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Peculiar Reaction of N^2-Acyl Derivatives of 2-Aryl-5-hydrazino-1,3-oxazole-4-carbonitriles with the Lawesson Reagent

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ABSTRACT: *Easily accessible N^2-acyl derivatives of 2-aryl-5-hydrazino-1,3-oxazole-4-carbonitriles react peculiarly with the Lawesson reagent. In addition to thionation, the reaction involves a recyclization to afford new substituted 2-(5-amino-1,3-thiazol-4-yl)-1,3,4-thiadiazoles. Their structure is corroborated spectroscopically and by the X-ray diffraction method.* © 2007 Wiley Periodicals, Inc. Heteroatom Chem 18:782–785, 2007; Published online in Wiley InterScience (www.interscience.wiley.com). DOI 10.1002/hc.20413

INTRODUCTION

The Lawesson reagent is known to be a useful tool for thionation of various carbonyl compounds (see, e.g., reviews [1,2]). However, thionation is rather commonly paralleled by phosphorylation, cyclization, and other as yet poorly understood processes. The present work elucidates a complicated reaction between the Lawesson reagent and the N^2-acyl derivatives of 2-aryl-5-hydrazino-1,3-oxazole-4-carbonitriles that are not merely thionated but also undergo recyclization. As a result, some novel 1,3,4-thiadiazole derivatives are obtained, which are substituted at position 2 with the 5-amino-2-aryl-1,3-thiazol-4-yl residues (Table 1).

RESULTS AND DISCUSSION

The previously found [3] cyclocondensation of easily accessible 2-acylamino-3,3-dichloroacrylonitriles with hydrazine hydrate was employed to prepare 2-aryl-5-hydrazino-1,3-oxazole-4-carbonitriles **1a,b**. As shown here, the latter are regioselectively acylated at the N^2 atom of the hydrazino group, if treated under mild conditions with acyl chlorides in the presence of dimethylaniline. Interestingly, the acylation conducted in the presence of triethylamine mostly involves the N^1 atom of the hydrazino group [4]. By comparing the IR and ^{1}H NMR spectra for isomeric acylated products, we have been able to fully ascertain that compounds **2a–d** are free of the primary amino group but contain, instead, the characteristic moiety C(O)NHNHHet (Table 2).

On heating compounds **2a–d** with the Lawesson reagent in dioxane, it is likely that thionation products **3a–d** initially formed and then undergo the cascade conversion **3** → **4** → **5** → **6** → **7** as shown in Scheme 1.

We first should note that the recyclization **3** → **4** → **5** is similar to the formerly studied

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TABLE 1 Physical and Analytical Data of Compounds **2** and **7**

Compound	*mp (°C)*	*Yield (%)*	*Mol. Formula (Mol. Wt.)*	*Analysis (%) Found (Calcd.)* C	H	N	S
2a	191–192[a]	87	$C_{12}H_{10}N_4O_2$ (242.2)	59.37 (59.50)	4.01 (4.16)	22.96 (23.13)	–
2b	200–201[a]	83	$C_{13}H_{12}N_4O_2$ (256.3)	61.01 (60.93)	4.73 (4.72)	21.80 (21.86)	–
2c	210–211[a]	95	$C_{18}H_{14}N_4O_2$ (318.3)	67.55 (67.91)	4.37 (4.43)	17.58 (17.60)	–
2d	273–274[a]	97	$C_{19}H_{16}N_4O_2$ (332.4)	68.51 (68.66)	4.59 (4.85)	16.71 (16.86)	–
7a	194–195[b]	61	$C_{12}H_{10}N_4S_2$ (274.4)	52.27 (52.53)	3.43 (3.67)	20.40 (20.42)	23.08 (23.37)
7b	212–213[b]	53	$C_{13}H_{12}N_4S_2$ (288.4)	59.91 (54.14)	4.05 (4.19)	19.33 (19.43)	22.14 (22.24)
7c	243–244[c]	75	$C_{18}H_{14}N_4S_2$ (350.5)	61.42 (61.69)	3.97 (4.03)	15.74 (15.99)	18.31 (18.30)
7d	254–255[c]	80	$C_{19}H_{16}N_4S_2$ (364.5)	62.39 (62.61)	4.13 (4.42)	15.25 (15.37)	17.44 (17.59)

[a] Recrystallization from MeCN.
[b] Recrystallization from the mixture benzene-hexane.
[c] Recrystallization from benzene.

[5] conversion of the adducts formed by aryl isothiocyanates and compounds **1a,b**. It is plausible that a significant part in this process is played by prototropic tautomers **4a–d** containing, instead of the aromatic oxazole nucleus, the nonaromatic oxazoline ring which opens more readily when attacked at the electrophilic C^5-center by the nucleophilic S-center of the thione group. Further intramolecular cyclization **6** → **7** represents a particular case of the 5-amino-1,3-thiazole ring closure favored by the appropriate mutual dispositions of the C≡N bond and the thionamide group (for another example, see [6]). It is not improbable that the cyclization proceeds rapidly not only as a result of heating but also due to the catalytic effect of the Lawesson reagent.

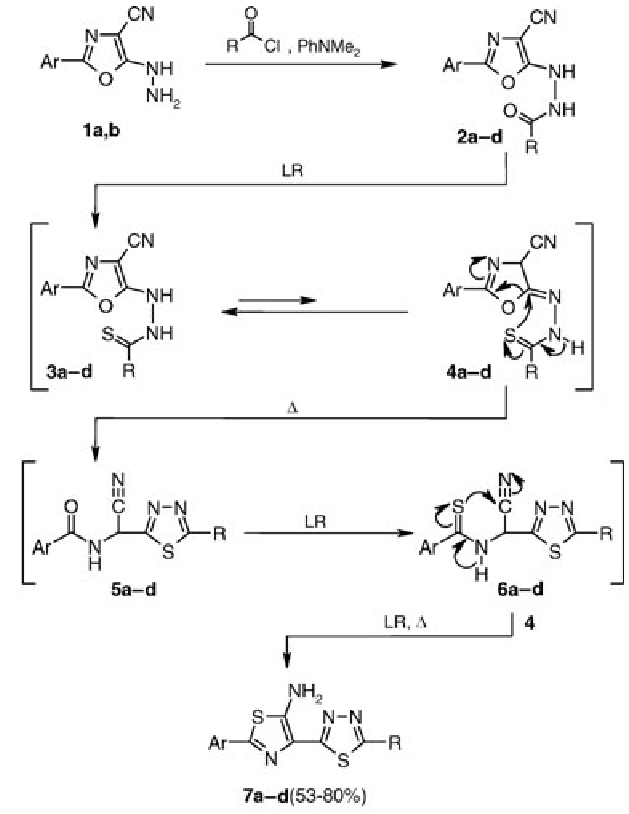
The above-discussed multistep processes furnish, in high yields, new sulfur-containing diazoles **7a–d**, which can be classed, on the one hand, with 1,3-thiazole derivatives and, on the other hand, with substituted 1,3,4-thiadiazoles. The primary amino group in their molecules manifests itself in the IR and ^{1}H NMR spectra (Table 2). In addition, unambiguous structural determination of one such compound, **7a**, was carried out by the X-ray diffraction analysis (Fig. 1 and Table 3).

The molecule in question is almost planar: the mean deviation from the least-squares plane of

TABLE 2 Spectroscopic Data of Compounds **2** and **7**

Compound	*IR (KBr) (cm^{-1})*	*^{1}H NMR (DMSO-d_6/TMS) δ,*
2a	1690 (NC=O), 2240 (C≡N), 3150–3350[a] (NH)	1.96 (s, 3H, CH_3), 7.49–7.81 (m, 5H, C_6H_5), 10.19 (br s, 1H, NH), 10.29 (br s, 1H, NH)
2b	1680 (NC=O), 2245 (C≡N), 3150–3350[a] (NH)	1.93 (s, 3H, CH_3), 2.38 (s, 3H, CH_3), 7.27–7.71 (m, 4H, C_6H_4), 10.07 (br s, 1H, NH), 10.25 (br s, 1H, NH)
2c	1640 (NC=O), 2240 (C≡N), 3200–3300[a] (NH)	2.40 (s, 3H, CH_3), 7.29–7.83 (m, 9H, C_6H_4, C_6H_5), 10.33 (br s, 1H, NH), 10.82 (br s, 1H, NH)
2d	1680 (NC=O), 2220 (C≡N), 3100–3370[a] (NH)	2.38 (s, 3H, CH_3), 2.40 (s, 3H, CH_3), 7.29–7.79 (m, 8H, $2C_6H_4$), 10.33 (br s, 1H, NH), 10.82 (br s, 1H, NH)
7a	3325, 3435 (NH_2)	2.73 (s, 1H, CH_3), 7.40 –(m, 5H, C_6H_5), 7.50 (br s, 2H, NH_2)
7b	3290, 3420 (NH_2)	2.37 (s, 1H, CH_3), 2.73 (s, 1H, CH_3), 7.28–7.64 (m, 4H, C_6H_4), 7.56 (br s, 2H, NH_2)
7c	3260, 3355 (NH_2)	2.37 (s, 1H, CH_3), 7.37–7.95 (m, 9H, C_6H_4,C_6H_5) 7.73 (br s, 2H, NH_2)
7d	3290, 3420 (NH_2)	2.36 (s, 3H, CH_3), 2.40 (s, 3H, CH_3), 7.23–7,83 (m, 8H, $2C_6H_4$), 7.63 (br s, 2H, NH_2)

[a] Associated bands.



1-7	a	b	c	d
Ar	Ph	4-MeC$_6$H$_4$	Ph	4-MeC$_6$H$_4$
R	Me	Me	4-MeC$_6$H$_4$	4-MeC$_6$H$_4$

SCHEME 1

non-hydrogen atoms does not exceed 0.0424 Å. The bond distances and angles in the molecule of compound **7a** agree with the structural formula of the compound. The primary amino group is coplanar with the rest of the molecule, as evidenced by the sum of the surrounding bond angles of the atom N4 (357(2)°), because of the conjugation between its lone electron pair and the π-system of the thiazole ring.

In the crystal state, there were found both intramolecular (N4–H41N$\cdots$N2; N4–H41N 0.84(2), H41N$\cdots$N2 2.26(2), N4$\cdots$N2 2.894(3) Å, N4–H41N–N2 132.5(19)°) and intermolecular (N4–H42N$\cdots$N1a; N4–H42N 0.79(3), H42N$\cdots$N1a 2.50(2), N4$\cdots$N1a 3.052(2) Å, N4–H42N–N1a 128(2)°) hydrogen bonds. The nitrogen atom N1 labeled with "a" is related to unlettered atoms by the following symmetry operation: $-x+2$, $-y+1$, $-z$.

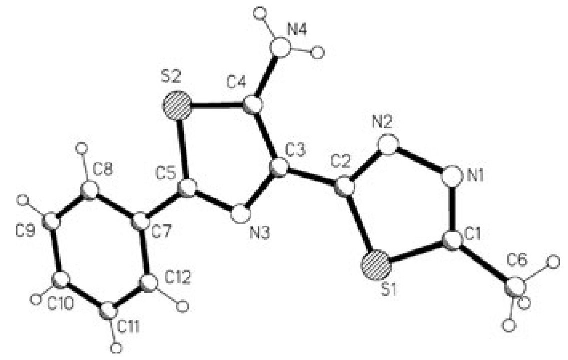


FIGURE 1 Perspective view and labeling scheme for the molecule **7a.**

EXPERIMENTAL

^{1}H NMR spectra were recorded on a Varian Gemini 300 spectrometer at 300 MHz using TMS as an internal standard. IR spectra were measured on a Specord M-80 spectrometer for KBr disks.

5-N^2-Acetyl (or 4-Methylbenzoyl)hydrazino-2-aryl-1,3-oxazol-4-carbonitriles **2a–d**

To a suspension of **1a,b** (10 mmol) obtained by the known procedure [4] in THF (25 mL) containing dimethylaniline (5 mL), a solution of acetyl chloride or 4-methylbenzoyl chloride (10 mmol) was added dropwise in THF (5 mL) at 10°C. The reaction mixture was stirred at ambient temperature for 10 h. Then, it was treated with water (100 mL), filtered, washed with ether, and purified by recrystallization from MeCN to give **2a–d** (Table 1).

2-Aryl-4-[5-methyl(4-methylphenyl)-1,3,4-thiadiazol-2-yl]-1,3-thiazol-5-amines **7a–d**

A mixture of **2a–d** (10 mmol) and Lawesson reagent (20 mmol) in dioxane (50 mL) was refluxed for 4 h, cooled, and treated with water (150 mL). Then, it was

TABLE 3 Selected Bond Lengths (Å) and Bond Angles (°) of **7a**

C(1)–N(1)	1.293(2)	C(2)–S(1)–C(1)	87.53(8)
C(2)–N(2)	1.315(2)	C(4)–S(2)–C(5)	89.54(8)
C(1)–S(1)	1.7255(16)	N(1)–C(1)–C(6)	123.70(16)
C(2)–S(1)	1.7254(17)	N(2)–C(2)–C(3)	124.23(15)
N(1)–N(2)	1.387(2)	C(5)–N(3)–C(3)	111.21(14)
C(3)–C(4)	1.379(2)	N(4)–C(4)–C(3)	128.16(17)
C(3)–N(3)	1.381(2)	C(1)–N(1)–N(2)	112.79(14)
C(5)–N(3)	1.303(2)	N(3)–C(5)–S(2)	114.18(12)
C(4)–S(2)	1.7236(16)		
C(5)–S(2)	1.7545(17)		
C(4)–N(4)	1.347(2)		

filtered, suspended in a saturated water solution of sodium hydrocarbonate, and left for 6 h. The residue was collected, washed with water, and purified by recrystallization from an appropriate solvent to give **7a–d** (Table 1).

X-Ray Structure Determination for 7a

Crystal Data. $C_{12}H_{10}N_4S_2$, M 274.36, monoclinic, space group $P2_1/n$ (N 14), $a = 5.5191(2)$, $b = 8.5465(3)$, $c = 25.9833(9)$ Å, $\beta = 91.141(2)^\circ$, $V = 1225.36(7)$ Å^3, $Z = 4$, $d_c = 1.487$ g cm^{-3}, $\mu = 0.420$ cm^{-1}, $F(000) = 568$, crystal size ca. $0.50 \times 0.22 \times 0.05$ mm.

Data Collection. All crystallographic measurements were performed at room temperature on a Bruker Smart Apex II diffractometer operating in the ω and φ scan modes. The cell parameters were obtained from the least-squares treatment of 4302 reflections in the θ range of 3.14°–30.12°. The intensity data were collected within the range of $3.14^\circ \leq \theta \leq 31.29^\circ$ using Mo K_α radiation ($\lambda = 0.71078$ Å). The intensities of 13,966 reflections were collected (3961 unique reflections). Data were corrected for Lorentz and polarization effects.

Structure Solution and Refinement. The structure was solved by direct methods and refined by the full-matrix least-squares technique in the anisotropic approximation for non-hydrogen atoms using the SHELXS97 and SHELXL97 programs [7,8]. Hydrogen atoms were located in the difference Fourier maps and refined isotropically. The SADABS absorption correction (the ratio of the minimum to maximum apparent transmission equal to 0.814339) was applied. In the refinement, 3961 reflections (3012 reflections with $I \geq 2\sigma(I)$) were used. Convergence was obtained at $R_1 = 0.0415$ and $wR_2 = 0.1033$, GOF = 1.054 (203 parameters; observed/variable ratio = 14.84; the largest and minimal peaks in the final difference map are 0.28 and –0.19 e/Å^3, the weighting scheme is as follows: $\omega = 1/[\sigma^2(F_o^2) + (0.0482P)^2 + 0.3915P]$, where $P = (F_o^2 + 2F_c^2)/3$). Full crystallographic details have been deposited at Cambridge Crystallographic Data Centre (CCDC). Any request to the CCDC for these materials should quote the full literature citation and reference number CCDC 627507.

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