

MANNICH REACTION OF 3-(HYDROXYPHENYL)ISOCOUMARINS

This report is devoted to study the Mannich reaction applying to arylisocoumarines in which the aromatic substituent at the third position is active in electrophilic substitution reactions due to the presence of the hydroxyl group. 3-(4-Hydroxyphenyl)-, 3-(2-hydroxy-5-methylphenyl)-, 3-(2,5-dihydroxyphenyl)-, and 3-(2-methoxy-4-hydroxyphenyl)isocoumarin were selected as the objects of investigation. The starting materials can be easily obtained by acylation of the corresponding phenol with homophthalic acid in the presence of a Lewis acid.

It proved impossible to execute the reaction of 3-(hydroxyphenyl)isocoumarins aminomethylation in classical Mannich reaction conditions; so to produce the target aminomethyl derivatives we have used formaldehyde amins – bis(dimethylamino)methane and bis(diethylamino)methane. A series of dialkylaminomethyl derivatives of isocoumarin were obtained, in all cases the substitution took place in the third position of the phenyl substituent. The reaction occurs by refluxing equimolar amounts of the products in a polar inert solvent, in a short time and with high enough yield; the obtained products can be isolated in the form of bases as well as in the form of hydrochlorides.

Double aminomethylation of 3-(4-hydroxyphenyl)isocoumarin – at positions 3', 5' – can probably be explained by both the smaller size of aminomethyl agent and the steric accessibility of the phenyl ring respective positions to attack, since only monoaminomethyl derivative formation were recorded in other cases. When there are two possible positions to aminomethylation 3-(2,5-dihydroxyphenyl)isocoumarin, product structure unambiguously established by the of ¹H NMR spectra data.

Under the same conditions and with the same efficiency aminomethylation to a third position of the phenyl substituent of 3-(2-hydroxy-5-methylphenyl)-3,4-dihydroisocoumarin was carried out.

Key words: isocoumarins (1H-isochromen-1-ones), amina, Mannich bases