Investigation of catalytic effect on carbon-carbon bond formation by Baylis-Hillman (BH) reaction between (2/3/4)-nitro-arylaldehyde and alkylacrylates and computational approaches through DFT functional

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ABSTRACT

The 4-diazabicyclo[2.2.2]octane, DABCO, had widely established with gigantic and celestial applications on catalysis for carbon-carbon bond formation reactions. Thus, it has been employed to synthesize the alkyl 2-(hydroxyl (nitrophenyl) methyl)acrylate by the reaction of arylaldehydes and alkylacrylates under a mild condition with good yields. First of all, reaction was examined effect of various solvents, such as water, MeOH, Dioxane, DMSO, t-Butanol, DMF, Toluene, and THF and THF was the best solvent in term of yield. Next, the room temperature (R.T) was the optimized condition than 60°C and 80°C. The overall reaction progress was monitored in presence of DABCO, Et3N, C2H5ONa, C4H9OK, (CH3)3COK and pyridine catalysts with THF solvents at room temperatures, and calculated the amount for superior of catalyst. There was no product obtained in presence of catalysts, such as Et3N, C2H5ONa, C4H9OK, (CH3)3COK and pyridine. But in present of DABCO, this reaction has proceeded and monitored the concentration of catalyst and various temperature effects on reaction progress. In addition, the computational approaches for speculative investigation of solvents effect has employed for predicting and comparatively verified with the proposed reaction mechanism in presence of DABCO catalyst through the Density Functional Theory (DFT). The most acceptable tools for the thermodynamic had been illustrated to get the reaction kinetics by formation energy, entropy, enthalpy for reactant, product and transition state. Finally, the Gibbs free energy for reactions from the reactants and product has calculated to predict the occurring spontaneously possibility with and without solvents, and it is said that the reaction is spontaneously occurred through the water, DMSO, THF solvent although it is opposed fact without solvent even other solvents. It might be concluded that the optimization conditions of reaction are the THF solvent in presence of 20% DABCO catalyst at room temperature with high (about 90%) throughout 6–8 h where the 4- position of nitro group in arylaldehyde is the most preferable in case of time and yield.

1. Introduction

Morita-Baylis-Hillman (MBH) reaction, which was modified in 1972 by Anthony B. Baylis and Melville E. D. Hillman, illustrated the carbon-carbon single bond formation between activated alkene and carbon electrophilic compounds [1, 2] but it was originated by K. Morita in 1968 [3]. Although, there were various approaches, for example aldol reaction [4], Reformatsky reaction [5], Grignard reaction [6], Diels-Alder reaction [7, 8], Wittig reaction [9, 10], and Heck reaction [11, 12, 13] for erection of carbon-carbon bond(s) with well established literatures, but the MHB has taken the vast attention with gigantic significance in organocatalysis and heterocyclic synthesis [14], enantioselective synthesis of spirocyclohexenes [15], organocatalytic asymmetric transformations [16], and synthesis of isatin-derived ketimines [17]. In addition, it belongs to the functional groups generation and atom economy [18], use non-metal and low toxic materials for catalysis [19, 20], mild conditions and compatibility of multiple functional groups [21, 22], synthesis of natural products and drug molecules [23], Chiral binaphthyl-derived amine-thiourea [24], organomatallic and heterocyclic synthesis [25]. But the main drawback of the MBH reaction is the use of toxic metal as catalysts [26]. Regarding that point, Hill and Isaacs et al. 1990 [27], Fort et al. 1992 [27], Lewis acids [28], Lewis bases [29], E.P. Kristin et al. in 2005 [30] and so many scientist performed numerous researches during 1990–2005 on the catalytic process. In addition, a
variety of 2-(1-hydroxyalkyl)-2-propenoic esters was prepared by using DABCO which has executed as a catalyst for coupling of aldehyde with methylacrylate [31], and Yong-Ling Shi and Min Shi proposed another similar concept for the DABCO-catalyzed reactions for salicyl N-tosylimine, with ethyl 2, 3-butadienoate and penta-3, 4-dien-2-one to produce the corresponding chromenes [31]. The stereoselective DABCOCatalyzed synthesis in (E)-α-ethyl-ω, β-unsaturated ester from allenylnitriles was accomplished by Yongsik Choe and Phil Ho Lee which opened a new dimension for application of DABCO for coupling reaction to form carbon-carbon bond without toxic metals [32]. The main fact of using DABCO as catalyst in MBH reaction is explained for its inexpensive and highly efficient catalytic activity, which has as well been developed for the cross-coupling of arylaldehydes with aryloboronic acids [33]. The total synthesis of syrxbutsins using the BH adduct of 2, 3-α-isopropylidene-R-glyceraldehyde and ethylacrylate as starting material followed by ring closing metathesis of the acrylate derivative [34]. In recent time, the most applicable and popular research on BH which was published by Nyoung Kim et al. for the synthesis of 3, 4-disubstituted 2(1H)-quinolones through intermolecular Friedel-Crafts reaction of N-arylamides of Baylis-Hillman adduct [35]. For having the vast applications of BH and MBH reactions, it has examined for the carbon-carbon unaccompanied bond construction between activated arylaldehydes and alkylacrylates in presence of DABCO catalyst which has as well modified by solvent and temperature effect; has been adding new dimension for synthesis of biologically significance molecules. Moreover, it must be noted for synthesis of alkyl 2-(hydroxyl (nitrophenyl) methyl) acrylate has no well-established methods for their synthesis. As a result, this study finds the sustainable method development with applying catalysts in temperature and solvents conditions that gives the assistance for introducing new method to get the high yield of methyl acrylate and its alkyl derivatives as well as less time and low cost.

Besides the experimental evidences, the computational approaches have been applied in view of thermodynamics and chemical reactivity for supporting about reaction mechanism with solvent effect [36]. To illustrate the solvents effect for formation of the carbon-carbon bond formation to form methyl acrylate and its alkyl derivatives from nitro arylaldehydes with different acrylates, the most accurate method of DFT has executed from material studio software [37], because it gives an extraordinary and accurate accomplishment for solving a potential problem of experimental work [38]. However, the accuracy of a theoretical method for some other problems may not entail precision for the crisis nearby. The potential energy, Gibbs free energy, HOMO-LUMO energy gap, chemical potential and entropy might be calculated for accurate explanation of catalytic and mechanistic studies of this reaction which can predict the possibility of occurring reaction with conditions. Some usual mechanistic steps, particularly carbon-carbon bond formation using solvent with catalyst, are sufficiently tractable in computational or quantum calculation [39, 40, 41, 42, 43, 44]. Finally, this theoretical hypothesis has used to understand by computational mechanistic results, specifically thermodynamic parameter and chemical reactivity of reactant, product and transition state to get accurate result which is compatible with experimental studies through the solvent and DABCO catalyst.

2. Experimental materials and methods

2.1. Methods and materials

IR spectra were recorded on a Shimadzu FTIR spectrophotometer and UV spectra were recorded in dry CHCl₃ with Shimadzu visible spectrophotometer. ¹H NMR and ¹³C NMR spectra were recorded on a Bruker DPX-400 spectrophotometer (400 MHz) using tetramethylsilane as internal reference. Analytical thin-layer chromatography (TLC) was performed on pre-coated silica gel 60 F-254 (E. Merck). Column chromatography was performed on silica gel (60–120 mesh). DABCO (1, 4-Diazabicyclo[2. 2. 2] octane), acrylates, aldehydes and other reagents were purchased from E. Merck (Germany) and Fluka (Switzerland).

2.2. General experimental methods

Typical reaction procedure for the preparation of alkyl 2-(Hydroxyl (nitrophenyl) methyl) acrylate 6-11

Alkyl 2-(hydroxyl (nitrophenyl) methyl) acrylate (6-11) were prepared from the reaction of nitro arylaldehydes with different acrylates in the presence of DABCO at room temperature. To a stirred solution of methyl acrylate (500 mg, 5.81 mmol) and DABCO (137 mg, 1.16 mmol, 20 mol %) in tetrahydrofuran (5 mL) at 28–30 °C, nitrobenzaldehyde (1932 mg, 12.78 mmol) was added slowly. Then the mixture was stirred for 6 h. The progress of the reaction was monitored by TLC. Then the solvent of the reaction mixture was removed by distillation and extracted by CHCl₃ solution (3 × 50 mL), the organic layer was washed with distilled water (3 × 50 mL) and dried over anhydrous Na₂SO₄. The crude product obtained after evaporation of the solvent was purified by chromatography on a column of silica gel (60–120 mesh) with ethyl acetate in n-hexane to yield light yellowish solid pure compound 6. The spots were visualized with UV light, the Rf value of TLC was at 0.6–0.65 which is acceptable to predict the monitoring reaction progress.

2.3. Characterisation by spectral data of synthesised compounds

All the synthesized compounds were characterized by their satisfactory spectroscopic (UV, IR, ¹H NMR, ¹³C NMR) and elemental analysis. The formation of the coupling products was established on the basis of the spectroscopic data observations. For the characterization by ¹H NMR spectrum of alkyl 2-(hydroxyl (nitrophenyl) methyl) acrylates (7) was accounted for the chemical shift at 8.11 (d, 2H, Ar-H), 7.52 (d, 2H, Ar-H), 6.35 (s,1H, 1-ethylen), 5.90 (s,1H, 1-ethylen), 5.61 (s, 1H, methine), 3.68 (s, 3H, CH₃). There was not presence any chemical shift at 9.45 ppm which was confirmed the absence of peak for –CHO group and in case of the –CH = CH₂ group of acrylates, the original peak of that ethylene group was shown at 6.05 ppm considering its conversion. However, the absence chemical shift at original peak region of –CHO and –CH = CH₂ groups pointed out the conversion into aldehyde group and ethylene group in alkyl 2-(hydroxyl (nitrophenyl) methyl) acrylates compound (6). For giving the strongest evidence for structural conversion, the ¹³C NMR spectrum of alkyl 2-(hydroxyl (nitrophenyl) methyl) acrylates (6) was accounted for the chemical shift at 166.33 (CO), 148.90 (Ar-C), 147.32 (Ar-C), 141.17 (1-ethylen), 127.459 (Ar-CH), 127.03 (1-ethylene), 123.53 (Ar-CH), 72.23 (C-methine), 52.14 (CH₃). For the fact of FTIR, the strongest peaks for stretching at about 3508.63 cm⁻¹ (O-H) asymmetry 3310.37 cm⁻¹ (O=H) symmetry make available the existence of C–C new bond formation at this point, on top of another three peaks at 1700 cm⁻¹ (C=O) asymmetry, 1670 cm⁻¹ (C=O) symmetry prove the existence of carboxylate ion, and 1350 cm⁻¹ for the –NO₂ group. Finally, the FTIR spectrum, ¹³C NMR spectrum, and ¹H NMR spectrum of compound 7, 8, 9, 10, and 11, were similar to compound 6 and confirmed their functional groups. Withal, the UV spectrum for compound 6 shows the similar absorption at about 394.50, 271.50, 218.50 nm wave-length which is almost similar to other compounds (7, 8, 9, 10 and 11).

Methyl 2-(hydroxy (4-nitrophenyl) methyl) acrylate 6

Light Yellowish solid; mp 72–73 °C, Yield: 92%, 1.266 g

IR: v max (KBr) 3508.37 (O–H), 2852–3108 (C–H), 1601.93 (C=O), 1530 (NO2), 700-1000 cm⁻¹.

UV (CHCl₃): λ max (KBr) 3508.37 (O–H), 2852–3108 (C–H), 1601.93 (C=O), 1530 (NO2), 700-1000 cm⁻¹.

HNM R (400 MHz, CDCl₃) δ (ppm) 8.11 (d, 2H, J = 8.4 Hz, Ar), 7.52 (d, 2H, J = 8.8 Hz, Ar), 6.35 (s, 1H, 1-ethylen), 5.90 (s,1H, 1-ethylen), 5.61 (s, 1H, methine), 3.68 (s, 3H, CH₃).

¹³C NMR (100 MHz, CDCl₃) δ (ppm) 166.33 (CO), 148.90 (Ar-C), 147.32 (Ar-C), 141.17 (1-ethylen-CD), 127.459 (Ar-CH), 127.03 (1-ethylene-CD), 123.53 (Ar-CH), 72.23 (C-methine-CD), 52.14 (CH₃-CD).

Anal. Calcd for C₁₂H₁₃NO₂: C, 55.70; H, 4.67; N, 5.90. Found: C, 55.85; H, 4.82; N, 6.10.
Ethyl 2-[hydroxyl (4-nitrophenyl) methyl] acrylate 7
Light yellowish liquid; Yield: 90%, 1.129 g
IR: \( \text{v}_{\text{max}} \) (KBr) 3500.92 (O-H), 2986–3134 (C-H), 1710 (C-O), 1610 (O-C), 1350 (NO2), 700–1000, cm\(^{-1}\).
UV (CHCl3): \( \lambda_{\text{max}} \) 336.00, 273.00, 218.80, 214.40, 204.60 nm.
\(^1\)H NMR (400 MHz, CDCl3) \( \delta \) (ppm) 8.16 (d, 2H, J = 7.08 Hz, Ar), 7.54 (d, 2H, J = 7.55 Hz, Ar), 6.37 (s, 1H, 1-ethylene), 5.85 (s, 1H, 1-ethylene), 5.60 (s, 1H, methine), 4.13 (q, 2H, J = 7.72, 7.71 Hz, \(-\text{OCH}_2\)), 3.48 (s, 1H, OH), 1.23 (t, 3H, J = 5.57, 5.58 Hz, CH3).
\(^13\)C NMR (100 MHz, CDCl3) \( \delta \) (ppm) 165.93 (CO), 148.77 (Ar-C), 147.35 (Ar-C), 141.20 (1-ethylene-CO), 137.24 (Ar-CH), 126.96 (1-ethylene), 123.54 (Ar-CH), 72.61 (C-methine), 61.29 (-OCH2), 13.98 (CH3).

DEPT: 127.34 (Ar-CH), 126.96 (1-ethylene), 123.54 (Ar-CH), 72.34 (C-methine), 61.29 (-OCH2), 13.98 (CH3).

Methyl 2-[hydroxy (3-nitrophenyl) methyl] acrylate 8
Colourless liquid; Yield: 83%, 1.143 g
IR: \( \text{v}_{\text{max}} \) (KBr) 3489.34 (O-H), 2987.84 (C-H), 1709.95 (C-O), 1531.53 (C=C), 1352.14 (NO2), 700-1000 cm\(^{-1}\).
UV (CHCl3): \( \lambda_{\text{max}} \) 676.50, 263.50, 224.50 nm.
\(^1\)H NMR (400 MHz, CDCl3) \( \delta \) (ppm) 8.26 (s, 1H, Ar), 8.14 (d, 1H, J = 7.2 Hz, Ar), 7.74 (d, 1H, J = 7.65 Hz, Ar), 7.52 (s, 1H, J = 8.0 Hz, Ar), 6.42 (s, 1H, 1-ethylene), 5.93 (s, 1H, 1-ethylene), 5.65 (s, 1H, methine), 3.76 (s, 3H, CH3).
\(^13\)C NMR (100 MHz, CDCl3) \( \delta \) (ppm) 166.39 (CO), 148.37 (Ar-C), 143.67 (Ar-C), 141.04 (1-ethylene), 132.68 (Ar-CH), 129.36 (Ar-CH), 127.26 (Ar-CH), 127.72 (Ar-CH), 121.57 (1-ethylene), 72.56 (C-methine), 52.19 (CH2).

Anal. Calcd for C12H13NO5: C, 57.37; H, 5.22; N, 5.58. Found: C, 57.52; H, 5.45; N, 5.78.
\(^1\)H NMR (400 MHz, CDCl3) \( \delta \) (ppm) 7.97 (d, 1H, J = 8 Hz, Ar), 7.75 (d, 1H, J = 7.2 Hz, Ar), 7.64 (t, 1H, J = 7.6 Hz, Ar), 7.46 (t, 1H, J = 7.2, 8.0 Hz, Ar), 6.39 (s, 1H, 1-ethylene), 6.20 (s, 1H, 1-ethylene), 5.75 (s, 1H, methine), 4.15 (Q, 2H, J = 4.6, 7.2 Hz, OCH2), 2.86 (s, 1H, OH), 1.21 (t, 3H, J = 7.2 Hz, CH3).
\(^13\)C NMR (100 MHz, CDCl3) \( \delta \) (ppm) 165.97 (CO), 144.81 (Ar-C), 140.90 (Ar-C), 136.22 (1-ethylene), 133.49 (Ar-CH), 128.93 (Ar-CH), 128.70 (Ar-CH), 126.29 (Ar-H), 124.57 (1-ethylene), 67.75 (C-methine), 61.20 (OCH2), 13.99 (CH3).

Anal. Calcd for C12H13NO5: C, 57.37; H, 5.22; N, 5.58. Found: C, 57.54; H, 5.38; N, 5.75.

It is reported here that the coupling between alkylacrylates with arylaldehydes were accomplished in presence of DABCO in good yield% (All of spectrum data was attached in supplementary file in Figure-S2, Table S1).

2.4. Computational details

To kick off, the development of chemical reaction mechanism through the solvent effect, the DFT functional has been employed from DMO1\(^3\) code of material studio 8.0. To perform this work, the B3LYP functional and DND basis set was used. In this case, the reactants and products were used to form the transition state. Next, the reactants, products and transition complexes were simulated using the B3LYP functional and DND basis set and recorded to the heat of formation, entropy, enthalpy and Gibbs free energy. Secondly, the evaluate the solvent effect, the reactant and product were also simulated using the same method and condition, and Water, MeOH, Dioxane, DMSO, t-Butanol, DMF, Toluene, and THF solvent were executed from the DFT methods to calculate the Gibbs free energy and heat of formation. On the other hand, to calculate the quantum properties, structural stability, the B3LYP functional and DND basis set from the DMO1\(^3\) code of material studio 8.0. The HOMO, LUMO and Electrostatic potential 3D map were optimized and analyzed for illustrate the chemical descriptors. At last for calculating the stereocentre of optimized molecules, the Gaussian 16 software packet was used for determination the stereoisomer for the synthesized molecules [45, 46]. In this case, the B3LYP function with 6-311G basis set from DFT functional method was performed for optimization. After optimization the stereoisomer of optimized molecules was determined to give specification of R and S center.

3. Results and discussions

3.1. Chemistry

The aldehydes and acrylates were used for synthesis of alky1 2-(hydroxyl (nitrophenyl) methyl) acrylate and its derivatives which were characterized by \(^1\)H NMR, \(^13\)C NMR, UV spectra and FTIR (attached the spectral diagram in supplementary file S2). The reaction progress was monitored in presence of various solvents medium to get the optimized products with high yield. No reaction was ensued without DABCO catalyst only using solvent. After adding solvent, this reaction was persisted the product where the 4-nitro arylaldehyde shows the highest yield rather than 3-nitro arylaldehyde and 2-nitro arylaldehyde, so that it must be concluded that the nitro group at 4-position of aryl ring was highly preferable for occurring this reaction. The main reason may be explained as that the higher distance of the nitro group would stay minimum static hindered for reactant during the reaction progress. On the other hand, another imperative memorandum is mentioned that larger alkyl chain of acrylate is required more time and low yield. For justification of reaction mechanism, the 1\(^{st}\) order is possible in presence of DABCO catalyst.

3.2. Proposed mechanism and effect of solvents as well as temperature

Effects of solvent, concentration of aldehydes and acrylates, and DABCO at different temperatures were premeditated, and it was recorded.
that the yield of the expected product depended on the nature of the base, temperature and solvents in presence of DABCO catalyst. To kick off, the solvent effects on the reaction was examined using a variety of solvents, such as 1, 4-dioxane, tetrahydrofuran (THF), dimethylsulfoxide (DMSO), dimethylformamide (DMF), dichloromethane (DCM), toluene, acetonitrile, t-butanol and methanol. Dioxane, DCM, t-butanol and DMSO. It is reported here alkyl 2-(hydroxy (nitrophenyl) methyl) acrylate 6–11 was obtained by treating 1 mol of acrylate with 2.2 mol of arylaldehyde (1–3) in the presence of DABCO (20 mol%) in anhydrous THF at room temperature for 6 h in pathway-3 and S1. The product was purified by chromatography on a column with ethyl acetate in n-hexane to pure compound 6 of 90% yield in optimization table, Entry-1. As higher yield of compound 6 was observed by using DABCO 20 mol%, Tetrahydrofuran (THF) solvent at R.T. for staring time 6 h are shown in optimization Table 1. From this table we observed MeOH was better solvent than others in this Tables 1, 2, 3, 4 Dioxan, Dichloromethane (DCM), t-Butanol and dimethyl sulfoxide (DMSO) were found to be poor solvent due to less solubility obtaining 50% yield in Entry-5. DMF and toluene were found to be the moderately good solvent to obtain 60% yield in Entry-6. When the reaction was carried out in neat conditions, the product was obtained in lower yield. THF was originated to be the best solvent accounting on basis of yields of product.

To optimize the reaction conditions, the reaction was observed at different temperature such as 80 °C, 60 °C and at room temperature. Room temperature was found to be the best condition for THF solvent. The yields got during heating are lower because of the parasitic reaction that can take place under these conditions between BH adducts and methanol which gives methylated ethers. The reaction was examined by employing different base catalyst, such as DABCO, Et3N, C2H5ONa, C4H9OK, (CH3)3COK and pyridine. When other base catalyst was employed without DABCO no product was observed after 6–24 h. The strong base (EtONa, tBUOK etc) does not facilitate this reaction and it is likely to witness trans-Esterification of the acrylic esters. But when DABCO was employed as catalyst, the product was obtained in 92% after only 6 h. So DABCO is the best base catalyst for this reaction. Then it was examined the reaction by employing a different amount of DABCO such as 10 mol%, 20 mol% and 100 mol%. Increasing the amount of DABCO from 10 to 100 mol%, did not increase the yield% of compound 6. The best result (90% yield) was got in case of 20 mol% DABCO catalyst. The examination of reaction time revealed that 6 h was found to be required to complete the reaction in presence of THF at room temperature. Therefore, the best reaction conditions were found to carry out the BH reaction with 2.2 equivalent of arylaldehyde 1–3 with 1 equivalent of acrylate 4–5 in presence of catalyst DABCO only (20 mol%) at room temperature in THF for 6 h. The coupling reactions of tolualdehyde, anisaldehyde, benzaldehyde, p-chlorobenzaldehyde, acetaldehyde, cinnamaldehyde, 4-formalbenzoic acid and 2-formalbenzoic acid with acrylates were performed under the same conditions, but no desired compound was afforded. On the other hand, the coupling reaction of methyl methacrylate, 2-hydroxy ethylmethacrylate and vinylacetate with arylaldehydes under the same conditions yielded no products. The BH reaction does not work with methymethacrylates and its derivatives because it requires the presence of a vinyl proton in the alpha position of the ester group. It was revealed that the methyl group at the vinyl position hindered the coupling reaction at the same position. All the synthesized compounds 6–11 were characterized by IR, UV, 1H NMR, 13CNMR, and elemental analysis. The analytical data of compound 6 was found to be compatible with literature data [47]. Although the detailed mechanism of the coupling reactions is yet to be clarified, it can be perceived that the reactions proceed according to Baylis-Hillman mechanism. It has undoubtedly transparent that the

### Table 1. Optimization for preparation of methyl 2-(hydroxy (4-nitrophenyl) methyl) acrylate 6.

| Entry/Serial no | Base catalyst (mol%) | Solvent | Temp. (°C) | Time (hr.) | Yield (%) |
|----------------|----------------------|---------|------------|------------|-----------|
| 1              | DABCO (20)           | THF     | R.T        | 6          | 90        |
| 2              | DABCO (10)           | THF     | R.T, 60, 80| 6 to 24    | 70        |
| 3              | DABCO (100)          | THF     | R.T, 60, 80| 6 to 24    | 60        |
| 4              | DABCO (20)           | MeOH    | R.T        | 6          | 80        |
| 5              | DABCO (20)           | Dioxane | R.T        | 6          | 50        |
| 6              | DABCO (20)           | DMF     | R.T        | 6 to 24    | Nil       |
| 7              | Et3N or C2H5ONa or C4H9OK or (CH3)3COK or Pyridine. | THF | R.T        | 6 to 24    | Nil       |

### Table 2. Data for proposed 1st order reaction mechanism.

| Step-I | Enthalpy ΔH, cal/mol | Entropy ΔS, cal/K/mol | E, Total energy, eV | Heat of formation Kcal/mol |
|--------|----------------------|-----------------------|---------------------|---------------------------|
| Step-I | R1 8222.714          | 298                   | 35677.45            | -27454.74                 | -2575.781 | 98.380          |
|        | TS-1 13045.71        | 298                   | 19167.02            | -6121.29                  | -2575.414 | 106.829          |
|        | P1 7249.348          | 298                   | 99.191              | -22309.57                 | -2576.001 | 93.298           |
| Step-II| R2 13116.063         | 298                   | 41970.61            | -28854.55                 | -4692.357 | 389.909          |
|        | TS-2 15403.19        | 298                   | 179.592             | -38115.22                 | -4710.573 | -30.180          |
|        | P2 12355.91          | 298                   | 133.763             | -27505.46                 | -4692.353 | 389.984          |
| Step-III| R3 12355.91         | 298                   | 133.763             | -27505.46                 | -4692.353 | 389.984          |
|        | TS3 16077.66         | 298                   | 132.387             | -28773.66                 | -3361.068 | 8.163            |
|        | P3 9156.11           | 298                   | 113.697             | -24289.01                 | -3350.089 | 261.343          |

#### THF solvent

| Step-I | Enthalpy ΔH, cal/mol | Entropy ΔS, cal/K/mol | E, Total energy, eV | Heat of formation Kcal/mol |
|--------|----------------------|-----------------------|---------------------|---------------------------|
| Step-I | R1 8177.648          | 298                   | 35299.59            | -27121.94                 | -2576.137 | 90.174           |
|        | TS1 13101.232        | 298                   | 49188.17            | -47876.93                 | -2575.657 | 101.245          |
|        | P1 7278.158          | 298                   | 99.466              | -22362.70                 | -2576.529 | 81.121           |
| Step-II| R2 13202.450         | 298                   | 42275.47            | -29673.02                 | -4693.128 | 372.120          |
|        | TS2 15532.802        | 298                   | 180.326             | -38204.04                 | -4711.093 | -42.165          |
|        | P2 12311.950         | 298                   | 133.632             | -27510.38                 | -4693.545 | 362.50           |
| Step-III| R3 12311.950        | 298                   | 133.632             | -27510.38                 | -4693.545 | 362.50           |
|        | TS3 10816.015        | 298                   | 135.184             | -29468.81                 | -3361.434 | -0.2828          |
|        | P3 9994.142          | 298                   | 112.024             | -24289.00                 | -3350.585 | 249.9055         |
presence of DABCO as base catalyst was indispensable condition for the coupling reaction between aldehyde and acrylate. The plausible mechanism is shown in the Figures 1 and 2 for 1st order and 2nd order reaction, respectively. However, Mc Quade et al; 2005; suggested a new mechanism based on the reaction rate data collected in aprotic solvents for BH reaction, that it is second order reaction in aldehyde with no catalyst but follows the first order in presence of DABCO catalyst [30]. For justification of proposed reaction mechanism, the computational tools were used.

3.3. Computational evidences for proposed mechanism and effect of solvents

According to the theory by Mc Quade and co-workers for reaction mechanism of Baylis-Hillman reaction in aprotic solvents, the rate of reaction is completely depending through the 1st order reaction kinetics in DABCO catalyst with acrylate reactant. For giving the strong evidence through the computational data, the formation energy for each stage of this proposed mechanism has illustrated in Figure 3 for both of solvent and without solvent medium.

First, it might be revealed for 1st order reaction that the heat of formation is lower in THF solvent than without solvents. However, it could be concluded in such way that this reaction is easily occurred in solvent medium which is the best supportive for experimental evidence of solvent effect. Second, the formation energy of reactant is lower than transition state but higher than product in step-I, II and III steps, shown in Figure 3, which can be said the occurring possibility of these steps.

On the other hand, the formation energy for 2nd order reaction, showing in Figure 3, of reactant, transition state and product are given this Figure 3 where the formation energy of all components without Table 3.

| Steps     | Enthalpy ΔH, cal/mol | Temp ΔT, K | Entropy, ΔS, cal/K/mol | TΔS | Free energy, ΔG, cal/mol | ΔE, Total energy, eV | Heat of formation Kcal/mol |
|-----------|----------------------|------------|-----------------------|-----|-------------------------|--------------------|--------------------------|
| Step-III B | R-3b | 17577.911 | 298 | 174.503 | 52001.89 | -34423.97 | -5974.135 | 768.627 |
| TS-3b     | 7474.837 | 298 | 104.802 | 31230.99 | -23756.15 | -5961.955 | 734.590 |
| P-3b      | 15968.143 | 298 | 154.285 | 45976.93 | -3008.78 | -5972.744 | 485.788 |
| Step-IV B | R-4b | 15931.941 | 298 | 157.523 | 46941.85 | -31009.90 | -5947.540 | 1435.042 |
| TS-4b     | 15931.941 | 298 | 157.523 | 46941.85 | -31009.90 | -5947.540 | 1435.042 |
| P-4b      | 15297.826 | 298 | 154.087 | 45917.92 | -30620.09 | -5943.904 | 1465.760 |

Table 4. Data of the Gibbs free energy for reaction for proposed 1st order reaction mechanism.

| Different stages | Free energy, ΔG, eV | ΔE, Total energy, eV | Escore − ΔG + ΔE | The Gibbs free energy for reaction | Occurring possibility |
|------------------|---------------------|----------------------|--------------------|-----------------------------------|----------------------|
| Step-I R- I      | -27454.74 -1.190    | -2575.781            | -2576.97           | +0.01                             | Not spontaneously    |
| TS- I            | -6121.29 -0.265     | -2575.414            | -2576.67           |                                   |                      |
| P- I             | -22309.57 -0.967    | -2576.001            | -2576.96           |                                   |                      |
| Step-II R-II     | -28854.55 -1.251    | -4692.357            | -4693.60           | +.06                              | Not spontaneously    |
| TS- II           | -38115.22 -1.652    | -4710.573            | -4712.22           |                                   |                      |
| P- II            | -27505.46 -1.192    | -4692.353            | -4693.54           |                                   |                      |
| Step-III R- III  | -27505.46 -1.192    | -4692.353            | -4693.54           | +1342.38                          | Not spontaneously    |
| TS- III          | -28773.66 -1.247    | -3361.068            | -3362.31           |                                   |                      |
| P- III           | -24725.59 -1.072    | -3350.089            | -3351.16           |                                   |                      |
| THF solvent R- I | -27121.94 -1.176    | -2576.137            | -2577.31           | -0.18                             | Spontaneously occurred |
| TS- I            | -47876.93 -2.0761   | -2575.657            | -2577.71           |                                   |                      |
| P- I             | -22362.70 -0.969    | -2576.529            | -2577.49           |                                   |                      |
| Step-II R-II     | -29073.02 -1.260    | -4693.128            | -4694.38           | -.35                              | Spontaneously occurred |
| TS- II           | -38204.04 -1.656    | -4711.093            | -4712.74           |                                   |                      |
| P- II            | -27510.38 -1.192    | -4693.545            | -4694.73           |                                   |                      |
| Step-III R- III  | -27510.38 -1.192    | -4693.545            | -4694.73           | +1343.10                          | Not Spontaneously occurred |
| TS- III          | -29468.81 -1.277    | -3361.434            | -3362.71           |                                   |                      |
| P- III           | -24289.00 -1.053    | -3350.585            | -3351.63           |                                   |                      |
solvent is higher than THF solvent medium. In case of step IIIb, the formation energy of reactant is higher than transition state and product, but it is opposite for IVB and VB step. It can be said that the reaction does not easily follow the 2nd order reaction as 1st order reaction. Therefore, the proposed reaction pathway 1 is highly reliable and empirical than reaction pathway 2.

3.4. Computational approaches for reaction mechanism in view of Gibbs free energy

The change in the Gibbs free energy for a reaction (\( \Delta G^\circ \)) is the difference between the free energy of the products and the free energy of the reactants. When the reactants have higher free energy than the products (\( \Delta G_{\text{rxn}}^\circ < 0 \)), the reaction is called exothermic reaction, it opposite event is called endothermic reaction.

Free energy or, more appropriately, Gibbs free energy (after the inventor of the concept, J. Willard Gibbs) is a composite thermodynamic concept involving both enthalpy and entropy. It is given by

\[
\Delta G = H - TS
\]

To explain the reaction pathway, the Gibbs free energy is a tool derived from thermodynamic study calculating both of experimental and theoretical chemistry or computational chemistry. For different reaction pathways occurring possibility depends on Gibbs free energy, lower Gibbs free energy indicates the higher occurring possibility. To say more, if change of Gibbs free energy for a reaction is negative, then it's spontaneous. If change of Gibbs free energy is positive, meaning the non-spontaneous.

In order to explain the reaction mechanism with the computational chemistry, the thermodynamics of reactant, transition state and product have been considered in this study by the DMol3 code of the material studio 8.0 [48,49]. At each step of the reaction mechanism for the reaction and product, Gibbs free energy and formation energy has determined. Tables 2, 3 show that the steps I and II occur spontaneously, but the subsequent steps are unlikely to occur spontaneously. With the first order reaction, it is seen that the last one is not happening spontaneously. However, when the reaction mechanism THF solvent is used, the Gibbs free energy value is reduced, and the reaction occurs spontaneously. Again, the kinetics of the reaction depends on the first and second steps. Thus, it can be said that the reaction through computational chemistry by thermodynamics calculations supports the reaction for 1st order and it is more convincing to solvent, THF.

According to the Gibbs free energy for reaction, it can be calculated by following equation for each step of predicted reaction mechanism

\[
\Delta G_{\text{reaction}} = E_{\text{corr (product)}} - E_{\text{corr (reactant)}}
\]

Figure 1. Proposed Reaction pathway-1 for 1st order reaction.

Figure 2. Proposed Reaction pathway-2 for 2nd order reaction.

Figure 3. a) Step-I for 1st and 2nd order reaction, b) Step-II for 1st and 2nd order reaction, c) Step-III for 1st order reaction, d) Step-IIIb for 2nd order reaction, e) Step-IVB for 2nd order reaction, f) Step-VB for 2nd order reaction for Heat of formation for all steps of 1st and 2nd order reaction mechanism.
Figure 4. Overall reaction progress pathway.

Figure 5. Comparison of heat of reaction in presence of eight solvents.
through DFT functionals for molecular geometry and optimization. After optimization, it was calculated the stereo isomer for products, shown in Figure 9 and Figure S1 (supplementary file). All of the products are S isomer in C-7 carbon atom which is also a chiral carbon of alkyl chain.

### 3.8. Chemical descriptors and HOMO and LUMO

Chemical parameters have served as a major catalyst for determining the chemical stability of any compound and their structural geometry. Table 7 describes the different values of these parameters, such as LUMO, HOMO, ionization potential, electron affinity, HOMO LUMO gap, chemical potential, hardness, electrons activity, electrophilicity, and softness. Table 7 shows that the value of LUMO is less than three times that magnitude of HOMO. Thus, the electrophilic groups of all these compounds tend to be much more attracted in the position of higher electronic denser portion. All these, energy gaps as expressed the $\epsilon_{HOMO} - \epsilon_{LUMO}$ between two orbitals are seen to be around 7.0 eV or slightly more. As aliphatic chain is occurred in their body, are caused for some variations in their chemical activity. The first is that the chemical potential energy levels of the chemical potential are close to -6.00 eV. There is a great deal of similarity between the compound and the chemical descriptors due a vast changing in their body chain. Their energy levels i.e. hardness values are around 3.0 eV while softness values are around 0.28 eV which indicates maximum chemical activity for organic compounds [39, 43, 50, 52, 53].

### 3.9. Frontier molecular orbital diagram in term of HOMO and LUMO

The LUMO and HOMO orbital diagrams indicate the most imperative parts of a molecule that can be joined by electrophilic and nucleophilic groups, resulting in a variety of chemical reactions. The LUMO and HOMO orbital diagrams are illustrated in Figure 10. First of all, the color green refers to the positive part of the orbital and the maroon color refers to the negative part. In the case of LUMO, it has been shown that lemon refers to the positive part and purple refers to the negative part. As it can be seen from Figure 10, these additions usually have three parts, benzene cycle, alkyl group, nitro group at side chain and ester group with negative atoms. Now, Figure 10 is how the reactivity of these functional groups but can be easily determined through this orbital picture. First, in the case of HOMO, alkyl chains and benzene rings are found more or less in this part of the world, even with the ester group, but the LUMO part is

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**Table 6. Thermodynamics data in various solvents effect.**

| Solvents     | $\Delta G$ for Reactant, eV | $\Delta G$ for Product, eV | $\Delta G$ for reaction, eV | Reaction possibility     |
|--------------|------------------------------|----------------------------|----------------------------|--------------------------|
| No solvent & DABCO | -25033.38                   | -24228.69                  | +804.69                    | Not Spontaneously occurred |
| Water        | -21409.17                   | -21622.23                  | -214.06                    | Spontaneously occurred   |
| MeOH         | -22624.34                   | -21603.37                  | +1020.97                   | Not Spontaneously occurred |
| Dioxane      | -24912.17                   | -24231.33                  | +680.83                    | Not Spontaneously occurred |
| DMSO         | -24683.72                   | -24905.77                  | -222.05                    | Spontaneously occurred   |
| t-Butanol    | -24893.33                   | -24247.92                  | +645.41                    | Not Spontaneously occurred |
| DMF          | -24863.58                   | -24189.01                  | +673.57                    | Not Spontaneously occurred |
| Toluene      | -24890.59                   | -24960.50                  | -69.91                     | Spontaneously occurred   |
| THF          | -24622.39                   | -24751.30                  | -128.91                    | Spontaneously occurred   |

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Figure 6. Comparison of Gibbs free energy for reactant in presence of eight solvents.

Figure 7. Comparison of Gibbs free energy for reactant in presence of eight solvents.

Figure 8. Comparison of Gibbs free energy for reaction in presence of eight solvents.
Figure 9. Sterio-centre for product 7.

Table 7. Frontier molecular orbitals and Reactivity descriptor analysis.

|     | ϵLUMO, eV | ϵHOMO, eV | Ionization potential (I), eV | Electron affinity (A), eV | ϵHOMO - ϵLUMO gap, eV | Chemical potential (μ), eV | Hardness (η), eV | Electrons activity (χ), eV | Electrophilicity (ω), eV | Softness (S), eV |
|-----|-----------|-----------|----------------------------|--------------------------|------------------------|---------------------------|----------------|--------------------------|------------------------|---------------|
| 06  | -9.78     | -2.3      | 9.790                      | 2.300                    | 7.480                  | -6.040                    | 3.740          | 6.040                    | 4.877                  | 0.267         |
| 07  | -9.87     | -2.46     | 9.870                      | 2.460                    | 7.410                  | -6.165                    | 3.705          | 6.165                    | 5.129                  | 0.270         |
| 08  | -10.1     | -2.41     | 10.100                     | 2.410                    | 7.690                  | -6.255                    | 3.845          | 6.255                    | 5.088                  | 0.260         |
| 09  | -9.92     | -2.48     | 9.920                      | 2.480                    | 7.440                  | -6.200                    | 3.720          | 6.200                    | 5.167                  | 0.269         |
| 10  | -9.77     | -2.68     | 9.770                      | 2.680                    | 7.090                  | -6.225                    | 3.545          | 6.225                    | 5.466                  | 0.282         |
| 11  | -9.8      | -2.47     | 9.800                      | 2.470                    | 7.330                  | -6.135                    | 3.665          | 6.135                    | 5.135                  | 0.273         |

Figure 10. HOMO, LUMO orbital diagram for (6–11).
only found in the nitro group benzene ring and its surrounding. Thus, it is clear that the functional group of the compound has a far-reaching effect for the addition of nucleophilic groups, and the nitro group for the addition of electrophilic groups.

3.10. Electrostatic potential charge distribution

The following electrostatic potential map shows how the molecules are distributed inside the charges through its full body. It may be influenced to form the weak bonds that are formed for the substance to bind to proteins as attracting to the hydrophobic and hydrophilic charges for which the charges are produced here for responsible that fact. In this context, by properties, it can be revealed whether matter has biological activity. The image below Figure 11 shows that there is a large gap between the positive and negative charges inside the substance as shown on the scale. This means that as the gap widens, there is a greater tendency for charges to be distributed and involved.

4. Conclusion

The synthesis of alkyl 2-[hydroxyl (nitrophenyl) methyl] acrylate in one step under mild conditions has been discussed in details of catalytic nature at optimized temperature and suitable solvents. To kick off, THF solvent is obtained the best solvent among 1, 4-dioxane, tetrahydrofuran (THF), dimethylsulfoxide (DMSO), dimethylformide (DMF), dichloromethane (DCM), toluene, acetonitrile, t-butanol and methanol, Dioxane, DCM, t-butanol. Next, 20 mol% of DABCO could be sustainable catalyst among 10%, and 100 % in presence of THF solvent. Moreover, this reaction does no precede in presence of Et3N or C2H5ONa or C2N6OK or (CH3)2COK or Pyridine catalysts having the THF solvent. For occurring this reaction in alkyl 2-[hydroxyl (nitrophenyl) methyl] acrylate and its derivates (06–11), it might be revealed that 4-position of nitro group in aryl acrylate is highly reactive for reactant due to low static hindered force occurring the proton transferring. Then, the synthesized acrylate derivates (06–11) were characterized by 1H NMR, 13C NMR FTIR and UV data. Finally, with the computational evidence, it could be said that this reaction follows the 2nd order reaction mechanism with THF solvent in presence of DABCO catalyst at room temperature for formation of carbon-carbon single bond between aryl acrylates and aldehydes. The control of stereochemistry of BH adducts and it might develop chemical transformation of –OH group at chiral centre and addition reaction at double bond. By the computational calculation, it was found that the synthesized acrylate derivates (06–11) are the S-stereoisomer at C7 carbon atom. At last, the HOMO and LUMO and energy gaps make the further study for the biological significances as bioactive molecules.

Declarations

Author contribution statement

Laila Arifun Nahar: Conceived and designed the experiments; Performed the experiments.
Ajoy Kumer: Performed the experiments; Analyzed and interpreted the data; Wrote the paper.
Md Wahab Khan: Contributed reagents, materials, analysis tools or data.
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L.A. Nahar et al. Heliyon 7 (2021) e08139

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