

## Regioselective Addition to Diarylideneacetones – Synthesis of 2-Oxo-1-Acyl-6-Aryl-4[(2-aryl)-vinyl]-Cyclohex-3-ene

M. Giasuddin Ahmed\*, U.K.R. Romman, Kawsari Akhter, Abdul Hakim Siddiki and M. Mostafizur Rahman

Department of Chemistry, Dhaka University, Dhaka-1000, Bangladesh

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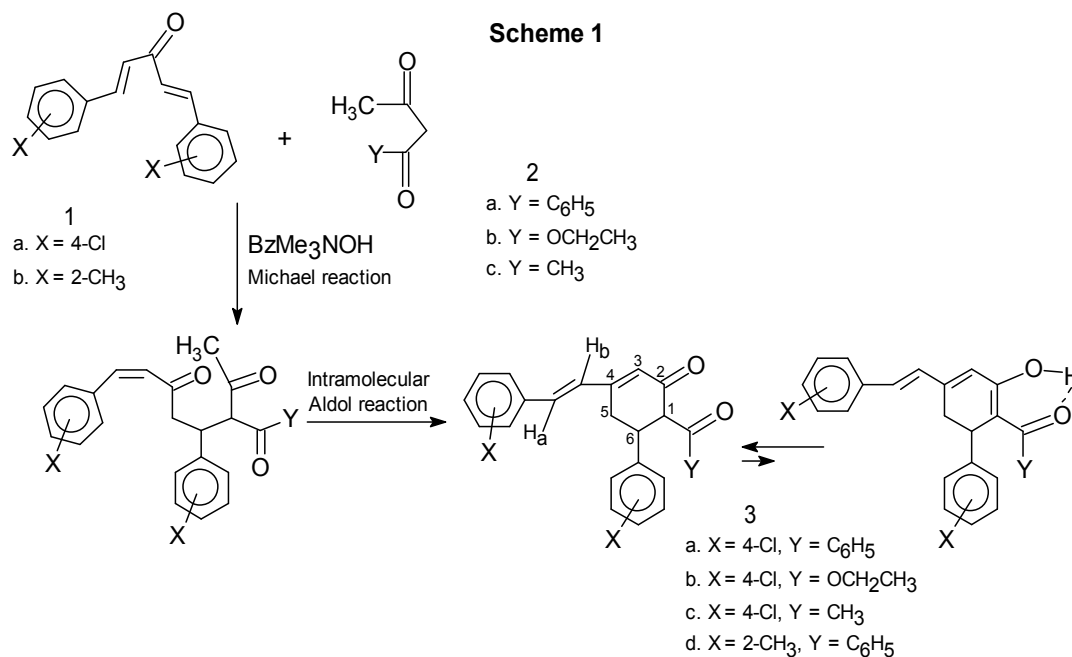
### Abstract

Benzyltrimethylammonium hydroxide (Triton-B) catalyzed reactions of di-4-chlorobenzylideneacetone **1a** with benzoylacetone **2a**, ethyl acetoacetate **2b** and acetylacetone **2c** give respectively 2-oxo-1-benzoyl-6-(4-chlorophenyl)-4-[2-(4-chlorophenyl)-vinyl]-cyclohex-3-ene **3a**, 2-oxo-6-(4-chlorophenyl)-4-[2-(4-chlorophenyl)-vinyl]-cyclohex-3-enecarboxylic acid ethyl ester **3b** and 2-oxo-1-acetyl-6-(4-chlorophenyl)-4-[2-(4-chlorophenyl)-vinyl]-cyclohex-3-ene **3c**. Under similar conditions, reaction of di-2-methylbenzylideneacetone **1b** with benzoylacetone **2a** gives 2-oxo-1-benzoyl-6-(2-methylphenyl)-4-[2-(2-methylphenyl)-vinyl]-cyclohex-3-ene **3d**.

### I. Introduction

Michael addition reaction<sup>1-6</sup> has received considerable attention over the years because of its synthetic utility. Kohler and co-workers reported<sup>1,2</sup> that the esters of cyanoacetic acid reacted rapidly with both dibenzylideneacetone and dianisylideneacetone in presence of a small amount of sodium methoxide. The products obtained were 1:1 adducts, 1:2-adducts and cyclic products from reactions of dibenzylideneacetone with esters of malonic acid under the influence of basic catalysts like piperidine and sodium methoxide<sup>3,4,12,14</sup>. In our laboratory we found<sup>7-10</sup> that

reactions of diarylideneacetones with cyanoacetamide and ethyl cyanoacetate gave styryl type products using both sodium ethoxide and anhydrous zinc chloride as catalysts. Our recent findings on the reactions of cyanoacetamide with diarylideneacetones using Triton-B as catalyst showed that cyclized products were formed<sup>13,15</sup>. In the present paper we would like to report the results of the reactions of di-4-chlorobenzylideneacetone **1a** with benzoylacetone **2a**, ethyl acetoacetate **2b**, acetylacetone **2c** and the reaction of di-2-methylbenzylideneacetone **1b** with benzoylacetone **2a** using Triton-B as catalyst (Scheme 1.)



### II. Experimental

The IR spectra were recorded as KBr pellet using SHIMADZU, IR-470 infrared spectrophotometer in the range of 4000-400 cm<sup>-1</sup>. The <sup>1</sup>H NMR spectra and <sup>13</sup>C NMR spectra were recorded in dpx BRUKER 400 MHz NMR spectrophotometer. TMS was used as an internal standard. The solvent used was d<sub>6</sub>-DMSO. The mass spectra were recorded in the JEOL JMS-HX 110A spectrophotometer.

The di-4-chlorobenzylideneacetone **1a** and di-2-methylbenzylideneacetone **1b** were prepared following literature method<sup>11</sup>.

#### General Procedure for the Synthesis of 3a-d

A mixture of diarylideneacetone (0.005 mol) and 1,3-diketone (0.005 mol) was dissolved in 80 ml of 1,4-dioxane

for (**3a-c**) and ethanol for **3d** in a round bottomed flask (250 ml). Triton-B (0.5 ml) was added to the above mentioned solution. The mixture was then stirred with a magnetic stirrer at room temperature (26-28 °C) for **3a**, **3c**, **3d** and 106 °C for **3b**. The progress of the reactions was followed by TLC on silica gel plates. The reaction mixture was stirred for 10 to 14 hours and then neutralized with 0.1N HCl acid and extracted with ether. Solvent was completely evaporated by vacuum evaporator. The residual solid mass was dissolved in hot chloroform in case of **3a**, **3c**, **3d** and ethanol in the case of **3b**. To these solutions 5.0 ml of 40<sup>o</sup>–60<sup>o</sup>C pet-ether (except **3b**) was added and kept over night. The solid crystalline precipitate was filtered off and recrystallized.

\*Author to whom all correspondence should made.

**Compound 3a** :  $R_f$  value 0.51 ( $\text{CHCl}_3$  :  $\text{EtOAc}$ =7:1), m.p.211-212  $^\circ\text{C}$ , Yield 40%; **IR** spectrum ( $\nu$  max in  $\text{cm}^{-1}$ ) : 3400, 3050, 2950,2900, 1695, 1660;  **$^1\text{H}$  NMR** ( $\delta$  value ) : 7.85-7.26 (m, 13H, Aromatic protons), 6.61 (d, 1H,  $J$ = 16.0 Hz,  $\text{H}_b$ ), 6.47 (d, 1H,  $J$ = 16.0 Hz,  $\text{H}_a$ ), 5.47 (s, 1H, H-3), 5.36 (d, 1H,  $J$ = 12.0 Hz, H-1), 3.97 (m, 1H, H-6), 3.17 (dd, 1H,  $J_{\text{gem}}=12.0$  Hz,  $\text{H}_{\text{eq-5}}$ ),2.36 (dd,1H,  $J_{\text{gem}}=12.0$  Hz,  $\text{H}_{\text{ax-5}}$ ). Mass spectra:  $m/z$  ( $\text{M}^+$ )= 447, calculated  $\text{M}^+$  = 447. Anal. calcd. for  $\text{C}_{27}\text{H}_{20}\text{Cl}_2\text{O}_2$  (447): C, 72.49; H, 4.51. Found C, 72.67; H, 4.36

**Compound 3b** :  $R_f$  value 0.82 ( $\text{CHCl}_3$  :  $\text{EtOAc}$ =7:1), m.p.158-159  $^\circ\text{C}$ , Yield 40%; **IR** spectrum ( $\nu$  max in  $\text{cm}^{-1}$ ) : 3415, 3050, 2990, 2950, 1720, 1640,  **$^1\text{H}$  NMR** ( $\delta$  value ) : 7.40 – 7.24 (m, 8H, Aromatic protons), 6.93 (d, 1H,  $J$ = 16.0 Hz,  $\text{H}_b$ ),6.87 (d, 1H,  $J$ = 16.0 Hz,  $\text{H}_a$ ), 6.19 (s, 1H, H-3), 4.05 (q, 2H,  $J$ =7.0 Hz,  $-\text{CH}_2-\text{CH}_3$ ), 3.73 (d, 1H,  $J$ = 12.0 Hz, H-1), 3.01-2.97 (m, 1H, H-6), 2.69 (dd, 1H,  $J_{\text{gem}}=20.0$  Hz,  $\text{H}_{\text{eq-5}}$ ), 2.64 (dd, 1H,  $J_{\text{gem}}=20.0$  Hz,  $J_{\text{aa}}= 8.0$  Hz ,  $\text{H}_{\text{ax-5}}$ ), 1.06 (t, 3H,  $J$ = 8.0 Hz,  $-\text{CH}_2-\text{CH}_3$ ). Mass spectra:  $m/z$  ( $\text{M}^+$ )=415, calculated  $\text{M}^+$  = 415. Anal. calcd. for  $\text{C}_{23}\text{H}_{20}\text{Cl}_2\text{O}_3$  (415): C, 66.52; H, 4.85. Found C, 66.37; H, 4.68

**Compound 3c** :  $R_f$  value 0.31 ( neat  $\text{CHCl}_3$  ), m.p.110-112  $^\circ\text{C}$ , Yield 62%; **IR** spectrum ( $\nu$  max in  $\text{cm}^{-1}$ ) : 3420, 3025, 2850, 2800, 1710, 1690;  **$^1\text{H}$  NMR** ( $\delta$  value ) : 7.45-7.34 (m, 8H, Aromatic protons), 6.57 (d, 1H,  $J$ = 16.0 Hz,  $\text{H}_b$ ), 6.43 (d, 1H,  $J$ = 16.0 Hz,  $\text{H}_a$ ), 5.43 (s, 1H, H-3), 4.26, (d, 1H,  $J$ = 12.0 Hz, H-1), 3.73 (dd, 1H,  $J_{\text{gem}}=12.0$  Hz,  $\text{H}_{\text{eq-5}}$ ), 3.01-2.96: (m, 1H, H-6), 2.20 (dd, 1H,  $J_{\text{gem}}=12.0$  Hz,  $\text{H}_{\text{ax-5}}$ ), 1.95 (s, 3H,  $\text{COCH}_3$ ).

**Compound 3d**:  $R_f$  value 0.84 ( $\text{CHCl}_3$ :  $\text{EtOAc}$ =7:1), m.p.168-169  $^\circ\text{C}$ , Yield 47%; **IR** spectrum ( $\nu$  max in  $\text{cm}^{-1}$ ): 3400, 3050, 2990, 2950, 1675, 1640.  **$^1\text{H}$  NMR** ( $\delta$  value): 7.83-6.91 (m, 13H, Aromatic protons), 6.25 (s, 1H, H-3), 4.94 (d, 1H,  $J$ = 12.0 Hz, H-1), 4.37- 4.30 (m, 1H, H-6), 3.15, (dd, 1H,  $J_{\text{gem}}=16.0$  Hz,  $\text{H}_{\text{eq-5}}$ ), 2.77 (dd, 1H,  $J_{\text{gem}}=12.0$  Hz,  $\text{H}_{\text{ax-5}}$ ), 2.46 (s, 3H,  $-\text{CH}_3$ ), 2.37 (s, 3H,  $-\text{CH}_3$ ). Mass spectra:  $m/z$  ( $\text{M}^+$ )=406, calculated  $\text{M}^+$  = 406 Anal. calcd. for  $\text{C}_{29}\text{H}_{26}\text{O}_2$  (406): C, 85.68; H, 6.45. Found C, 85.51; H, 6.39

### III. Results and Discussion

The reactions of **1a** & **1b** with **2a-d** in Triton-B led to the isolation of **3a-d** compounds. Assignment of structure to the compounds (**3a-d**) was made on the basis of their IR,  $^1\text{H}$  NMR,  $^{13}\text{C}$  NMR and mass spectral data.

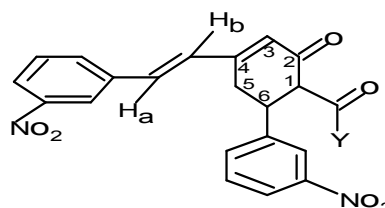
**Table 1.**  $^{13}\text{C}$ -NMR spectral data

Carbon atoms	Compounds ( $\delta$ value in ppm)			
	<b>3a</b>	<b>3b</b>	<b>3c</b>	<b>3d</b>
CO ph	207.06			198.47
COCH <sub>3</sub>			206.96	
C-2 Ketonic C=O	197.61	193.76	205.89	196.79
C=O of ester		169.64		
C-4', C-4''	142.46	144.35	142.06	
C-2', C-2''				140.39
Aromatic and Olefinic Carbons	137.35- 128.11	139.70- 127.12	137.00- 128.20	136.90- 125.90
C-1	61.31	60.54	57.67	59.92
C-3	125.67	123.26	125.64	125.38
C-4		155.29		156.26
C-5	43.76	33.01	41.55	38.23
C-6	52.34	43.13	43.70	32.98
O-CH <sub>2</sub> - CH <sub>3</sub>		61.25		
O-CH <sub>2</sub> - CH <sub>3</sub>		14.12		
COCH <sub>3</sub>			31.16	
CH <sub>3</sub>				19.98
CH <sub>3</sub>				19.81

In the IR spectrum of **3a** the characteristic stretching frequency for the  $\text{C}=\text{C}-\text{C}=\text{O}$  was observed at  $1695\text{cm}^{-1}$ . The enolic form although not enough in concentration for NMR, in IR it showed a stretching at  $3400\text{cm}^{-1}$  for  $-\text{OH}$ .

In  $^1\text{H}$  NMR of **3a** the  $\delta$  values and  $J$  values are in well agreement with the structure. The  $J$  value of 16 Hz for the doublet shows that  $\text{H}_a$  and  $\text{H}_b$  are trans-disposed. The coupling pattern and  $J$  values of the remaining protons are evident from the data given under compound **3a** in the Experimental.

The  $\delta$  values for different carbons in compound **3a** are shown in Table 1 and the values are found to be consistent with the literature values<sup>17</sup>. Any peak due to C-4 could not be detected in the C-13 NMR probably due to its quaternary nature. Similar observation was made in the C-13 NMR of some similar compounds like (A) synthesized previously in our laboratory.



(A)

The peak due to molecular ion  $M^+$  (447) corresponds to molecular mass of the compound **3a**. The experimental values of elemental analysis also correspond to the calculated values.

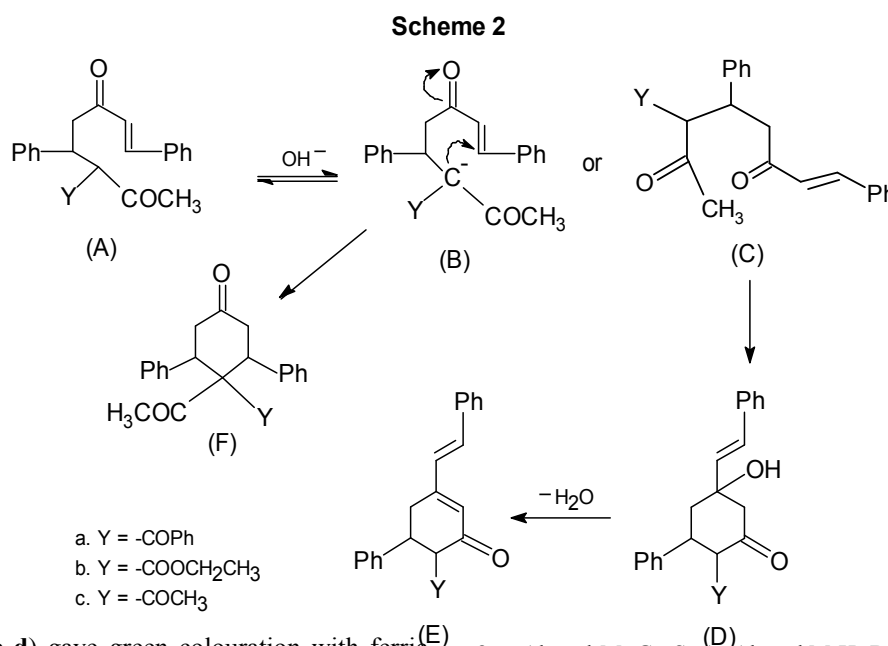
The spectral data of the remaining compounds **3b-3d** can be similarly explained as in the case of **3a** to confirm their structures.

The formation of the products may be explained by the cyclisation of the initially formed Michael adduct undergoing an intermolecular aldol-type reaction (Scheme 1). Since all the active methylene compounds contained –COCH<sub>3</sub> group as a common group used in the present investigation, the products obtained from all these reactions

are also showed similar structures containing a common styryl unit.

The preference of aldol type addition over Michael type addition may be explained by the Frontier Orbital Theory. The rationalization of the reactions mentioned above is based on the preference of a comparatively hard nucleophile – hard electrophile (C→E) reaction over a soft nucleophile – soft electrophile reaction (B→F) since Coulombic term showed to be more contributory than the Frontier orbital term in the Klopman and Salem equation<sup>16</sup> (Scheme 2)

**1a** also reacts with **2b** in presence of sodium ethoxide catalyst to produce the same product **3a**. But the yield is low.



The compounds (**3a-d**) gave green colouration with ferric chloride indicating the presence of enolic structure which was also supported by their IR spectra. However, we could not observe any enolic protons in their <sup>1</sup>H NMR spectra. It existed mostly in keto form probably due to steric inhibition in the coplanar hydrogen bonded enol form by the adjacent acetyl, benzoyl and ester groups. This suggested that the keto form is predominant and the enol form is sterically hindered.

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