NOVEL METHODS FOR INTRODUCING A TWO-CARBON UNIT AT EITHER THE 3- OR 4-POSITION OF THE ISOQUINOLONE RING BY MEANS OF PHOTO[2+2]CYCLOADDITION REACTION¹⁾

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A novel method is described for introducing a two-carbon unit at either the 3- or 4-position of the 1-isoquinolone ring. The method for the synthesis of the 4-vinyl or 4-ethynyl derivative of isoquinolone consists of 1) photoaddition of the isoquinolone to chloroethylenes and 2) base treatment of the major (head-to-tail) adduct giving the 4-substituted isoquinolones. Similarly, by using 3-methoxyisoquinolone and vinyl acetate in step 1) and an acidic condition in step 2), a formylmethyl group is introduced into the 3-position of the isoquinolone ring.

KEYWORDS photo[2+2]cycloaddition; 1,1-dichloroethylene; 4-vinyl-1-isoquinolone; 4-ethynyl-1-isoquinolone; 3-formylmethyl-1-isoquinolone; photochemical cyclobutanation; 1-isoquinolone

Photochemical cyclobutanation of a cyclic enone system, coupled with subsequent C-C bond fission in the strained four-membered ring, provides a useful method for the construction of a variety of complex carbon frameworks.³⁻⁶⁾ Our continuing studies concerning the application of this method to heteroaromatic compounds⁶⁻⁸⁾ have led us to examine the chemical behaviour of the adducts (**A**) obtained from 1-isoquinolones (**1a**, **1b** and their 3-methoxy derivatives) and an appropriate olefin, with an expectation that the cyclobutanes thus formed would undergo C-C bond fission between 2- and 2a- (a-bond cleavage) or 1- and 8b-positions (b-bond cleavage) to give isoquinolones having a two-carbon unit at either the 4- or 3-position.

Here, we report that, while treatment of the adduct (**A**) obtained by photoaddition of 1-isoquinolones (**1**) to chloroethylenes with a base afforded the 4-substituted 1-isoquinolones (**B**), treating the adduct, derived by photoaddition of 1-isoquinolone having an alkoxyl group at 3-position to vinyl acetate, with an acid gave the 3-substituted derivative (**C**).

The adduct (**2b**) obtained by the photoaddition of 2-methyl-1-isoquinolone (**1b**) to 1,1-dichloroethylene⁹⁾ was treated with a base (t-BuOK-THF/reflux) to give 4-(1-chlorovinyl)-2-methyl-1-isoquinolone (**3b**: mp 89-90 °C)¹⁰⁾ in a quantitative yield. When the adduct (**2a**) derived from **1a** was used in this reaction, 4-ethynylisoquinolone [**4a**: mp 231-232 °C,

ν_{KBr} , 2110, 1650 cm^{-1} , $^1\text{H-NMR}$ δ ; 4.33 (s, $\equiv\text{C-H}$) was formed in 71% yield as a sole product. The formation of the latter product probably proceeds via the allene species (5) as the intermediate from 3a. Catalytic hydrogenation of the 4a over Lindlar's catalyst afforded in an almost quantitative yield the corresponding 4-vinyl derivative (6a: mp 167-169 $^{\circ}\text{C}$). The same type of transformation was also carried out using the adduct (7: either endo- or exo-isomer) of 1-isoquinolones and vinyl chloride to give directly the vinylisoquinolones (6a and 6b: oil) in yields of 92 and 98%, respectively. The ease of the desired C-C bond fission depends upon the stereochemistry of the adduct and the endo-adduct (7-endo) was found to be cleaved even by NaOH-MeOH/reflux, while the exo-adduct (7-exo) was stable under the same condition. Since only the minor adduct (7-endo) has a trans relationship between 8b-H and 1-Cl atoms, the cleavage probably proceeds in two steps via the cyclobutene (8) as the intermediate.

a-bond cleavage reaction

Since this type of reaction proceeded smoothly even by using the adduct derived from 1-isoquinolones and tetrachloroethylene, the method seems to have wide applicability for the introduction of a variety of a two-carbon unit at the 4-position of the isoquinolone ring. Obviously from the data shown above, this type of reaction (a-bond cleavage) would proceed in the [2+2]-adducts having a suitable leaving group at the 1-position. Actually when the 2-chloro derivatives (9) were employed in the above reaction, only the starting material was recovered unchanged.

Obvious extension of the above a-bond cleavage reaction then suggested that treatment of the cyclobut[g]isoquinolones having a hydroxyl group at the 1-position under suitable condition would give 3-formylmethylisoquinolones (b-bond cleavage products). This expectation was realized by the following experiment. The adduct (10: a ca. 5:2 mixture of endo- and exo isomers¹¹⁾) obtained from 3-methoxy-2-methyl-1-isoquinolone and vinyl acetate¹²⁾ was treated with an acid ($\text{BF}_3\text{-Et}_2\text{O}/\text{CH}_3\text{CN}$, at room temperature) to give the expected isoquinolone (11) in 40% yield. Contrary to the a-bond cleavage reactions, the methoxyl group at 2a-position in the adduct (10) acts as the leaving group.

b-bond cleavage reaction

The scope of the two types of bond cleavage reactions (a and b) used to synthesize isoquinolones having a functionalized C-2 unit at the 3- or 4-position is now under investigation, together with the use of a 4-vinyl derivative as the diene in the Diels-Alder reaction.¹³⁾

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- 10) All new compounds were identified either by elemental analysis or by high-resolution mass spectra and the structures were supported by acceptable spectral data.
- 11) Two isomers could be separated into the major (mp 80-81 °C) and minor adducts (oil), in which the former could be assigned as the endo isomer due to ca. 1 Hz long-range coupling (W-conformation, cf. the puckered conformation shown by formula 10-endo) between 2-endo- and 8b-protons.
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