromethane): δ 9.62 (d, 1H, H-6), 8.95 (m, 2H, H-8,9), 8.60 (m, 3H, H-7,2',6'), 7.75 (m, 3H, H-3',4',5'), 3.11 (s, 3H, S-CH_3).

Anal. Calcd. for $C_{14}H_{12}IN_3S$: C, 44.11, H, 3.17; N, 11.02. Found: C, 44.28; H, 3.12; N, 10.91.

Reaction of 1-Thiolates **7a,b** with Trimethyloxonium Hexafluorophosphate.

General Procedure.

A suspension of 1-thiolate **7a,b** (1 mmole) and trimethyloxonium hexafluorophosphate (0.21 g, 1 mmole) was stirred in dry dichloromethane (10 ml) at room temperature for 24 hours. The suspension was mixed with ether (10 ml) and filtered to give a mixture which contained 1-methylthiopyrido[2,1-*f*]-*as*-triazinium hexafluorophosphate **9a,b**, (A = PF_6) and 2-methyl-1(2*H*)-thionopyrido[2,1-*f*]-*as*-triazinium hexafluorophosphate salts **8a,b**, (A = PF_6) in different ratios (Table I). The product was investigated without recrystallization.

Compounds **9a** (A = PF_6) and **8a** (A = PF_6) had the following spectral properties; ir (potassium bromide): 3120, 3110, 3070, 2910, 1610, 1580, 1550, 1480, 1450, 830, 550 cm^{-1}; ^{1}H-nmr (trifluoroacetic acid + DMSO-d_6): δ 9.44 (d, 1H, H-6), 9.19 (s, H-3), 8.86 (m, 2H, H-8,9), 8.57 (m, H-3,7), 3.95 and 2.93 (two singlets, 3H, N-CH_3 and S-CH_3; ratio: 20:80).

Anal. Calcd. for $C_8H_8F_6N_3PS$: C, 29.73; H, 2.49; N, 13.00. Found: C, 29.48; H, 2.62; N, 12.85.

Compound **9b** (A = PF_6) had the following spectral properties; ir (potassium bromide): 3110, 3070, 2910, 1610, 1585, 1570, 1540, 1480, 1455, 840, 550 cm^{-1}; ^{1}H-nmr (trifluoroacetic acid + DMSO-d_6): δ 9.46 (s, 1H, H-6), 9.0-8.3 (m, 5H, H-7,8,9 and 2',6') 7.70 (m, 3H, H-3',4',5'), 3.10 (s, 3H, S-CH_3). In the spectrum of the crude product a singlet with very small intensity could be found at 3.93 ppm, which was assigned to the N-CH_3 group of **8b** (A = PF_6).

Anal. Calcd. for $C_{14}H_{12}F_6N_3PS$: C, 42.11; H, 3.03; N, 10.52. Found: C, 42.33; H, 3.21; N, 10.45.

1-Phenylpyrido(2,1-*f*)-*as*-triazinium-3-thiolate (**12**).

A suspension of **10** (2.23 g, 10 mmoles) and phosphorus pentasulfide (3.33 g, 15 mmoles) in dry pyridine (100 ml) was stirred at 100° for 10 minutes. The hot mixture was poured onto ice-water (200 ml). The crystals were filtered, the mother liquor was extracted with chloroform (3 x 50 ml). The organic solution was dried on magnesium sulfate, filtered and evaporated *in vacuo*. The residue was recrystallized from a mixture of acetonitrile (50 ml) and dimethylformamide (20 ml) to give ochreyellow needles (1.0 g, 42%), mp 186-187°; ir (potassium bromide): 3050, 1590, 1560, 1470, 1440; ^{1}H-nmr (DMSO-d_6): δ 9.06 (d, 1H, H-6), 8.15 (m, 3H, H-7,8,9), 7.73 (m, 5H, Ph).

Anal. Calcd. for $C_{13}H_9N_3S$: C, 65.25; H, 3.79; S, 13.40. Found: C, 65.41; H, 3.58; S, 13.28.

3-Methylthio-1-phenylpyrido[2,1-*f*]-*as*-triazinium Iodide (**13**, R = Me, A = I).

A suspension of **12** (0.24 g, 1 mmole) in dimethylformamide (5 ml) was stirred at room temperature with methyl iodide (1.4 g, 0.6 ml, 10 mmoles) for 2 days. The suspension was mixed with ether (15 ml) and filtered to give orange crystals (0.36 g, 94%), mp 235-237°; ir (potassium bromide): 3060, 3020, 2920, 1610, 1590, 1580, 1540, 1480, 1440 cm^{-1}; ^{1}H-nmr (trifluoroacetic acid + perdeuterio nitromethane): δ 9.36 (d, 1H, H-6),

Table V

Physical, Analytical and Spectral Data of Phenylated Products

Substrate	Product	Yield (%)	MP (°C) (solvent)	IR (cm^{-1}) (Potassium bromide)	^{1}H-NMR (δ ppm) (Trifluoroacetic acid)	Analyses (%) Calcd./Found C H N
4a	**14**	35	223-226 [b]	3110, 3090, 1725, 1630, 1590, 1560, 1490, 1080	9.36 (d, 1H, H-6), 9.06 (m, 2H, H-8,9), 8.67 (m, 2H, H-3,7), 7.71 (m, 5H, N-Ph)	$C_{13}H_{10}BF_4N_3O$ 50.20 3.21 13.51 49.86 3.45 13.32
4d	**3d** [a]	61	240-242 [b]	3350, 3240, 3020, 1726, 1610, 1550, 1510, 1060	9.36 (d, 1H, H-6), 9.2-8.4 (m, 3H, H-7,8,9), 8.27 (m, 2H, H-2',6'), 8.82 (m, 3H, H-3',4',5')	$C_{13}H_{10}BF_4N_3O$ 50.20 3.21 13.51 50.42 3.38 13.27
7a	**15a**	35	192-195 [c]	3120, 3100, 3060, 1610, 1580, 1550, 1480, 1050	9.44 (d, 1H, H-6), 9.0 (m, 3H, H-3,8,9), 8.66 (m, 1H, H-7), 7.66 (s, 5H, S-Ph)	$C_{13}H_{10}BF_4N_3S$ 47.73 3.08 12.58 47.52 3.19 12.64
7b	**15b**	57	230-233 [d]	3040, 1600, 1530, 1480, 1440, 1420, 1080	9.54 (d, 1H, H-6), 9.0-8.8 (m, 2H, H-8,9), 8.61 (m, 1H, H-7), 8.07 (m, 2H, 3-Ph), 7.7 (m, 5H, S-Ph), 7.6-7.3 (m, 3H, 3-Ph)	$C_{19}H_{14}BF_4N_3S$ 56.60 3.50 10.42 56.74 3.82 10.35
10	**11** [e]	72	220-223 [c]	3130, 3090, 3060, 1580, 1550, 1460, 1050	9.22 (d, 1H, H-6), 8.86 (m, 2H, H-8,9), 8.48 (m, 1H, H-7), 7.88 (m, 5H, 1-Ph), 7.47 (m, 5H, O-Ph)	$C_{19}H_{14}BF_4N_3O$ 58.94 3.64 10.85 58.85 3.52 10.93
12	**13** [e]	42	205-208 [c]	3080, 1610, 1570, 1540, 1440, 1080	9.06 (d, 1H, H-6), 8.8 (m, 2H, H-8,9), 8.46 (m, 1H, H-7), 7.87 (m, 5H, 1-Ph), 7.74 (m, 5H, S-Ph)	$C_{19}H_{14}BF_4N_3S$ 56.60 3.50 10.42 56.38 3.68 10.73

[a] Following the general procedure, no phenylated product was formed. The reaction gave only the protonated derivative **3b** of **4d**. [b] Dimethylformamide/ethyl acetate. [c] Acetonitrile/ethyl acetate. [d] Ethanol/water. [e] R = Ph, A = BF_4.

8.70 (m, 2H, H-8,9), 8.47 (m, 1H, H-7), 7.83 (m, 5H, Ph), 2.79 (s, 3H, S-CH_3).

Anal. Calcd. for $C_{14}H_{12}IN_3S$: C, 44.11; H, 3.17; N, 11.02. Found: C, 44.38; H, 3.08; N, 10.86.

3-Methylthio-1-phenylpyrido[2,1-*f*]-*as*-triazinium Hexafluorophosphate (**13**, R = Me, A = PF_6).

A suspension of **12** (0.24 g, 1 mmole) and trimethyloxonium hexafluorophosphate (0.21 g, 1 mmole) in dry dichloromethane (10 ml) was stirred at room temperature for 24 hours, then was mixed with ether (20 ml), and filtered to give white crystals (0.39 g, 97%); mp 225-230°; ir (potassium bromide): 3100, 3050, 2920, 1610, 1595, 1580, 1540, 1480, 1440, 830, 550 cm^{-1}; ^{1}H-nmr (trifluoroacetic acid): δ 9.40 (d, 1H, H-6), 8.84 (m, 2H, H-8,9), 8.51 (m, 1H, H-7), 7.87 (m, 5H, Ph), 2.85 (s, 3H, S-CH_3).

Anal. Calcd. for $C_{14}H_{12}F_6N_3PS$: C, 42.11; H, 3.03; N, 10.52. Found: C, 42.39; H, 3.18; N, 10.34.

Reaction of Olates **4a**, **4d** and **10** and Thiolates **7a**, **7b** and **12** with Diphenyliodonium Fluoroborate.

General Procedure.

A suspension of the olates **4a**, **4d**, **10** (1 mmole) or thiolates **7a**, **7b** and **12** (1 mmole) and diphenyliodonium fluoroborate (0.37 g, 1 mmole) in benzonitrile (5 ml) was refluxed for 10 minutes. A second portion of diphenyliodonium fluoroborate (0.37 g, 1 mmole) was added to the mixture and refluxed for 30 minutes. The resulting solution was cooled, mixed with ether (30 ml), whereupon a gum was separated. The etheral solution was decanted, the residue dissolved in boiling ethanol (2 ml), cooled, filtered off and recrystallized from a mixture of acetonitrile and ethyl acetate to give the product (Table V).

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