A NOVEL METHOD FOR MICHAEL ADDITION AND EPOXIDATION OF CHALCONES IN A WATER SUSPENSION MEDIUM: A COMPLETELY ORGANIC SOLVENT-FREE SYNTHETIC PROCEDURE

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Abstract - Very efficient Michael addition reactions of amines, thiophenol and methyl acetylacetate to chalcone, and epoxidation of chalcone derivatives with NaOCl, in a water suspension medium have been developed as completely organic solvent-free reactions.

Introduction

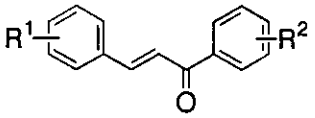
The Michael addition reaction is very useful for carbon-hetero atom and carbon-carbon bond formations, and epoxidation is also very important in organic synthesis. We report organic solvent-free Michael addition and epoxidation reactions of chalcones which are carried out in a water suspension medium containing a surfactant. The reaction product can be collected just by filtration. This method has a big advantage, since no organic solvent is necessary during the reaction and separation of the product, and since the water medium containing surfactant can be recycled, no polluted material is produced. Furthermore, although Michael addition reaction of amines to chalcones in organic solvents does not give the addition product in a pure state because of its reversibility in solution,[1] the reaction in a water suspension medium gives the pure addition product in high yield because of the absence of this reversibility in the solid state.

Results and Discussion

Michael Addition Reactions of Amines to Chalcones in a Water Suspension. As a typical example, a suspension of powdered chalcone (**1 a**) in a small amount of water containing *n*BuNH$_2$ (**2 e**) and the surfactant hexadecyltrimethylammonium bromide (**3 a**) was stirred at room temperature for 4 h. The reaction product was filtered and air dried to give the Michael addition product (**4 e**) as a colorless powder in 98% yield. The filtrate, containing **3 a** and small amounts of **2e** and **4 e**, can be used for the next identical reaction. By the same procedure, Michael addition reactions of the various amines (**3 a-q**) to (**1 a**) were carried out and pure amine-chalcone adducts were obtained in good yields (Table 1). The solubility of the amines in water is not related to the efficiency of the reaction. Amines (**2h-k**) which are poorly soluble in water reacted with **1 a** in the water suspension as effectively as the water soluble amines (Table 1). These Michael adducts cannot be obtained in a pure state through reaction in organic solvents. For example, when a solution of **1 a** and **2 e** in toluene was stirred at room temperature, and solvent evaporated below 40 °C in vacuo, a mixture of **4 e** and **1 a** was obtained as an oily material which contained **4 e** in only 38% yield (^{1}H NMR analysis in CDCl$_3$). Furthermore, due to the equilibrium in solution, it is difficult to isolate **4** in a pure state from the mixture. For example, ^{1}H NMR spectral analysis showed that a solution of pure **4 e** (0.1 g) in toluene (1 mL) consists of 53% of **4 e** and 47% of **1 a**. As far as we are aware, only **4 n** has been prepared previously in a pure crystalline state by the reaction of **1 a** and **2 n** in a sealed tube at 100 °C.[2]

Pure crystalline samples of **4e, 4h-k, 4 n** and **4p-q** are all much more stable in the solid state than in solution. However, even in the solid state, these were gradually decomposed at room temperature and were completely degraded to chalcone and amine after about one week.

During the Michael addition reaction in water suspension medium, the surfactant plays an important role. In its absence, powdered **1 a** coagulates and is not dispersed in water. Therefore the relationship between the structure of the surfactant and efficiency of the reaction was studied. As summarized in Table 2, hexadecyltrimethylammonium bromide (**3 a**) and chloride (**3 b**), and bis(dodecyl)dimethylammonium bromide worked very well, and therefore most reactions were carried out by using the surfactant (**3 a**) or (**3 b**). A plausible interpretation



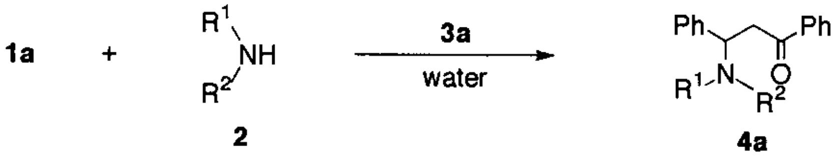
1

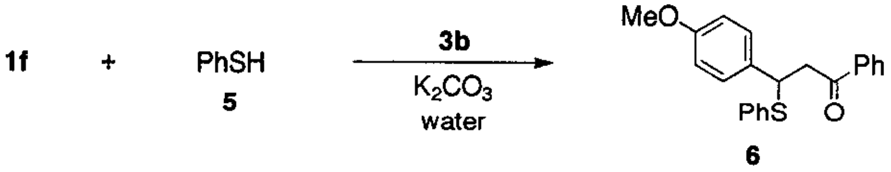
a: $R^1=R^2=H$
b: $R^1=m\text{-Me}, R^2=H$
c: $R^1=p\text{-Me}, R^2=H$
d: $R^1=p\text{-Cl}, R^2=H$
e: $R^1=p\text{-Br}, R^2=H$
f: $R^1=p\text{-MeO}, R^2=H$
g: $R^1=H, R^2=p\text{-Me}$
h: $R^1=H, R^2=p\text{-Cl}$
i: $R^1=H, R^2=p\text{-Br}$
j: $R^1=H, R^2=p\text{-MeO}$
k: $R^1=R^2=p\text{-Me}$
l: $R^1=R^2=p\text{-Cl}$

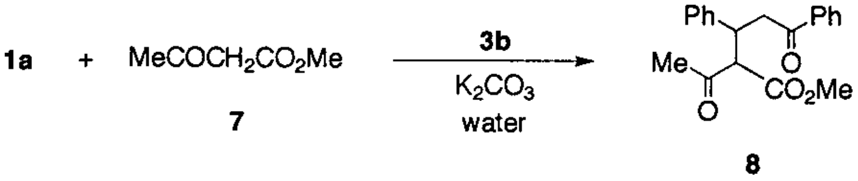
$C_{16}H_{33}N^+Me_3 \cdot X^-$

3

a: X=Br
b: X=Cl







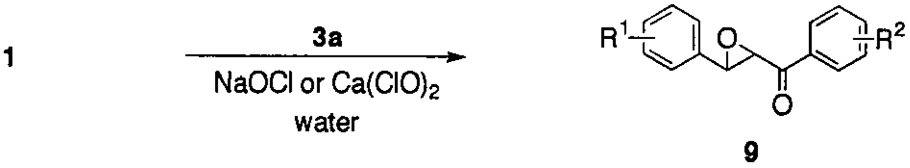
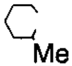
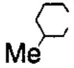
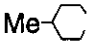


Table 1. Michael Addition Reactions of Amines (**2**) to Chalcone (**1a**) in a Water Suspension Medium Containing **3a** as a Surfactant

	Amine **2**		Reaction time (h)	Product	
	R^1	R^2			yield (%) [a]
a	Me	H	48	—	— [b]
b	Et	H	48	—	— [b]
c	*n*Pr	H	48	—	— [b]
d	*i*Pr	H	48	—	— [b]
e	*n*Bu	H	4	**4e**	98
f	*s*Bu	H	48	—	— [b]
g	*t*Bu	H	48	—	— [b]
h	*n*Pen	H	0.7	**4h**	98
i	*n*Hex	H	0.3	**4i**	96
j	*n*Oct	H	0.3	**4j**	93
k	C_6H_{11}	H	48	**4k**	93
l	Ph	H	48	—	— [b]
m	Et	Et	48	—	— [b]
n			5	**4n**	93
o			48	—	— [b]
p			0.5	**4p**	95
q			2	**4q**	96

[a] Isolated yields.

[b] No reaction occurred.

Table 2. Effect of Surfactant on Michael Addition Reactions of **2e** to **1a** in a Water Suspension Medium [a)]

Surfactant	Reaction time (h)	Yield (%)
$(Me(CH_2)_3)_4N^+ \cdot Br^-$	48	— [b)]
$(Me(CH_2)_3)_4N^+ \cdot SCN^-$	48	— [b)]
$C_6H_5N^+Me_3 \cdot Br^-$	48	— [b)]
$C_9H_{19}N^+Me_3 \cdot I^-$	50	93
$C_{13}H_{27}N^+Me_3 \cdot I^-$	50	92
$C_{16}H_{33}N^+Me_3 \cdot Br^-$ (**3a**)	4	98
$C_{16}H_{33}N^+Me_3 \cdot Cl^-$ (**3b**)	10	96
$C_{16}H_{33}N^+Me_3 \cdot I^-$	70	96
$C_{16}H_{33}N^+nPr_3 \cdot Br^-$	8	98
$(C_{12}H_{25})_2N^+Me_2 \cdot Br^-$	5	91
$(Cl^-Me_3N^+CH_2CH_2COOCH_2)_2 \cdot 2H_2O$	52	97

[a)] A mixture of **1a** (0.2 g, 0.96 mmol), **2e** (0.077 g, 1.1 mmol), the surfactant (0.024 mmol) and water (2 mL) was stirred at room temperature, and the reaction product (**4e**) was filtered and dried.

[b)] Reaction did not occur and **1a** was recovered unchanged.

for the role of surfactant is a formation of a micelle in which molecules of reactant and reagent aggregate in the best position to cause efficient reaction. In order to form the best micelle for the reaction, the surfactant (**3**) which has a hexadecyl chain would be the best. Formation of inclusion crystals of onium salts such as ammonium and phosphonium with various kinds of alcohol and phenol guest compounds has been reported.[3-5] However, inclusion crystals of **1 a** and **3** have not yet been isolated. Nevertheless, the formation of the micelle is not essential for the solvent-free Michael addition reaction, because simple mixing of **1 a** with **2** in the absence of water and **3** also gave **4** in good yield. In this case, however, the reaction product (**4**) should be washed with water in order to remove excess amine. For example, when a mixture of powdered **1 a** with **2 e** was stirred at room temperature for 10 min, the mixture first liquidized and then gradually solidified. The solidified product was washed with water and air dried to give **4 e** as colorless powder in quantitative yield.

We have published many solid state organic reactions so far, however, organic solvents are *finally necessary for isolation of the product by extraction.*[6-7] However, the Michael addition reaction in the water suspension is completely free from organic solvent both during the reaction and isolation of the product.

Michael addition of thiophenol (**5**) to *p*-methoxychalcone (**1 f**) also proceeded efficiently in a water suspension medium. For example, when a mixture of **1 f**, **5**, K_2CO_3, **3 b** and water was stirred for 24 h at room temperature and the reaction product was filtered and air dried, the addition product (**6**) was obtained in 92% yield. Although similar Michael addition reactions can be carried out in solution,[8] the procedure of the solid state reaction is rather simple, economical and free from polution problems involving organic solvents.

The Michael addition reaction in a water suspension medium is also applicable to carbon-carbon bond formation. A mixture of **1 a**, methyl acetylacetate (**7**), **3 a**, and water was stirred for 5 h at room temperature and the reaction product filtered and dried to give the addition product (**8**) in 98% yield. Although a similar solvent-free Michael addition reaction of **1 a** with diethyl malonate at 60 °C has been reported, organic solvent was still necessary to isolate the product from the reaction mixture.[9]

Epoxidation of Chalcones with NaOCl in a Water Suspension. Furthermore, the water suspension method can also be applied to epoxidation reactions of chalcones with NaOCl. A mixture of **1 a, 3 a**, and commercially available 11% aqueous NaOCl was stirred at room temperature for 24 h. The reaction product was filtered and dried to give **9 a** in quantitative yield. This procedure was applied to various kinds of chalcone derivatives, and **1 b-i** were oxidized efficiently giving the corresponding epoxides (**9b-i**), respectively, in good yields (Table 3). In the case of **1 h** and **1 i**, the oxidation reaction proceeds very fast. This organic solvent-free reaction procedure is much more simple and convenient in comparison with usual epoxidation reaction with NaOCl in organic solvent.[10] $Ca(OCl)_2$ can also be used for this epoxidation reaction in water suspension (Table 3). In the case of **1 g** and **1 h**, the reaction proceeds extremely fast. However, here the reaction product should be isolated from water insoluble $Ca(OCl)_2$ by extraction with organic solvent. Furthermore, in the case of **1 d-f** and **1 j**, the reaction products did not require extraction with ether from the reaction mixture (Table 3).

Table 3. Epoxidation Reactions of Chalcones in a Water Suspension Medium Containing **3a** as a Surfactant

Chalcone	Product	Reagent NaOCl [a)] Reaction time (day)	NaOCl [a)] yield (%)	Ca(ClO)$_2$ [b)] Reaction time (day)	Ca(ClO)$_2$ [b)] yield (%)
1a	**9a**	1	100	1	77
1b	**9b**	2	80	2	70
1c	**9c**	2	85	2	89
1d	**9d**	4	85	7	— c)
1e	**9e**	2	90	7	— c)
1f	**9f**	1	78	7	— c)
1g	**9g**	2	36	0.04	77
1h	**9h**	0.4	90	0.1	95
1i	**9i**	0.3	99	3	78
1j	**9j**	1	93	7	— c)
1k	**9k**	5	43	5	50
1l	**9l**	5	30	4	82

a) Commercially available 11% aqueous solution was used and products were collected by filtration.

b) Commercially available powder was used and products were collected by extraction with ether.

c) Reaction products were not extracted with ether from reaction mixture.

EXPERIMENTAL

Measurement of IR and ^{1}H NMR Spectra. IR spectra were measured as Nujol mulls. ^{1}H NMR spectra were measured in CDCl$_3$. ^{1}H NMR spectra of unstable **4a-l** in CDCl$_3$

were measured at a concentration of 0.02 g pure sample in 0.5 mL of $CDCl_3$ immediately after preparation of the solution, which are contaminated by 10-20% of **1 a-l** through equilibrium.

Chalcones. Chalcones (**1 a-l**) were prepared by base-catalyzed condensation reaction of benzaldehyde with the appropriate acetophenone derivative according to the reported procedures. **1 a** mp 53-55 °C (lit.,[11] 57-58 °C); **1 b** mp 58-60 °C (lit.,[12] 59-60 °C); **1 c** mp 92-96 °C (lit.,[13] 96.5 °C); **1 d** mp 112-115 °C (lit.,[14] 114-115 °C); **1 e** mp 123-127 °C (lit.,[15] 127-128 °C); **1 f** mp 70-73 °C (lit.,[16] 77.5 °C); **1 g** mp 74-76°C (lit.,[13] 77 °C); **1 h** mp 94-96 °C (lit.,[11] 94-95 °C); **1 i** mp 103-105 °C (lit.,[17] 104-105 °C); **1 j** mp 103-107 °C (lit.,[18] 107 °C); **1 k** mp 127-129 °C (lit.,[19] 127.5-129 °C) ans **1 l** mp 154-156 °C (lit.,[20] 155-157 °C).

Michael Addition Products of Amines to Chalcones (4e). Representative example; a suspension of powdered **1 a** (0.2 g, 0.96 mmol), **3 a** (8.5 mg), **2 e** (77 mg, 1.1 mmol) and water (2 mL) was stirred at rt for 4 h. The reaction product was filtered and air dried to give **4 e** as colorless powder (0.27 g, 98%, mp 61-63 °C). IR: 3315 (NH) and 1682 cm^{-1} (C=O); ^1H NMR δ 0.84-0.94 (m, 3H, CH_3), 1.28-1.40 (m, 4H, CH_2), 1.66 (s, 1H, NH), 2.36-2.54 (m, 2H, CH_2), 3.23-3.39 (m, 2H, CH_2), 4.27-4.30 (q, *J*= 4.8 Hz, 1H, CH) and 7.23-8.04 (m, 10H, Ph). Anal. Calcd for $C_{19}H_{23}NO$: C, 81.10; H, 8.24; N, 4.68. Found: C, 81.27; H, 8.32; N, 4.68. By the same procedure, the following addition products were obtained.

4h. colorless powder (98%, mp 45-47 °C). IR: 3315 (NH) and 1670 cm^{-1} (C=O); ^1H NMR δ 0.82-0.87 (m, 3H, CH_3), 1.23-1.25 (m, 4H, CH_2), 1.40-1.45 (t, *J*=7.5 Hz, 2H, CH_2), 1.83 (s, 1H, NH), 2.37-2.49 (m, 2H, CH_2), 3.19-3.36 (m, 2H, CH_2), 4.26-4.30 (m, 1H, CH) and 7.23-8.01 (m. 10H, Ph). Anal. Calcd for $C_{20}H_{25}NO$: C, 81.31; H, 8.53; N, 4.74. Found: C, 81.10; H, 8.74; N, 4.92.

4i. colorless powder (96%, mp 48-50 °C). IR: 3300 (NH) and 1665 cm^{-1} (C=O); ^1H NMR δ 0.82-0.88 (m, 3H, CH_3), 1.23-1.43 (m, 8H, CH_2), 1.69 (s, 1H, NH), 2.41-2.46 (m, 2H, CH_2), 3.27-3.32 (m, 2H, CH_2), 4.26-4.30 (q, *J*=6.0 Hz, 1H, CH) and 7.22-8.02 (m, 10H, Ph). Anal. Calcd for $C_{21}H_{27}NO$: C, 81.51; H, 8.79; N, 4.53. Found: C, 81.25; H, 8.90; N, 4.60.

4j. colorless powder (93%, mp 46-48 °C). IR: 3305 (NH) and 1680 cm^{-1} (C=O); ^1H NMR δ 0.84-0.89 (t, *J*= 6.9 Hz, 3H, CH_3), 1.14-1.43 (m, 12H, CH_2), 1.82 (s, 1H, NH), 2.35-2.53 (m, 2H, CH_2), 3.24-3.40 (m, 2H, CH_2), 4.26-4.31 (q, *J*= 4.8 Hz, 1H, CH) and 7.23-8.04 (m, 10H, Ph). Anal. Calcd for $C_{23}H_{31}NO$: C, 81.85; H, 9.26; N, 4.15. Found: C, 81.80; H, 9.23, N, 4.18.

4k. colorless powder (93%, mp 36-38 °C). IR: 3320 (NH) and 1675 cm^{-1} (C=O); ^1H NMR δ 1.07-1.70 (m, 10H, CH_2), 2.04 (s, 1H, NH), 2.27-2.30 (t, *J*= 4.8 Hz, 1H, CH), 3.23-3.28 (m, 2H,

CH_2), 4.48-4.52 (q, *J*= 5.1 Hz, 1H, CH) and 7.22-8.02 (m, 10H, Ph). Anal. Calcd for $C_{19}H_{23}NO$: C, 82.04; H, 8.20; N, 4.56. Found: C, 81.90; H, 8.47; N, 4.70.

4n. colorless powder (93%, mp 87-91 °C, lit.,[2a] 95-96 °C, lit.,[2b] 91-92 °C). IR: 1675 cm^{-1} (C=O); ^1H NMR δ 1.25-1.32 (m, 2H, CH_2), 1.47-1.50 (m, 4H, CH_2), 2.26-2.46 (m, 4H, CH_2),3.34-3.61 (m, 2H, CH_2), 4.21-4.25 (t, *J*= 6.9 Hz, 1H, CH) and 7.20-8.02 (m, 10H, Ph). Anal. Calcd for $C_{19}H_{23}NO$: C, 81.87; H, 7.90; N, 4.77. Found: C, 81.63; H, 8.10; N, 4.88.

4p. colorless powder (95%, mp 83-85 °C). IR: 1675 cm^{-1} (C=O); ^1H NMR δ 0.67-0.88 (m, 3H, CH_3), 1.26-1.97 (m, 7H, CH_2 and CH), 2.72-2.82 (q, *J*= 10.2 Hz, 2H, CH_2), 3.64-3.77 (m, 2H, CH_2), 4.22-4.26 (t, *J*= 6.9 Hz, 1H, CH) and 7.20-8.04 (m, 10H, Ph). Anal. Calcd for $C_{21}H_{25}NO$: C, 82.04; H, 8.20; N, 4.56. Found: C, 81.81; H, 8.47; N, 4.33.

4q. colorless powder (96%, mp 94-96 °C). IR: 1680 cm^{-1} (C=O); ^1H NMR δ 0.84-0.86 (d, *J*= 5.7 Hz, 3H, CH_3), 1.08-2.08 (m, 7H, CH_2 and CH), 2.80-2.84 (d, *J*= 11.4 Hz, 2H, CH_2), 3.45-3.72 (m, 2H, CH_2), 4.20-4.25 (t, *J*= 6.0 Hz, 1H, CH) and 7.20-8.05 (m, 10H, Ph). Anal. Calcd for $C_{21}H_{25}NO$: C, 82.04; H, 8.20; N, 4.56. Found: C, 82.17; H, 8.24; N, 4.32.

Michael Addition of Thiophenol 5 to *p*-Methoxychalcone (1f). A mixture of powdered **1f** (0.5 g, 2.1 mmol), **5** (0.25 g, 2.3 mmol), **3b** (67 mg), K_2CO_3 (87 mg) and water (5 mL) was stirred at rt for 24 h. The reaction product was filtered and air dried to give **6** as a colorless powder (0.67 g, 92%, mp 71-73 °C). IR: 1680 cm^{-1} (C=O); ^1H NMR δ 3.49-3.68 (m, 2H, CH_2), 3.74 (s, 3H, CH_3), 4.91-4.95 (m, 1H, CH) and 7.76-7.88 (m, 14H, Ph). Anal. Calcd for $C_{22}H_{20}O_2S$: C, 75.83; H, 5.79. Found: C, 75.78; H, 5.95.

Michael Addition of Methyl Acetylacetate (7) to Chalcone (1a). A mixture of powdered **1a** (0.5 g, 2.4 mmol), **7** (0.31 g, 2.64 mmol), **3b** (67 mg), K_2CO_3 (0.1 g) and water (5 mL) was stirred at rt for 5 h. The reaction product was filtered and air dried to give **8** as a colorless powder (0.75 g, 98%, mp 124-126 °C). IR: 1740, 1710 and 1680 cm^{-1} (C=O); ^1H NMR δ 2.28 (s, 3H, CH_3), 3.36-3.46 (m, 2H, CH_2), 3.477 (s, 3H, CH_3), 4.16-4.22 (m, 1H, CH), 4.15-4.23 (s, 1H, CH) and 7.23-8.04 (m, 10H, Ph). Anal. Calcd for $C_{20}H_{20}O_4$: C, 74.05: H, 6.22. Found: C, 74.13; H, 6.41.

Expoxidation of Chalcones (1a-l) with NaOCl. Representative example; a mixture of **1a** (0.2 g, 0.96 mmol), **3a** (0.02 g) and commercially available 11% aqueous NaOCl (2 mL) was stirred at rt for 24 h. The reaction product was filtered and air dried to give **9a** (0.215 g, 100%, mp 87-89 °C (lit.,[21] 89-90 °C)). IR: 1690 cm^{-1} (C=O); ^1H NMR δ 4.09 (d, *J*=2.0 Hz, 1H, CH), 4.31 (d, *J*=2.0 Hz, 1H, CH) and 7.26-8.04 (m, 10H, Ph). Anal. Calcd for $C_{15}H_{12}O_2$: C, *80.34; H, 5.39. Found: C, 80.07; H, 5.56. By similar treatments of* ***1b-l*** *with NaOCl, epoxides* (**9b-l**) were obtained in the yields shown in Table 3. The structures of **9b-l** were elucidated by comparison of their mp with those of authentic samples and by their elemental analyses. **9b** mp 79-81 °C (lit.,[21] 81-83 °C); Anal. Calcd for $C_{16}H_{14}O_2$: C, 80.65; H, 5.92. Founc: C, 80.59; H, 6.07. **9c**: mp 70-72 °C (lit.,[22] 77-78 °C); Anal. Calcd for $C_{16}H_{14}O_2$: C, 80.65; H, 5.92. Found: C, 80.49; H, 6.02. **9d**: mp 66-68 °C (lit.,[23] 69-70 °C); Anal. Calcd for $C_{15}H_{11}O_2Cl$: C, 69.64; H, 4.29. Found: C, 69.45; H, 4.32. **9e** mp 73-75 °C (lit.,[21] 77-78 °C); Anal. Calcd for $C_{15}H_{11}O_2Br$: C, 59.43; H, 3.66. Found: C, 59.15; H, 3.36. **9f** mp 60-62 °C (lit.,[22] 60-63 °C); Anal. Calcd for $C_{16}H_{14}O_3$: C75.58; H, 5.55. Found: C, 75.51; H, 5.55. **9g** mp 81-83 °C (lit.,[22] 84-86 °C); Anal. Calcd for $C_{16}H_{14}O_2$: C, 80.65; H, 5.92. Found: C, 80.52; H, 5.98. **9h** mp 116-118 °C (lit.,[24] 123 °C); Anal. Calcd for $C_{15}H_{11}O_2Cl$: C, 69.64; H, 4.29. Found: C, 69.53; H, 4.33. **9i** mp 123-125 °C (lit.,[25] 125 ° C); Anal. Calcd for $C_{15}H_{11}O_2Br$: C, 59.43; H, 3.66. Found: C, 59.15; H, 3.36. **9j** mp 60-62 °C (lit.,[26] 60-62 °C); Anal. Calcd for $C_{16}H_{14}O_3$: C, 75.58; H, 5.55. Found: C, 75.55; H, 5.44. **9k** mp 98-100 °C (lit.,[27] 106 °C); Anal. Calcd for $C_{17}H_{16}O_2$: C, 80.66; H, 6.36. **9l** mp 115-117 °C (lit.,[20] 120 °C); Anal. Calcd for $C_{15}H_{10}O_2Cl_2$: C, 61.46; H, 3.44. Found: C, 61.18; H, 3.19.

Epoxidation of Chalcones (1a-l) with $Ca(OCl)_2$. Representative example; a mixture of **1h** (0.2 g, 0.826 mmol), $Ca(OCl)_2$ (2 g, 14 mmol), **3b** (0.02 g) and water (10 mL) was stirred at rt for 3 h. The reaction mixture was extracted with ether (200 mL) and the ether solution was washed with water and dried over $MgSO_4$. Evaporation of the solvent gave **9h** as colorless crystals (0.2 g, 95%, mp 116-118 °C (lit.,[24] 123 °C)). IR: 1680 cm^{-1} (C=O); ^{1}H NMR δ 4.06 (d, J=1.7 Hz, 1H, CH), 4.26 (d, J=1.7 Hz, 1H, CH) and 7.23-7.98 (m, 9H, Ph). These spectral data were identical to those of **9h** prepared by the epoxidation of **1h** with NaOCl. By the same procedure, **1a-c, 1g-i** and **1k-l** were also oxidized efficiently with $Ca(OCl)_2$ (Table 3).

ACKNOWLEDGEMENTS

We are grateful for a Grant-in-Aid for Scientific Research on Priority Areas, No. 06242105 from the Ministry of Education, Science, Sports and Culture.

REFERENCES

1 F. M. Menger and J. H. Smith, *J. Am. Chem. Soc.*, 1969, **91**, 4211.

2 (a) N. S. Kozlov and G. N. Kozlov, *Zh. Obshch. Khim.*, 1963, **33**, 2184. (b) P. A. Barrett, Brit. 765,874 (*Chem. Abstr.*, 1957, **51**, 14892h).

3 F. Toda, K. Tanaka, T. Okada, S. A. Bourne, and L. R. Nassimbeni, *Supramol. Chem.*, 1994, **3**, 291.

4 K. Tanaka, K. Tamura, and F. Toda, *J. Chem. Soc., Perkin Trans.* 2, 1995, 1571.

5 F. Toda, K. Tanaka and H. Sawada, *J. Chem. Soc., Perkin Trans.* 1, 1995, 3065.

6 F. Toda, *Synlett.*, 1993, 303.

7 F. Toda, *Acc. Chem. Res.*, 1995, **28**, 480.

8 R. Annunziata, M. Cinquini, and S. Colonna, *Chem. & Ind.* (London), 1980, 238.

9 A. Loupy, J. Sansoulet, A. Zaparucha, and C. Merienne, *Tetrahedron Lett.*, 1989, **30**, 333.

10 S. Marmor, *J. Org. Chem.*, 1963, **28**, 250.

11 S. Itsuno, M. Sakakura, and K. Ito, *J. Org. Chem.*, 1990, **55**, 6049.

12 R. E. Lyle and L. P. Paradis, *J. Am. Chem. Soc.*, 1955, **77**, 6668.

13 V. Hanzlik and A. Bianehi, *Ber.*, 1899, *32*, 2282.

14 V. Alex, *Bull. Soc. Chim. Romania*, 1936, **18A**, 93.

15 W. B. Black and R. E. Lutz, *J. Am. Chem. Soc.*, 1955, **77**, 5134.

16 J. Frederick, J. Dippy, and E. Reginald, *Rec. Trav. Chim.*, 1937, **56**, 1000.

17 W. Dilthey, *J. Prakt. Chem.*, 1921, **101**, 202.

18 H. Burton and D. A. Munday, *J. Chem. Soc.*, 1954, 1456.

19 C. Weygand and A. Matthes, *Ann.*, 1926, **449**, 29.

20 H. O. House, *J. Am. Chem. Soc.*, 1956, **78**, 2298.

21 B. Marmsan and H, Wynberg, *J. Org. Chem.*, 1979, **44**, 2312.

22 H. O. House and R. D. Ryerson, *J. Am. Chem. Soc.*, 1961, **83**, 979.

23 S. Bodforss, *Chem. Ber.*, 1956, **49**, 2795.

24 H. Jörlander, *Ber.*, 1917, **50**, 406.

25 G. Sipos, G. Schöbel, and L. Baláspiri, *J. Chem. Soc., C* 1970, 1154.

26 G. Drefahl, M. Hartmann, and H. Grosspietsh, *Chem. Ber.*, 1958, **91**, 755.

27 P. Sohar and G. Sipos, *Acta Chim.*, 1971, **68**, 149.

Received, 23rd May, 1997