

Reaction of acylisothiocyanates with 5-isopropoxy-4-methyloxazole

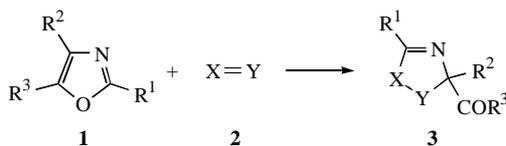
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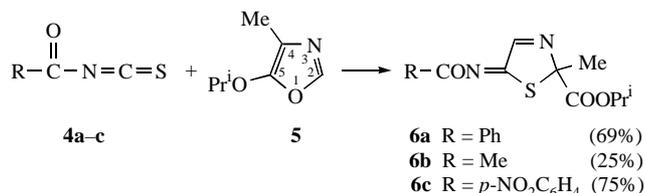
Formal [3+2]-cycloaddition of acylisothiocyanates to 5-isopropoxy-4-methyloxazole gives derivatives of 5-acylimino-3-thiazoline.

In recent years, extensive studies have been carried out on the formal [3+2]-cycloaddition to oxazoles **1** accompanied by opening of the oxazole ring and formation of another heterocycle **3** (Scheme 1).



Scheme 1

A series of 'ene' components **2** of this reaction, such as C=C,¹ C=N,² N=N,^{2,3} C=O,^{2,4} and N=O⁵ bonds have been studied; the addition of oxazoles to the C=S group of thioaldehydes generated *in situ* has also been reported.⁶



Scheme 2

We found that acylisothiocyanates **4a–c** reacted with 5-isopropoxy-4-methyloxazole **5** to give hitherto unknown 5-acylimino-2-isopropoxycarbonyl-2-methyl-3-thiazolines **6a–c**, *i.e.* the transformation occurred *via* formal [3+2]-cycloaddition of the C=S bond of acylisothiocyanate to the 2nd and 4th atoms of the oxazole ring (Scheme 2). Thus, we show for the first time

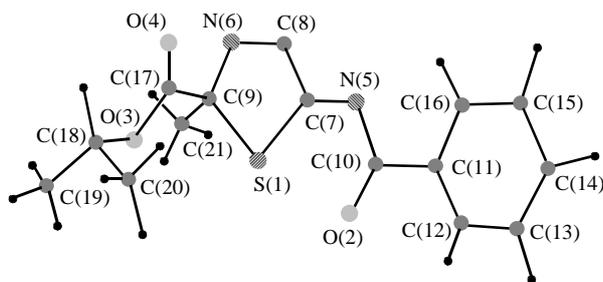


Figure 1 The structure of compound **6a**. Bond lengths (Å): S(1)–C(7) 1.763(5), S(1)–C(9) 1.859(6), O(2)–C(10) 1.227(8), O(3)–C(17) 1.345(7), O(3)–C(18) 1.461(7), O(4)–C(17) 1.226(8), N(5)–C(7) 1.283(8), N(5)–C(10) 1.421(7), N(6)–C(8) 1.292(9), N(6)–C(9) 1.401(7), C(7)–C(8) 1.429(9), C(9)–C(17) 1.492(10), C(9)–C(21) 1.513(8), C(10)–C(11) 1.519(10), C(11)–C(12) 1.341(8), C(12)–C(13) 1.391(10), C(13)–C(14) 1.363(9), C(14)–C(15) 1.417(10), C(15)–C(16) 1.435(10), C(16)–C(11) 1.383(8), C(18)–C(19) 1.527(8), C(18)–C(20) 1.512(10). Bond angles (°): C(7)–S(1)–C(9) 89.3(3), S(1)–C(7)–C(8) 107.5(5), S(1)–C(7)–N(5) 128.5(5), N(5)–C(7)–C(8) 124.0(6), C(7)–C(8)–N(6) 120.6(6), C(8)–N(6)–C(9) 112.0(6), S(1)–C(9)–N(6) 110.0(5), S(1)–C(9)–C(17) 104.0(5), S(1)–C(9)–C(21) 110.9(5), N(6)–C(9)–C(17) 109.9(5), N(6)–C(9)–C(21) 111.0(5), C(17)–C(9)–C(21) 110.8(6), C(7)–N(5)–C(10) 115.7(5), O(2)–C(10)–N(5) 125.6(7), O(2)–C(10)–C(11) 120.1(7), N(5)–C(10)–C(11) 114.3(5), C(10)–C(11)–C(12) 118.9(6), C(10)–C(11)–C(16) 119.6(7), C(12)–C(11)–C(16) 121.4(7), C(11)–C(12)–C(13) 121.3(6), C(12)–C(13)–C(14) 119.3(8), C(13)–C(14)–C(15) 121.5(8), C(14)–C(15)–C(16) 117.0(6), C(15)–C(16)–C(11) 119.2(7), C(9)–C(17)–O(4) 124.9(7), O(3)–C(17)–O(4) 120.7(6), O(3)–C(17)–C(9) 114.4(5), O(3)–C(18)–C(19) 104.6(3), O(3)–C(18)–C(20) 105.8(6), C(17)–O(3)–C(18) 119.4(5), C(19)–C(18)–C(20) 110.2(6).

that oxazoles react by the above mechanism not only with heteroolefins but also with heterocumulenes.[†]

The structure of adduct **6a** was confirmed by X-ray diffraction analysis[‡] (Figure 1), while the structures of compounds **6b,c** were established by comparing their ¹H and ¹³C NMR and mass spectra with those of compound **6a**.

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[†] 5-Benzoylimino-2-isopropoxy-2-methyl-3-thiazoline **6a** was obtained by refluxing oxazole **5**⁷ (1.0 g, 7.1 mmol) and isothiocyanate **4a** (1.16 g, 7.1 mmol) in toluene for 7 h under argon. The resulting mixture was chromatographed on a column with SiO₂ using benzene as an eluent to give 1.50 g of compound **6a** as large yellow prisms, mp 84–85.5 °C (from hexane), *R_f* (Silufol, Et₂O–benzene, 1:1) 0.53–0.56. Found (%): C 59.00, H 5.36, N 9.29, S 10.30. Calc. for C₁₅H₁₆N₂O₃S (%): C 59.19, H 5.30, N 9.21, S 10.53.

¹H NMR (300 MHz, CDCl₃) δ: 1.23 [m, 6H, CH(CH₃)₂], 2.00 (s, 3H, CH₃), 5.04 [m, 1H, CH(CH₃)₂], 7.51 (m, 3H, Ph), 8.30 (t, 3H, Ph and N=CH). ¹³C NMR (75.5 MHz, CDCl₃) δ: 21.3 [q, CH(CH₃)₂], 24.7 (q, CH₃), 70.7 [d, CH(CH₃)₂], 93.7 (s, S–C–CH₃), 128.5 and 130.4 (d, Ph, *o*- and *m*-CH), 133.7 (d, Ph, *p*-CH), 134.4 (s, Ph, quaternary C), 163.7 (d, N=CH), 167.1 (s, N=C–S), 177.6 and 178.3 (s, N–C=O and O–C=O). MS (EI, 70 eV) *m/z* 304 [M]⁺.

Adducts **6b** [bp 144–145 °C (1 mmHg)] and **6c** (mp 99–101.5 °C) were synthesized similarly to adduct **6a**.

[‡] X-ray diffraction analysis. Crystals of compound **6a** in the form of tetrahedral prisms were grown from pentane, triclinic, *a* = 10.164(1) Å, *b* = 9.732(1) Å, *c* = 7.877(1) Å, *α* = 96.40(1)°, *β* = 93.30(1)°, *γ* = 98.92(1)°, *Z* = 2, space group *P* $\bar{1}$, C₁₅H₁₆N₂O₃S. A complete set of 1295 independent reflections with *I* > 2σ(*I*) was obtained on a RED-4 four-circle automatic diffractometer (λ Cu-Kα, graphite monochromator, ω–θ/2θ scanning, θ ≤ 60°).

The structure of compound **6a** was solved by a direct method. The coordinates of non-hydrogen atoms were refined by the least-squares method in an anisotropic approximation; the hydrogen atom coordinates were refined isotropically. The final value of *R* was 0.07. Atomic coordinates, bond lengths and thermal parameters have been deposited at the Cambridge Crystallographic Data Centre (CCDC). For details, see Notice to Authors, *Mendeleev Commun.*, 1998, issue 1. Any request to the CCDC should quote the full literature citation and the reference number 1135/23.