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Research article

A modified claisen- schmidt protocol for synthesis of 1,3-diaryl-2- propen-1-one (chalcone)

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ABSTRACT

We here reports a modified improved method for synthesis of 1,3-diaryl-2-propen-1-one, rely on base catalyze condensation of arylmethyl ketone with aromatic aldehyde. This method however to an extent analogues to classical methodology thou minute changes in reactant charging sequence, prominent control over their dropping rate, and strict temperature regulation enhance its synthetic utility. disintegration.

Keywords: chewable tablet, gum core, antioxidant, compressibility etc.

INTRODUCTION

1,3-diaryl-2-propen-1-ones (chalcone) are key pharmacophores in terms of pharmacological activities, acting as a universally accepted synthetic intermediate for yielding heteroaromatic ring systems as well as substituted steroidal derivatives. Phytochemically, they are close congeners (precursor) of bioactive flavonoid, isoflavonoids & their analogues, but unique among in terms of a dual ring system connected to each other via three carbon bridge enveloping keto-ethylenic moiety. Generally, occurs naturally, the extraction, isolation, and purification of these magical moiety employs tedious, time-consuming, complicated procedures, which are rarely comparable with synthetic procedures in terms of end product yield, purity, net reaction time, ease of procedure, & eco-handy technique. Thus, numerous synthetic strategies were developed, each with its own pros & cons; however, utility of Claisen-Schmidt condensation (Scheme-01) is still undeniable as a synthetic feasible tool for this molecule [1].

Formation, reaction failure, self-condensation of ketonic-enolate, side reactions, impure product, & lower yield. Therefore in view of above restriction and our own intention towards synthesis of 1,3-diaryl-2-propen-1-one optimized various reaction parameters by blind shuffling the quantity of reactants, their time frame & sequence of charging, solvents, amount & nature of bases, reaction time, reaction temperature and thus ends-up our journey on an procedure extremely reliable both in terms of synthetic feasibility and eco-handy technique in synthesis of this molecule [2].

MATERIALS & METHODS

All the reagents and solvents used in this experimentation are acquired from the common store of the University Institute of Pharmacy, CSJM University, Kanpur, India and used as such without any modification unless or until specified. The physiochemical & spectral properties of the synthesised compounds were reported in Tables 02 & 03. 1H NMR spectra were recorded with a Bruker Avance II 300 NMR

Ar-COCH3 + NaOH + CH3OHAr'-CHO

Dropwise spectrometer. The chemical shifts were recorded

Ar-CO-CH=CH-Ar' in parts per million (ppm) and were reported

relative to the TMS. Mass spectra data were recorded on Waters Q-TOF Premier-HAB213 Scheme-01[3].

Adopting the conventional Claisen-Schmidt procedure in parallel in our lab, we encountered problems such as prolonged reaction time, excessive solvent requirement, and sticky product system in ESI mode. The FT-IR spectra of synthesised compounds were recorded on PerkinElmer Spectrum version 10.03.06. The melting point was recorded by open capillary method and is uncorrected [4].

Experimental

Classical method[27]	Modified method	General note
Equimolar quantities (0.01M) of arylmethyl ketone & aromatic aldehydes were dissolved in ethanol (40ml) in a round bottom flask placed in ice bath. To this aqueous NaOH (10ml; 60%) were added dropwise with continuous stirring for 30-minutes. The mixing was continued for next 2-3 hrs at room temperature. The mixture was kept in refrigerator for overnight when it become quite thick. Then it was diluted with ice cold water, dried in air, and recrystallized from methanol.	In a clean conical flask (100ml), NaOH (10%; 5ml) was transferred followed by methanol (10ml). The flask was then immersed in an ice-chest and temperature was recorded with sensitive thermometer (50°C), once reading fixed at 0°C aromatic aldehyde (0.01M) was transferred; stirring initiated. Immediately, but slowly & steadily arylmethyl ketone (0.01M; 08- drops/min.) was dropped-in and stirring was continued while maintaining the reaction temperature not greater than 5°C. Soon reaction mixture becomes slightly yellowish color indicating reaction progression. Once addition was completed, ice-chest was replaced to cold water-bath (20°C), stirring resumed 2-hrs more. The content was refrigerated (if required) overnight, filtered off, and washed thoroughly from cold water and then from chilled ethanol. The product was air dried and washes from ethanol (10ml). Chalcone so obtained was sufficiently pure for further usage however its purity can be asses by thin layer chromatography (TLC) employing ethylacetate:petroleum ether in a ratio of 6:4.	*Reaction superiority* Required lesser amount of base & solvent compare to classical procedure for equal quantities of reactants. Condensation between enolates of arylmethyl ketone can be efficiently controlled. No problem of sticky product formation. Prevent side reactions. High quality product can be synthesized. Overall lesser reaction time. No need of intermittent reaction monitoring. Minimize reaction failure. Recrystallization may or may not be required. *Reaction limitation* Lethargy procedure. Drop-in rate of arylmethyl ketone must be optimum. Required strict control of reaction temperature.

RESULTS & DISCUSSION

Table 1:

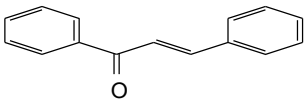
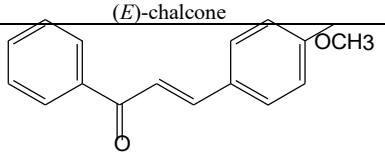
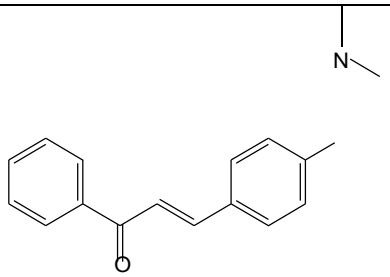
Reactants	Structure & chemical name	Formula & Mol. weight	Melting point (°C) Reported	Melting point (°C) Found	Yield (%)
Acetophenone & benzaldehyde	 (*E*)-chalcone	$C_{15}H_{12}O$; 208	56-57	57	87
Acetophenone & 4-Methoxy benzaldehyde	 (*E*)-3-(4-methoxyphenyl)-1-phenylprop-2-en-1-one	$C_{16}H_{14}O_2$; 238	77-78	79	89
Acetophenone & 4-Dimethylamin o benzaldehyde	 (*E*)-3-(4-(dimethylamino)phenyl)-1-phenylprop-2-en-1-one	$C_{17}H_{17}NO$; 251	111-113	110	91

Table 2:

Spectral data		
IR (KBr) cm^{-1}	**NMR (δ, ppm)**	**Mass (m/e)**
3030 (CH-Ar), 1558 (C=O), 1598 (C=C)	7.7 (d 1Hα) 8.0 (1Hβ) 7.4-7.9 (m, 10H-Ar-H)	208
2955 (CH-Ar), 1658 (C=O), 1598 (C=C), 1111 (-OCH_3)	7 (d 1Hα) 8.1 (d,1Hβ) 6.4-8.1 (m, 9H-Ar-H), 3.6 (s, 3H, -OCH_3)	238
2906 (CH-Ar), 1661 (C=O), 1599 (C=C), 1313 (CN)	6.9 (d 1Hα) 8.0 (d,1Hβ) 7.0-7.5 (m, 9H-Ar-H), 2.6 (s, 6H, -$N(CH_3)_2$	251

Table 03:

Reaction parameters	Classical method	Modified method
Reactants required	Aromatic ketone, aromatic aldehydes, & their substituted derivatives	Aromatic ketone, aromatic aldehydes, & their substituted derivatives
Reactants quantities	0.01M	0.01M
Reactant charging sequence	Both at same time	Aromatic aldehyde followed by aromatic ketone
Reactants charging rate	Not specified	Not more than 10-drops/min. incase aromatic ketone is liquid at room temperature and a pinch or slightly more if same exist as solid at room temperature

A minor change in sequence of reactants charging, their dropping rate, and strict temperature control during overall reaction would yield a method highly versatile and reliable in terms of chalcone synthesis and its purity. Thus modified Claisen-Schmidt procedure (table 01) we herein reported is highly versatile, efficient, cost effective, and devoid of any reaction failure, side reactions, sticky product formation, inferior product yield, and purity problem comparatively (table 04). We also here suggest that this methodology is equally effective in synthetic procedure of various chalcones and their derivatives since this procedure enables an extraordinary command over generation and condensation of (nucleophile) with subsequent electrophile thereby enhance productivity along with purity gradification [5].

CONCLUSION

The modified Claisen-Schmidt reaction reported here can be used as an alternative for synthesis of chalcone owing to its superiority over classical method.

Conflict of interest

The authors declare they had no conflict of interest.

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