Reactions of Acyl Isothiocyanates with Diphenyldiazomethane: a Route to Oxazole Derivatives and Thietan-3-imines

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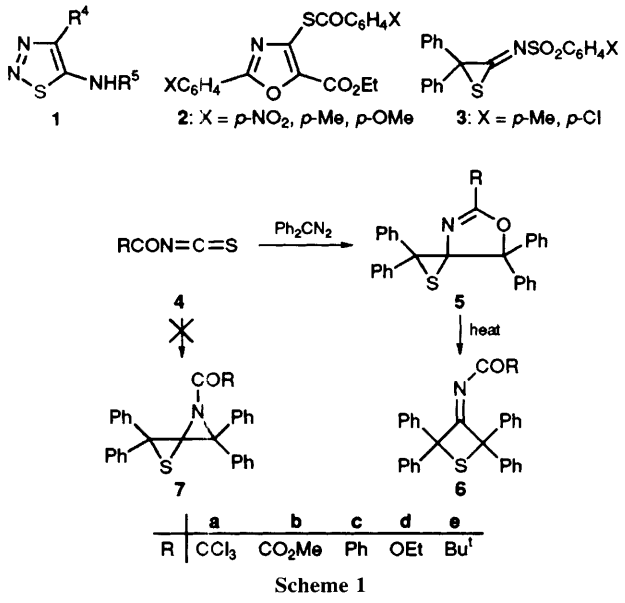
Acyl isothiocyanates **4a–e** react with two equivalents of diphenyldiazomethane at room temperature to give the 4,5-dihydro-1,3-oxazole-4-spiro-2′-thiiranes **5a–e** which isomerize thermally to the thietan-3-imines **6a–e**.

The reactions of diazomethane and monosubstituted diazoalkanes with isothiocyanates constitute a well established method for the synthesis of 5-amino-1,2,3-thiadiazoles **1**.[1] This method is general and allows the introduction of a large variety of substituents at the 4- and 5-positions; *i.e.* alkyl, aryl, acyl, alkoxycarbonyl, carbamoyl, sulfonyl and phosphoryl. In addition, no side products are formed except for the reactions of some *p*-substituted benzoyl isothiocyanates with ethyl diazoacetate which furnish the oxazoles **2** together with the expected thiadiazoles.[2]

Disubstituted diazoalkanes, in general, are much less reactive towards isothiocyanates. The only reactions thus far reported are those of diphenyldiazomethane with the strongly electrophilic arylsulfonyl isothiocyanates, leading to *N*-sulfonyl substituted thiiranimines **3**; these are derived formally from decomposition of the non-aromatic adducts, 1,2,3-thiadiazol-5(4*H*)-imines.[3] Reactions of acyl isothiocyanates with disubstituted diazomethanes have so far not been reported although some of them, such as trichloroacetyl isothiocyanate, are powerful electrophilic reagents which combine with alkyl azides in a complex manner.[4] This investigation disclosed the unexpected behaviour of the title reactions.



Scheme 1

When trichloroacetyl isothiocyanate **4a** was allowed to react with diphenyldiazomethane in diethyl ether at room temperature, nitrogen was evolved and a precipitate (37%) with mp 132 °C was formed. From the filtrate an isomer (43%) with mp 162 °C was obtained after chromatographic purification. The lower-melting compound was found to be unstable and rearranged into the higher melting isomer in refluxing dichloromethane, or simply when allowed to stand in the NMR tube ($CDCl_3$ solution) at room temperature. Both compounds exhibit the same mass spectrum with a weak molecular ion peak at *m/z* 535 (0.4%), indicating that they are composed of two diphenylcarbene units and one isothiocyanate unit. Microanalysis of the most stable isomer confirmed this conclusion.

The higher melting isomer is easily characterized as the thietan-3-imine **6a** since its symmetrical structure is apparent from the ^{13}C NMR spectrum where only 8 signals are observed. This implies that *Z–E* isomerization about the imine function is fast on the NMR timescale, a phenomenon well known for other imines bearing electron-withdrawing groups at nitrogen.[5] No broadening of the NMR absorptions was observed when a deuteriochloroform solution of compound **6a** was cooled to −45 °C. The IR absorptions at 1720 and 1695 cm^{-1} are also compatible with a C=NCOCCl$_3$ group, and the fragments in the mass spectrum at *m/z* 337 (19%) for $Ph_2C{=}C{=}NCOCCl_3^{\cdot+}$, *m/z* 192 (100%) for $Ph_2\overset{+}{C}{-}CN$ and at *m/z* 121 (25%) for $PhCS^+$ are in compliance with structure **6a**.

In contrast with compound **6a**, the phenyl groups of the lower-melting isomer are magnetically non-equivalent in the ^1H and ^{13}C NMR spectra, suggesting two spiro compounds, **5a** and **7a**, to be considered. The IR spectrum, however, leaves no doubt that structure **5a** is the correct one, since it exhibits a C=N stretching vibration at 1632 cm^{-1} in agreement with literature reports on 4,5-dihydrooxazoles;[6] normal acylaziridines are known to absorb at 1670–1690 cm^{-1} and a trichloromethyl substituent should move the frequency to still a higher value.

Similar results were obtained when the acyl isothiocyanates **4b–e** were treated with diphenyldiazomethane (Tables 1, 2): the spiro compounds **5b–e** were collected as precipitates when the reactions were carried out in concentrated diethyl ether solutions at room temperature, whereas the thietan-3-imines **6b–e** were isolated after heating in chloroform. In the case of **5d** rearrangement already occurred partly during the synthesis at room temperature and also when the ^{13}C NMR spectrum was recorded in deuteriochloroform.

The melting points of the spiro compounds are not sharp due to isomerization and in the cases of **5c,e** also loss of sulfur. This

Table 1 Characterization of the 4,5-dihydro-1,3-oxazole-4-spiro-2′-thiiranes **5**

				^{13}C NMR ($CDCl_3$) δ				
Compound	Yield (%)	Mp/°C	IR(KBr) ν/cm^{-1}	C–2	Spiro–C	C–5	C–3′	Other signals[a]
5a	37[b]	132 (decomp.)	1632s	162.5	90.7	99.0	64.7	86.6 (CCl_3)
b	60	147 (decomp.)	1646m, 1757s	156.7	90.9	96.3	65.0	53.4 (OMe), 157.5 (CO ester)
c	67	144 (decomp.)	1624s	165.3	93.4	94.2	64.2	
d	51[c]	131 (decomp.)	1646s	163.6	92.5	96.6	—[d]	14.4 and 67.7 (OEt)
e	73	137 (decomp.)	1632s	175.4	92.5	93.6	63.7	27.2 and 33.8 (But)

[a] The phenyl C-atoms absorb at δ 126–132 (CH) and 137–144 (C_i). [b] Together with 43% of **6a**. [c] Together with 7% of **6d**. [d] Not observed.

Table 2 Characterization of the thietan-3-imines **6**[a]

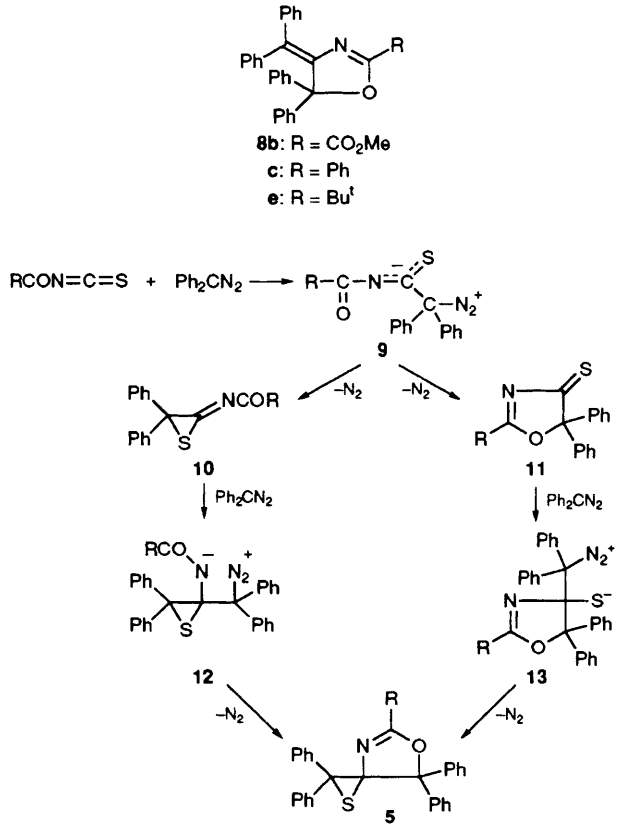
Compound	Yield (%) **5** → **6**	Mp/°C	IR(KBr) ν/cm^{-1}	^{13}C NMR ($CDCl_3$) δ C–2/4	C–3	N–C=O	Other signals[b]
6a	83	162	1720s, 1695s	74.9	170.1[c]	176.7[c]	91.7 (CCl_3)
b	72	187	1749s, 1700s	75.0	170.9	164.7	53.0 (OMe), 157.6 (CO ester)
c	92	161	1703s, 1672s	75.7	168.6	175.7	
d	96	197	1709s, 1683s	74.8	172.5	159.2	13.7 and 62.4 (OEt)
e	70	162	1719s, 1677s	75.1	168.0	189.5	26.4 and 41.2 (Bu^t)

[a] The compounds were recrystallized from Et_2O–*n*-pentane (**6a**), Et_2O (**6b**) or CH_2Cl_2–*n*-hexane (**6c–e**) and gave satisfactory C,H analyses. [b] The phenyl C-atoms absorb at δ 127–129 (3 signals) and 140.2–141.7 (C_i). [c] The reverse assignment is possible.

Table 3 Characterization of the 4-alkylidene-4,5-dihydro-1,3-oxazoles **8**[a]

Compound	Yield (%)[b]	Mp/°C	IR(KBr) ν/cm^{-1}	^{13}C NMR ($CDCl_3$) δ C–2	C–4	C–5	Other signals[c]
8b	95	172	1740s, 1648m	156.4	149.5	97.2	53.3 (OMe), 158.0 (CO)
c	90	162	1647m	165.9	152.0	95.4	
e	73	147	1643m	177.3	152.3	95.0	27.5 and 33.7 (Bu^t)

[a] The compounds were recrystallized from CH_2Cl_2–*n*-hexane. [b] Prepared from the spiro compounds **5** and triphenylphosphine in dichloromethane at room temperature. [c] The Ph and Ph_2C= atoms absorb at δ 126–132 and 136–141.



Scheme 2

has been verified by analysing the NMR spectra of **5c,e** after melting, showing the presence of the thietanes **6c,e** and the 4-alkylidene-1,3-oxazoles **8c,e**. The latter were prepared independently by desulfurization of compounds **5c,e** with triphenylphosphine (Table 3). Compounds **5a,b** gave only **6a,b**, and compound **5d** gave predominantly **6d** in addition to an unknown compound upon melting.

A rational mechanism for the formation of the unexpected spiro compounds is depicted in Scheme 2 and involves the formation of the betaine **9** in the first step of the reaction. This intermediate can lose nitrogen and cyclize in two ways; either to the thiiranimine **10**, similar to **3**, or to the oxazole **11**. Since these heterocycles could not be observed in the reaction mixtures, even when an equimolar amount of diphenyldiazomethane was used, we assume that their electrophilic exocyclic double bond, C=N or C=S, react instantaneously with a second molecule of diphenyldiazomethane. The resulting betaines **12** and **13** are then transformed into the products **5a–e** after extrusion of nitrogen. The betaines **9**, **12** and **13** may equilibrate with the corresponding ring-closed heterocycles, which, in fact, are the intermediates if the reactions of diphenyldiazomethane with the hetero double bonds C=S and C=N proceed by a concerted 1,3-dipolar cycloaddition mechanism.[7]

Received, 31st August 1994; Com. 4/05316H

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