ISSN 1009-3095 *Journal of Zhejiang University(SCIENCE)* V.1, No.2, P.184-185, Apr.-Jun., 2000
184 http://www.zju.edu.cn; http://www.zjupress.com; http://www.chinainfo.gov.cn/periodical

STUDY ON STABLE NITROXYLS(II): SYNTHESIS OF SPIN LABELED PHENOXYACETATES AS POTENTIAL AUXINS

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Received Dec.16, 1998; revision accepted May.15, 1999

Abstract: The syntheses and characterization of six new spin labeled phenoxyacetates as potential auxins are discribed.

Key words: auxins, nitroxyls, phase-transfer catalyses, characterization
Document code: A **CLC number:** O623.626

INTRODUCTION

Stable nitroxyls have been used extensively as spin labels in various biological systems (Sankarapandi et al., 1994; Kocherginsky et al., 1995) and drugs. Some nitroxyls were demonstrated to comprise a new class of compounds with potential for selective cutaneous radioprotection without systemic absorption (Goffiman et al., 1992). We reported that the introduction of the nitroxyl group into some anticancer drug molecules such as podophyllotoxin, resulted in significant improvement in the pharmacological properties of the drugs (Wang et al., 1993; Wang et al., 1997; Chen et al., 1987). Phenoxyacetic acids and their derivatives are synthetic auxins; some of them had been used as growth regulators for plants and as weed killers (Fawcett et al., 1957; Li 1993). Spin labeled auxins may be useful probes for research on the action mechanism of auxins by ESR technology. In this paper, we describe a facile syntheses of spin labeled phenoxyacetates 3a-f by solid-liquid phase-transfer catalytic method, as shown in Scheme 1.

EXPERIMENTAL DETAILS

All melting points were obtained on Kofler melting point apparatus and were uncorrected. Elemental analysis was recorded on a 1106 instrument. IR spectra were recorded on a Nicolet-5DX spectrometer and ESR spectra were obtained by using a Bruker-200D-SRC spectrometer.

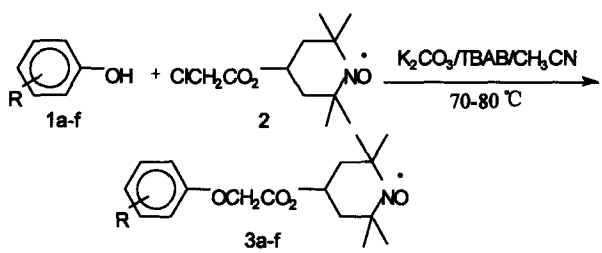

Fig.1 Synthesis of spin labeled phenoxylacetates
(a. R = H; b. R = 4-OCH_3; c. R = 4-Cl; d. R = 4-Br; e. R = 2,4-di-Cl; f. R = 4-NO_2)

4-Chloroacetyl-2,2,6,6-tetramethyl-1-oxypiperidine(2) was prepared according to reported procedure (Wang et al., 1992).

General procedure for synthesis of 3a-f: A mixture of the phenol ethers 1a-f (1 mmol), 4-choroacetyl-2, 2, 6, 6-tetramethyl-1-oxypiperidine (2) (1.2 mmol), TBAB(1.5 μmol) and anhydrous K_2CO_3(1.2 mmol) in dry acetonitrile (10 ml) was stirred vigorously at 70-80 ℃ for 4-6 hrs. All reactions were monitored by TLC (Silica GF_{254} plate, cyclohexane : EtOAc = 15 : 1). The mixture was cooled to room temperature, then diluted with EtOAc (100 ml), and then washed with brine (50 ml) and H_2O (50 ml). The organic phase was dried with anhydrous Na_2SO_4, and evaporated to dryness under reduced pressure. The residues were purified by recrystallization from hexane to give 3a-f, re-

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spectively.

RESULTS AND DISCUSSION

The structure determination of the phenoxyacetates 3a-f was based on their characteristic IR and ESR spectra, as well as their elementary analysis data. Analysis data are shown in Table 1 and 2.

Table 1 Physical data of spin labeled auxins 3a-f

Compound*	Yield (%)	m.p. (℃)	IR(cm^{-1})		
			C=O	Aromatic C=C	N-O
3a	82	69-70	1740	1610,1500,1490	1360
3b	86	54-55	1740	1600,1500,1460	1360
3c	81	73-74	1758	1597,1490,1430	1340
3d	82	81-82	1758	1604,1490,1430	1360
3e	78	79-80	1760	1590,1490,1430	1360
3f	36	122-123	1744	1612,1510,1440	1340

* ESR(solid): single line, $g = 2.005 - 2.007$, $\Delta H = 2.10 - 3.52 \times 10^{-3}T$

Phenoxyacetates were usually obtained by the condensation of phenoxyacetic acid or its chloride with the correspondent alcohol (Rozantsev et al., 1963; Hisa et al., 1969). The work-up and purification of the product are quite cumbersome (Hisa et al., 1969). In contrast to those methods, our process employed the solid-liquid phase-transfer catalytic reaction method which is facile and efficient. In conclusion, we report a facile synthesis for the spin labeled phenoxy- acetates as potential auxins with good yields (except 3f). The results of ongoing biological activity tests and ESR researches of compounds 3a-f will be published elesewhere.

Table 2 Elementary analysis data of spin labeled auxins 3a-f

Compound	Formula	Calcd./Found (%)		
		C	H	N
3a	$C_{17}H_{24}NO_4$	66.67/66.80	7.84/7.86	4.58/4.75
3b	$C_{17}H_{26}NO_5$	64.28/64.00	7.74/7.70	4.17/4.20
3c	$C_{17}H_{23}ClNO_4$	59.91/60.10	6.75/6.70	4.11/4.09
3d	$C_{17}H_{23}BrNO_4$	59.99/59.20	5.97/5.93	3.64/3.72
3e	$C_{17}H_{22}Cl_2NO_4$	54.40/54.94	5.87/5.92	3.73/3.82
3f	$C_{17}H_{23}N_2O_6$	58.12/58.37	6.55/6.72	7.98/7.81

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