Review

β-Isothiocyanatoketones: A Convenient Source of Heterocyclic Compounds

Sham M. Sondhi*, Nirupma Singh, and Shefali Rajvanshi

Department of Chemistry, I. I. T. Roorkee, Roorkee-247667 (UA) India

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Summary. The preparation of β-isothiocyanatoketones and their reactions leading to formation of pyrimidine and bicyclic, tricyclic, tetracyclic, and pentacyclic heterocyclic compounds are reviewed. A few references concerning the rearrangement of heterocyclic compounds are also included. Some of the compounds reported have shown good antiinflammatory activity.

Keywords. Isothiocyanatoketones; Bi-, tri-, tetra-, and pentacyclic; Pyrimidines; Antiinflammatory.

Introduction

Isothiocyanatoketones are important reagents for the synthesis of various heterocyclic compounds. There is only scattered information available in literature about the synthetic utility of β-isothiocyanatoketones and thus an attempt was made to bring available information together in this review.

Synthesis of β-Isothiocyanatoketones

Several methods for the preparation of β-isothiocyanatoketones are available. Thus, Bruson [1] synthesized a number of ketothiocyanates 2a—2g by addition of HSCN to α, β-unsaturated ketones (Scheme 1). 2-Methyl-2-thiocyanato-4-pentanone (3) was synthesized by Mathes et al. [2] by following the reaction of Scheme 2. Further examination of 3 by Mathes [3] using IR revealed quite conclusively that 3 was 2-methyl-2-isothiocyanato-4-pentanone and not 2-methyl-2-thiocyanato-4-pentanone. A number of β-isothiocyanatoketones 4a—4d were synthesized by Bhanot et al. [4] (Scheme 3).

* Corresponding author. E-mail: sondify@iitr.ernet.in
Scheme 1

\[
\begin{align*}
2a: & \quad R^{'1} = CH_3, \quad R^{'2} = CH_3, \quad R^{'3} = H, \quad R^{'4} = CH_3 \\
2b: & \quad R^{'1} = CH_3, \quad R^{'2} = CH_3, \quad R^{'3} = H, \quad R^{'4} = Me_2C=CH- \\
2c: & \quad R^{'1} = Et_2CH-, \quad R^{'2} = H, \quad R^{'3} = H, \quad R^{'4} = CH_3 \\
2d: & \quad R^{'1} = n-C_6H_{13}-CH-Et, \quad R^{'2} = H, \quad R^{'3} = H, \quad R^{'4} = CH_3 \\
2e: & \quad R^{'1} = R^{'2} = (CH_2)_{n-} \quad R^{'3} = R^{'4} = (CH_2)_{n-} \\
2f: & \quad R^{'1} = Et_2CH-, \quad R^{'2} = H, \quad R^{'3} = R^{'4} = (CH_2)_{n-} \\
2g: & \quad R^{'1} = CH_3, \quad R^{'2} = R^{'4} - CH_2C(CH_3)_{2}CH_2-, \quad R^{'3} = H \\
\end{align*}
\]

\[\text{Scheme 1}\]

\[
\begin{align*}
(CH_3)_2C=CHCOCH_3 & \xrightarrow{NH_2SCN/HCl} (CH_3)_2C=CHCOCH_3 \text{SCN} \\
\end{align*}
\]

\[\text{Scheme 2}\]

\[
\begin{align*}
R^{'1} & \quad R^{'2} \quad R^{'3} \quad R^{'4} \\
4a: & \quad CH_3, \quad CH_3, \quad CH_3 \quad CH_3 \\
4b: & \quad C_2H_5, \quad CH_3, \quad C_2H_5 \quad C_2H_5 \\
4c: & \quad CH_3, \quad CH_3, \quad C_2H_5 \quad C_2H_5 \\
4d: & \quad CH_3, \quad CH_3, \quad C_6H_{15} \quad C_6H_{15} \\
\end{align*}
\]

\[\text{Scheme 3}\]

\[
\begin{align*}
R^{'1} & \quad R^{'2} \quad R^{'3} \quad R^{'4} \\
a: & \quad H, \quad H, \quad CH_3 \\
b: & \quad H, \quad H, \quad H \\
c: & \quad H, \quad CH_3, \quad H \\
d: & \quad H, \quad CH_3, \quad CH_3 \\
e: & \quad H, \quad Ph, \quad H \\
\end{align*}
\]

\[\text{Scheme 4}\]