

Reactions of 4-Aryl-1H-1,2,3-Triazoles with Cycloalkenones and Epoxides: Synthesis of 2,4- and 1,4-Disubstituted 1,2,3-Triazoles

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Abstract : The Huisgen's 1,3-dipolar [3+2] cycloaddition of organic azides and alkynes often give the mixtures of both the regioisomers 1,4- and 1,5- disubstituted 1,2,3-triazoles. Later, in presence of metal salts (click chemistry) such as copper(I)-catalyzed azide-alkyne cycloaddition (CuAAC) was used for the synthesis of 1,4-disubstituted 1,2,3-triazoles as a sole products regioselectively. Also, the 'click reactions' of Ruthenium-catalyzed azides-alkynes cycloaddition (RuAAC) is used for the synthesis of 1,5-disubstituted 1,2,3-triazoles as a single isomer. The synthesis of 1,4- and 1,5-disubstituted 1,2,3-triazoles has become the gold standard of 'click chemistry' due to its reliability, specificity, and biocompatibility. The 1,4- and 1,5-disubstituted 1,2,3-triazoles have emerged as one of the most powerful entities in the varieties of biological properties like antibacterial, antitubercular, antitumor, antifungal and antiprotozoal activities. Some of the 1,4,5-trisubstituted 1,2,3-triazoles exhibit Hsp90 inhibiting properties. The 1,4-disubstituted 1,2,3-triazoles also play a big role in the area of material sciences. The triazole-derived oligomeric, polymeric structures are the potential materials for the preparation of organic optoelectronics, silicon elastomers and unimolecular block copolymers. By the virtue of hydrogen bonding and dipole interactions, the 1,2,3-triazole moiety readily associates with the biological targets. Since, the 4-aryl-1H-1,2,3-triazoles are stable entities, they are chemically robust and very less reactive. In this regard, the addition of 4-aryl-1H-1,2,3-triazoles as nucleophiles to α,β -unsaturated carbonyls and nucleophilic substitution with the epoxides constitutes a powerful and challenging synthetic approach for the generation of disubstituted 1,2,3-triazoles. Herein, we have developed aza-Michael addition of 4-aryl-1H-1,2,3-triazoles to 2-cycloalken-1-ones in the presence of an organic base (DABCO) in acetonitrile solvent leading to the formation of disubstituted 1,2,3-triazoles. The reaction provides 1,4-disubstituted triazoles, 3-(4-aryl-1H-1,2,3-triazol-1-yl)cycloalkenones in major amount along with 1,5-disubstituted 1,2,3-triazoles, minor regioisomers with excellent combined chemical yields (upto99%). The nucleophilic behavior of 4-aryl-1H-1,2,3-triazoles was also tested in the ring opening of meso-epoxides in the presence of organic bases (DABCO/Et₃N) in acetonitrile solvent furnishing the two regioisomers 1,4- and 1,5-disubstituted 1,2,3-triazoles. Thus, the novelty of this methodology is synthesis of diversified disubstituted 1,2,3-triazoles under metal free condition. The results will be presented in detail.

Keywords : aza-Michael addition, cycloalkenones, epoxides, triazoles

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