

Ring Transformation of 2-Substituted Isothiazol-3(2*H*)-ones to 3,4-Dihydro-1,3-thiazin-4(2*H*)-ones by a Novel Carbene Addition–Ring Expansion Sequence

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Rhodium(II)-catalysed addition of diazo compounds to 2-substituted isothiazol-3(2*H*)-ones (1) results in a ready conversion into hitherto unknown 3,4-dihydro-1,3-thiazin-4(2*H*)-ones (2) in high yield.

Despite the presence of an ambiphilic S–N linkage in mononuclear isothiazoles, their chemistry is characterised by a scarcity of reactions involving ring transformations.¹ Even for the non-aromatic 2-substituted isothiazol-3(2*H*)-ones (1), which possess a labile S–N bond,² such reactions are rare. Apart from a report of their photoisomerization to thiazol-2-(3*H*)-ones,³ only two other closely related examples are known. Both involved rearrangement to the dihydrothiazinone ring system of isothiazolones derived from penicillin *S*-oxides, either under basic conditions⁴ or upon reduction with zinc

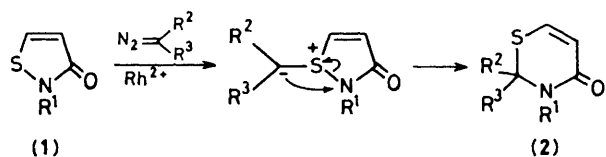
dust.⁵ We now report that the metal-catalysed reaction of 2-substituted isothiazol-3(2*H*)-ones (1) with diazo compounds is a novel and high yielding method for preparing 3,4-dihydro-1,3-thiazin-4(2*H*)-ones (2). The ready availability of the starting materials (1)⁶ and the simplicity of the procedure makes the method an attractive route to this little known⁷ class of compounds, the oxygen analogues of which have received considerable attention⁸ because of their biological activity.

The following experimental procedure is typical. A mixture

Table 1. Preparation of 3,4-dihydro-1,3-thiazin-4(2*H*)-ones (2).

R ¹	R ²	R ³	% Yield	M.p./°C	δ (CDCl ₃)/p.p.m.		J/Hz
					H-5	H-6	
Et	CO ₂ Me	CO ₂ Me	70	133.5–135 ^a	6.89	7.75	6.0
Et	COMe	CO ₂ Et	74	120.5–121.5 ^b	6.87	7.45	6.0
Et	COMe	COMe	58	127.5–128 ^a	6.92	7.50	6.0
Et	–CO·OCMe ₂ O·CO–		74	162.5–163 ^c	7.05	7.62	6.0
CO ₂ Me	–CO·OCMe ₂ O·CO–		95	193–194 ^b	7.28	8.18	6.0 ^e
Et	– <i>o</i> -C ₆ H ₄ –C ₆ H ₄ – <i>o</i> -CO–		91	148–149.5 ^d	6.07	6.28	5.8
Et	–COCH ₂ CMc ₂ CH ₂ CO–		65	116–117 ^a	6.93	7.54	6.6

^a Ether. ^b CH₂Cl₂–ether. ^c CHCl₃–ether. ^d Ethanol. ^e Determined for (CD₃)₂SO solution.



Scheme 1

of *N*-ethylisothiazol-3-one (**1**; $R^1 = \text{Et}$) (1.23 g), rhodium(II) acetate (15 mg), and dimethyl diazomalonate (1.42 g) in dry benzene (20 ml) was boiled under reflux for *ca.* 4 h until nitrogen evolution had ceased. Removal of solvent *in vacuo* followed by recrystallisation from ether afforded the pure dihydrothiazinone (**2**; $R^1 = \text{Et}$; $R^2 = R^3 = \text{CO}_2\text{Me}$) as colourless crystals (1.65 g; 70%). Further dihydrothiazinones similarly produced from (**1**; $R = \text{Et}$ or CO_2Me) by reaction with other diazo compounds are listed in Table 1, together with yields, melting points, and ^1H n.m.r. data. The structure of the products (**2**) was established from their elemental analyses and complementary spectral data, and in particular, by the presence of distinctive doublet ^1H n.m.r. resonances due to olefinic protons at shifts which compared favourably with literature values for related compounds.⁹

The most likely mechanism for the conversion of (**1**) into (**2**) is shown in Scheme 1 and involves the trapping of a carbene or carbenoid species¹⁰ to form an intermediate sulphonium ylide, which undergoes ring expansion by a 1,2-shift. This reaction sequence is notable in that it constitutes a new type of S–N cleavage of the isothiazole ring system induced by carbenes. No products of carbene addition to the double bond were detected.

Similar reactions of the parent compound (**1**; $R^1 = \text{H}$), which is better formulated as 3-hydroxyisothiazole,¹¹ failed to yield a dihydrothiazinone.† Instead, (**1**; $R^1 = \text{H}$) reacted preferentially with the catalyst as a bidentate ligand to form a

† 3-Hydroxyisothiazoles have been converted into 1,3-thiazine derivatives by reaction with substituted formamides under Vilsmeier conditions.¹²

red crystalline rhodium complex $[\text{Rh}_2(\text{C}_3\text{H}_2\text{NOS})_4]$, m.p. 155 °C (decomp.), ν_{max} 1630 cm^{-1} .

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