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ScienceDirect
Journal of Molecular Catalysis A: Chemical 273 (2007) 169–176
JOURNAL OF MOLECULAR CATALYSIS A: CHEMICAL
www.elsevier.com/locate/molcata

Preparation of mono- and diacetyl 4,4′-dimethylbiphenyl and their corresponding carboxylic acids: Reactivity, selectivity and isomer distribution studies via Lewis acid catalyzed Friedel-Crafts acetylation/oxidation

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Received 22 December 2006; accepted 27 March 2007
Available online 31 March 2007

Abstract

Shape selective acetylation of 4,4′-dimethylbiphenyl using anhydrous aluminum chloride as catalyst is an effective route for the production of mono- and di-acetyl-4,4′-dimethylbiphenyl. Preparations, characterization and a catalytic study of the Friedel-Crafts acetylation of 4,4′-dimethylbiphenyl, involving use of the Perrier addition procedure are carried out in a range of solvents and under a variety of experimental conditions. The obtained ketones are isolated and identified by various physico-chemical techniques. Mono acetylation of 4,4′-dimethylbiphenyl afforded a mixture of two isomeric acetyl dimethylbiphenyls. In chloroalkane or carbon disulfide solvent, the yields of isomers were in the order: 2 -> 3-; in nitromethane 3-isomer predominated. On the other hand diacetylation of the hydrocarbon gave only the 2,3′-diacetyl isomer. The mono- and di-ketones are converted to the corresponding carboxylic acids. 2-Acetyl-4,4′-dimethylbiphenyl was prepared by indirect multi-step synthetic routes. 3-D molecular modelling supports the positional assignment of the acetyl group with the results obtained from the electronic spectra.

Keywords: Friedel-Crafts acetylation; 4,4′-Dimethylbiphenyl; Catalytic activity; Selectivity; Lewis acid

1. Introduction

The Friedel-Crafts acylation reaction is one of the most significant one-step routes for the synthesis of aromatic ketones, which are of special importance for the preparation of intermediates in manufacturing fine chemicals, polymers and semiconductors [1,2] and pharmaceuticals [3]. The dicarboxylic acids of dimethyl biphenyl and their derivatives have been used as medication for the treatment of cancer [4].

Friedel-Crafts reactions can be characterised in a general sense as acid-catalysed irreversible electrophilic substitution reactions of high selectivity. They are essentially reactions between an acyl component and an aromatic substrate, occurring in the presence of a catalyst, to give an aromatic ketone [5]. It is recognized that many acylations depend critically on the experimental conditions used (time, temperature, mode of addition of reactants, overall concentrations of reactants and the solvent). Many workers, mostly with the sole aim of preparing particular ketones, have carried out Friedel-Crafts acylations of aromatic hydrocarbons [6]. The study of acylations of 4,4′-dimethylbiphenyl (Ia) was not considered by any worker until Liebermann [7] reported the Friedel-Crafts investigations employing oxalyl chloride and aluminium chloride in an attempt to synthesize polycyclic aromatic compounds and obtained a quinone derivative, labelled it as 2,7-dimethylphenanthrenequinone. 4,4′-Dimethylbiphenyl (DMBPh) has been reported [8] to give, on sulfonation, a mixture of 4,4′-dimethyl-3,3′- and 2,3′-disulfonic acids. Nitration has been shown [9,10] to afford either 2-nitro- or 2,3′-dinitro-4,4′-dimethylbiphenyl. Chlorination of 4,4′-dimethylbiphenyl was reported by De la Mare et al. [11] to give a mixture of 2-chloro- and 3-chloro-4,4′-dimethyl-biphenyl. Gore has studied more

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doi:10.1016/j.molcata.2007.03.069

Table 1
Effect of type of solvent used on the %conversion and isomer distribution at two different reaction temperatures (25 and 45 °C) at 3 h reaction time

Solvent	Temperature (°C)	Overall yield	Isomer distribution (%)		
			2-Acetyl-DMBPh	3-Acetyl-DMBPh	4-Methyl-biphenyl
$CHCl_3$	25	1.20	99.88	–	0.12
$CHCl_3$	45	1.36	99.85	–	0.15
$ClCH_2CH_2Cl$	25	16.14	76.35	23.16	0.49
$ClCH_2CH_2Cl$	45	18.21	53.11	46.31	0.58
CS_2	25	40.24	88.78	10.41	1.81
CS_2	45	42.24	75.19	23.09	1.92
CH_3NO_2	25	2.18	–	100.00	–
CH_3NO_2	45	2.49	–	100.00	–
C_6H_5Cl	25	22.59	77.02	2.32	0.66
C_6H_5Cl	45	24.68	76.22	3.07	0.71

Table 2
Effect of reaction time on the overall yield and isomer distribution on the acetylation of 4,4′-dimethylbiphenyl in $ClCH_2CH_2Cl$ solvent at 25 °C

Time (h)	Overall yield (%)	Isomer distribution (%)		
		2-Acetyl-DMBPh	3-Acetyl-DMBPh	4-Methyl-biphenyl
3	16.14	76.35	23.16	0.49
12	31.74	86.01	13.48	0.51
24	48.40	93.16	6.12	0.72
72	56.22	95.86	3.29	0.85

Table 3
Effect of reaction time on the overall yield and isomer distribution on the acetylation of 4,4′-dimethylbiphenyl in $CHCl_3$ solvent at 25 °C

Time (h)	Overall yield (%)	Isomer distribution (%)		
		2-Acetyl-DMBPh	3-Acetyl-DMBPh	4-Methyl-biphenyl
3	1.20	99.88	–	0.12
12	6.55	99.81	–	0.19
24	10.31	99.78	–	0.22
72	22.84	99.72	–	0.28

Table 4
Effect of reaction time on the overall yield and isomer distribution on the Friedel-Crafts acetylation of 4,4-dimethylbiphenyl in nitromethane solvent at 25 °C reaction temperature

Time (h)	Overall yield (%)	Isomer distribution (%)	
		2-Acetyl-DMBPh	3-Acetyl-DMBPh
3	2.18	–	100.00
12	2.76	–	100.00
24	3.21	–	100.00
72	9.22	–	100.00

Table 5
Effect of reaction time on the overall yield and isomer distribution on the acetylation of 4,4′-dimethylbiphenyl in carbon disulphide solvent at 25 °C

Time (h)	Overall yield (%)	Isomer distribution (%)		
		2-Acetyl-DMBPh	3-Acetyl-DMBPh	4-Methyl-biphenyl
3	40.24	88.78	10.41	1.81
12	51.77	69.20	28.78	2.02
24	58.38	63.66	34.17	2.17
72	62.65	61.52	37.24	2.24

systematically the Friedel-Crafts acylation of certain halogeno- and alkyl-substituted benzenes and naphthalene and related compounds [6]. In the last decade various heterogeneous catalysts such as HZSM-5, have been used as catalysts in other types of acylation for 4,4′-dimethylbiphenyl [12,13].

The literature on the Friedel-Crafts acetylation reaction of 4,4′-dimethylbiphenyl reveals no previous attempts. A systematic study of Friedel-Crafts acetylation of hydrocarbons, using the Perrier addition procedure (involves addition of the hydrocarbon to the preformed acetyl chloride–aluminium chloride complex), has now been undertaken. Reaction conditions were varied, in order to obtain optimum yields of the acylated product. A range of solvents were also used to achieve the mono- and diacetyl-4,4′-dimethylbiphenyl. Quantitative analysis was performed by GLC; the data are collected in Tables 1–6. All mono and diketones synthesized along with the corresponding carboxylic acids were isolated from the reaction mixture and securely identified by their ^1H NMR, IR, elemental analysis and UV and mass spectra in some cases.

2. Experimental

2.1. Materials

4,4′-Dimethylbiphenyl, acetyl chloride, anhydrous aluminium chloride, 4-methyl-biphenyl, 4-chloroacetophenone, hydrochloric acid and ammonium hydroxide are from Aldrich, 4-amino-3-bromotoluene, copper(II) cyanide, *tert*-butylnitrite, methyl iodide, magnesium, D_2O, anhydrous sodium sulfate, sodium hypochlorite solution (NaOCl) (6% available chlorine), are from BDH. Alumina for column chromatography was obtained from R.D.H. Preparative TLC (silica gel PLC) was used size 20 cm × 40 cm, thickness 2.0 mm and silica gel used for column chromatography was 230–400 mesh ASTM from

Table 6
Effect of hydrocarbon:acetyl chloride:aluminium chloride molar ratio on the overall yield and isomer distribution on the acetylation of 4,4′-dimethylbiphenyl in 1,2-dichloroethane at 80 °C

Molar ratio DMB:AcCl:$AlCl_3$	Overall yield (%)	Isomer distribution (%)			
		2-Acetyl-DMBPh	3-Acetyl-DMBPh	2,3′-Diacetyl-DMBPh	4-Acetyl-biphenyl
1:1:1	48.40	93.26	6.11	–	0.63
1:2:2	76.22	–	–	100.00	–
1:4:4	90.20	–	–	100.00	–
1:6:6	91.06	–	–	100.00	–

Merck. All solvents used were of analytical purity from Fluka and were dried over anhydrous calcium chloride or anhydrous sodium sulfate prior to use in the acetylation reactions.

2.2. Apparatus

IR spectra were measured as KBr discs or as thin films of Nujol on a Pye Unicam sp3-300 spectrophotometer. UV–vis spectra were measured by Pye Unicam 8-400 in chloroform or *n*-hexane. ^{1}H-NMR spectra were recorded on a Varian FT-80 MHz and Bruker 100 MHz for solutions in deuterated chloroform, using tetramethylsilane as an internal standard. GLC analyses were carried out with a stainless steel column (2 m × 2.2 mm i.d.) packed with SE-30 (10%) on acid-washed Chromosorb W (80–100 mesh). Nitrogen (flow rate 15 lb in.$^{-2}$) was used as carrier gas at 250 °C; a Pye Unicam 204 instrument fitted with flame ionization detector was used. Peak areas were measured by Pye Unicam DP 88 electronic integrator. Mass response towards the different compounds was determined, and appropriate corrections were applied. Elemental analyses were carried out in Alfred Bernhard Mikroanalytisches Laboratorium, Germany. Mass spectra were obtained on a VG MassLab 12-250 GC mass spectrometer.

2.3. General acetylation procedure

Friedel-Crafts acetylation: equimolar quantities of the reactants were brought together under the Perrier conditions, i.e. the catalyst and acylating agent were allowed to react prior to addition of the substrate. A solution of 4,4′-dimethylbiphenyl (0.455 g, 0.0025 mol) in the chosen solvent (20 ml) was added dropwise over 5 min to a stirred mixture of acetyl chloride and aluminium chloride in the same solvent (10 ml) at 25 °C. Stirring was continued at 25 or 45 °C for a further 3 h or as described in the tables. The mixture was then added to an excess of crushed ice and 3 M HCl. The organic phase was separated, the extract was added to washing (solvent) of the acid layer and the combined extracts were washed with water (5 × 50 ml) and the solvent removed by rotary evaporator (and the organic layer washed with 150 ml of 3 M NaOH in the case of nitromethane). The viscous residue was dissolved in benzene and passed through a short column of silica gel (Merck type ASTM 230-4) to remove any polymeric materials. The eluent was then analyzed quantitatively by GLC. The overall yield of products is presented in the tables. Mono and diketones synthesized were directly isolated from reaction mixture and securely identified by their ^{1}H NMR, IR, mass spectra and elemental analysis.

2.4. Preparations of acetyl isomers

2.4.1. 2-Acetyl-4,4′-dimethylbiphenyl

To a stirred solution of acetyl chloride (0.785 g; 0.01 mol) and aluminium chloride (1.33 g; 0.01 mol) in chloroform (10 ml), 4,4′-dimethylbiphenyl (1.82 g; 0.01 mol) in the same solvent (20 ml) was added dropwise (20 min) and the mixture was stirred at 25 °C for 72 h. The dark brown oil obtained was chromatographed over silica gel/petroleum ether first to get rid of the remaining starting hydrocarbon, and then the ketone was obtained by using benzene as an eluent. Evaporation of benzene affords brown oil. This was subjected to preparative TLC (silica gel–benzene). The pure ketone (0.43 g; 19% was obtained as yellow oil: ν_{max} (neat) 1685 (C=O) cm^{-1}; δ ($CDCl_3$) 2.10 (s, 6H, 4-CH_3 and 4′-CH_3), 2.49 (s, 3H, 2-CH_3CO), 7.16–7.31 (6H, m, aromatic H), 7.53 (d, $J_{3,5}$ = 1.9 Hz, 1H, H-3); λ_{max} = 256 nm, ε_{max} = 12,600; *m/z* 224 $[M]^+$, 209 [base peak, $M-CH_3]^+$, 181 $[M-COCH_3]^+$, 76 $[C_6H_4]^+$, 43 $[COCH_3]^+$.

2.4.1.1. Preparation of 2-acetyl-4,4′-dimethylbiphenyl by stepwise synthetic route.

(I) 4-Amino-3-cyanotoluene: 4-amino-3-bromotoluene (10 g; 0.05 mol) and copper(II) cyanide (15 g, 0.17 mol) in pyridine (30 ml) was refluxed for 8 h. The solid obtained after cooling was extracted with chloroform (5 × 50 ml), washed with ammonium hydroxide solution 1 M (1000 ml), HCl solution 1 M (1000 ml), then with water. The solid obtained was purified by column chromatography (silica gel–benzene). 4-Amino-3-cyanotoluene (MeOH) was obtained as a yellow solid (2.35 g; 33%), mp 62–63 °C; lit 63 [14], ν_{max} (KBr) 2221 (C≡N) cm^{-1}.

(II) 2-Cyano-4,4′-dimethylbiphenyl: a mixture of 4-amino-3-cyanotoluene (0.5 g; 0.004 mol) and *tert*-butylnitrite (0.6 g) was left stirring at 25 °C for 20 min. Dried toluene (17 ml) was added and stirred for another 5 min. The mixture was heated (oil bath) at 45 °C until evolution of gas ceased. The mixture was left at room temperature for 30 min and then refluxed (oil bath) at 125 °C for 2 h. Toluene and low boiling products were removed by rotary evaporator. The residue was purified by column chromatography (silica gel–benzene). The extract was washed

with 30% HCl then water. Yellow oil was obtained (0.23 g; 30%), ν_{max} (neat) 2220 (C≡N) cm^{-1}.

(III) 2-Acetyl-4,4′-dimethylbiphenyl: 2-cyano-4,4′-dimethylbiphenyl (0.203 g; 0.001 mol) was added to methyl magnesium iodide [prepared from methyl iodide (0.71 g), Mg (0.122 g) and dried ether (15 ml)] in dried toluene (15 ml) for 15 min. After evaporation of ether, the mixture boiled gently for 4 h. After cooling, an excess of ammonium chloride solution was added, extracted with benzene. An oily liquid was obtained by evaporation of benzene, which was boiled again with 30% HCl (30 ml) for 5 h. Cooled, extracted with $CHCl_3$, washed with water and dried. Evaporation of $CHCl_3$ a brown viscous liquid was obtained, purified by column chromatography (alumina-benzene). Evaporation of benzene, a yellow oil was obtained (0.09 g; 41%), ν_{max} (neat) 1685 (C=O) cm^{-1}, and showed the same NMR spectrum as well as same retention time with the product obtained from the direct acetylation.

2.4.1.2. 3-Acetyl-4,4′-dimethylbiphenyl. To a stirred solution of acetyl chloride (1.507 g; 0.019 mol) and aluminium chloride (2.56 g; 0.019 mol) in nitromethane (40 ml), 4,4′-dimethylbiphenyl (3.5 g; 0.019 mol) in the same solvent (35 ml) was added dropwise (20 min) and the mixture was stirred at 25 °C for 120 h. The ketone (0.39 g; 9%) was obtained as a yellow oil (by preparative TLC. using silica gel–benzene); ν_{max} (neat) 1681 (C=O) cm^{-1}; δ ($CDCl_3$) 2.14 (s, 3H, 4′-CH_3), 2.51 (s, 3H, 4-CH_3), 2.55 (s, 3H, 3-CH_3CO), 7.12–7.51 (m, 6H, aromatic H), 7.75 (d, $J_{2,6}$ = 1.9 Hz, 1H, H-2); λ_{max} = 251 nm, ε_{max} = 17,800; *m/z* 224 $[M]^+$, 209 [base peak, $M-CH_3]^+$, 181 $[M-COCH_3]^+$, 76 $[C_6H_4]^+$, 43 $[COCH_3]^+$.

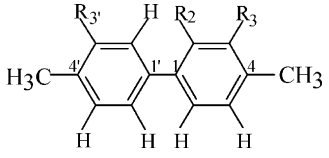
2.4.1.3. 2,3′-Diacetyl-4,4′-dimethylbiphenyl. To a stirred solution of acetyl chloride (1.568 g; 0.02 mol) and aluminium chloride (2.668 g; 0.02 mol) in dichloroethane (20 ml), 4,4′-dimethylbiphenyl (0.91 g; 0.005 mol) in the same solvent (20 ml) was added (5 min), and the mixture was stirred at 25 °C for 1 h and then heated under reflux for 22 h. The residue obtained was purified by column chromatography (silica gel–benzene). The ketone (1.12 g; 84%) was obtained as a yellow solid, mp 55–56 °C, ν_{max} (KBr) 1679 (C=O) cm^{-1}, δ ($CDCl_3$) 2.07 (s, 3H, 4′-CH_3), 2.49 (s, 3H, 2′-CH_3CO), 2.50 (s, 3H, 4-CH_3), 2.57 (s, 3H, 3-CH_3CO), 7.01–7.33 (m, 4H, aromatic H), 7.48 (d, $J_{2,6}$ = 2.0 Hz, 1H, H-2), 7.72 (d, $J_{3',5'}$ = 1.9 Hz, 1H, H-3′).

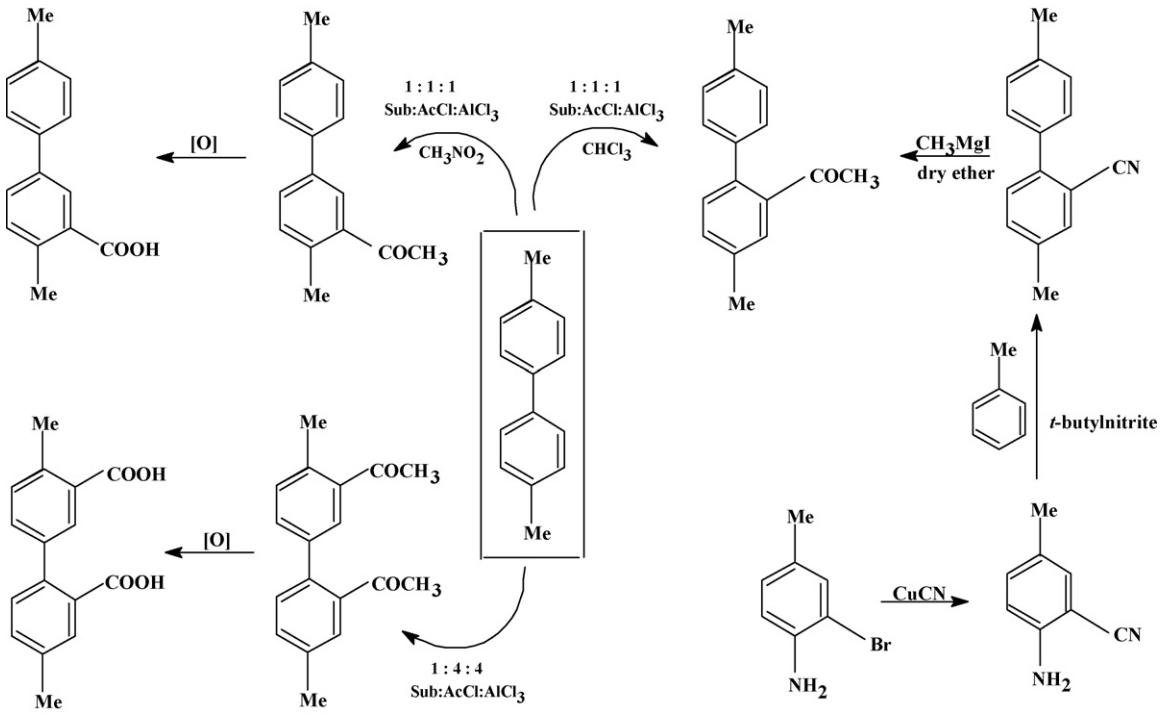
2.4.1.4. 4,4′-Dimethylbiphenyl-3-carboxylic acid. A mixture of 3-acetyl-4,4′-dimethylbiphenyl (0.55 g; 0.002 mol), sodium hydroxide (0.2 g) and sodium hypochlorite (NaOCl), 6% available chlorine (20 ml) was boiled for 5 h. Additional quantities of hypochlorite solution (7 ml) were added to the mixture after 1, 2, 3 and 4 h. After cooling, the solution was acidified with 50% HCl and the precipitate was extracted with ether (4 × 25 ml), washed with water then with dilute sodium hydroxide. The basic layer was separated, acidified with dilute HCl and a precipitate was formed which was extracted with ether. The acid was obtained after ether evaporation as yellow crystals (0.34 g; 61%), mp 144–146 °C (benzene–Ligroine). ν_{max} (KBr) 1688 (C=O) and 3045 (OH) cm^{-1} δ ($CDCl_3$) 2.39 (s, 3H, 4′-CH_3), 2.67 (s, 3H, 4-CH_3), 8.29 (d, $J_{2,6}$ = 1.85 Hz, 1H, H-2), 7.27–7.55 (m, 6H, aromatic H), 10.94 (s, 1H, 3-COOH exchangeable with D_2O), (found C, 79.32; H, 6.09%; $C_{15}H_{14}O_2$ requires C, 79.65; H, 6.19%).

2.4.1.5. 4,4′-Dimethyl biphenyl-2,3′-carboxylic acid. This acid was prepared from 2,3′-acetyl-4,4′-dimethylbiphenyl (0.25 g; 0.009 mol) following the procedure described in (d); white crystals (0.14 g; 55%) were obtained, mp 210–212 °C (benzene–Ligroine). ν_{max} (KBr) 1684 (C=O) and 3053 (OH) cm^{-1}, δ ($CDCl_3$) 2.46 (s, 3H, 4-CH_3), 2.67 (s, 3H, 4′-CH_3), 4.58 (s-br, 2H, 2- and 3′-COOH exchangeable with D_2O), 7.89 (s, 1H, H-3); 7.98 (s, 1H, H-2′), 7.28–7.63 (m, 4H, aromatic H), (found C, 71.29; H, 5.08%; $C_{16}H_{14}O_4$ requires C, 71.11; H, 5.19%).

3. Results and discussion

The symmetry of the 4,4′-dimethylbiphenyl molecule limits the number of isomeric mono-substituted derivatives to two, those with substituents at position 2- and 3-. Systematic investigations of the Friedel-Crafts acetylation of 4,4′-dimethylbiphenyl have now been undertaken in detail in an attempt to prepare the mono and di-ketones by direct electrophilic substitution reaction in good yield. The reaction mixtures were examined for their isomer proportions by gas–liquid chromatographic analysis. The identity of each component of an acetylation product was established by comparison of the retention times of each component on the GLC chromatogram with the retention time of the pure compounds or authentic samples determined under identical conditions. In some cases, it was thus necessary to prepare by unambiguous routes the pure ketones expected to be present in the acetylation product. The ^1H NMR spectra of the isomers isolated from the reaction mixture have been discussed in detail [15]. The chemical shift of the methyl protons could be used as an indication for the position of substitution of an acetyl or a methyl group linked to the aromatic rings [16,17]. The IR technique further supports the positional assignment. The IR absorption bands of the C=O stretching vibration of the acetyl group at position 2 and 3 appeared at 1685–1679 cm^{-1}, which elaborate a carbonyl group sterically hindered by the adjacent phenyl or methyl groups. The carbonyl band shifted to a lower wave number in comparison to acetophenone (1690 cm^{-1}) [18]. Mass spectra also support their structures by existence of the molecular ion peak $[M]^+$. The breakdown of the two mono acetyl isomers under electron impact follows almost the same mass fragmentation pathways. The major fragment ions observed in the mass spectra were $[M-CH_3]^+$, $[M-COCH_3]^+$, $[C_6H_4]^+$ and $[COCH_3]^+$.





Scheme 1. Acetylation/oxidation reaction pathways of 4,4′-dimethylbiphenyl.

Mono and di-acetylation of hydrocarbon 4,4′-dimethylbiphenyl were carried out using the appropriate molar proportions of the hydrocarbon (substrate), acetyl chloride (acylating agent) and aluminium chloride (catalyst) in the chosen solvent applying Perrier addition method unless otherwise stated (Scheme 1). 4,4′-Dimethylbiphenyl was acetylated using equimolar quantities of acetyl chloride and aluminium chloride (1:1:1) in various solvents and at different reaction temperatures. Two oily isomers were obtained, 2-acetyl- and 3-acetyl-4,4′-dimethylbiphenyl which were oxidized to the corresponding carboxylic acids. To be more accurate unambiguous routes synthesized one of the isomer, viz. 2-acetyl- isomer. The diacetyl isomer was also obtained by direct acetylation of the hydrocarbon and oxidized to the corresponding dicarboxylic acid.

Diacetylation of the substrate using four times excess of the acetylating agent and catalyst gives only one diketone, i.e. 2,3′-diacetyl-4,4′-dimethylbiphenyl, in good yield on using all the studied solvents. The formation of only a single di-substitution product under the above conditions may be due to the deactivation of the α-phenyl ring by the acetyl group because of their combined −I (inductive) and −M (mesomeric) effects.

Our preliminary investigation of the acetylation of 4,4′-dimethylbiphenyl indicated the formation of additional compounds (i.e. 4-methylbiphenyl and 4-chloroacetophenone which is not found in the 4,4′-dimethylbiphenyl used); 4-methylbiphenyl has been formed in trace amounts (1–2%) may be due to possible rearrangement or isomerization of the hydrocarbon 4,4′-dimethylbiphenyl, such process is usual in similar reactions [19]. In case of acetylation in chlorobenzene, 4-chloroacetophenone was formed. The retention times of these two compounds corresponded to the retention times of authentic samples.

Different parameters have been studied to attain the best suited conditions for the preparations of mono and di-acetyl isomers such as effect of temperature, solvent, type of addition, time and reactant molar ratio and the results are listed in Tables 1–6 and Figs. 1 and 2. Table 7 represents the retention time in centimetres and in seconds along with the relative retention time for comparison.

3.1. Effect of reaction conditions on reactivity, selectivity and isomer distribution

3.1.1. Solvent effects

To understand the influence of solvent used, a variety of solvents with different polarities have been employed in the

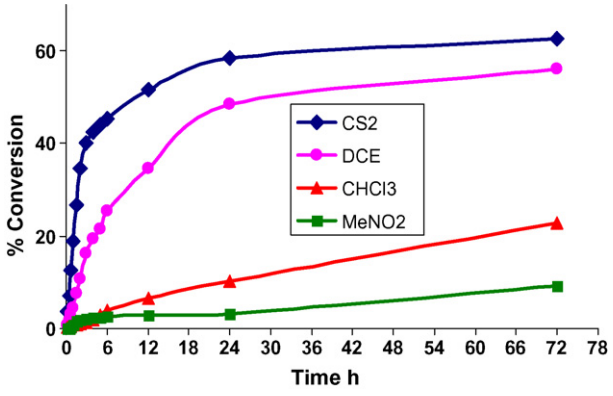


Fig. 1. %Conversion of 4,4′-dimethylbiphenyl under different types of solvents.

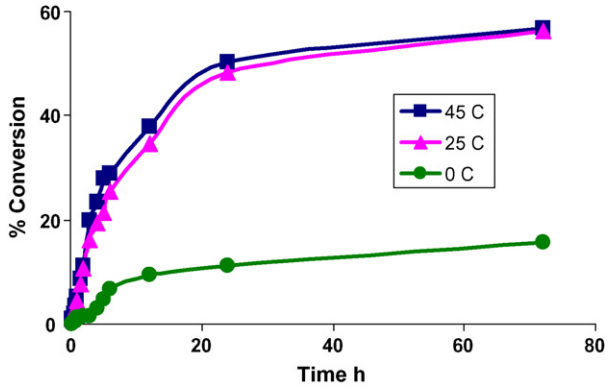


Fig. 2. Effect of reaction temperature on the overall yield in 1,2-dichloroethane solvent.

Friedel-Crafts ketone synthesis (Table 1, Fig. 1). Nitromethane and carbon disulfide are the most commonly used solvents which at the same time govern the types of acylation reaction, viz. essentially homogeneous and heterogeneous, respectively. A polar solvent, such as nitromethane, dissolves (and solvates) not only aluminium chloride but also the [$RCO^+ \cdot AlCl_3X^-$] complex, and usually also the aluminium chloride complex of the resulting ketones; the reaction is homogeneous. In non-polar solvents such as carbon disulfide, neither aluminium chloride nor its complex with acyl halides is appreciably soluble; the reaction is largely heterogeneous throughout its course. Intermediate between these extremes are such chlorinated solvents as 1,2-dichloroethane, chloroform or chlorobenzene, which do not appreciably dissolve aluminium chloride but are excellent solvents for the acylating complex and fair solvents for the final complex.

The results show that the solvent has a marked effect on the overall efficiency of acetylation (overall yield), isomer distribution and selectivity. Low conversion was obtained in chloroform and nitromethane and moderate acetylation yield were achieved in 1,2-dichloroethane and chlorobenzene, whereas a good yield was attained in carbon disulfide solvent in comparison with other solvents. The ratio of 2-:3- substitution of 4,4′-dimethylbiphenyl is influenced to a large extent by the type of solvent used, i.e. only one acetyl isomer, viz. 3-acetyl isomer was formed in nitromethane solvent, whereas, in other solvents a mixture of the 2- and 3-regioisomers was formed. The low reactivity of the 2-position in acetylation is due to steric hindrance, coupled with the large steric requirements possessed by the acetylation species.

Table 8
UV absorption spectra measured in chloroform solution: 1×10^{-4} mol l^{-1}

Compound	λ_{max} (nm)	ε_{max} (mol^{-1} m^2)
2,2′-Dimethylbiphenyl	242	11,000
4,4′-Dimethylbiphenyl	256	20,000
2-Acetyl-4,4′-dimethylbiphenyl	256	12,600
3-Acetyl-4,4′-dimethylbiphenyl	251	17,800

The acetyl isomer distribution of 4,4′-dimethylbiphenyl allows a discussion on the competition of the directing effects of the methyl and tolyl substituents. In the following discussion it will, in the first instance, be assumed that non of the reaction mixtures were exhaustively investigated for minor components or rearranged side products, and that the proportions of monoacetyl derivatives represent the proportions of attack on the corresponding positions by acetyl chloride. It is interesting that, in terms of the additively principle, the orientation in this compound can be said to be controlled essentially by the relative *meta*-orientating power of the group. The methyl and tolyl substituents have similar activating powers towards the *ortho*-position for each substituent, but for the *meta*-position the methyl group is activating and the tolyl group is deactivating, so substitution occurs *meta* rather than *ortho* to the methyl group. This type of analysis reveals the theoretical and practical difficulties in determining relative directing power of two substituents from orientation obtained by putting two substituents in competition within the same molecule. Therefore, the above explanation indicates the high reactivity of the 2-position in chloroalkanes or carbon disulfide solvents. The high yield of the 3-acetyl isomer in nitromethane solution, however, is due to the formation of a bulky addition complex, viz. $CH_3COCl \cdot AlCl_3 \cdot (MeNO_2)_n$, which would not find spatial accommodation to react at the 2-position.

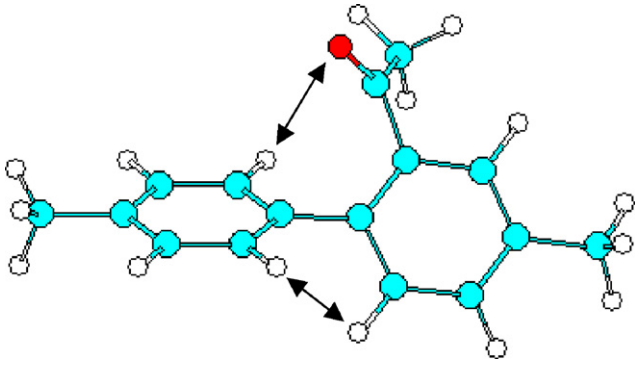
In order to provide further evidence for the structure elucidation of 2-acetyl and 3-acetyl-4,4′-dimethylbiphenyl, it was desirable to examine the UV spectra of the above ketones and compare them with that of 2,2′- and 4,4′-dimethylbiphenyl. The positions and extinctions data of the UV absorption band (band corresponding to the $n \rightarrow \pi^*$ transition of the carbonyl group) are recorded in Table 8.

Positions and extinctions data of the UV absorption bands are interpreted in terms of steric and conjugation effects. Substitution of a methyl group *ortho* to the biphenyl bond causes a rotation of the two rings relative to one another compared to biphenyl itself. In the same way, substitution of acetyl group in the position *ortho* to the biphenyl bond causes a rotation of

Table 7
GLC analysis, retention time (in cm and s) with the relative retention time of the 4,4′- dimethylbiphenyl and its acetyl isomers and other by-products

Compound	Retention time (RT) in cm[a]	Retention time (RT) in s	Relative retention time
4,4′-Dimethylbiphenyl	1.33	159	1.00
4-Chloroacetophenone	1.72	205	1.29
2-Acetyl-4,4′-dimethylbiphenyl	2.19	263	1.65
3-Acetyl-4,4′-dimethylbiphenyl	2.91	349	2.20
2,3′-Diacetyl-4,4′-dimethylbiphenyl	4.58	549	3.45
4-Methylbiphenyl	0.88	105	0.66

[a] Chart speed 300 mm/h.



Scheme 2. 3D modeling for the optimized geometry of 2-Ac-4,4′-DMB.

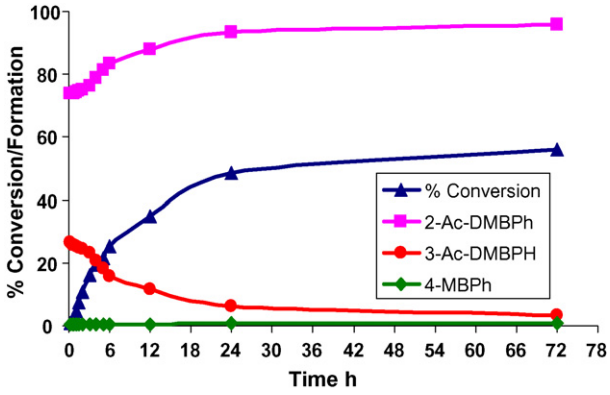


Fig. 3. Effect of reaction time on the %conversion and product selectivity in 1,2-dichloroethane.

the two rings relative to one another, which in turn induce a rotation of the acetyl group relative to the plane of the benzene ring to which it is attached. The position of substitution could be confirmed and interpreted in terms of steric and conjugation effects from the UV spectra [20] and dynamic study [21]. Oshaughnessy et al. [22] showed a similar molecular extinction coefficient value in other solvents. Also the same effects were observed in the electronic spectra of methyl-substituted acetophenones [23].

It is clear that the acetyl group at position-2 will interpenetrate with the hydrogen at 2′-position, which causes the two rings to rotate to some extent and in turn obstruct resonance between the two aromatic rings. This behaviour was compared with the same results that are found in case of 2,2′-dimethylbiphenyl. This explains the change in molecular extinction coefficient value.

To assist our elucidation on the positional effect of the acetyl group on the rotation angle of the two rings relative to one another, a 3D modeling software (HyperChem Version 6.01) was used to calculate the dihedral angle (torsion angle) between the two rings of 2-acetyl-4,4′-dimethylbiphenyl using Parametric Method (PM3), performing the semi-empirical Self-Consistent Field (SCF) theory for the geometry optimization. It was found that the angle between the two phenyl rings lies between 44.31 and 46.06°, and the distance between 6- and 6′-H and between 2′-H and O is 2.15 and 2.94 Å, respectively (Scheme 2). In agreement with the earlier reported, it was found that the dihedral angle between the two rings of biphenyl molecule is $26 \pm 5°$ [24], whereas in 2,2′-dimethylbiphenyl system this angle becomes 70.5 or close to perpendicular [25–27]. The same observations were found with 4,4′-dimethylbiphenyl-2,2′-dicarboxylic acid [28,29], the twist angles of the two biphenyl were 68.1 and 64.6°.

3.1.2. Temperature effect

Three different reaction temperatures (0, 25 and 45 °C) were selected to study the effect of reaction temperature on the yield or conversion as well as isomer distribution. Fig. 2 shows the influence of reaction temperature on the overall yield in 1,2-dichloroethane solvent. Table 1 shows the %conversion at two different temperatures using all the studied solvents. At moderate temperature (25 °C), carbon disulfide was a good solvent for the formation of 2-acetyl isomer in high yield. At higher temperature (45 °C) no significant effect was found on both yield and isomer distribution. At 0 °C, the reaction was found to be very slow which is predictable. In the case of chloroform and chlorobenzene at reflux, the reaction was not showing good results due to formation of a high percentage of polymeric materials and other by-products due to acetylation of the solvent itself in the case of chlorobenzene.

3.1.3. Effect of time

Tables 2–5 show the effect of reaction time on the acetylation reaction in different solvents. It was found that the percentage conversion increased with time, whereas the %selectivity showed different trends. Fig. 3 shows the %conversion and selectivity with time for acetylation of the hydrocarbon at 25 °C in 1,2-dichloroethane as a typical example. It was interesting to find that the isomer distribution was also affected largely and the reaction became more selective towards the 2-acetyl isomer and increased from ∼76 to ∼96 with increasing reaction time from 3 to 72 h which is due to high reactivity of the 2-position. The %conversion increased slightly on increasing the reaction time to 120 h in 1,2-dichloroethane and nitromethane solvents. In case of chlorobenzene, on increasing reaction time to 72 h, the overall yield increased to ∼52% in which more than 40% of 4-chloroacetophenone was formed.

3.1.4. Effect of reactants molar ratio: (substrate:acylating agent:catalyst)

Table 6 represents the results of acetylation of 4,4′-dimethylbiphenyl using 1:1:1 molar ratio, the keto isomers 2- and 3- were detected. When an excess of acetyl chloride and aluminium chloride were used, only one isomer was formed, i.e. 2,3′-diacetyl-4,4′-dimethylbiphenyl(Id). Increasing the molar ratio of substrate:AcCl:$AlCl_3$ from 1:1:1 to 1:6:6 only one isomer was isolated (diacetyl isomer) and no mono acetyl isomer were detected by GLC. It was found from Table 6 that increasing the molar ratio above 1:2:2 would increase the %yield only. It was concluded that a 1:4:4 molar ratio was the best ratio to get a high yield of 2,3′-diacetyl-4,4′-dimethylbiphenyl.

3.1.5. Type of addition

Two different types of addition (i.e. Perrier and antiPerrier) were used to show the effect of type of addition. It was found

that the type of addition has no significant effect on both the %yield and isomer distribution.

4. Conclusions

The main aim of the present work was to investigate in detail the activity and selectivity of Friedel-Crafts acetylation of 4,4′-dimethylbiphenyl as well as to prepare the mono- and diacetyl isomers in good yields as earlier works were incomplete. The substrate was acetylated using equal molar of hydrocarbon, acylating agents and catalyst in various solvents at different temperatures leading to a mixture of 2-acetyl and 3-acetyl 4,4′-dimethylbiphenyl. The results obtained indicate that in chloroalkanes or carbon disufide, the 2-acetyl isomer predominates. In nitromethane, however, the reactivity sequence is $3 \rightarrow 2$-. The best conditions to obtain the 2-acetyl isomer were found to be 1:1:1 molar ratio of the hydrocarbon: acylating agent: catalyst, 25 °C and 72 h, in dichloroethane. While in nitromethane solvent, the 3-acetyl isomer (100% selectivity) was formed using a 1:1:1 molar ratio, at 25 °C in 72 h reaction time, although in low yield. In the case of the diacetyl isomer, the best-suited condition is 1:4:4 molar ratio in 1,2-dichloroethane at 45 °C (reflux) for 3 h with 100% selectivity.

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