REACTIONS OF BENZOYL ISOTHIOCYANATES WITH 5-SUBSTITUTED TETRAZOLES

Michal UHER, Jozef FOLTÍN, František POVAŽANEC and Jaroslav KOVÁČ

Department of Organic Chemistry,
Slovak Institute of Technology, 880 37 Bratislava

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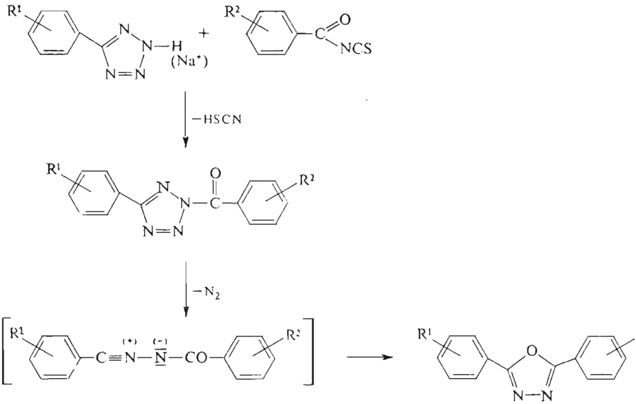
A method of preparing 2,5-disubstituted 1,3,4-oxadiazoles from benzoyl isothiocyanates and 5-substituted tetrazoles is described. The transformation of the tetrazole into a 1,3,4-oxadiazole ring takes place readily under neutral conditions giving high yields of the desired products.

The reaction of isothiocyanates with 5-phenyltetrazole was first described by Huisgen and coworkers.[1] Of the reactions of benzoyl isothiocyanates only the one with 5-aminotetrazole[2,3] has been described thus far. The cited authors performed the reaction in pyridine, and the formation of 5-benzoylaminotetrazole was confirmed by using



$R^1 = H$; $4-NO_2$; $4-CH_3O$; $3-Cl$
$R^2 = H$; $4-NO_2$

I

SCHEME 1

^{15}N-labelled benzoyl isothiocyanate (elimination of HSCN *via* intramolecular N,N-transacylation). Treatment of 5-substituted tetrazoles with acid anhydrides or acid chlorides yields unstable N-acyltetrazoles[4]. Heating of the latters gives, *in situ*, nitrilimines which, by intramolecular 1,5-dipolar cyclization, afford the corresponding 1,3,4-oxadiazoles[5]. We have also described preparation of 2- and 2,5-substituted 1,3,4-oxadiazoles from tetrazoles and a dicyclohexylcarbodiimide-carboxylic acid adduct[6]. Other methods of preparing 1,3,4-oxadiazoles have been described in the literature[7-11].

In connection with our work on the use of benzoyl isothiocyanates for preparing heterocyclic substances[12,13] we now describe reactions of benzoyl isothiocyanates with 5-substituted phenyltetrazoles. To study these reactions benzoyl and 4-nitrobenzoyl isothiocyanates have been chosen.

Reactions of benzoyl isothiocyanates with 5-(R^1-phenyl)tetrazoles were performed in mesitylene at 160–170°C. When sodium salts of 5-(R^1-phenyl)tetrazoles were used the temperature of the reactions was 100–120°C. The structure of the prepared substances was investigated and the obtained results suggested that 1,3,4-oxadiazole derivatives had been formed. This was confirmed by the reaction[4] of 5-phenyltetra-

TABLE I

Synthesized 2-(R^2-Phenyl)-5-)R^1-phenyl)-1,3,4-oxadiazoles

Compound	R^1 R^2	Formula (m.w.)	M.p., °C yield, g	Solvent
Ia	H H	$C_{14}H_{10}N_2O$ (222·2)	137[a] 80	ethanol
Ib	4-NO_2 H	$C_{14}H_9N_3O_3$ (267·2)	206[a] 85	acetone
Ic	4-CH_3O H	$C_{15}N_{12}N_2O_2$ (252·3)	147[a] 85	ethanol
Id	3-Cl H	$C_{14}H_9ClN_2O$[b] (256·8)	117–118	acetone
Ie	4-NO_2 4-NO_2	$C_{14}H_8N_4O_5$ (312·2)	305[a] 80	acetic acid
If	4-CH_3O 4-NO_2	$C_{15}H_{11}N_3O_4$ (297·3)	227–228[a] 95	benzene

[a] Lit.[4]: *Ia*, m.p. 137–138°C; *Ib*, m.p. 206·5–208°C; *Ic*, m.p. 149–149·5°C; *Ie*, m.p. 309–310°C; *If*, m.p. 229–230°C. [b] For $C_{14}H_9ClN_2O$ (247·5) calculated: 10·90% N, 14·81% Cl; found: 10·80% N, 13·68% Cl.

zole with benzoyl chloride in pyridine: spectral characteristics and melting points of 2,5-diphenyl-1,3,4-oxadiazole prepared in the two independent manners were identical (Table I).

The formation of 1,3,4-oxadiazole derivatives involves probably a nucleophilic substitution reaction of the tetrazole ring and the carbonyl carbon atom of benzoyl isothiocyanates. The assumed mechanism is shown in Scheme 1. The intermediate formation of SCN^- ion was proved by the $FeCl_3$-test. The advantages of the method described herein lie in the fact that the reaction is easy to handle, it can be performed under neutral conditions and affords high yields (73–95%) of highly pure products.

EXPERIMENTAL

The used benzoyl isothiocyanates[14] and 5-(R^1-phenyl)tetrazoles[15] were prepared as described. The UV spectra for 3—5 . 10^{-3}M ethanolic solutions were measured with a Specord UV VIS (Zeiss) spectrometer using a 10 mm cell. The IR spectra (KBr technique, 1 : 300 substrate-KBr ratio) were obtained with a UR-20 (Zeiss) instrument. Mass spectra (70 eV, emission 100 μA) were recorded with an AEI MS-902 S spectrometer applying the direct sample-introduction technique; the temperature of the ionizing chamber was 100°C.

Reactions of 5-(R^1-Phenyl)tetrazoles with Benzoyl Isothiocyanates

A mixture of the respective benzoyl isothiocyanate (0·01 mol) and 5-(R^1-phenyl)tetrazole, or its sodium salt (0·01 mol) in mesitylene (10 ml) was heated at 160—170°C (or 100—120°) for 1 h, or until evolution of nitrogen ceased. After cooling, the product was precipitated by addition of light petroleum, filtered, the filtrate was concentrated at reduced pressure, and the crude product was recrystallized (for solvents see Table I).

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