Synthesis of 2-Aryl and 2-Heterocyclyl-2H-benzo[e]-1,2,3,4- thiatriazin-1,1-dioxides

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Summary: Several 2-(substituted) aryl-2H-benzo[e]-1,2,3,4-thiatriazin-1,1-dioxides (III) have been prepared in good yields, by the nitrosation of N-aryl-2-aminobenzenesulphonamides(II): derived from the reduction of corresponding N-aryl-2-nitrobenzenesulphonamides(I). 2-cyclohexyl, 2-benzyl and some heterocyclyl derivatives have also been prepared, the latter however, in lower yields. The mass spectra of these compounds show fragmentation patterns closely related to those observed in photolysis or thermolysis studies of such compounds. The infra- red spectra of these compounds have also been discussed.

Introduction

Benzothiatriazin-1,1-dioxides are an important class of nitrogen-sulphur heterocycles, and their various derivatives have found a number of important applications. Thus, the 2-methyl, 2-phenyl and 2,2-ethylene bis-1,2,3,4-benzothiatriazin-1,1-dioxides have been used as polymerization catalysts [1]. 2-Phenyl, 2-ter-butyl, 2-methyl, 2-cyclohexyl and 2-isopropyl derivatives have been employed as blowing agents [2] in the production of cellular rubber and plastics. 6-Chloro-2-methyl/ benzyl-7-methyl sulphamoyl benzothiatriazindioxides (IV) are an important class of diuretics [3,4,5]. The 7-nitro derivatives (V) had been used as dyeing precursors [6] stable to heat, storage and handling. Recently the use of various 2-alkyl, alkenyl, acyl, cycloalkyl and aryl derivatives in the preparation of heat-sensitive recording materials [7] giving sharp and clear images, had been reported. Thermolysis of 2-phenyl-2H-benzothiatriazin-1,1-dioxide in the presence of copper [8], as well as photolysis yields the dibenzo[c,e] 1,2-thiatriazin-1,1-dioxides (sultan) [9] while the sterically hindered 2-mesityl derivative affords the four-membered benzofused heterocyclic system 2-mesityl-2H-benzo[c]-1,2-thiazet-1,1-dioxide [10], inaccessible through other ways. Although some patents claim to synthesize the aryl derivatives in general, however, only a few of them had been supported by real physical data and incidentally no heterocyclyl deriva-

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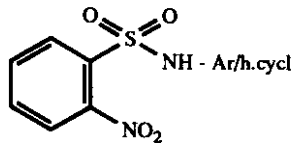
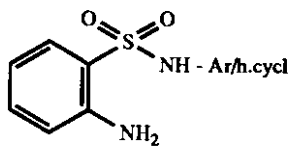


(I)



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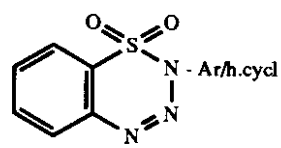

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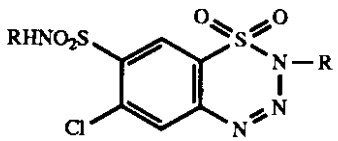

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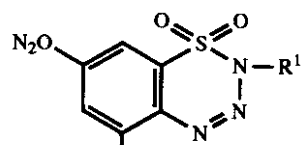


(V)

R = methyl, isopropyl, benzyl, cyclohexyl etc.

R^1 = H, Cl, Br, NO_2
R^2 = ethyl, 2-hydroxyethyl, allyl, cyclohexyl, benzyl etc.

Table 1: N-Aryl/h.cycl-2-nitrobenzenesulphonamides (I)

Compd.	Aryl/heterocyclyl group	m.p. (°C)	Yield (%)	IR (cm^{-1})
a	Phenyl	104-105 (114-115) [14]	70 (72) [14]	3310, 1536, 1365, 1167
b	2'-Methylphenyl	134-135 (137-138) [11]	70 (75) [11]	3392, 1548, 1332, 1173
c	4'-Methylphenyl	105-106 (114-116) [11]	62 (65) [11]	3340, 1530, 1326, 1137
d	3',4'-Dimethylphenyl	131-132	83	
e	2'-Methoxyphenyl	87-89 (91-92) [11]	63	3340, 1530, 1326, 1137
f	4'-Methoxyphenyl	127-130	74	
g	4'-Fluorophenyl	107-109	85	
h	3'-Chlorophenyl	115-116	90	
i	4'-Chlorophenyl	102-104	58	3392, 1548, 1332, 1137
j	4'-Bromophenyl	184-186	63.6	
k	4'-Iodophenyl	92-94	69.4	3340, 1530, 1326, 1137
l	Benzyl	91-92	95	
m	Cyclohexyl	84-86	72.5	
n	(3'-Pyridinyl)methyl	146-147	45.5	
o	2'-Pyridyl	122-124	26	
p	3'-Pyridyl	152-154	55.4	3238, 1536, 1131, 1122
q	2'-Pyrimidyl	112-114	15.2	
r	3,5-Dimethylpyrimidyl	144-146	9.9	3340, 1530, 1326, 1137
s	3-(1',2',4'-Triazolyl)	174-178	89.2	
t	2-Benzothiazolyl	190	25.5	3392, 1548, 1332, 1137
u	2-Benzimidazolyl	194-196	78.6	
v	2-Thiazolyl	184-186	57	3392, 1548, 1332, 1137
w	8-Quinolinyl	144-145	65	

tive has ever been reported. In this article we wish to describe the synthesis of some new 2-aryl and 2-heterocyclyl compounds along with their infra-red and mass spectral data.

Thus, N-aryl-2-nitrobenzenesulphonamides (Ia-w, Table 1) were easily prepared by the reaction of 2-nitrobenzensulphonylchloride with arylamines using dry pyridine [11] or dry benzene [9] as solvent. The reduction to the corresponding N-aryl-2- amino-benzenesulphonamides (IIa-w, Table 2) was accomplished using zinc-2N-hydrochloric acid [12], zinc-calcium chloride [9] or stannous chloride-conc. hydro chloric acid [13]. The yields were quite good in the

Table 2: N-Aryl/h.cycl-2-aminobenzenesulphonamides (II)

Compd	m.p. (°C)	Yield (%)	IR (cm^{-1})
a	112-114 (119-120) [14]	82 (85) [14]	3460, 3400, 1320, 1158
b	133-134 (137-138) [11]	85 (88) [11]	3502, 3394, 1320, 1140
c	117-119 (125-126) [11]	72 (76)	3466, 3376, 1326, 1137
d	108-110	83	
e	104-105 (102-103) [11]	53.5 (55) [11]	3452, 3360, 1325, 1130
f	91-93	68	
g	106-108	58	
h	176-177	98	3502, 3394, 1320, 1140
i	112-114	72	
j	Oil	52	
k	70-72	48	3466, 3376, 1326, 1137
l	69-71	86.5	3502, 3394, 1320, 1140
n	Oil	40	
o	198-200	25	
p	182-184	72	3430, 3340, 1323, 1125
q	-	27	
r	-	12	
s	290 (decomp)	56	
t	244-246 (decomp)	37	3454, 3364, 1314, 1137
u	225-228	35	
v	-	-	
w	-	-	

case of N-aryl, N-cyclohexyl, N-aralkyl but poor to moderate in the case of N-heterocyclyl compounds, using any of these methods. In fact, despite repeated efforts, some of the heterocyclyl compounds could not be reduced using any of these methods.

Diazotisation of the sodium N-aryl/heterocyclyl-2-aminobenzenephonamides [14] in 2N hydrochloric acid at 0-5° followed by basification with aqueous ammonia liberated the thiatriazindioxides (IIIa-p,t; Table 3). It may be noted from Table 3 that, the thermal and photostability of 2-heterocyclyl derivatives is enhanced as compared to the 2-aryl, 2-benzyl, 2-methyl-(3'-pyridyl) or 2-cyclohexyl compounds as indicated by the relatively higher melting points and stability towards the laboratory light of the former.

The infra-red spectra of these compound clearly provide evidence of the changes occuring in conversion of (I) to (III) via (II). Thus, the nitro-compounds (I) showed strong absorption at ca 3256 cm^{-1} for -SO_2NH- stretching and at 1524-1534 cm^{-1} for NO_2 stretchings, in addition to the peaks at 1330-1320 cm^{-1} and 1170-1150 cm^{-1} for SO_2 absorptions. The amino derivatives (II) were characterized by the lack of absorption due to NO_2 stretchings and by the appearance of two sharp distinct peaks at ca 3430 cm^{-1} and 3340 cm^{-1} due to unsymmetrical and symmetrical -NH_2 stretchings respectively. In constrast the infra-red spectra of benzothiatriazin-1,1-dioxides(III) showed a complete absence of -NH absorptions due to either -SO_2NH or -NH_2, while the appearance of absorption at ca 1570 cm^{-1} due to -N=N- was noticed.

The mass spectra of these compounds did not show, normally, an M^+ peak owing to the thermal instability of the molecular ion. FAB technique (acid + glycerol matrix) had to be employed to obtain the molecular ion. The most prominent fragmentions invariably corresponded to the M-28 and M-92 due to the loss of nitrogen and the subsequent extrusion of sulphur dioxide, respectively. The characteristic fragmentation pattern for two specific cases, 2-(4'-methoxyphenyl)-2H-benzo[e]-1,2,3,4-thiatriazin-1,1-dioxide (III_f) and 2-(2'-pyridyl)-2H-benzo[e]-1,2,3,4-thiatriazin-1,1-dioxide (III_o), are illustrated by schemes 1 and 2 respectively. Thus the loss of stable nitrogen molecule from 2-(4'-methoxyphenyl)-2H-benzo[e]-1,2,3,4-thiatriazin-1,1-dioxide (III_f) (Scheme-1) leads to either the 2-(4'-methoxyphenyl)-2H-benzo[c]-1,2-thiazet-1, 1-dioxide (1) or the 5-methoxyphenyl benzo[c,e]-1, 2-thiazin-1, 1-dioxide (sultam) (2b) for med *via* the tautometric (2a), as the base peak. Extrusion of the methyl radical from (1) results in the phenothiazinone dioxide ion (3b) *via* its isomeric intermediate (3a). Alternatively, the isomeric fragment (3c) results from (2b). Subsequent elimination of SO_2 gives the carbazolone derivative (4) which looses CO to give the ion (5).

Table 3: Ar/h.cycl-2H-benzo[e]-1,2,3,4-thiatriazin-1,1dioxides (III)

Compd	m.p. (°C)	Yield (%)	M.S. (m/z)
a	104-106 (decomp) (111) [11]	92 (96)	IR 2926, 1575, 1332, 1161 cm^{-1}
b	106-108 (decomp)	85	273 (M^+), 245, 181
c	107-109	65	273 (M^+), 245, 181
d	103-105	60	287 (M^+), 259, 195
e	106-108	52	289 (M^+), 259
f	83-84	72	289 (M^+), 261, 246, 182, 154
g	62-63	75	277 (M^+), 249
h	74-76	70	293 (M^+), 265, 201
i	101-102	60	293 (M^+), 265, 201, 166
j	101-102	65	338 (M^+), 340 (M^+), 310, 246
k	182-184	85	385 (M^+), 355, 291
l	104-105	81	273 (M^+), 245, 181
m	76-78	62	265 (M^+), 237, 173
n	97-99	65	274 (M^+), 246, 219, 181, 141
o	360-362	52	260 (M^+), 232, 168, 141
p	325-330	68	260 (M^+), 232, 168
q	-	-	-
r	-	-	-
s	-	-	-
t	discolours above120 melts 172-178	25	
u	-	-	-
v	-	-	-
w	-	-	-

Notes for tables 1-3

(i) For known compounds the structures confirmed by the IR spectral data and melting points only (I, II, a-c,e;IIIa). The literature values (m.p. & yield %) given in paranthesis.

(ii) The M^+ for thiatriazindioxides were obtained using FAB (acid + glycerol matrix).

(iii) The dashes refer to compounds which did not give satisfactory IR spectra and had very high melting points, hence the M.S. were not taken.

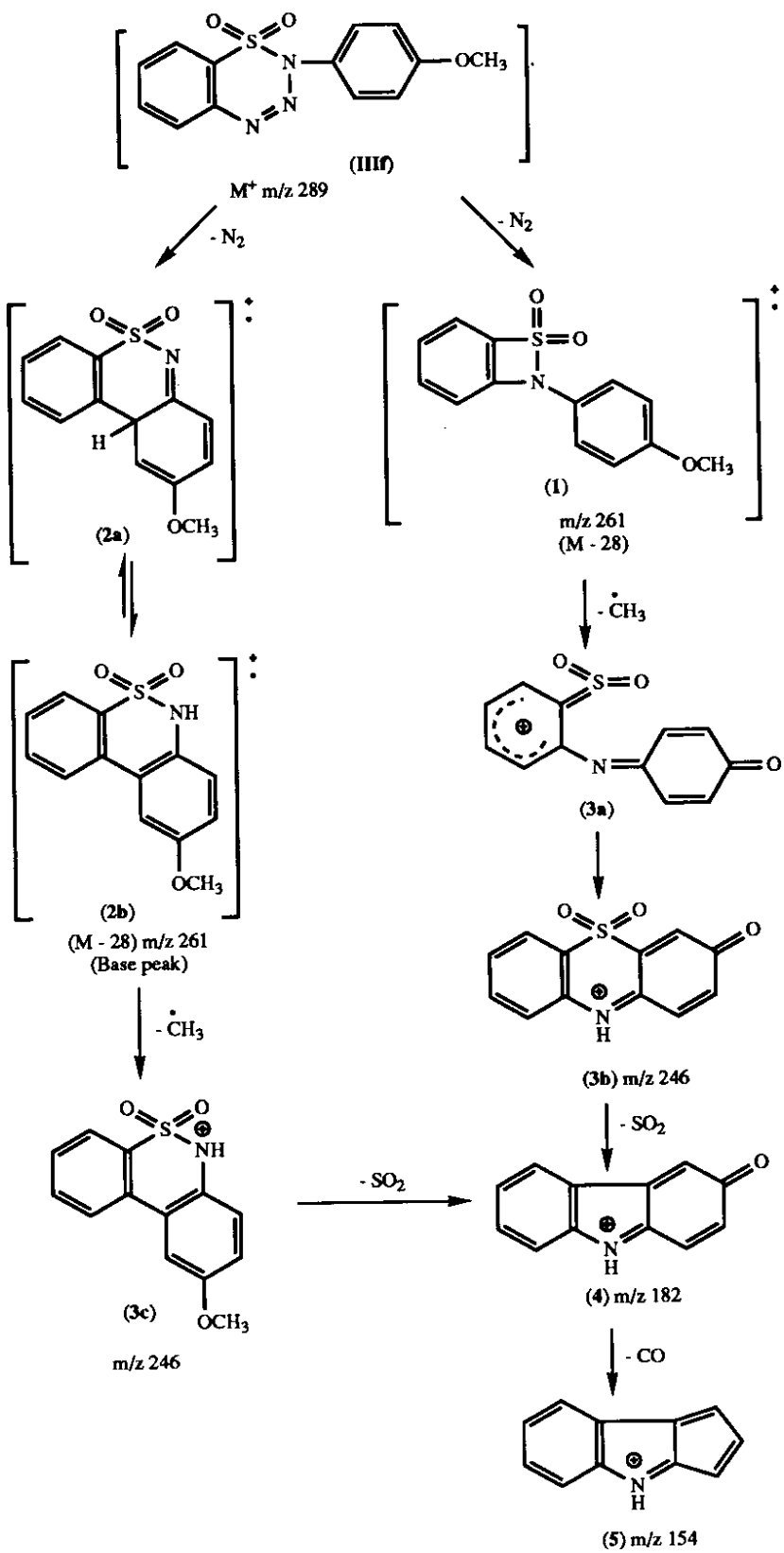
The possible fragmentation pattern for 2-(2'-pyridyl)-2H-benzo[e]-1,2,3,4-thiatriazin-1,1-dioxide (III_o) is shown in Scheme 2. The M-28 fragment (m/z 232) may correspond to (6) or (7b). Either fragment (7b) or (8b) obtained from (6) *via* (8a), looses SO_2 to afford the same pyridoindole fragment (9) which corresponds to the base peak in this case. Loss of HCN from (9) results in the ion-radical (1) which further looses C_2H_2 to give the indole ion-radical (11).

Experimental

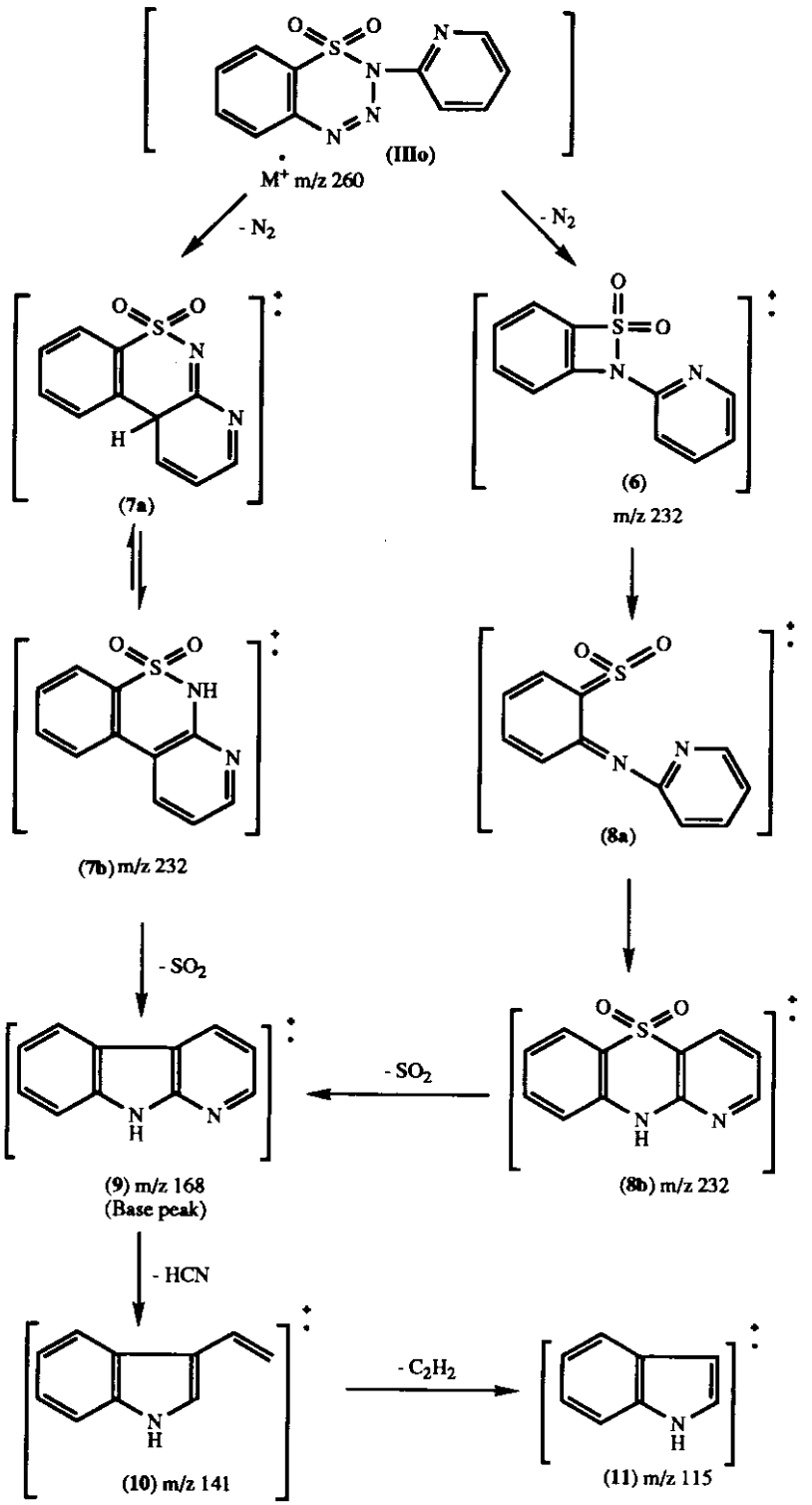
Melting points which were determined using a MEL-TEMP MP-D apparatus are uncorrected. Infra-red spectra of all compounds were recorded on a Hitachi Model-270 spectrophotometer as KBr discs. FAB mass spectra were recorded by the DS-55 Mass Spectrometry Data System King's College, London. Acid + glycerol matrix was used to obtain the molecular ions. 2-Nitrobenzenesulphonyl chloride was the commercial Aldrich product while the aryl/heterocyclyl amines were mostly from E. Merck. The physical and mass spectral data of all compounds are listed in Tables 1-3.

Preparation of N-(4'-methoxyphenyl)-2-nitrobenzenesulphonamide (I_f)

The general procedures for preparation of N-aryl-2-nitro-benzenesulphonamides (I) is exemplified by the synthesis of the title compound (I_f). 2-Nitrobenzenesulphonyl chloride (2.215 g, 0.01 mol) was added portionwise to a stirred solution of the 4'-methoxyaniline (1.35 g; 0.011 mol) in dry pyridine (15 ml). The reaction mixture was stirred for a further 15 minutes and then poured into cold water (150 ml) for precipitation. The precipitates were recrystallized from aqueous ethanol, as light yellow crystals (2.23 g; 0.0075 mol, 74%) m.p. 127-130°; IR (KBr); 3256 (SO_2NH-), 1533 (-NO_2), 1506 (Ar), 1374, 1164 (SO_2) cm^{-1}.



Scheme 1: Fragmentation pattern for 2-(4'-methoxyphenyl)-2H-benzo[e]-1,2,3,4-thiatriazin-1, 1-dioxide (**IIIf**).



Scheme 2: Mass fragmentation pattern of the 2-(2'-pyridyl)-2H-benzo[e]-1,2,3,4-thiatriazin-1, 1-dioxide (**IIIo**).

Preparation of N-(4'-methoxyphenyl)-2-aminobenzenesulphonamide (IIf)

With minor differences, the reductions were carried out as described for the following compound.

Method-A [12]

N-(4'-Methoxyphenyl)-2-nitrobenzenesulphonamide (If; 3.0 g, 0.01 mol) was dissolved in a mixture of ethanol (90 ml) and 2N hydrochloric acid (45 ml). Zinc dust (2.4 g, 0.038 mol) was added with stirring and the solution refluxed for 6-10 hrs. The excess of zinc was filtered off, the reaction mixture was poured into water and pH adjusted using aqueous sodium bicarbonate for precipitation. The pprecipitates were recrystallized from aqueous ethanol as off-white needles (2.0 g, 0.0072 mol, 72%) m.p. 91-93°; IR (KBr): 3502, 3394 ($-NH_2$), 3250 (SO_2NH), 1488, 1374, 1140 (SO_2) $cm.^{-1}$

Method-B [13]

The reduction of (If) was also carried out by adding simultaneously (If; 3.0 g. 0.01 mol) and conc. hydrochloric acid (8 ml) to a warm solution of stannous chloride dihydrate (7.4 g, 0.,033 mol) in ethanol (50 ml). The reaction mixture was refluxed for 2 hr., the excess solvent removed by evaporation and poured into water. The precipitated compound (IIf) was recrystallized from aqueous ethanol (2.0 g, 0.0074 mol, 74%).

Method-C [8]

A mixture of the nitro-compound (If; 3.0 g, 0.01 mol), zinc powder (1.9 g, 0.029 mol) and calcium chloride dihydrate (0.85 g, 0.005 mol) in aqueous ethanol (78%, 30 ml) were refluxed for 3 hr. and then poured into ice. Usual work-up afforded the amino-compound (IIf; 1.89 g, 0.0068 mol, 68%).

2-(4'-Methoxyphenyl)-2H-benzo[e]-1,2,3,4-thiatriazin-1,1- dioxide (IIIf)

N-(4'-Methoxyphenyl)-2-aminobenzenesulphonamide (IIf; 2.78 g, 0,01 mol) sodium hydroxide (0.5 g, 0.0125 mol) and sodium nitrite (0.7 g, 0.01 mol) were dissolved in distilled water 25 ml) and the resulting solution added dropwise to a stirred solution of conc. hydrochloric acid (5 ml) in water (25 ml) maintaining the temperature at or below 0°. After completion of the addition, the stirring was continued for 15-20 minutes. The reaction mixture was then filtered and diluted if necessary. Basification with aqueous ammonia precipitated the title thiatriazindioxide as light pinkish powder sensitive to laboratory light. This was recrystallized from ether-petroleum ether as light pink needles (2.0 g, 0.0072 mol, 72%) m.p. 83-84° (with decomposition and explosive violence). IR (KBr): 3088, 1575 (N=N), 1338, 1185, 774 cm^{-1}. EIMS (acid + glycerol matrix) m/z 289 (M^+). EIMS: m/z 261 (100.0), 246 (59.6), 182 (34.6), 154 (32.4), 127 (25.0) (% INT NREF given in parantheses).

Acknowledgement

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