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Novel Conversion of 2-(4-Dimethylaminoaryl)-1,4-diphenylbutane-1,4-diones into 3-(4-Dimethylaminoaryl)-1-phenylpropenones via Debenzoylation and Oxidation

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It was found that 1,4-diketones such as 1,4-diphenyl-1,4-butanediones containing *N,N*-dimethylaminophenyl (pDPB) and *N,N*-dimethylaminonaphthyl (nDPB) at C2 are converted into 3-(4-dimethylaminoaryl)-1-phenylpropan-1-ones (pPPA and nPPA) by treatment with $Ca(OH)_2$ in methanol, which was easily oxidized to enone, i.e., 3-(4-dimethylaminophenyl)-1-phenylpropenones (pPPE and nPPE), when treated with 2,3-dichloro-5,6-dicyano-1,4-benzoquinone (DDQ) in dichloromethane.

key words: 1,4-diphenyl-1,4-butanedione, 1-phenylpropan-1-one, 1-phenyl-propenone, calcium hydroxide, DDQ

INTRODUCTION

Chalcones are a group of enone compounds with wide distribution in nature [1,2].

Many of them are known to exhibit antioxidant activities which are related to their ability to chelate metal ions and scavenge singlet oxygen, superoxide radicals, peroxyl radicals, hydroxyl radicals, and peroxynitrite. Enones have also been used as the starting materials in conjugate addition of many organic molecules [3-7]. It was found that enones such as **5** and **6** are produced from 1,4-diketones such as **1** and **2** via debenzoylation and oxidation. To the best of our knowledge, this kind of debenzoylation in the reactions of 1,4-diketones, i.e., **1** and **2** has not been reported yet. We here describe that enone such as aminochalcone **5** and its naphthyl analog **6** can be produced by the reaction of 1,4-diphenyl-1,4-butanediones (pDPB **1** and nDPB **2**) with calcium hydroxide followed by oxidation with 2,3-dichloro-5,6-dicyano-1,4-benzoquinone (DDQ).

MATERIALS AND METHODS

Materials

Two starting materials, 2-(4-dimethylaminophenyl)-1,4-diphenylbutan-1,4-dione (pDPB) **1** and 2-(4-dimethylaminonaphthyl)-1,4-diphenylbutan-1,4-dione (nDPB) **2** were prepared from dibenzoylmethane and *N,N*-dimethylaniline or *N,N*-dimethyl-1-naphthylamine [8]. Calcium hydroxide and 2,3-dichloro-5,6-dicyano-1,4-benzoquinone (DDQ) were purchased from Aldrich Chemical Co. and used without further purification. Methanol and methylene chloride used in the reactions were obtained from Ducksan Chemical Co. and distilled before use. Silica gel (Kieselgel 60 F254, Merck Co.) was used for thin layer chromatography. Kieselgel G (230-400 mesh) purchased from Merck Co. was used for liquid column chromatography. Hexane and ethyl acetate were also obtained from Ducksan Chemical Co. to use as the eluent in TLC and column chromatography.

Methods

^1H and ^{13}C NMR spectra were recorded on a Jeol JMN EX-400 spectrometer. Proton chemical shifts (δ) are recorded in ppm downfield from tetramethylsilane (TMS), and ^{13}C resonances were recorded using the $CDCl_3$ resonance (77.0 ppm) of the solvent as an internal standard and reported in ppm downfield from TMS. Infrared (IR) spectra were recorded on a Nicolet 5-DXB Fourier transform (FT) spectrophotometer in KBr pellets or NaCl cell, in which peaks are reported in reciprocal centimeters (cm^{-1}). UV-visible spectra were recorded on a Beckman DU 7500 spectrophotometer. Mass spectra were determined at 40-70 eV with a Hewlett-Packard 5985A GC/MS spectrometer by electron impact (EI) method. All reactions were carried out under dry nitrogen atmosphere in oven-dried glassware. Evaporation of solvents was carried out with a rotary evaporator using vacuum pump.

Preparation of 3-(4-dimethylaminophenyl)-1-phenylpaopan-1-one (pPPA) 3

2-(4-Dimethylaminophenyl)-1,4-diphenylbutan-1,4-dione (pDPB) **1** (36.2 mg, 0.1 mmol) was treated with $Ca(OH)_2$ (15.0 mg, 0.2 mmol) in methanol (20 mL) at room temperature under stirring for 5 h. The reaction mixture was concentrated in vacuo followed by liquid column chromatography (silica gel, 230-400 mesh) using hexane-ethyl acetate (12:1, v/v) as the eluents to isolate 22.8 mg (0.09 mmol) of 3-(4-dimethylaminophenyl)-1-phenylpropan-1-one (pPPA) **3** in 90 % yield.

Spectral data of **3**: UV (MeOH) λ_{max} 248, 310 nm; IR (KBr)

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3080, 2924, 2854, 1684, 1615, 1480, 1447, 1348, 1205, 1164, 1059, 1164, 1059, 976, 946, 814, 745, 691 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.96(2H, d, J=7.2), 7.55(1H, t), 7.45(2H, t), 7.13(2H, d, J=8.8), 6.70(2H, d, J=8.4), 3.26(2H, t, -C<u>H</u>$_2$ CH_2CO), 2.97(2H, t, -CH_2C<u>H</u>$_2$CO), 2.91(6H, s, -$N(CH_3)_2$); ^{13}C NMR (100 MHz, $CDCl_3$) δ 199.5(-C=O), 149.4, 137.1, 133.0, 129.5, 128.5, 113.2, 40.8, 37.7, 29.2, 18.6; Mass (m/e) 253(M), 134, 77.

Preparation of 3-(4-dimethylaminonaphthyl)-1-phenylpaopan-1-one (nPPA) 4

2-(4-Dimethylaminonaphthyl)-1,4-diphenylbutan-1,4-dione **2** (nDPB) (16.5 mg, 0.04 mmol) was treated with $Ca(OH)_2$ (5.9 mg, 0.08 mmol) in methanol (20 mL) under stirring for 5 h. The reaction mixture was concentrated in vacuo followed by liquid column chromatography (silica gel, 230-400 mesh) using hexane-ethyl acetate (12:1, v/v) as the eluents to isolate 9.7 mg (0.032 mmol) of 3-(4-dimethylaminonaphthyl)-1-phenylpropan-1-one (nPPA) **4** in 80% yield. **4**: UV (MeOH) λ_{max} 240, 282, 311 nm; IR (KBr) 3066, 2927, 2850, 1732, 1689, 1462, 1394, 1283, 1203, 1135, 1074, 1049, 969, 828, 769, 745, 692 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 8.31(1H, d, J=7.8), 8.01(1H, d, J=7.4), 7.96(2H, d, J=6.8), 7.56~ 7.50(3H, m), 7.44(2H, t), 7.31 (1H, d, J=8.0), 7.02(1H, d, J= 7.6), 3.47 (2H, t,), 3.41 (2H, t, -CH_2-), 2.88(6H, s, 2xCH_3); ^{13}C NMR (100 MHz, $CDCl_3$) δ199.5(-C=O), 149.9, 136.9, 133.0, 132.7, 131.8, 129.3, 128.6, 128.0, 126.0, 125.9, 124.9, 124.8, 123.9, 113.8, 45.3(2xCH_3), 39.9, 29.7, 27.0; Mass (m/e) 303 (M).

Preparation of 3-(4-Dimethylaminophenyl)-1-phenylpropenone (pPPE) 5

The pPPA **3** (20 mg, 0.08 mmol) was treated with 2,3-dichloro-5,6-dicyano-1,4-benzoquinone (DDQ, 36.3 mg, 0.16 mmol) in dichloromethane (20 mL) under stirring for 2 h. The reaction mixture was concentrated in vacuo followed by liquid column chromatography (silica gel, 230-400 mexh) using hexane-ethyl acetate (9:1, v/v) as the eluents to isolate 17.1 mg (0.07 mmol) of 3-(4-dimethylaminophenyl)-1-phenylpropenone (pPPE) **5** in 85% yield. **5**: UV (MeOH) λ_{max} 421, 264 nm, IR (KBr) 3020, 2923, 1736, 1532, 1469, 1249, 1021 cm^{-1}; ^1H-NMR (400 MHz, $CDCl_3$) δ 8.00 (2H), 7.78 (1H, C<u>H</u> =CHCO, J=15.6), 7.56-7.47 (5H), 7.36 (1H, CH=C<u>H</u>CO, J= 15.6), 6.70 (2H), 3.04 (6H); ^{13}C-NMR (100 MHz, $CDCl_3$) δ 190.9, 152.1, 146.0, 139.2, 132.1, 130.5, 128.4, 122.6, 116.9, 111.9, 40.3; High Resolution Mass (EI), m/e Calcd for $C_{17}H_{17}NO$ 251.1310, Found 251.1312.

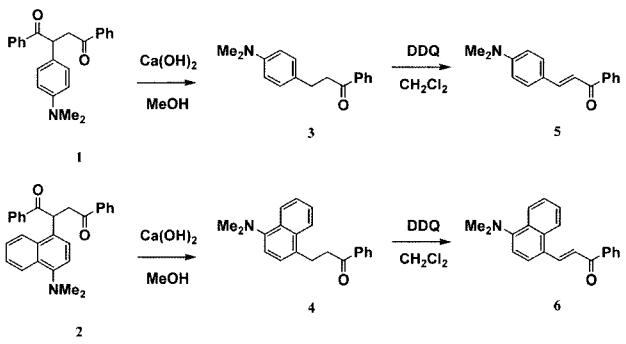
Preparation of 3-(4-Dimethylaminonaphthyl)-1-phenylpropenone (nPPE) 6

The nPPA **4** (9.10 mg, 0.03 mmol) was treated with 2,3-dichloro-5,6-dicyano-1,4-benzoquinone (DDQ, 13.6 mg, 0.06 mmol) in dichloromethane (20 mL) under stirring for 2 h. The reaction mixture was concentrated in vacuo followed by liquid column chromatography (silica gel, 230-400 mesh) using hexane-ethyl acetate (9:1, v/v) as the eluents to give 7.2 mg (0.024 mmol) of 3-(4-dimethylaminonaphthyl)-1-phenylpropenone **6** in 81% yield.

6: UV (MeOH) λ_{max} 248, 405 nm; IR (KBr) 3060, 2925, 2857, 1730, 1666, 1584, 1455, 1381, 1262, 1099, 1031, 802, 701 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ8.58 (1H, d, C<u>H</u>= CHCO, J=15.6), 8.20(1H, d, J=6.8), 8.18(1H, d, J=6.8), 8.00 (2H, d, J= 7.6), 7.82(1H, d, J=8.0), 7.65(1H, t) 7.52(1H, t), 7.50(1H, CH= C<u>H</u>CO, J=15.6), 7.47(3H, t, ph), 7.01(1H, d, J= 8.4), 2.79(6H, s, 2xCH_3); ^{13}C NMR (100 MHz, $CDCl_3$) δ 194.8(-C=O), 167.7, 142.0, 138.9, 137.6, 132.7, 132.3, 130.9, 128.6, 128.2, 126.2, 125.3, 125.0, 124.8, 124.6, 117.2, 113.0, 45.0(2x<u>C</u>H_3); HRMS Calcd for $C_{21}H_{19}NO$: 301.1467. found: 301.1467.

RESULTS AND DISCUSSION

1,4-Diketones have been extensively employed in the syntheses of a variety of cyclic compounds such as furans, thiophenes, etc. [9, 10]. We have been interested in the reactions of 1,4-diketones with *N,N*-dimethylaniline and metallic cations. We found that 1,4-diphenyl-1,4-diketones such as **1** and **2** having 4-dimethylaminoaryl groups at C2 undergo debenzoylation to give the corresponding 1-phenylpropan-1-ones, i.e., **3** and **4** in good yields. When 2-(4-dimethylaminophenyl)-1,4-diphenylbutan-1,4-dione (pDPB) **1** was treated with $Ca(OH)_2$ in methanol, a simple ketone, 3-(4-dimethylaminophenyl)-1-phenylpropan-1-one (pPPA) **3** was produced in 93% yield. It was also found that the ketone **3** was oxidized easily to give a yellow-colored enone (λ_{max} = 421 nm in MeOH), i.e., 3-(4-dimethylaminophenyl)-1-phenyl-propenone (pPPE) **5** by treatment with DDQ in methanol. In the same manner, another 1,4-diketone, 2-(4-dimethylaminonaphthyl)-1,4-diphenylbutan-1,4-dione (nDPB) **2** was also converted into a ketone, 3-(4-dimethylaminoaryl)-1-phenylpropan-1-ones (nPPA) **4** in 90% yield, when treated with $Ca(OH)_2$ in methanol, which was also found to be oxidized to give a yellow-colored enone dye (λ_{max} = 410 nm in MeOH), i.e., 3-(4-dimethylaminonaphthyl)-1-phenylpropenones (nPPE) **6**, when treated with DDQ in methanol. It is interesting to note that simple ketones such as **3** and **4** are produced from 1,4-diketones such as **1** and **2** via debenzoylation in one pot.



Scheme 1.

UV-visible spectra of the photoproducts **1** and **2**, produced from dibenzoylmethane and *N,N*-dimethylaniline, primary products **3** and **4**, and final products **4** and **5** were compared in methanol at room temperature, in which the longest absorption bands were observed at 305 and 336 nm, 310 and 311 nm, and 421 and 416 nm, respectively (Figures 1 and 2). The longest absorption bands of enone dyes **5** and **6** were red shifted, in comparison with the starting materials, which is due to the formation of carbon-carbon double bonds between two chromophores, i.e., 4-dimethylaminoaryl and benzoyl group, to give π-conjugated systems.

In summary, it was found for the first time that 1,4-diketones such as 2-(4-dimethylaminophenyl)-1,4-diphenylbutan-1,4-dione (pDPB) **1** and 2-(4-dimethylaminonaphthyl)-1,4-diphenylbutan-1,4-dione (nDPB) **2** undergo debnzoylation to give simple ketones, i.e., pPPA **3** and nPPA **4** in good yields, when they were treated with $Ca(OH)_2$ in methanol at room temperature. In addition, they were easily oxidized to give yellow-colored enones dyes, i.e., pPPE **5** and nPPE **6** by treatment with DDQ in dichloromethane.

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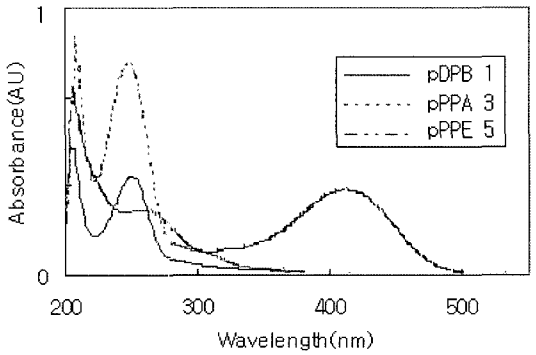

Figure 1. Comparison of UV-visible spectra of pDPB **1**, pPPA **3**, and pPPE **5** in methanol at room temperature.

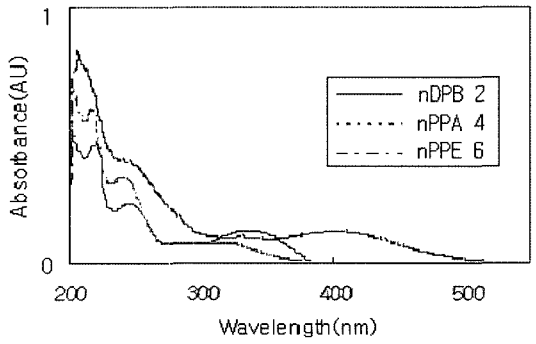

Figure 2. Comparison of UV-visible spectra of nDPB **2**, nPPA **4**, and nPPE **6** in methanol at room temperature.

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Spectral data of **2**: UV (MeOH) λ_{max} 336, 245 nm, IR (KBr) 3066, 2965, 1723, 1669, 1595, 1447, 1387, 1279, 696 cm^{-1}; ^{1}H-NMR (400 MHz, $CDCl_3$) δ 8.26 (1H), 8.14 (1H), 8.00 (2H), 7.73 (2H), 7.61-7.43 (5H), 7.28 (3H), 7.13 (1H), 6.79 (1H), 5.65 (1H, t, -C<u>H</u>CH_2-, J=7.2 Hz), 3.86 (2H, d, -CHC<u>H</u>$_2$-, J=7.2 Hz), 2.78 (6H); ^{13}C-NMR (100 MHz, $CDCl_3$) δ 195.8 (C=O), 136.0, 133.8, 133.2, 132.6, 132.3, 131.2, 129.1, 128.7, 128.6, 128.4, 127.3, 127.1, 126.1, 125.0, 124.8, 124.1, 123.6, 113.5, 57.3 (-<u>C</u>HCH$_2$-), 45.3 (2CH_3), 32.6 (-CH<u>C</u>H$_2$-); Mass (EI) m/e 407 (M), 302, 184, 105.
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