

Rapid Communication

Cu(II)-catalyzed Michael addition of 1,3-dicarbonyl compounds

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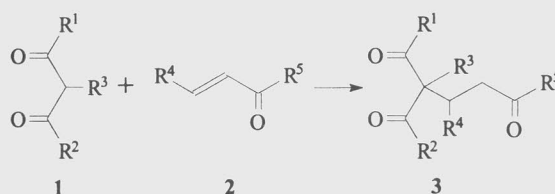
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Copper sulphate pentahydrate catalyses the C-C bond formation *via* Michael addition of 1,3-dicarbonyl compounds **1** under mild and neutral conditions at ambient temperature and furnishes the products **3** in high yields.

Michael reaction is one of the most efficient methods for effecting carbon-carbon bond formation¹ and has wide synthetic applications². One of the most efficient tools is the conjugated addition of nucleophiles to activated double bonds (addition of organometallics to α,β -enones). The classical Michael addition of β -dicarbonyl compounds to α,β -unsaturated ketones catalyzed by strongly basic alkoxides suffers from some drawbacks, namely retro-addition, bis-addition, subsequent condensations and other reactions leading to the formation of considerable amounts of by-products in numerous instances¹. In recent years various catalysts such as phase transfer catalysts³, transition metal complexes³, lanthanides⁴, alumina⁵, SnCl_4 ³, TiCl_4 ³, CsF ⁶, $\text{Bu}_2\text{Sn}(\text{OTf})_2$ ⁷ and $\text{BF}_3\text{Et}_2\text{O}$ ⁷ were proposed to circumvent this problem. But a serious limitation of some of these catalysts is towards the use of MVK, the simplest enone, as an acceptor due to its high tendency to polymerise, under certain reaction conditions^{6,8}. Herein we wish to report the use of a new catalyst copper sulphate pentahydrate in tetrahydro-furan for carbon-carbon bond formation⁹ under mild and neutral conditions. The reaction proceeds efficiently giving the products in excellent yields at ambient temperature.

In a typical procedure, copper sulphate pentahydrate¹⁰ (5 m moles, 1.25g) was taken in 15 mL of THF in a 50 mL round bottom flask. To this acetylacetone (10 m moles, 1 mL) was added and the mixture stirred for 15 min., and then benzalacetone (10 m moles, 1.46g) added to it. The resulting mixture was stirred at room temperature for about 12 hr. After the completion of reaction (TLC) dichloromethane (20 mL) was added and the resulting mixture washed with water. The organic layer was dried over anhydrous sodium sulphate and distilled. The residue on purification by passing through a short column of silica gel using



chloroform as eluent afforded the Michael adduct (entry 1) in 85% yield without the formation of any side product. Similar treatment of other 1,3-diketones gave the corresponding Michael adducts in 70-85% yields and the typical results are summarised in Table I. The Michael adducts thus obtained gave satisfactory spectroscopic and analytical data and were in full agreement with those of known products.

The scope of the reaction was studied by changing the structure of the Michael donors and acceptors. Both cyclic and acyclic β -keto esters were used in this reaction and in all cases the desired Michael adducts were obtained in high yields. Stirring the reaction

Table I — $\text{CuSO}_4 \cdot 5\text{H}_2\text{O}$ -catalyzed Michael addition of 1,3-dicarbonyl compounds

entry	R	R ²	R ³	R ⁴	R ⁵	Reaction period (hr)	Yield ^a %
1	Me	Me	H	Ph	Me	12	85
2	Me	Me	H	H	Me	13	80
3	Me	OEt	H	Ph	Ph	15	70 ^b
4	Me	Me	H	Ph	Ph	12	82
5	Me	OEt	H	-(CH ₂) ₃ -		8	80
6	Me	Me	H	-(CH ₂) ₃ -		8	85
7	Me	OEt	H	Ph	Me	16	78
8	Me	OEt	H	H	Me	15	80
9	OEt	-(CH ₂) ₃ -	H	H	Me	28	85
10	OEt	-(CH ₂) ₄ -	H	H	Me	30	80
11	OEt	OEt	H	Ph	Ph	16	80

^aAll the yields refer to isolated chromatographically pure compounds.

^bFurther increasing the reaction period gave no significant improvement in yields but rather decomposition of product occurred

mixture at room temperature for a period of 8 to 30 hr was necessary to reach high conversion but control experiments showed that in the absence of the catalyst even after 72 hr only about ten percent of the starting material was converted to the desired product. Furthermore, it is to be noted that highly pure products were obtained using this simple procedure and in most cases no further purification was needed⁸. In all cases, hydrolysis of the ester functionality was not observed. Also, the yields were generally higher than those reported for 1,4-additions catalysed by mild Lewis acids in common organic solvents.

In conclusion, catalysis of the Michael reaction of β -dicarbonyl compounds by inexpensive $\text{CuSO}_4 \cdot 5\text{H}_2\text{O}$, offers a significant improvement over the existing methods and would thus help facile entry into a host of new Michael adducts of potentially high synthetic utility. The selectivity of this method is excellent in most of the cases, reaction conditions are mild and neutral, and performance is reasonably easy (no inert or anhydrous conditions, simple work-up procedure).

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- 10 Copper sulphate pentahydrate used was of commercial grade and procured from Central Drug House (P) Ltd, New Delhi 110002.