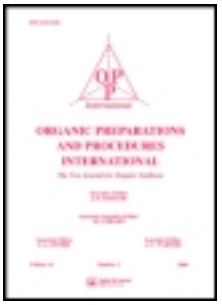

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A FACILE SYNTHESIS OF ARYL ISOTHIOCYANATES FROM ARYLAMINES

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A FACILE SYNTHESIS OF ARYL ISOTHIOCYANATES FROM ARYLAMINES

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(03/14/00)

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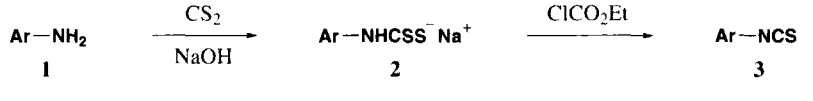
Aryl isothiocyanates, used as intermediates for the preparation of medicinal antibacterial, antitumor or anti-AIDS agents,[1] agricultural fungicides[2] or herbicides[3] and other various heterocyclic compounds,[4] are commonly prepared from arylamines by treatment with carbon disulfide, ammonia and lead nitrate[5] or by treatment with thiophosgene.[6] Other synthesis methods from monoarylthioureas,[6] phosphoramidates[7] or aryliminodithiazoles[8] have also been reported. However, most of these methods are laborious and suffer from low yields. Aryl isothiocyanates can be also prepared by the modified Kaluza method in three steps: first, the formation of the dithiocarbamate salt from an amine, carbon disulfide and triethylamine in benzene or ether; secondly, formation of the carboethoxy dithiocarbamate by treatment of the dithiocarbamate salt with ethyl chloroformate in chloroform; and thirdly, decomposition of the carboethoxy dithiocarbamate with base to yield the isothiocyanate.[9] We now report a more straightforward and convenient synthesis of aryl isothiocyanates from arylamines on the basis of Kaluza method as shown in the following equation. Aryl amines (**1a-l**) readily reacted with carbon disulfide and sodium hydroxide in water to give sodium aryldithiocarbamates (**2a-l**), which were treated directly with ethyl chloroformate at 35-40° to give aryl isothiocyanates (**3a-l**).



a) Ar = *o*-FC_6H_4 e) Ar = 3,4-$F_2C_6H_3$ i) Ar = *o*-ClC_6H_4
b) Ar = *p*-FC_6H_4 f) Ar = 2,3,4-$F_3C_6H_2$ j) Ar = 2,6-$Cl_2C_6H_3$
c) Ar = *m*-FC_6H_4 g) Ar = 3,4-$ClFC_6H_3$ k) Ar = *m*-ClC_6H_4
d) Ar = 2,4-$F_2C_6H_3$ h) Ar = C_6H_5 l) Ar = *o*-BrC_6H_4

EXPERIMENTAL SECTION

IR spectra were determined as films on a Nicolet FT-IR-20SX Infrared Spectrophotometer. Mass spectra were obtained on a Hitachi M80 spectrometer. Elemental analyses were performed on an Italian MOD1106 microanalyzer.

Table 1. Physical and Spectroscopic Data of Compounds **3a-l**

Cmpd	bp (°C/Torr)	lit. bp (°C/Torr)	Yield (%)	IR (cm^{-1})	MS m/z (M^+)
3a	103-104/8[i]		68	2033, 1601, 1598	153
3b	95-97/8	228[5]	72	2040, 1590, 1504	153
3c	94-96/8[ii]		54	2038, 1596, 1508	153
3d	85-86/8[iii]		89	2049, 1602, 1501	171
3e	82-84/8	68-70/4[10]	78	2050, 1600, 1500	171
3f	80-82/8	96-97/17[11]	86	2018, 1500, 1490	189
3g	110-112/8	115-117/11[10]	82	2000, 1580, 1480	187, 189
3h	85-87/8	96-98/15[12]	56	2062, 1591, 1488	135
3i	120-122/8	120/8[8]	79	2050, 1580, 1460	169,171
3j	122-124/8[iv]		62	2030, 1540, 1420	203,205, 207
3k	115-117/8	120/8[13]	78	2052, 1589, 1475	169, 171
3l	116-118/8	140-143[13]	69	2028, 1560	213, 215

i) *Anal.* Calcd for C_7H_4FNS: C, 54.89; H, 2.63; N, 9.14. Found: C, 54.71; H, 2.64; N, 9.20. ii) *Anal.* Calcd for C_7H_4FNS: C, 54.89; H, 2.63; N, 9.14. Found: C, 54.84; H, 2.64; N, 9.15. iii) *Anal.* Calcd for $C_7H_3F_2NS$: C, 49.12; H, 1.77; N, 8.18. Found: C, 49.22; H, 1.76; N, 8.19. iv) *Anal.* Calcd for $C_7H_3Cl_2NS$: C, 41.20; H, 1.48; N, 6.86. Found: C, 41.31; H, 1.47; N, 6.88.

Aryl Isothiocyanates (3a-l).- To a stirred mixture of carbon disulfide (45.6 g, 0.60 mole), sodium hydroxide (16.0 g, 0.40 mole) and water (80 mL) at 2-5° was added dropwise the amine (0.40 mole) over a period of 30 min. After stirring at 40-45° for 24 h, the lower layer of carbon disulfide was removed and the upper aqueous layer containing intermediate **2** was washed with benzene (3 x 100 mL). To this aqueous solution was added dropwise ethyl chloroformate (0.4 mole) at 35-40° and the resulting mixture was stirred for about 40 min at the same temperature. Then the lower organic phase was separated, washed with water (3 x 50 mL), dried over anhydrous magnesium sulfate and distilled *in vacuo* to give pure **3** (**Table 1**).

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SYNTHESIS OF 1,9-DIAMIDINIUMACRIDINE AS A POTENTIAL RECEPTOR FOR PHOSPHATE ESTER RECOGNITION

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One of the most intriguing topics in biochemistry is the regulation of enzyme structure and function by phosphorylation of serine, threonine, and tyrosine residues.[1] Phosphorylation is the most abundant post-translational modification of proteins and results in covalent but easily reversible regulation. It has been demonstrated that phosphatases play key roles in tumor suppression, the control of normal and neoplastic cell growth, and cell proliferation.[2,3] At the present time there are relatively few examples of synthetic phosphate ester binding receptors.[4] In a continuing effort to design receptors for phosphate recognition,[5-8] 1,9-diamidiniumacridine (**7**) was synthesized in order to test its ability to bind to phosphate mono-esters (**8**) (Fig. 1).