

## PREPARATION OF 2- AND 2,5-DISUBSTITUTED 1,3,4-OXADIAZOLES FROM TETRAZOLES AND CARBOXYLIC ACIDS

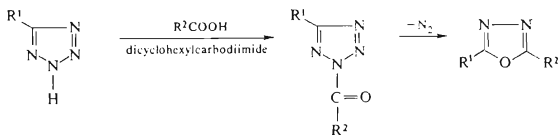
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The intermediate N-acylated tetrazoles, prepared from 5-substituted tetrazoles, N,N'-dicyclohexylcarbodiimide and carboxylic acids, undergo decomposition to form 2-, or 2,5-disubstituted 1,3,4-oxadiazoles in high yield.

In continuance of our study of 2,5-disubstituted 1,3,4-oxadiazoles<sup>1</sup> we found a novel process of transformation of 5-substituted tetrazoles to 2-, or 2,5-substituted 1,3,4-oxadiazoles. Treatment of 5-substituted tetrazoles with acid anhydrides or chlorides leads to 1,3,4-oxadiazoles<sup>2,3</sup>. Aiming to generalize the Huisgen synthesis, we investigated another method of activation of carbonyl groups without preparation of acid chlorides or anhydrides, what is advantageous primarily with substances susceptible to acid medium. Such a reagent is the adduct of dicyclohexylcarbodiimide with carboxylic acids, which furnishes in the presence of 5-substituted tetrazole the corresponding N-acyl derivative. The latter decomposes thermally under liberation of nitrogen; the zwitterion thus formed is transformed to a substituted 1,3,4-oxadiazol in a high yield. This method enables to prepare, in addition to 2,5-disubstituted



1,3,4-oxadiazoles, also 2-substituted 1,3,4-oxadiazoles from tetrazoles; the latter could not be obtained due to instability of formic chloride. This method makes it possible to transform carbonyl group to 2-substituted 1,3,4-oxadiazolyl grouping and consequently, to exploit this reaction for protecting carboxyl group in carboxylic acids.

TABLE I  
Characteristic Data of Substituted 1,3,4-Oxadiazoles

Compound	R <sup>1</sup>	R <sup>2</sup>	Yield %	Solvent	M.p., °C	Ref.
1	4-NO <sub>2</sub> C <sub>6</sub> H <sub>4</sub>	H	84	CH <sub>3</sub> CH <sub>2</sub> OH	156–157	4
2	C <sub>6</sub> H <sub>5</sub>	H	82	CCl <sub>4</sub>	154–156	4
3	C <sub>6</sub> H <sub>5</sub>	CH <sub>3</sub>	78	CCl <sub>4</sub>	65–66	2
4	4-NO <sub>2</sub> C <sub>6</sub> H <sub>4</sub>	CH <sub>3</sub>	92	CH <sub>3</sub> CH <sub>2</sub> OH	172–174	2
5	C <sub>6</sub> H <sub>5</sub>	CH <sub>2</sub> Cl	81	CCl <sub>4</sub>	118–119	2
6	C <sub>6</sub> H <sub>5</sub>	C <sub>4</sub> H <sub>3</sub> O	86	CCl <sub>4</sub>	103–104	5
7	C <sub>4</sub> H <sub>3</sub> O	C <sub>6</sub> H <sub>5</sub>	74	CCl <sub>4</sub>	103–104	5
8	C <sub>6</sub> H <sub>5</sub>	C <sub>6</sub> H <sub>5</sub>	94	CCl <sub>4</sub>	137–138	2
9	4-NO <sub>2</sub> C <sub>6</sub> H <sub>5</sub>	C <sub>6</sub> H <sub>5</sub>	85	CH <sub>3</sub> CH <sub>2</sub> OH	207–208	2
10	C <sub>4</sub> H <sub>3</sub> O	C <sub>4</sub> H <sub>3</sub> O	65	CCl <sub>4</sub>	140–142	6
11	C <sub>6</sub> H <sub>5</sub>	X <sup>a</sup>	62	CH <sub>3</sub> CH <sub>2</sub> OH	208–209	3
12	C <sub>4</sub> H <sub>3</sub> O	X <sup>a</sup>	29	CH <sub>3</sub> CO <sub>2</sub> C <sub>2</sub> H <sub>5</sub>	235–237	1

<sup>a</sup> X = 2-[2-(5-Nitro-2-furyl)viny].

## EXPERIMENTAL

The above-mentioned 1,3,4-oxadiazoles were alternatively prepared according to<sup>1–6</sup>. The IR spectra were measured with a UR-20 (Zeiss, Jena), the UV spectra with a UV-VIS Specord (Zeiss, Jena) and the <sup>1</sup>H-NMR spectra with a Tesla BS 487 C (80 MHz) apparatuses. All spectral characteristics of substituted oxadiazoles prepared by both procedures were found to be identical. Melting points were measured with a Kofler micro hot-stage and the mixed melting points did not reveal any depression.

### 1,3,4-Oxadiazoles

5-Substituted tetrazole (10 mmol) was added to a solution of dicyclohexylcarbodiimide (2.1 g, 10 mmol) and carboxylic acid (10 mmol) in toluene (15 ml). The mixture was heated to 120°C, the solvent distilled off after 15 min and the residue crystallized from a suitable solvent (Table I).

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