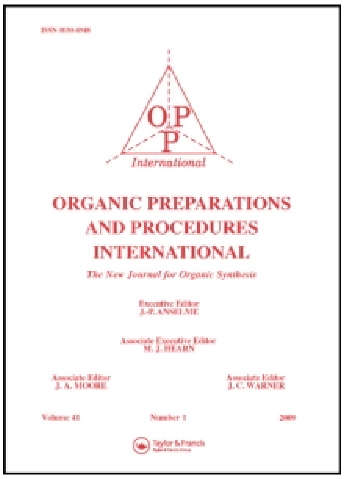

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A NOVEL CLASS OF OXAZOLE DERIVATIVES. 4-ACYL-2-ARYLTHIO-5-ETHOXYOXAZOLES

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A NOVEL CLASS OF OXAZOLE DERIVATIVES.

4-ACYL-2-ARYLTHIO-5-ETHOXYOXAZOLES

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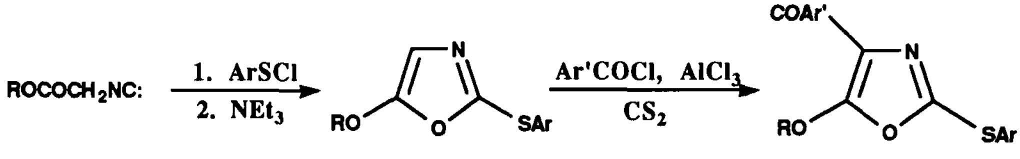
Oxazole derivatives are an important class of heterocycles[1], and substituted oxazoles[2,3] are useful intermediates in organic synthesis. In a previous paper,[2] we described the synthesis of 2-arylthio-5-ethoxyoxazoles **1** starting from alkyl isocyanoacetates and aryl sulfenyl chlorides. In order to evaluate the reactivity of these compounds towards electrophilic species, we attempted their acylation with acyl chlorides in the presence of aluminum chloride. These attempts were successful, giving 4-acyl-2-arylthio-5-ethoxyoxazoles **2** in fair yields.



1 2

a) Ar = 2-$NO_2C_6H_4$, Ar' = C_6H_5 b) Ar = 2-$NO_2C_6H_4$, Ar' = 4-$CH_3C_6H_4$
c) Ar = 2-$NO_2C_6H_4$, Ar' = 4-$CH_3OC_6H_4$ d) Ar = 2-$NO_2C_6H_4$, Ar' = 4-ClC_6H_4
e) Ar = 2-NO_2-4-ClC_6H_3, Ar' = C_6H_5 f) Ar = 2-NO_2-4-ClC_6H_3, Ar' = 4-$CH_3C_6H_4$
g) Ar = 2-NO_2-4-ClC_6H_3, Ar' = 4-$CH_3OC_6H_4$

The success of the above acylation is probably due to the presence of the arylthio and the alkoxy groups that enhance the reactivity of the oxazole ring towards electrophilic substitution. Although 4-oxazolin-2-ones can be N-acylated by acid chlorides to afford substituted oxazoles,[4] to our knowledge the present acylation is the first example of direct acylation at the 4-position of oxazoles. Evidence for the formation of 4-acyl-2-arylthio-5-alkoxyoxazoles **2** was provided by IR spectra of these compounds (1720 cm^{-1} carbonyl). Further confirmation of the structure was obtained by comparing the ^1H NMR spectra of compounds **1** and **2**; the singlet at about δ 6.36 due to the H-4 of **1** disappears and a series of signals due to the protons of the ArCO moiety appears. Physical, analytical and spectral data of compounds **2a-g** are summarized in Tables 1 and 2.

EXPERIMENTAL SECTION

Melting points were obtained in open capillary tubes and are uncorrected. The IR spectra were measured with a Perkin-Elmer 881 apparatus (KBr discs). Unless otherwise stated the ^1H NMR spectra were recorded with a Varian Gemini 200 apparatus for $CDCl_3$ saturated solutions. Chemical shifts are reported in ppm (δ) from TMS. Reagent grade carbon disulfide was dried over P_4O_{10} and distilled prior to use.

Table 1. Analytical Data of 4-Acyl-2-arylthio-5-ethoxyoxazoles (**2a-g**)

Cmpd	Empirical Formula	Analysis Calcd (Found)		
		C	H	N
2a	$C_{18}H_{14}N_2O_5S$	58.37 (58.46)	3.81 (3.78)	7.57 (7.61)
2b	$C_{19}H_{16}N_2O_5S$	59.37 (59.31)	4.20 (4.28)	7.29 (7.36)
2c	$C_{19}H_{16}N_2O_6S$	57.00 (57.07)	4.03 (3.98)	7.00 (7.05)
2d	$C_{18}H_{13}ClN_2O_5S$	53.41 (53.48)	3.24 (3.27)	6.92 (6.88)
2e	$C_{18}H_{13}ClN_2O_5S$	53.41 (53.37)	3.24 (3.30)	6.92 (6.86)
2f	$C_{19}H_{15}ClN_2O_5S$	54.49 (54.42)	3.61 (3.70)	6.69 (6.73)
2g	$C_{19}H_{15}ClN_2O_6S$	52.48 (52.51)	3.48 (3.53)	6.44 (6.40)

Table 2. Physical, IR and ^{1}H NMR Spectral Data of 4-Acyl-2-arylthio-5-ethoxyoxazoles (**2a-g**)

Cmpd	mp[a] (°C)	Yields (%)	IR CO (cm^{-1})	^{1}H NMR (δ)
2a	139-140	49	1712	4.50-4.39 (q, 2H, CH$_2$); 1.45-1.37 (t, 3H, CH$_3$)
2b	128-129	57	1721	8.35-7.31 (m, 8H, H-aromatic); 4.36-4.25 (q, 2H, CH$_2$); 2.37 (s, 3H, CH$_3$); 1.30-1.23 (t, 3H, OCHC$\underline{H}_3$)[b]
2c	109-110	60	1719	8.33-7.07 (m, 8H, H-aromatic); 4.37-4.25 (q, 2H, CH$_2$); 3.82 (s, 3H, OCH$_3$); 1.32-1.23 (t, 3H, CH$_3$)[b]
2d	150-152	25	1719	4.48-4.38 (q, 2H, CH$_2$); 1.42-1.34(t, 3H, CH$_3$)
2e	103-105	42	1724	4.48-4.37 (q, 2H, CH$_2$); 1.42-1.36 (t, 3H, CH$_3$)
2f	129-132	47	1720	4.48-4.37 (q, 2H, CH$_2$); 2.39 (s, 3H, CH$_3$); 1.42-1.36 (t, 3H, OCH$_2$C$\underline{H}_3$)
2g	122-123	48	1718	4.48-4.37 (q, 2H, CH$_2$); 3.84 (s, 3H, OCH$_3$); 1.44-1.36 (t, 3H, CH$_3$)

a) Recrystallized from EtOH. b) Solvent: DMSO-d$_6$.

4-Acyl-2-arylthio-5-alkoxyoxazoles (2a-g).- A saturated solution of **1** (15.0 mmol) and the appropriate acid chloride (15.0 mmol) in carbon disulfide [CAUTION] was added all at once to a well-stirred suspension of finely ground aluminum chloride (3 g, 22.5 mmol) in carbon disulfide (20 ml). The resulting mixture was stirred for 2 hrs and then 50 g of crushed ice were added. The organic layer was separated, dried over calcium chloride and then evaporated to dryness. The residue was washed with a little isopropyl ether (**CAUTION: Peroxides**) and then recrystallized from suitable solvent.

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