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VANILLIN ESTERS IN REACTIONS WITH INDAN-1,3-DIONE

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2-Methoxy-4-(12-oxo-12H-benzo[f]indeno[1,2-b]quinolin-13-yl)phenyl esters of carboxylic acids were synthesized by the three component condensation of indan-1,3-dione, 2-naphthylamine, and O-acylvanillin. 2-Arylidenindan-1,3-diones formed during the reaction were isolated.

Keywords: 2-arylidenindan-1,3-diones, O-acylvanillins, indan-1,3-dione, 2-methoxy-4-(12-oxo-12H-benzo[*f*]indeno[1,2-*b*]quinolin-13-yl)phenyl esters of carboxylic acids, 2-naphthylamine.

Thanks to its high reactivity, indan-1,3-dione is widely used in synthetic organic chemistry, including the synthesis of heterocyclic compounds [1, 3].

In the present work we have presented the results of a study of a three component condensation of indan-1,3-dione **1**, 2-naphthylamine **2**, and vanillin esters **3a-h.** The condensation was carried out by heating equimolar amounts of the components in ethanol. We assumed that formation of the final heterocyclic compound of the indenoquinoline series occurred *via* intermediate amino ketone **A**, which then lost a water molecule and cyclized to the corresponding 4-(12,13-dihydro-12-7H-benzo[*f*]indeno[1,2-*b*]quinolin-13-yl)-2-methoxyphenyl esters of the carboxylic acids **5a-h**. Oxidation of the latter gave 2-methoxy-4-(12-oxo-12H-benzo[*f*]indeno[1,2-*b*]quinolin-13-yl)phenyl esters of the carboxylic acids **6a-h**.

In all the experiments under the experimental conditions the esters **5a-h** were found in mixtures with 2-methoxy-4-(12-oxo-12H-benzo[*f*]indeno[1,2-*b*]quinolin-13-yl)phenyl esters of the carboxylic acids **6a-h** in a ratio of 1:9 according to the ^{1}H NMR spectra. At recrystalization of compounds **5a-h** their further oxidation occurs and separation of them from the reaction mixture in pure form proved impossible. In view of the difficulty of separating compounds **5a-h** and **6a-h**, immediate dehydration of the mixture obtained by boiling in nitrobenzene for 3-4 h was carried out.

During monitoring of the course of the reaction we established that 4-[(1,3-dihydro-1,3-dioxo-2H-inden-2-ylidene)methyl]-2-methoxyphenyl esters of the carboxylic acids **4a-h** were always present in the reaction mixture. From this it can be proposed that condensed reaction products of the dihydrobenzoindenoquinoline series **5a-h** are formed by reaction of the 2-arylideneindan-1,3-diones **4a-h** with 2-naphthylamine **2**.

To confirm this idea we have synthesized 4-[(1,3-dihydro-1,3-dioxo-2H-inden-2-ylidene)methyl]-2-methoxyphenyl esters of the carboxylic acids **4a-h** by the reaction of indan-1,3-dione with O-acylvanillins **3a-h** and condensing them with 2-naphthylamine **2** under analogous conditions. Mixtures of the esters **5a-h** and **6a-h** were formed as a result of the condensation, analogous to the mixtures from the three component condensation of compounds **1**, **2**, and **3a-h**.

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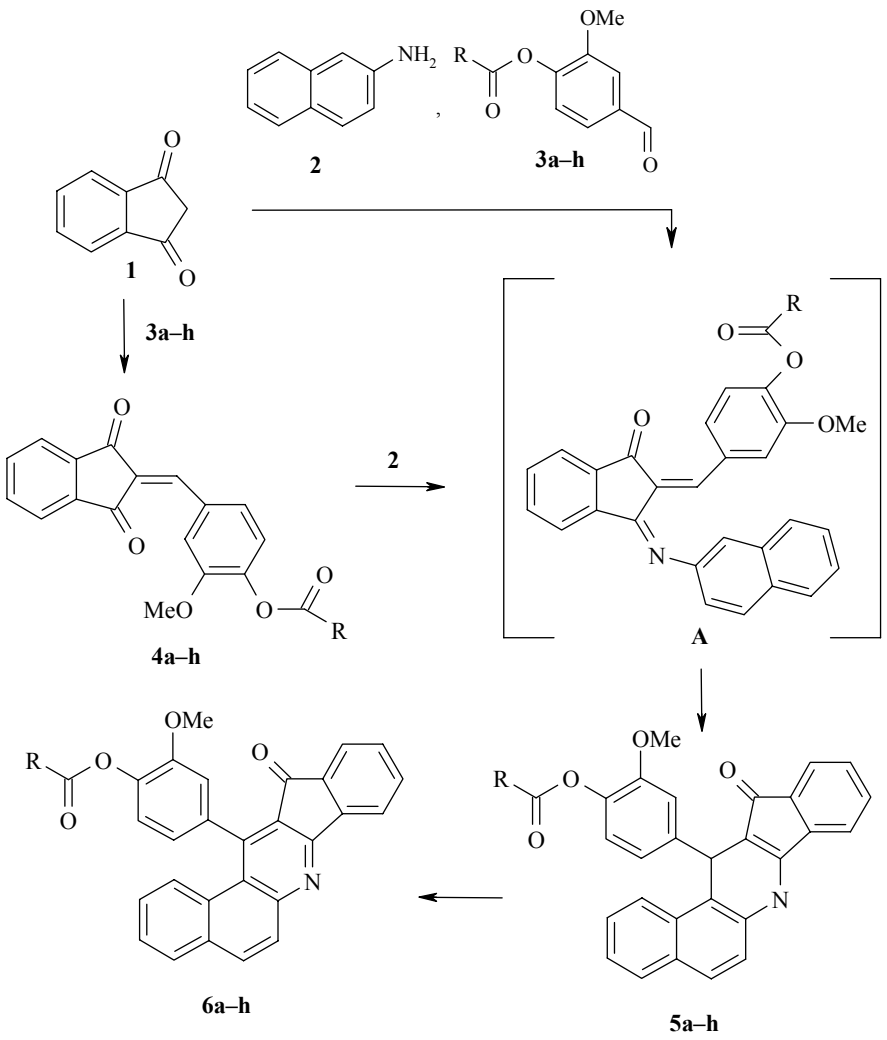

3,4,6 a R = Me, **b** R = Et, **c** R = Pr**, d** R = *i*-Pr, **e** R = Bu, **f** R = Am, **g** R = Hex, **h** R = Hept

The synthesized esters **6a-h** are crystalline substances with a yellowish color (Table 1).

The IR spectra of compounds **4a-h** contain intense absorption bands in the 1580-1600 cm^{-1} region, due to stretching vibrations of carbonyl groups conjugated to the benzene ring, and absorption bands of similar intensity in the 1740-1760 cm^{-1} region due to ester carbonyl groups. In the IR spectra of compounds **6a-h** there are absorption bands of medium intensity at 1560-1580 cm^{-1} ascribed to stretching vibrations of carbonyl groups conjugated to benzene and naphthalene nuclei, while the ester carbonyl groups give intense absorptions in the 1710-1730 cm^{-1} range.

Analysis of the mass spectra of compounds **4a-h** and **6a-h** indicates the stability of these compounds to electron impact. In the mass spectra of compounds **4a-h** and **6a-h** there are high intensity molecular ion peaks $[M^+]$ (*I* 100%) and satisfactorily intense peaks for ions with *m/z* 120 (*I* = 40-50%) for compounds **4a-h**, and with *m/z* = 281 (*I* = 60 -70%) for compounds **6a-h**, corresponding to the ions $[M - CH_3OC_6H_3OCOR]^+$.

The ^1H NMR spectra of compounds **6a-h** (Table 2) correspond to a benzoindenoquinoline structure in the position and multiplicity of the signals of the aromatic protons. The methine proton of compounds **4a-h** is conjugated with two carbonyl group, appears at weak field in the spectra as a singlet at 8.74-8.85 ppm, which corresponds with the position of the methine proton in the spectra of analogous compounds [4].

TABLE 1. Characteristics of Compounds **4a-h** and **6a-h**

Compound	Empirical formula	Found, % / Calculated, %			mp, °C	Yield, %
		C	H	N		
4a	$C_{19}H_{14}O_5$	70.78 / 70.80	4.39 / 4.35	—	163	69
4b	$C_{20}H_{16}O_5$	71.38 / 71.43	4.73 / 4.76	—	160	62
4c	$C_{21}H_{18}O_5$	72.03 / 72.00	5.13 / 5.14	—	140	67
4d	$C_{21}H_{18}O_5$	71.98 / 72.00	5.09 / 5.14	—	162-164	52
4e	$C_{22}H_{20}O_5$	72.55 / 72.53	5.46 / 5.49	—	130-132	49
4f	$C_{23}H_{22}O_5$	73.07 / 73.01	5.80 / 5.82	—	126-127	48
4g	$C_{24}H_{24}O_5$	73.44 / 73.46	6.15 / 6.12	—	128	50
4h	$C_{25}H_{26}O_5$	73.91 / 73.89	6.37 / 6.40	—	124	58
6a	$C_{29}H_{19}NO_4$	78.16 / 78.20	4.31 / 4.27	3.11 / 3.15	236	75
6b	$C_{30}H_{21}NO_4$	78.45 / 78.43	4.61 / 4.57	3.02 / 3.05	250	64
6c	$C_{31}H_{23}NO_4$	78.61 / 78.65	4.83 / 4.86	3.01 / 2.96	252	74
6d	$C_{31}H_{23}NO_4$	78.65 / 78.65	4.88 / 4.86	2.97 / 2.96	274	72
6e	$C_{32}H_{25}NO_4$	78.90 / 78.85	5.10 / 5.13	2.90 / 2.87	281	70
6f	$C_{33}H_{27}NO_4$	79.00 / 79.04	5.36 / 5.39	2.81 / 2.79	280	57
6g	$C_{34}H_{29}NO_4$	79.25 / 79.22	5.67 / 5.63	2.75 / 2.72	273	54
6h	$C_{35}H_{31}NO_4$	79.37 / 79.39	5.88 / 5.86	2.68 / 2.65	279	50

TABLE 2. ^{1}H NMR Spectra of Compounds **4a-h** and **6a-h**

Compound	Chemical shifts, δ, ppm (*J*, Hz)			
	CH (1H, s)	OCH_3 (3H, s)	R	H_{Ar}
1	2	3	4	5
4a	8.85	4.00	2.20 (3H, s, CH_3)	7.20 (1H, s); 7.70 (3H, m); 8.10 (2H, m)
4b	8.75	4.00	1.25 (3H, t, *J* = 6.9, $CH_2\underline{CH_3}$); 2.75 (2H, q, *J* = 6.7, $\underline{CH_2}CH_3$)	7.30 (1H, d, *J* = 7.8); 7.82 (1H, s); 7.91 (3H, m); 8.00 (2H, m)
4c	8.74	3.98	1.09 (3H, t, *J* = 6.4, $(CH_2)_2\underline{CH_3}$); 1.75 (2H, m, $CH_2\underline{CH_2}CH_3$); 2.59 (2H, t, *J* = 6.7, $\underline{CH_2}CH_2CH_3$)	7.15 (1H, d, *J* = 8.2); 7.83 (1H, s); 7.90 (3H, m); 8.00 (2H, m)
4d	8.72	3.99	1.30 (6H, d, *J* = 6.8, $(\underline{CH_3})_2CH$); 2.80 (1H, m, $(CH_3)_2\underline{CH}$)	7.19 (1H, d, *J* = 8.0); 7.85 (1H, s); 7.93 (3H, m); 8.00 (2H, m)
4e	8.75	4.00	1.0 (3H, t, *J* = 6.5, $(CH_2)_3\underline{CH_3}$); 1.50 (2H, m, $(CH_2)_2\underline{CH_2}CH_3$); 1.75 (2H, m, $CH_2\underline{CH_2}CH_2CH_3$); 2.60 (2H, t, *J* = 7.0, $\underline{CH_2}(CH_2)_2CH_3$)	7.15 (1H, d, *J* = 8.2); 7.82 (1H, s); 7.89 (3H, m); 8.00 (2H, m)
4f	8.77	4.00	1.0 (3H, t, *J* = 6.9, $(CH_2)_4\underline{CH_3}$); 1.45 (4H, m, $(CH_2)_2\underline{CH_2}\underline{CH_2}CH_3$); 1.75 (2H, m, $CH_2\underline{CH_2}(CH_2)_2CH_3$); 2.58 (2H, t, *J* = 6.8, $\underline{CH_2}(CH_2)_3CH_3$)	7.15 (1H, d, *J* = 7.8); 7.84 (1H, s); 7.87 (3H, m); 8.00 (2H, m)
4g	8.75	4.00	0.98 (3H, t, *J* = 6.4, $(CH_2)_5\underline{CH_3}$); 1.42-1.78 (8H, m, $CH_2(\underline{CH_2})_4CH_3$); 2.55 (2H, t, *J* = 6.7, $\underline{CH_2}(CH_2)_4CH_3$)	7.15 (1H, d, *J* = 8.3); 7.85 (1H, s); 7.89 (3H, m); 8.00 (2H, m)

TABLE 2 (continued)

1	2	3	4	5
4h	8.73	3.96	0.96 (3H, t, J = 6.5, $(CH_2)_6\underline{CH_3}$); 1.40-1.80 (10H, m, $CH_2\underline{(CH_2)_5}CH_3$); 2.50 (2H, t, J = 6.3, $\underline{CH_2}(CH_2)_5CH_3$)	7.13 (1H, d, J = 8.0); 7.82 (1H, s); 7.86 (3H, m); 8.04 (2H, m)
6a	—	3.75	2.18 (3H, s, CH_3)	6.73 (1H, d, J = 7.8); 7.00 (1H, s); 7.20 (2H, m); 7.50 (3H, m); 7.68 (1H, d, J = 7.4); 7.75 (1H, t, J = 6.5); 7.87 (1H, d, J = 8.2); 8.00 (3H, m)
6b	—	3.73	1.22 (3H, t, J = 6.4, $CH_2\underline{CH_3}$); 2.67 (2H, q, J = 7.0, $\underline{CH_2}CH_3$)	6.90 (1H, d, J = 7.8); 7.08 (1H, s); 7.22 (2H, m); 7.50 (3H, m); 7.65 (1H, d, J = 7.4); 7.73 (1H, t, J = 6.7); 7.85 (1H, d, J = 8.2); 8.10 (3H, m)
6c	—	3.75	1.04 (3H, t, J = 6.7, $(CH_2)_2\underline{CH_3}$); 1.62 (2H, m, $CH_2\underline{CH_2}CH_3$); 2.52 (2H, t, J = 6.4, $\underline{CH_2}CH_2CH_3$)	6.95 (1H, d, J = 7.4); 6.98 (1H, s); 7.12 (2H, m); 7.63 (3H, m); 7.70 (1H, d, J = 8.2); 7.79 (1H, t, J = 6.7); 7.92 (1H, d, J = 8.0); 8.13 (3H, m)
6d	—	3.72	1.30 (6H, d, J = 6.8, $(\underline{CH_3})_2CH$); 2.78 (1H, m, $(CH_3)_2\underline{CH}$)	6.82 (1H, d, J = 8.0); 7.00 (1H, s); 7.25 (2H, m); 7.48 (3H, m); 7.60 (1H, d, J = 7.9); 7.73 (1H, t, J = 6.3); 7.92 (1H, d, J = 8.2); 8.10 (3H, m)
6e	—	3.73	1.0 (3H, t, J = 6.6, $(CH_2)_3\underline{CH_3}$); 1.43-1.75 (4H, m, $CH_2\underline{(CH_2)_2}CH_3$); 2.60 (2H, t, J = 6.7, $\underline{CH_2}(CH_2)_2CH_3$)	6.76 (1H, d, J = 7.8); 6.98 (1H, s); 7.02 (2H, m); 7.43 (3H, m); 7.65 (1H, d, J = 8.2); 7.70 (1H, t, J = 6.4); 7.84 (1H, d, J = 7.6); 8.16 (3H, m)
6f	—	3.75	1.0 (3H, t, J = 6.5, $(CH_2)_4\underline{CH_3}$); 1.40-1.60 (6H, m, $CH_2\underline{(CH_2)_3}CH_3$); 2.58 (2H, t, J = 6.3, $\underline{CH_2}(CH_2)_3CH_3$)	6.93 (1H, d, J = 7.9); 7.15 (1H, s); 7.27 (2H, m); 7.50 (3H, m); 7.62 (1H, d, J = 7.5); 7.84 (1H, t, J = 6.8); 8.03 (1H, d, J = 8.2); 8.16 (3H, m)
6g	—	3.72	0.98 (3H, t, J = 6.7, $(CH_2)_5\underline{CH_3}$); 1.42-1.78 (8H, m, $CH_2\underline{(CH_2)_4}CH_3$); 2.55 (2H, t, $\underline{CH_2}(CH_2)_4CH_3$)	6.90 (1H, d, J = 7.9); 7.05 (1H, s); 7.34 (2H, m); 7.52 (3H, m); 7.65 (1H, d, J = 7.7); 7.79 (1H, t, J = 6.7); 7.95 (1H, d, J = 7.9); 8.17 (3H, m)
6h	—	3.74	0.98 (3H, t, J = 6.5, $(CH_2)_5\underline{CH_3}$); 1.52-1.76 (8H, m, $CH_2\underline{(CH_2)_4}CH_3$); 2.50 (2H, t, J = 6.5, $\underline{CH_2}(CH_2)_4CH_3$)	6.75 (1H, d, J = 7.6); 7.00 (1H, s); 7.31 (2H, m); 7.54 (3H, m); 7.66 (1H, d, J = 7.9); 7.73 (1H, t, J = 6.3); 7.93 (1H, d, J = 7.6); 8.08 (3H, m)

EXPERIMENTAL

Mass spectra were recorded with a Finnigan MAT INCOS 50 (70 eV). IR spectra were recorded with a Nicolet Protege Fourier spectrometer. ^{1}NMR spectra of DMSO-d_6 solutions with TMS as internal standard were recorded with Bruker AC-500 (500 MHz) and Tesla BS-567 (100 MHz) spectrometers. Melting points were determined with a Kofler block.

O-Acylvanillins 3a-h. Absolute pyridine (0.25 mol) and the corresponding acid chloride (0.20 mol) (added in small portions), prepared by boiling the carboxylic acid (1 mol), $SOCl_2$ (1.3 mol), and absolute benzene (500 ml) for 6 h, followed by removal of the benzene, and distilling the residue, were added to a stirred solution of vanillin (0.2 mol) in absolute CH_2Cl_2 (500 ml). The reaction mixture was boiled for 1 h, the CH_2Cl_2

was evaporated off on a water bath, the residue was dissolved in benzene (500 ml), washed with water twice, washed with 5% aqueous $NaHCO_3$ three times, and dried over $CaCl_2$. The solvent was distilled off and the residue was distilled or recrystallized from a 1:1 mixture of benzene and hexane.

Compound 3a. Yield 92%; mp 78-79°C (mp 77-79°C [5]). ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 2.32 (3H, s, CH_3); 3.92 (3H, s, OCH_3); 7.18 (1H, d, *J* = 7.1, H_{arom}); 7.48 (2H, m, H_{arom}); 9.92 (1H, s, CHO).

Compound 3b. Yield 79%; mp 33-34°C .^{1}H NMR spectrum, δ, ppm (*J*, Hz): 1.25 (3H, t, *J* = 6.9, $CH_2\underline{CH_3}$); 2.52 (2H, q, *J* = 6.7, $\underline{CH_2}CH_3$); 3.84 (3H, s, OCH_3); 7.13 (1H, d, *J* = 7.4, H_{arom}); 7.42 (2H, m, H_{arom}); 9.88 (1H, s, CHO). Found, %: C 63.29; H 5.73. $C_{11}H_{12}O_4$. Calculated, %: C 63.46; H 5.77.

Compound 3c. Yield 81%; bp 137-138°C (0. 5 mm Hg), n_D^{20} 1.5281. ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 1.02 (3H, t, *J* = 6.2, $(CH_2)_2\underline{CH_3}$, 1.63 (2H, m, $CH_2\underline{CH_2}CH_3$); 2.51 (2H, t, *J* = 6.7, $\underline{CH_2}CH_2CH_3$); 3.84 (3H, s, OCH_3); 7.15 (1H, d, *J* = 7.7, H_{arom}); 7.40 (2H, m, H_{arom}); 9.90 (1H, s, CHO). Found, %: C 64.11; H 7.02. $C_{12}H_{16}O_4$. Calculated, %: C 64.28; H 7.14.

Compound 3d. Yield 89%; mp 29-30°C .^{1}H NMR spectrum, δ, ppm (*J*, Hz): 1.35 (6H, d, *J* = 6.8, $CH(\underline{CH_3})_2$); 2.88 (1H, m, $\underline{CH}(CH_3)_2$); 3.90 (3H, s, OCH_3); 7.21 (1H, d, *J* = 7.5, H_{arom}); 7.50 (2H, m, H_{arom}); 9.96 (1H, s, CHO). Found, %: C 64.72; H 6.19. $C_{12}H_{14}O_4$. Calculated, %: C 64.86; H 6.31.

Compound 3e. Yield 76%; bp 149-150°C (0.5 mm Hg), n_D^{20} 1.5273. ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 0.96 (3H, t, *J* = 6.8, $(CH_2)_3\underline{CH_3}$); 1.20-1.90 (4H, m, $2CH_2$); 2.62 (2H, t, *J* = 6.5, $\underline{CH_2}(CH_2)_2CH_3$); 3.96 (3H, s, OCH_3); 7.15 (1H, d, *J* = 7.8, H_{arom}); 7.38 (2H, m, H_{arom}); 9.90 (1H, s, CHO). Found, %: C 66.01; H 6.62. $C_{13}H_{16}O_4$. Calculated, %: 66.10; H 6.77.

Compound 3f. Yield 85%; bp 155-156°C (0.5 mm Hg); n_D^{20} 1.5068. ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 0.90 (3H, t, *J* = 6.2, $(CH_2)_4\underline{CH_3}$); 1.12-1.90 (6H, m, $3CH_2$); 2.58 (2H, t, *J* = 6.5, $\underline{CH_2}(CH_2)_3CH_3$); 3.88 (3H, s, OCH_3); 7.13 (1H, d, *J* = 7.3, H_{arom}); 7.44 (2H, m, H_{arom}); 9.95 (1H, s, CHO). Found, %: C 67.19; H 7.23. $C_{14}H_{18}O_4$. Calculated, %: 67.20; H 7.20.

Compound 3g. Yield 82%; bp 163-164°C (0.5 mm Hg); n_D^{20} 1.5092. ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 0.96 (3H, t, *J* = 6.3, $(CH_2)_5\underline{CH_3}$); 1.15-1.88 (8H, m, $4CH_2$); 2.51 (2H, t, *J* = 6.5, $\underline{CH_2}(CH_2)_4CH_3$); 3.86 (3H, s, OCH_3); 7.12 (1H, d, *J* = 7.0, H_{arom}); 7.45 (2H, m, H_{arom}); 9.91 (1H, s, CHO). Found, %: C 68.22; H 7.59. $C_{15}H_{20}O_4$. Calculated, %: 68.18; H 7.57.

Compound 3h. Yield 77%; bp 170-171°C (0.5 mm Hg); n_D^{20} 1.5079. ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 0.92 (3H, t, *J* = 6.4, $(CH_2)_6\underline{CH_3}$); 1.32-1.64 (10H, m, $5CH_2$); 2.60 (2H, m, $\underline{CH_2}(CH_2)_5CH_3$); 3.88 (3H, s, OCH_3); 7.14 (1H, d, *J* = 7.2, H_{arom}); 7.47 (2H, m, H_{arom}); 9.90 (1H, s, CHO). Found, %: C 68.83; H 7.69. $C_{16}H_{22}O_4$. Calculated, %: 69.06; H 7.91.

Interaction of Indan-1,3-dione 1,2-Naphthylamine 2, and O-Acylvanillin Alkanoates 3a-h (General Method). A solution of 2-naphthylamine **2** (1.43 g, 0.01 mol) in ethanol (10 ml) and a solution of the corresponding ester **3a-h** (0.01 mol) in ethanol (10 ml) were added to a solution of indan-1,3-dione **1** (0.01 mol) in ethanol (10 ml). The reaction mixture was boiled for 30-60 min. The precipitate which formed when the mixture was cooled was separated, added to nitrobenzene (15 ml), and boiled for 3-4 h. The solvent was evaporated, and the solid residue was washed with ether and crystallized from a 1:3 mixture of ethanol and benzene.

Synthesis of 4-[(1,3-Dihydro-1,3-dioxo-2H-inden-2-ylidene)methyl]-2-methoxyphenyl Esters of Carboxylic Acids 4a-h (General Method). A mixture of indan-1,3-dione **1** (1.46 g, 0.01 mol) and the corresponding O-acylvanillin **3a-h** (0.01 mol) in ethanol (20 ml) was boiled for 2-3 h. The precipitate was separated and crystallized from butanol.

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