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TETRALONE ESTERS AS INTERMEDIATES FOR THE SYNTHESIS OF PODOPHYLLOTOXIN DERIVATIVES VIA CYCLOPROPA NATION OF CHALCONES

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Abstract: Cyclopropyl ester (8a-f) were synthesized by the cyclopropanation of chalcones (7a-e) in dry benzene using powdered sodium in 80-85% yield. Preparation of tetralone ester (4a-e), an intermediate for the synthesis of podophyllotoxin derivatives by Lewis acid (SnCl₄) catalyzed cyclization of (8a-e) is also described here.

Podophyllotoxin (1) and several of its analogous are used as cytotoxic spindle poisons and antitumor agents, some at clinical level. Recently Lee et al. discovered that some modified derivatives of podophyllotoxin possess anti-HIV (AIDS) property. In earlier parts of the series, we have reported the synthesis of analogous of 1 and β-apoticropodophyllin (2), with a view to study their structure-antimitotic activity relationship. We found some of these derivatives possess higher activity and some have lower activity when compared to the parent molecules. Now we have envisaged that modifying ring A and pendent ring C in 1

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and 2 might enhance their biological activity and hence decided to synthesize the analogues 3a-e.

Several synthetic routes other than Gensler's have been reported for the synthesis of 1 via the tetralone ester 4. In the present paper, we adopted Murphy's method because it requires easily available starting materials. Starting material for the synthesis of 4 is the chalcone (7), which was easily prepared by stirring a equal molar solution of 3-methyl-4-methoxy-acetophenone (5) and aromatic aldehyde (6) in methanol containing one equivalent of sodium hydroxide pellets at room temperature for 5 to 10 minutes. Cyclopropyl ketoesters (8) were synthesized via cyclopropanation of 7 using cyano ethyl acetate by employing the method of Rai ital. In a typical procedure, a solution of 7 in benzene containing cyanoethyl acetate was treated with sodium powder at room temperature and then was refluxed for 12 hrs. After the workup gave 82% of cyclopropyl ester (8) and 10% of ketoacid (9). The formation of 9 was confirmed by its conversion to 8 in almost quantitative yield using ethanol and sulphuric acid. Formation of the cyclopropyl ring system in 8 was confirmed by $^1$H NMR, (multiplet at δ 2.20-2.35 ppm). The products isolated were characterized by IR, $^1$H NMR, and also mass spectra, which showed the acyl cation as base peak and other fragments formed through a identical fragmentation pattern.

In the present paper we adopted Murpy's method for the cyclization of 8 to give tetralone 4. In a typical procedure, reaction of cyclopropyl esters 8 with two equivalents of SnCl₄ in nitrobenzene at room temperature for 6 to 7 hr. yielded
Podophyllotoxin Derivatives

\[ \text{PODOPHYLLOTOXIN DERIVATIVES} \]

\[ \text{1181} \]

\[ \text{1} \]

\[ \text{2} \]

\[ \text{3} \]

\[ \text{4} \]

\[ \text{5} \]

\[ \text{6} \]

\[ \text{7 (cis/trans)} \]

\[ \text{8} \]

\[ \text{9} \]

\[ \text{a. } R = R' = R'' = H \]
\[ \text{b. } R = R'' = H; R' = \text{OCH}_3 \]
\[ \text{c. } R = R' = \text{OCH}_3; R'' = H \]
\[ \text{d. } R = R' = R'' = \text{OCH}_3 \]
\[ \text{e. } R = R' = H; R'' = \text{NO}_2 \]
tetralone ester 4 in 60-65% yield. The NMR spectrum of 4a exhibited a doublet at 
δ 4.55 ppm (J=6Hz) for the dibenzylic proton C1-H. The large J value of 6 Hz 
indicated that C2-H and C1-H in 4a were diaxial. Hence, the C2-ethoxycarbonyl and 
C1-phenyl groups should be trans to each other, a configuration being 
thermodynamically more stable.

Experimental Section:

Melting points were taken on open capillary and are uncorrected. IR spectra were 
recorded on a Perkin Elmer 399 spectrometer. 1H NMR spectra were recorded on 
Jeol 60 MHz NMR spectrometer using CDCl3 as solvent and TMS as internal 
reference. The chemical shifts are expressed in δ ppm. Mass spectra were recorded 
on Hitachi RMU-61 spectrophotometer and important fragments are given with the 
relative intensities in the bracket. Thin layer chromatography were obtained on 
Merk silica gel G coated on glass plates.

General procedure for the preparation of chalcones (7a-e): A typical 
procedure is described for the preparation of 1-(3'-methyl-4'-methoxyphenyl)-3-
phenyl-prop-2-ene-1-one (7a) :- A solution of 3-methyl-4-methoxy acetophenone 
(5, 1.0 g, 6.2 mmol) and benzaldehyde (6a, 0.65 g, 6.2 mmol) in methanol (25 mL) 
was treated with sodium hydroxide pellets (0.25 g) and stirred for 15 minutes at 
room temperature, wherein chalcone 7a precipitated. The precipitate was then 
filtered off, washed thoroughly with water and dried to yield 7a. It was then 
recrystallized from 50% aqueous ethanol give a light yellow, crystalline compound 
in 80% (1.22 g) yield, m.p.= 86°C, IR (KBr): 1600 (C=C), 1605, 1657 (CO) cm⁻¹;
1H NMR (CDCl₃): δ 2.25 (s, 3H, CH₃), 3.90 (s, 3H, OCH₃), 6.80 (bd, 2H, -HC=CH-), 7.0-7.20 (m, 5H, Ar-H), 7.20-7.30 (d, 1H, Ar-H), 7.50-7.65 (bd, 2H, Ar-H); Anal. Calcd. for C₁₇H₁₆O₂ C, 80.92; H, 6.40%; Found C, 80.86; H, 6.42%.

1-(3'-Methyl-4'-methoxyphenyl)-3-(4''-methoxyphenyl)-prop-2-ene-1-one

(7b): Obtained from 3-methyl-4-methoxy acetophenone (5, 1.0 g, 6.2 mmol) and p-anisaldehyde (6b, 0.84 g, 6.2 mmol) as pale yellow crystalline solid in 85% (1.47 g), m. p. = 62-64°C, IR (KBr): 1605 (C=C), 1610, 1667 (CO) cm⁻¹; 1H NMR (CDCl₃): δ 2.30 (s, 3H, CH₃), 3.85 (s, 3H, OCH₃), 3.90 (s, 3H, OCH₃), 6.80 (bd, 2H, -HC=CH-), 6.90-7.0 (bd, 1H, Ar-H), 7.50-7.70 (d, 4H, Ar-H), 7.80-7.90 (d, 2H, Ar-H); Anal. Calcd. for C₁₈H₁₈O₃ C, 76.56; H, 6.43%; Found C, 76.46; H, 6.47%.

1-(3'-Methyl-4'-methoxyphenyl)-3-(3''',4'''-dimethoxyphenyl)-prop-2-ene-1-one

(7c): Obtained from 3-methyl-4-methoxy acetophenone (5, 1.0 g, 6.2 mmol) and 3,4-dimethoxybenzaldehyde (6c, 1.03 g, 6.2 mmol) as pale yellow crystalline solid in 82% (1.56 g), m. p. = 93-95°C, IR (KBr): 1600 (C=C), 1605, 1657 (CO) cm⁻¹; 1H NMR (CDCl₃): δ 2.30 (s, 3H, CH₃), 3.85 (s, 6H, OCH₃), 3.92 (s, 3H, OCH₃), 6.70-6.95 (d, 2H, -HC=CH-), 7.10-7.30 (bd, 1H, Ar-H), 7.50-7.55 (d, 2H, Ar-H), 7.60-7.75 (d, 1H, Ar-H), 7.80-7.90 (d, 2H, Ar-H); Anal. Calcd. for C₁₉H₂₀O₄ C, 73.06; H, 6.45% Found C, 73.01; H, 6.44%.
1-(3'-Methyl-4'-methoxyphenyl)-3-(3",4",5"-trimethoxyphenyl)-prop-2-ene-1-one (7d) - Obtained from 3-methyl-4-methoxy acetophenone (5, 1.0 g, 6.2 mmol) and 3,4,5-trimethoxybenzaldehyde (6d, 1.22 g, 6.30 mmol) as pale yellow crystalline solid in 85% (1.78 g), m. p. = 88-89°C, IR (KBr): 1605 (C=C), 1616, 1662 (CO) cm\(^{-1}\); \(^1\)H NMR (CDCl\(_3\)): \(\delta\) 2.30 (s, 3H, CH\(_3\)), 3.85 (s, 9H, OCH\(_3\)), 3.90 (s, 3H, OCH\(_3\)), 6.80 (w, 2H, -HC=CH-), 6.40 (s, 2H, Ar-H), 6.50 (s, 1H, Ar-H), 7.70-7.80 (d, 2H, Ar-H); Anal. Calcd. for C\(_{20}\)H\(_{22}\)O\(_5\) C, 70.16; H, 6.48%: Found C, 70.10; H, 6.50%.

1-(3'-Methyl-4'-methoxyphenyl)-3-(3"-nitrophenyl)-prop-2-ene-1-one (7e) - Obtained from 3-methyl-4-methoxy acetophenone (5, 1.0 g, 6.2 mmol) and 3-nitrobenzaldehyde (6e, 0.94 g, 6.2 mmol) as pale brown crystalline solid in 78% (1.47 g), m. p. = 134-36°C, IR (KBr): 1605 (C=C), 1610, 1672 (CO) cm\(^{-1}\); \(^1\)H NMR (CDCl\(_3\)): \(\delta\) 2.30 (s, 3H, CH\(_3\)), 3.90 (s, 3H, OCH\(_3\)), 6.70-6.90 (bd, 2H, HC=CH-), 7.20 (s, 1H, Ar-H), 7.30-8.00 (m, 6H, Ar-H); Anal. Calcd. for C\(_{17}\)H\(_{15}\)N\(_2\)O\(_4\) C, 68.66; H, 5.09; N, 4.71%: Found C, 68.74; H, 6.39; N, 4.75%.

General procedure for the preparation of cyclopropyl ketoesters (8): A typical procedure is described for the preparation of ethyl-2-(3'-methyl-4'-methoxybenzoyl)-3-phenyl cyclopropane-1-carboxylate (8a) - Freshly distilled cyanoethyl acetate (0.45 g, 4.0 mmol) was added into a magnetically stirred suspension of powdered sodium (0.18 g, 8 m atom) in dry benzene (25 mL) in a 100 ml round bottomed flask fitted with guard tube. Chalcone (7a, 1.02 g, 4.0
mmol) was added and the mixture stirred at room temperature. After 24 hrs, reaction mixture was washed successively with 5% NaOH (2 X 15 mL), brine solution (2 X 15 mL) and dried over anhydrous Na$_2$SO$_4$. Evaporation of the solvent under reduced pressure yielded a pasty mass, which after purification over chromatography yielded the cyclopropyl ester in 82% (1.12 g) yield as a pale yellow oil. Alkaline extract on acidification with conc. HCl at 5°C gave a pasty mass, which was then extracted into ether layer and dried over anhydrous Na$_2$SO$_4$. Evaporation of the solvent gave keto acid (9a) as a pale yellow oil in 10% (0.125 g) yield.

**Esterification of keto acid (9a):** Solution of keto acid (9, 0.125 g) in absolute ethanol (10 mL) was treated with conc. H$_2$SO$_4$ acid (0.5 mL) and refluxed for 4 hrs. After 4 hr, solvent was evaporated off, neutralized with 5% sodium bicarbonate solution and then extracted into ether. The ethereal layer was washed thoroughly with water (2 X 20 mL), brine solution (1 X 15 mL) and dried over anhydrous sodium sulphate. Evaporation of the solvent under reduced pressure yielded a pasty mass, which after purification over chromatography yielded the cyclopropyl ester (8a) in 95% (0.128 g) yield as a pale yellow oil, IR (KBr): 1605 (C=C), 1680 (CO), 1750 (ester CO) cm$^{-1}$, $^1$H NMR (CDCl$_3$): $\delta$ 0.95-1.12 (t, 3H, CH$_3$), 2.30 (s, 3H, CH$_3$), 2.20-3.35 (m, 3H, C$_1$, C$_2$, C$_3$-H), 3.70-3.95 (q, 2H, OCH$_2$), 3.90 (s, 3H, OCH$_3$), 7.00-7.20 (m, 5H, Ar-H), 7.25-2.35 (d, 1H, Ar-H), 7.80-7.90 (d, 2H, Ar-H); Mass spectrum, m/z (relative intensity): 338 (M', 10), 310 (M', -C$_2$H$_4$, 8), 265 (M'-73,
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14), 252 (M'–86, 52), 237 (M'–101, 32), 149 (ArCO' , 100);
Anal. Calcd. for C21H22O4 C, 74.52; H, 6.56%; Found C, 74.59; H, 6.39%.

**Ethyl-2-(3'-methyl-4'-methoxybenzoyl)-3-(4''-methoxyphenyl)-cyclopropane-1-carboxylate (8b)** : Obtained from (7b, 1.0 g, 3.2 mmol) and cyanoethyl acetate (0.36 g, 3.2 mmol) as pale yellow oily product in 85% (1.08 g) yield, IR (KBr): 1605 (C=C), 1678 (CO), 1755 (ester CO) cm⁻¹, ¹H NMR (CDCl₃); δ 0.95-1.10 (t, 3H, CH₃), 2.30 (s, 3H, CH₃), 2.20-3.35 (m, 3H, C₁, C₂, C₃-H), 3.70-3.90 (q, 2H, OCH₂), 3.90 (s, 3H, OCH₃), 3.95 (s, 3H, OCH₃), 7.00-7.20 (d, 2H, Ar-H), 7.25-7.35 (d, 1H, Ar-H), 7.60-7.80 (bd, 4H, Ar-H); Mass spectrum, m/z (relative intensity): 368 (M', 12), 340 (M'–C₂H₄, 11), 295 (M'–73, 20), 282 (M'–86, 71), 267 (M'–101, 15), 149 (ArCO', 100); Anal. Calcd. for C₂₂H₂₄O₅ C, 71.72; H, 6.57%; Found C, 71.78; H, 6.425%.

**Ethyl-2-(3'-methyl-4'-methoxybenzoyl)-3-(3''-4''-dimethoxyphenyl)-cyclopropane-1-carboxylate (8c)** : Obtained from (7c, 1.0 g, 3.2 mmol) and cyanoethyl acetate (0.36 g, 3.2 mmol) as pale yellow oily product in 85% (1.08 g) yield, IR (KBr): 1605 (C=C), 1678 (CO), 1755 (ester CO) cm⁻¹, ¹H NMR (CDCl₃); δ 1.00-1.10 (t, 3H, CH₃), 2.30 (s, 3H, CH₃), 2.20-3.30 (m, 3H, C₁, C₂, C₃-H), 3.70-3.95 (q, 2H, OCH₂), 3.85 (s, 6H, OCH₃), 3.90 (s, 3H, OCH₃), 7.00-7.10 (s, 2H, Ar-H), 7.25-7.35 (d, 1H, Ar-H), 7.60-7.75 (d, 1H, Ar-H), 7.80-7.90 (d, 2H, Ar-H); Mass spectrum, m/z (relative intensity):
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398 (M', 11), 370 (M'-C,H, 7), 325 (M'-73, 18), 312 (M'-86, 55), 297 (M'-101, 32), 149 (ArCO', 100); Anal. Calcd. for C23H26O6 C, 69.33; H, 6.58%. Found C, 69.40; H, 6.55%.

Ethyl-2-(3'-methyl-4'-methoxybenzoyl)-3-(3'',4'',5''-dimethoxyphenyl)-cyclopropane-1-carboxylate (8d) :- Obtained from (7d, 1.0 g, 2.9 mmol) and cyanoethyl acetate (0.33 g, 2.9 mmol) as pale red oily product in 82% (1.02 g) yield, IR (Nujol): 1605 (C=C), 1678 (CO), 1760 (ester CO) cm⁻¹, ¹H NMR (CDCl₃); δ 0.95-1.10 (t, 3H, CH₃), 2.30 (s, 3H, CH₃), 2.20-3.35 (q, 3H, C₁, C₂, C₃-H), 3.70-3.85 (q, 2H, OCH₂), 3.85 (s, 9H, OCH₃), 3.90 (s, 3H, OCH₃), 7.00-7.20 (d, 2H, Ar-H), 7.25-2.35 (d, 1H, Ar-H), 7.80-7.90 (d, 2H, Ar-H); Mass spectrum, m/z (relative intensity): 428 (M', 12), 400 (M'-C₂H₄, 9), 355 (M'-73, 25), 342 (M'-86, 56), 327 (M'-101, 15), 149 (ArCO', 100); Anal. Calcd. for C₂₄H₂₈O₇ C 67.26; H, 6.59%. Found C, 67.20; H, 6.63%.

Ethyl-2-(3'-methyl-4'-methoxybenzoyl)-3-(3''-nitrophenyl)-cyclopropane-1-carboxylate (8e) :- Obtained from (7e, 1.0 g, 3.4 mmol) and cyanoethyl acetate (0.38 g, 3.4 mmol) as pale red oily product in 80% (1.03 g) yield, IR (Nujol): 1362 (sym NO₂), 1522 (asym NO₂), 1600 (C=C), 1678 (CO), 1745 (ester CO) cm⁻¹, ¹H NMR (CDCl₃); δ 0.95-1.12 (t, 3H, CH₃), 2.30 (s, 3H, CH₃), 2.20-3.35 (m, 3H, C₁, C₂, C₃-H), 3.70-3.95 (q, 2H, OCH₂), 3.90 (s, 3H, OCH₃), 7.00-7.20 (m, 4H, Ar-H), 7.25-2.35 (d, 1H, Ar-H), 7.80-7.90 (d, 2H, Ar-H); Mass spectrum,
m/z (relative intensity): 383 (M⁺, 10), 355 (M⁺-C₂H₄, 12), 310 (M⁺-73, 16), 297 (M⁺-86, 56), 282 (M⁺-101, 21), 149 (ArCO', 100); Anal. Calcd. for C₂₁H₂₁NO₆ C, 65.77; H, 5.52; N, 3.65%; Found C, 65.73; H, 5.44; N, 3.69%.

**General procedure for the preparation of tetralone esters (4):** A typical procedure is described for the preparation of *ethyl-6-methyl-7-methoxy-1-phenyl-4-oxo-2-naphthoate (4a)*: Solution of cyclopropyl ketoester (8a, 0.80 g, 2.36 mmol) in nitrobenzene (10 mL) was added dropwise to a magnetically stirred solution of anhydrous stannic chloride (0.54 g, 4.6 mmol) in nitrobenzene (10 mL) for half an hour at 0°C and further stirred for 6 hrs. After treating with 5N HCl (5 mL), the organic layer was washed with 10% NaOH (2 X 10 mL) and finally with water. Brown gummy product obtained after steam distillation of the solvent was purified by column chromatography using chloroform as eluant to yield tetralone ester 4a as red semisolid in 65% (0.52 g) yield, IR (KBr): 1605 (C=C), 1670 (CO), 1725 (ester CO) cm⁻¹, ¹H NMR (CDCl₃): δ 0.9-1.2 (t, 3H, CH₃), 2.1 (s, 3H, CH₃), 2.85 (d, 2H, J=6Hz, C₈-H), 3.1-3.25 (m, 1H, C₇-H), 3.70-3.90 (q, 2H, OCH₂), 3.95 (s, 3H, OCH₃), 4.55 (d, 1H, J=6Hz, C₁-H), 7.1-7.8 (m, 7H, Ar-H); Anal. Calcd. for C₂₁H₂₂O₄ C, 74.52; H, 6.56%; Found C, 74.47; H, 6.55%.

*Ethyl-6-methyl-7-methoxy-1-(4'-methoxyphenyl)-4-oxo-2-naphthoate (4b)*: Prepared from (8b, 0.80 g, 2.17 mmol) in dry benzene containing stannic chloride (0.5g, 4.2 mmol) as brown gummy product in 60% (0.48 g) yield, IR (KBr): 1610 (C=C), 1678 (CO), 1750 (ester CO) cm⁻¹, ¹H NMR (CDCl₃): δ 0.9-1.10 (t, 3H,
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CH₃), 2.2 (s, 3H, CH₃), ), 2.80 (d, 2H, J=5.5Hz, C₂-H), 3.1-3.25 (m, 1H, C₂-H), 3.65-3.80 (q, 2H, OCH₂), 3.85 (s, 3H, OCH₃), 3.90 (s, 3H, OCH₃), 4.55 (d, 1H, J=5.5Hz, C₁-H), 6.7-7.8 (m, 6H, Ar-H); Anal. Calcd. for C₂₂H₂₄O₅
C, 71.72; H, 6.57%; Found C, 71.69; H, 6.62%.

Ethyl-6-methyl-7-methoxy-1-(3',4'-dimethoxyphenyl)-4-oxo-2-naphthoate (4c)
-Prepared from (8c, 0.80 g, 2.01 mmol) in dry benzene containing stannic chloride (0.50 g, 4.2 mmol) as brown gummy product in 62% (0.49 g) yield, IR (KBr): 1613 (C=C), 1670 (CO), 1750 (ester CO) cm⁻¹, 'H NMR (CDCl₃) δ 0.9-1.1 (t, 3H, CH₃), 2.15 (s, 3H, CH₃), ), 2.85 (d, 2H, J=6Hz, C₃-H), 3.1-3.25 (m, 1H, C₂-H), 3.60-3.75 (q, 2H, OCH₂), 3.80 (s, 6H, OCH₃), 3.85 (s, 3H, OCH₃), 4.55 (d, 1H, J=6Hz, C₁-H), 6.8-7.8 (m, 5H, Ar-H); Anal. Calcd. for C₂₃H₂₆O₆
C, 69.33; H, 6.58%; Found C, 69.32; H, 6.59%.

Ethyl-6-methyl-7-methoxy-1-(3',4',5'-trimethoxyphenyl)-4-oxo-2-naphthoate (4d)
-Prepared from (8d, 0.80 g, 1.86 mmol) in dry benzene containing stannic chloride (0.5 g, 4.2 mmol) as brown gummy product in 62% (0.49 g) yield, IR (Nujol): 1605 (C=C), 1678 (CO), 1755 (ester CO) cm⁻¹, 'H NMR (CDCl₃) δ 1.0-1.3 (t, 3H, CH₃), 2.2 (s, 3H, CH₃), ), 2.85 (d, 2H, J=6Hz, C₃-H), 3.1-3.25 (m, 1H, C₂-H), 3.60-3.80 (q, 2H, OCH₂), 3.82 (s, 6H, OCH₃), 3.85 (s, 6H, OCH₃), 4.55 (d, 1H, J=6Hz, C₁-H), 6.4-7.5 (bm, 4H, Ar-H); Anal. Calcd. for C₂₄H₂₈O₇
C 67.26; H, 6.59%; Found C, 67.30; H, 6.56%.

Ethyl-6-methyl-7-methoxy-1-(3'-nitrophenyl)-4-oxo-2-naphthoate (4e)
-Prepared from (8e, 0.81 g, 2.08 mmol) in dry benzene containing stannic chloride
(0.5 g, 4.2 mmol) as brown gummy product in 60% (0.49 g) yield, IR (KBr): 1600 (C=C), 1683 (CO), 1734 (ester CO) cm\(^{-1}\), \(^1\)H NMR (CDCl\(_3\)) \(\delta\) 1.0-1.3 (t, 3H, CH\(_3\)), 2.15 (s, 3H, CH\(_3\)), 2.85 (d, 2H, \(J=6\text{Hz}\), C\(_3\)-H), 3.1-3.25 (m, 1H, C\(_2\)-H), 2.95 (d, 2H, CH\(_2\)), 3.60-3.75 (q, 2H, OCH\(_2\)), 3.80 (s, 3H, OCH\(_3\)), 4.55 (d, 1H, \(J=6\text{Hz}\), C\(_1\)-H), 6.7-8.1 (m, 6H, Ar-H); Anal. Calcd. for C\(_{21}\)H\(_{21}\)NO\(_6\) C, 65.77; H, 5.52; N, 3.65% Found C, 65.81; H, 5.55; N, 3.63%.

REFERENCES:


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