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UNUSUAL BEHAVIOUR OF DIETHYLBROMOMALONATE WITH 2-HYDROXYDESOXYBENZOINS. CONVENIENT SYNTHESIS OF 2-ARYL-3(2H)-BENZOFURANONES

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ABSTRACT : Formation of 2-aryl-3(2H) benzofuranones in the reaction of diethylbromomalonate with 2-hydroxydesoxybenzoins is reported alongwith their further conversion into 2-arylbenzofurans.

Many naturally occurring compounds possessing 2-arylbenzofuran as the core structure are known to possess interesting biological properties. Some of these e.g. Eupomatenoids, Vignafurans, Neolignans have emerged in recent years as substances of considerable biological interest.

In view of the potent biological activities of these compounds, various synthetic routes are reported in the literature for 2-arylbenzofurans[1-6]. Similarly 2-aryl-3(2H)- benzofuranones which could be the

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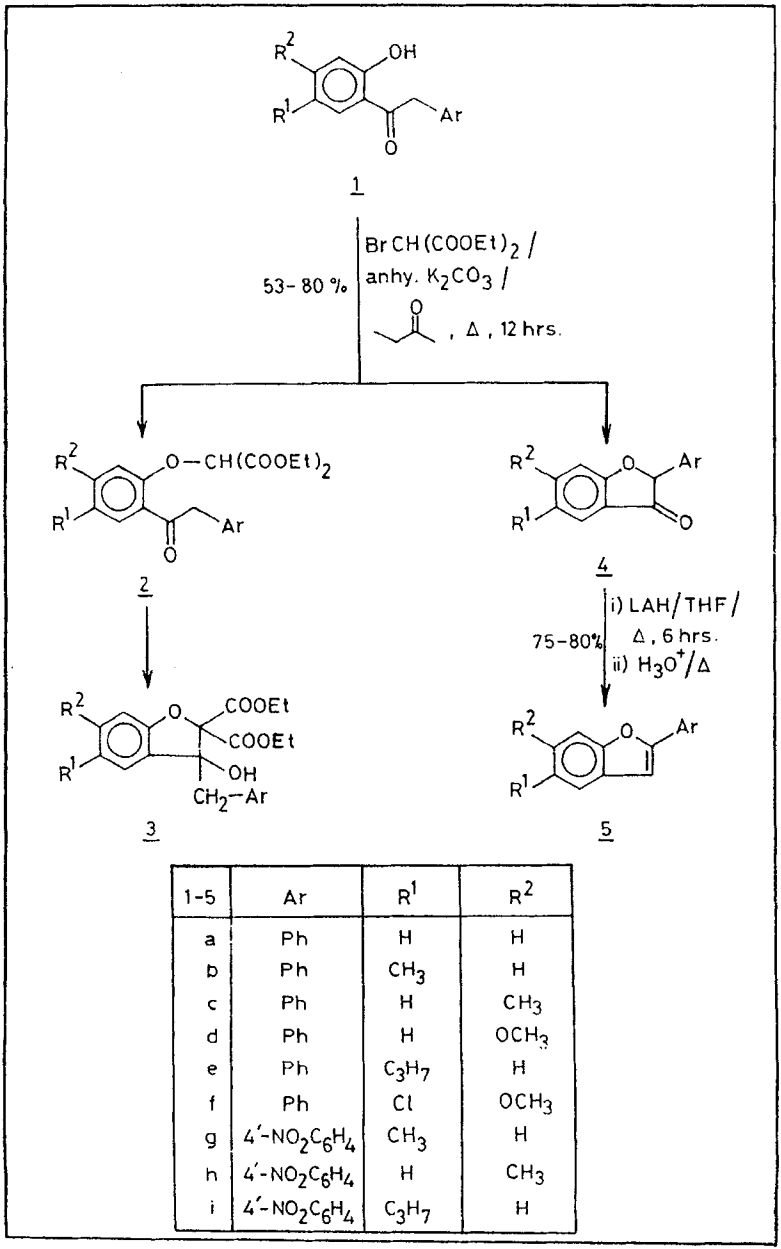
most obvious synthons for these systems are also known for their biological activities[7]. The earlier approaches[7-14] to these systems suffered mainly in yield and critical reaction conditions.

While studying the reaction of diethylbromomalonate with various substrates, we noticed an unusual behaviour of this reagent with 2-hydroxydesoxybenzoin which resulted in the formation of 2-phenyl-3(2H)-benzofuranone. This interesting observation constitutes the subject matter of this paper.

When 2-hydroxydesoxybenzoin was reacted with diethylbromomalonate in presence of anhydrous potassium carbonate and methyl ethyl ketone, usual work up of the reaction mixture provided a neutral product mp 217° along with diethylmalonate. The neutral product was devoid of ester grouping and any exchangeable proton as evident from its PMR, indicating that expected product 1 or 3 was not formed in this reaction while IR of the compound showed presence of a carbonyl function. The elemental analysis suggested the molecular formula as $C_{14}H_{10}O_2$. Based on this data, it appeared to be 2-phenyl-3(2H)-benzofuranone, a compound reported to have m.p. 219[14]. Thus in this reaction an intramolecular cyclization has occurred with the formation of 2-phenyl-3(2H)-benzofuranone 4a. This interesting



1-5	Ar	R^1	R^2
a	Ph	H	H
b	Ph	CH_3	H
c	Ph	H	CH_3
d	Ph	H	OCH_3
e	Ph	C_3H_7	H
f	Ph	Cl	OCH_3
g	4′-$NO_2C_6H_4$	CH_3	H
h	4′-$NO_2C_6H_4$	H	CH_3
i	4′-$NO_2C_6H_4$	C_3H_7	H

observation was then further exploited and several 2-aryl-3(2H)-benzofuranones were obtained in moderate yields, 4b-i.

As mentioned earlier, these compounds could be easily converted into 2-aryl-benzofurans merely by reduction and dehydration. Thus as a test case, three 2-aryl-3(2H)-benzofuranones 4b,d,e were converted into the corresponding benzofurans 5b,d,e whose spectral data was in complete accordance with the structure.

From these results it appears that probably diethyl bromomalonate is acting as a brominating agent and bringing about bromination at the reactive methylene followed by cyclization, thus furnishing 2-aryl-3(2H)-benzofuranones. The mechanistic aspects of this reaction are under investigation.

This method comprising of easily available starting compounds, milder reaction conditions, simple work up with moderate yields has wider applicability and is thus much more advantageous than the earlier known methods for benzofuranones.

EXPERIMENTAL :

2-Aryl-3(2H)-benzofuranones 4a-i - General Procedure :

A mixture of appropriate 2-hydroxydesoxybenzoin (1a-i, 0.005 mole), diethylbromomalonate (0.0075 mole),

anhydrous K_2CO_3 (0.015 mole) and dry methyl ethyl ketone (15 ml) was refluxed for 12h. The mixture was then filtered and the residue was washed thoroughly with hot methyl ethyl ketone (2 x 10 ml). The combined filtrate on removal of solvent furnished a sticky product contaminated with diethylmalonate. This after trituration with hot hexane (50ml) provided a white solid which on further purification through column chromatography (n-hexane-eluent) and crystallization (n-hexane-ethylacetate) provided the desired products 4a-i.

Yields of isolated products are mentioned. All the melting points are uncorrected. IR Spectra were measured on a Perkin-Elmer 599B and 337 IR spectrophotometer. ^1H NMR spectra are recorded on Jeol Fx-90Q Spectrometer and Mass Spectra on a Finnigan Mat 1020c Spectrometer. Satisfactory micro analyses were obtained with $\pm$0.3% for C and H.

2-phenyl-3(2H) benzofuranone-4a : White solid 65% yield m.p. 217° (lit m.p. 219[14]) IR (Nujol) 1705cm^{-1} ^1H NMR ($CDCl_3$)δ 6.8-7.6 (m,10H,C_2-H,Harom).

5-Methyl-2-phenyl-3(2H)benzofuranone-4b : White solid 68% yield. m.p. 234° (lit m.p. 234[15]) IR (Nujol) 1750cm^{-1} ^1H NMR ($CDCl_3$)δ 2.28 (s,3H,-CH_3), 6.8 -7.6 (m,9H,C_2-H, Harom).

6-Methyl-2-phenyl-3(2H)-benzofuranone-4c : White solid 58% yield. m.p. 253°. IR (Nujol)1740cm^{-1};^{1}H NMR ($CDCl_3$)δ2.34 (s, 3H,-CH_3), 6.8(b s.1H, C_7-H), 7.17-7.51 (m,8H, C_2-H, Harom).

6-Methoxy-2-phenyl-3(2H)-benzofuranone-4d : White solid 67% yield m.p. 234° IR (Nujol) 1725 cm^{-1}.^{1}H NMR ($CDCl_3$)δ 3.77(s, 3H,-OCH_3), 6.48 (b s.1H,C_7-H), 7.17-7.51(m, 8H, C_2-H, Harom).

5-Propyl-2-phenyl-3(2H)-benzofuranone-4e : White solid. 64% yield. m.p. 184°. IR(Nujol)1717cm^{-1};^{1}H NMR($CDCl_3$)δ 0.9(t, J=8Hz, 3H, -CH_3), 1.31-1.82 (m,2H-CH_2-CH_3),2.6 (t,J=8Hz,2H, -CH_2-Ar), 7.1-7.85 (m,9H,C_2-H, Harom);MS m/e(%) 252(M^+, 42), 251 (100), 223(39), 165(14),77(17).

5-Chloro-6-methoxy-2-phenyl-3(2H)-benzofuranone-4f : White solid 80% yield. m.p. 272°. IR (Nujol) 1710cm^{-1} .^{1}H NMR ($CDCl_3$)δ 4.1(s , 3H, -OCH_3), 6.8 (s ,1H,C_7-H),7.4-7.8 (m,7H, C_2-H, H-arom).

5-methyl-2(4′-nitrophenyl)-3(2H)benzofuranone-4g : White solid. 63% yield m.p. 175°. IR (Nujol) 850, 1520, 1740 cm^{-1} ^{1}H NMR ($CDCl_3$)δ 2.3 (s, 3H, -CH_3). 7-7.6(m, 6H, C_2-H, Harom), 8.2 (d, J=8Hz, 2H, C_3′,C_5′,H).

6-Methyl-2-[4′-nitrophenyl]-3(2H)- benzofuranone-4h : White solid 63% yield. m.p. 262°. IR (Nujol)850,1520, 1720 cm^{-1} ^{1}H NMR ($CDCl_3$)δ2.5 (s,3H,-CH_3), 7.1-7.9 (m, 6H,C_2-H, Harom), 8.3 (d, J=8Hz, 2H, C_3′,C_5′-H).

5-propyl-2[4'nitrophenyl]-3(2H)-benzofuranone-4i : White granules. 53% yield. m.p. 199-201°. IR (Nujol) 860, 1520, 1740 cm^{-1}. ^1H NMR ($CDCl_3$)δ 0.9 (t,J=7Hz, 3H, $-CH_3$),1.4-1.9 (m, 2H, $-CH_2-CH_3$), 2.6 (t, J=7Hz, 2H, $-CH_2$ -Ar), 7.3-7.9 (m, 6H, C_2-H, Harom), 8.2(d, J=8Hz, 2H, C_3,C_5'-H).

5-Methyl-2-phenyl-benzofuran-5b: White solid. 75% yield. m.p. 124° (lit. m.p. 126-9[16]), ^1H NMR ($CDCl_3$)δ 2.5 (s,3H, $-CH_3$), 7.0-7.3 (m, 6H, C_3-H, Harom),7.7-8.1 (m,3H, Harom).

6-Methoxy-2-phenyl-benzofuran-5d : White solid 75% yield m.p. 73° (lit. m.p.79-81[17]). ^1H NMR ($CDCl_3$)δ 3.9 (s, 3H, $-OCH_3$), 6.9-7.77 (m, 7H,C_3-H, Harom),7.9 (d,2H,C_2,C_6'-H). MS m/e(%) 224(M^+, 86), 209(100), 152(33), 105(19).

5-Propyl-2-phenyl-benzofuran-5e : White solid.80% yield. m.p. 83-85°. ^1H NMR ($CDCl_3$)δ 0.9(t, J=8Hz, 3H, $-CH_3$), 1.5-1.9 (m,2H,$-CH_2-CH_3$), 2.7(t,J=8Hz, 2H,$-CH_2$ -Ar), 7.1 (s, 1H, C_3-H), 7.3-7.6(m, 6H, Harom), 8.0 - 8.1(m, 2H, C_2',C_6'-H).

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