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UV Light Assisted Green Cross-Aldol Condensation in Aqueous Medium

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Abstract: ***An environment-friendly green procedure is developed for Ultra Violet Ray assisted cross aldol condensation between a cycloalkanone and aromatic aldehyde in the existence of a LBSC (Lewis Base Surfactant Combined Catalyst). Triethanolamine acts as the base for aldol condensation as well as catalyzing the reaction by phase transfer and the desired aqueous phase synthesis is achieved. UV Ray is used as the specific source of energy in contrast to the conservative heating which minimizes unwanted bi-product generation and improves yield.***

Keywords: LBSC, UV-Light Assisted Reaction, Aqueous Organic Chemistry, Aldol Reaction

1. Introduction

Water is nowadays considered the most preferred solvent to perform chemical operations from the sustainable chemistry point of view, as it is non-toxic, affordable, safe, and poses no risk to the environment.Nevertheless, as a solvent for organic processes, water is either rarely utilized or rarely considered. The majority of organic molecules' limited solubility in pure water is undoubtedly one of the main constrain.Our objective is to build a greener catalytic system that makes it possible to use water as a solvent for a variety of chemical processes.Using surfactants or surfactant-like ligands[1] that dissolve organic compounds or create monophasic dispersions with them in water might help overcome the disadvantage in the usage of water (problem of solubility). Triethanolamine (TEOA) has been employed in the manufacture of metal/metal oxide nanoparticles as a ligand that resembles a surfactant.[2]TEOA has been utilized[3] as a LBSC, acting as both a surfactant to solubilize organic reactants in aqueous media and a base to activate substrate molecules.

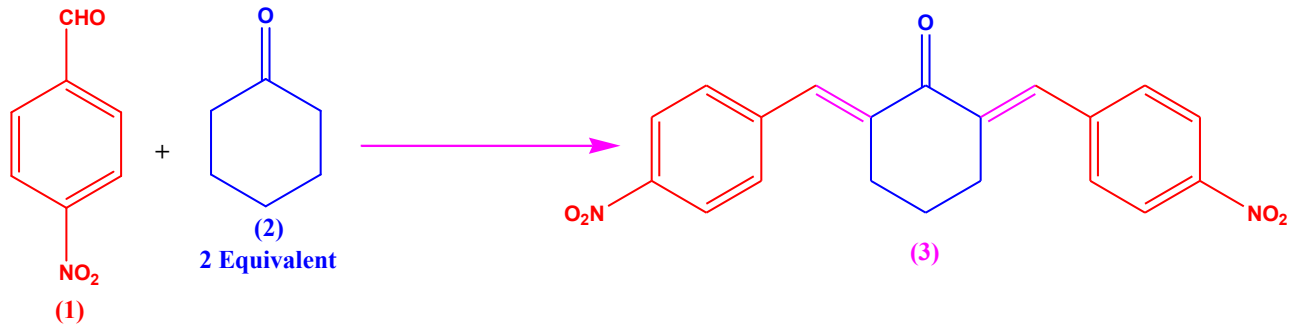
In several instances, the traditional techniques for creating these heterocyclic systems necessitate prolonged heating, which is linked to a waste of energy and time. UV-irradiation has developed into an efficient, eco-friendly approach for selective organic synthesis in recent years. UV-assisted synthesis is compatible with the concepts of green chemistry since it has several benefits, including easier set-up, faster reaction times, cleaner products, and product selectivity.

The α, α′-bis (substituted benzylidene) cycloalkanones are essential building blocks of potentially medicinal heterocyclic compounds, pharmaceuticals, agrochemicals intermediates, perfumes as well as novel organic materials for cytotoxic analogous[4], nonlinear optical applications, and liquid-crystalline polymers units.[5]Strong acid or base catalysts could be used to facilitate the operation of a cross aldol type reaction, which can be used to prepare them. The corresponding intended products are only partially produced by this process of condensation due to side and reverse reactions (like the self-condensation of aldehydes and ketones).[6, 7]Numerous techniques have been devised for the production of these kinds of compounds. Several metals (II) ion complexes, including Zn (II), Ni (II), Co (II), Fe (II) & Mn (II) have been employed as catalysts[8]; but the yields generated were not very promising. In other instances, Cp_2ZrH_2, [7]bis (*p*-ethoxyphenyl) telluroxide (BOMPTO), [9] $RuCl_3$[10], SmI_3[11], Cp_2TiPh_2[12], $TiCl_3$ (SO_3CF_3)[13], KF-Al_2O_3[14], $FeCl_3$[15], BF_3•OEt_2[16], $InCl_3$[17], $LiClO_4$[18] as well as silica sulfuric acid[19]were also utilized to catalyze the reaction. Among the shortcomings of the published procedures include the creation of a mixture of products, low yields, lengthy reaction times, and the employment of toxic reagents.

On the basis of their widespread relevance, it is essential to further establish more competent and expedient approaches to develop such considerable heterocyclic compounds. In the communication, a greener UV Light -assisted protocol for crossed Aldol condensation in existence of green, an effective, as well as inexpensive catalyst TEOA within an aqueous medium is reported.

2. Results and Discussion

We examined the synthesis ofα, α′-bis (substituted benzylidene) cycloalkanone **3** from the condensation of 1 equivalent of cyclohexanone (**1**) with two equivalents of 4-nitrobenzaldehyde (**2**) in the existence of a series of catalysts to improve the reaction condition during initial exploratory reactions.



Scheme 1

It was seen that when the reaction was performed no product was obtained even after 12 h (Entry 1). Reaction with different Brønsted as well as Lewis acid catalysts gave poor yield in the range (20-45 %). A moderate yield of the matching product 3 was attained from the reaction with triethylamine as the catalyst and Lewis base (Table 1, entry 10). The target molecule 3's yield increased (Table 1, entry 11) when the reaction was carried out with the SDS/triethylaminecatalyst combination. We considered a catalyst with strong Lewis basicity and surfactant characteristics to encourage the crossing aldol condensation process in light of the preceding findings (Table 1, entries 10, 11).We have recommended TEOA as the catalyst for the crossing aldol condensation in the LBSC and to our satisfaction, TEOA produced good findings (Table 1, entry 12).

Table 1: Optimization of catalyst for the Crossed Aldol Condensation [a]

Entry	Catalyst	Time (hour)	Yield[b] (%)
1	-	12	Trace
2	Nano Al_2O_3	4	21
3	Nano SiO_2	4	27
4	L-Proline	4	31
5	*p*-toluene sulphonic acid	3	34
6	Nano ZnO	4	39
7	Acetic Acid	2	43
8	TUD	2	52
9	DBU	2	58
10	Triethylamine	2	68
11	Triethylamine/SDS	1	73
12	TEOA	0.5	81

[a] Cyclohexanone (**1a**) (1 mmol), 4-nitrobenzaldehyde (**2a**) (2 mmol) have been irradiated using UV light in 5ml water in the prevalence of 15 mol percent of the catalyst.
[b] The pure product's isolated yield.

Table 2 summarises the findings of the screening process that was conducted to study the effectiveness of various solvents and reaction conditions in the reaction. Compound 3 was generated in modest yields when ethanol, DMSO, or DMF were used as the reaction medium instead of methanol (Table 2, entries 1-4). Poor yields of the product were obtained when $CHCl_3$, acetone, and toluene were employed as the solvent (Table 2, entries 5–7). Water was superior to other solvents, as evidenced by the 81 percent yield of the intended product (3a) in the reaction carried out in water (Table 2, entry 8).One important element that only influences the reaction rate and product yield is the catalyst concentration. To investigate this The reaction was carried out at various TEOA concentrations—10, 15, 20, and 25 mol percent. The product was obtained in yields of 77 percent, 81 percent, 84 percent, and 84 percent, respectively (Table 2).Changing the reaction mode from thermal to photochemical results in a further enhancement in the yield of the product (Table 2, entry 10). This significant increase in the product yield upon changing the reaction condition from thermal to photochemical condition can be attributed to lesser self-condensation and polymerization reactions in the case of UV light assisted reactions.

Table 2: Screening of solvents and reaction condition optimization [a]

Entry	TEOA (mol%)	Solvent	Reaction Condition	Yield[b] (%)
1	15	Methanol	80 °C; Heat	42
2	15	Ethanol	80 °C; Heat	49
3	15	DMSO	80 °C; Heat	51
4	15	DMF	80 °C; Heat	46
5	15	$CHCl_3$	80 °C; Heat	39
6	15	Acetone	80 °C; Heat	28
7	15	Toluene	80 °C; Heat	34
8	15	Water	80 °C; Heat	81
9	10	Water	80 °C; Heat	77
10	20	Water	80 °C; Heat	84
11	25	Water	80 °C; Heat	84
12	**20**	**Water**	**RT; UV**	**92**

[a] Cyclohexanone (**1a**) (1 mmol), 4-nitrobenzaldehyde (**2a**) (2 mmol) were irradiated using UV light in 5ml solvent in the incidence of specific TEOA catalytic load.
[b]The pure product's isolated yield.

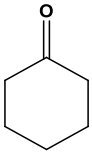
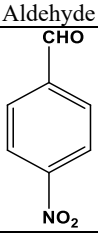
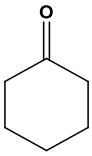
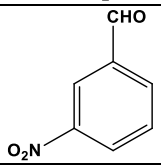
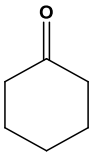
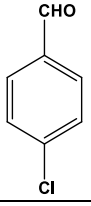
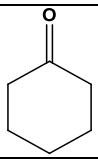
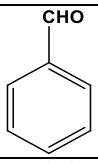
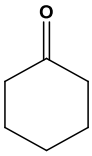
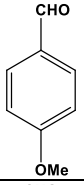
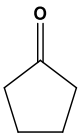
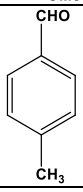
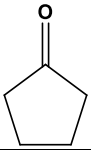
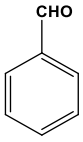
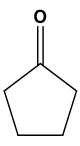
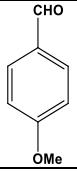
The observations mentioned above show that the reaction proceeds wellin the existence of 20 mol% of TEOA in aqueous medium under influence of UV Light. The mildreaction conditions and formation of almost negligible side products are the primarybenefits of this reaction protocol in water.

Now with this new green protocol, we explored the synthetic applicability of this protocol with a set of ketones as well as aldehydes. The symmetrically substituted α, α′-bis (substituted benzylidene) alkanones were smoothly synthesized in this protocol. The electron-rich aldehydes showed poor reactivity due to obvious reasons as the reaction was much faster for the electron-defficient aldehydes.

TEOA is an organic base that is sterically hindered and non-nucleophilic. It is particularly useful in preventing the development of undesirable byproducts. The LBSC is a novel kind of catalyst that functions as a surfactant to create

a colloidal suspension as well as a catalyst to stimulate the substrate molecules. It is important to note that the reaction mass that was initially floating was transformed into a homogenous mixture by the TEOA addition to the reaction flask. After stirring, the mixture turned into a white, turbid emulsion. The production of micelles or colloidal aggregates resembling micelles is implied by this ocular observation. Triethanolamine's ability to function as a surfactant is what is responsible for the development of the emulsion, and this ability ought to be crucial for accelerating the rate of reaction. In other words, such colloidal vesicles functioned as an efficient reaction sphere in water. The reaction in the existence of micelles might be driven by a hydrophobic force that reduces the reactants into an extremely compact complicated arrangement inside a confined hydrophobic domain. Despite having a relatively short carbon chain, TEOA aggregates via forming intermolecular H-bonds, which leads to the creation of micelle-like colloidal aggregates after this kind of polymerization.

Table 3: Substrate the scope of this green protocol of aldol condensation

Entry	Ketone	Aldehyde	Product	Time (Minute)	Yield (%)	m. p. (°C)	m.p. (Lit.)
1			3a	30	92	158	161-162
2			3b	20	95	189	188-190
3			3c	35	88	146	147-148
4			3d	60	82	119	117-118
5			3e	105	77	163	164-165
6			3f	25	89	242	243-244
7			3g	40	81	186	188-190
8			3h	50	88	243	243-244

3. Conclusion

In conclusion, a greener UV light-assisted synthetic protocol of crossed aldol condensation reaction is developed which offers a milder reaction condition for sensitive scaffolds for organic synthesis.

4. Experimental

TMS (Tetramethylsilane) was employed as an internal standard for the ^{13}C-NMR and ^{1}H-NMR spectrum studies, which were performed on Bruker-Advance Digital 75 and 300MHz equipment.A Perkin Elmer RX-1 FTIR spectrophotometer has been used to record infrared spectra with KBr pellets within reflection mode. On Kofler Block equipment, melting points were examined. Iodine vapour exposure and UV light monitoring were employed in the analytical TLC process using Merck aluminum-blocked silica gel plates covered by silica gel G. The organic reactions were conducted utilizing synthetic grade chemicals from E-Merck, Spectrochem, andSigma-Aldrich. After being thoroughly distilled and dried, every solvent utilized in the procedure was removed. An EXCEL IMPEX UV lamp was the UV instrument that was utilized.

Characterization Data

2, 6-Bis (4-nitrobenzylidene)cyclohexanone (3a): ^{1}H NMR ($CDCl_3$, 300 MHz) δ: 1.86-1.82 (m, 2H, CH_2), 2.91 (t, J=6.0 Hz, 4H, $2CH_2$), 7.7—8.1 (m, 8CH, arom), 8.35 (s, 2H, 2=CH); ^{13}C NMR (75.0 MHz, $CDCl_3$) δ: 187.7, 147.8, 144.5, 141.2, 141.3, 127.4, 123.2, 27.2; IR (KBr) v: 3075, 2932, 1711, 1586, 1512, 1341 cm^{-1}.

2, 6-Bis (3-nitrobenzylidene)cyclohexanone (3b): ^{1}H NMR ($CDCl_3$, 300 MHz) δ: 1.8-1.9 (m, 2H, CH_2), 2.965 (t, J=5.6 Hz, 4H, CH_2), 7.61—7.84 (m, 6CH, arom), 8.2 (d, J=8.0 Hz, 2H, arom), 8.28 (s, 2H, =CH); IR (KBr) v: 3076, 2948, 1667, 1610, 1517, 1347, 1262 cm^{-1}.

2, 6-Bis (4-chlorobenzylidene)cyclohexanone (3c): ^{1}HNMR ($CDCl_3$, 300 "MHz) δ: 1.76—1.88 (m, 2H, CH_2), 2.85 (t, J=6.0 Hz, 4H, $2CH_2$), 7.32—7.46 (m, 8CH, arom), 7.48 (s, 2H, 2=CH); IR (KBr) v: 2936, 1661, 1607, 1578, 1267, 830 cm^{-1}.

2, 6-Di (benzylidene)cyclohexanone (3d): ^{1}H NMR ($CDCl_3$, 300 MHz) δ: 1.72—1.86 (m, 2H, CH2), 2.90 (t, J=6 Hz, 4H, $2CH_2$), 7.23—7.65 (m, 10H, CH arom), 7.85 (s, 2H, 2=CH); ^{13}C NMR (75.0 MHz, $CDCl_3$) δ: 187.6, 144.5, 141.9, 134.2, 128.1, 127.2, 27.1; IR (KBr) v: 3071, 3026, 2928, 1652, 1603, 1578 cm^{-1}.

2, 6-Bis (4-methoxybenzylidene)cyclohexanone (3e): ^{1}H NMR ($CDCl_3$, 300 MHz) δ: 1.71—1.74 (m, 2H, CH_2), 2.82 (t, J=5.4 Hz, 4H, $2CH_2$), 3.76 (s, 6H, 2-OCH_3), 6.92—7.40 (m, 8H, CH arom), 7.72 (s, 2H, 2=CH); ^{13}C NMR (75.0 MHz, $CDCl_3$) δ: 187.8, 161.6, 144.7, 141.1, 127.9, 114.5, 56.6, 27.8; IR (KBr) v: 3015, 2931, 1652, 1559, 1501, 1256 cm^{-1}.

2, 5-Bis (4-methylbenzylidene)cyclopentanone (3f): ^{1}H NMR ($CDCl_3$, 300 MHz) δ: 2.36 (s, 6H, $2CH_3$), 3.08 (s, 4H, $2CH_2$), 7.13—7.15 (m, 4H, 4CH), 7.35—7.40 (m, 6H, 6CH); ^{13}C NMR (75.0 MHz, $CDCl_3$) δ: 188.5, 144.9, 142.1, 136.3, 131.1, 128.4, 126.8, 23.0, 20.7; IR (KBr) v: 2919, 1681, 1612, 1593 cm^{-1}.

2, 5-Di (benzylidene)cyclopentanone (3g): ^{1}H NMR ($CDCl_3$, 300 MHz) δ: 3.18 (s, 4H, $2CH_2$), 7.30—7.40 (m, 6H, 6CH), 7.55—7.60 (m, 6H, 6CH); ^{13}C NMR (75.0 MHz, $CDCl_3$) δ: 188.6, 144.9, 142.8, 133.8, 128.1, 127.8, 126.1, 22.0); IR (KBr)v: 3058, 3012, 2916, 1682, 1628, 1591 cm^{-1}.

2, 5-Bis (4-methoxybenzylidene)cyclopentanone (3h): ^{1}H NMR ($CDCl_3$, 300 MHz) δ: 3.02 (s, 4H, $2CH_2$), 3.80 (s, 6H, 2 -OCH_3), 6.82—6.86 (m, 4H, 4CH), 7.50—7.55 (m, 6H, 6CH); ^{13}C NMR (75.0 MHz, $CDCl_3$) δ: 26.1, 55.2, 114.1, 128.3, 132.0, 133.9, 135.7, 160.2, 196.7; IR (KBr)"v: 3072, 2839, 1685, 1582 cm^{-1}.

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