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Studies on Sigmatropic Rearrangements: Thermal Rearrangement of 3-(*meta*-Substituted Aryloxymethyl) Coumarins

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Summary. At elevated temperatures, the 3-(*meta*-substituted aryloxymethyl) coumarins **3a–e** and **3g-k** undergo sigmatropic rearrangements to give the hydroxylated 3-benzylcoumarins **4a–e** and **4g–k**. Upon methylation and subsequent oxidation with N-bromo succinimide, the 3-(chlorosubstituted benzyl) coumarins **4a**, **4m** and **4n** afford 3-(chlorosubstituted benzoyl) coumarins **8a**, **8m**, and **8n**.

Keywords. 3-Chloromethyl coumarin; Sigmatropic rearrangement; Sigmatropic shift; *NBS*.

Untersuchungen von sigmatropen Umlagerungen: Thermische Umlagerung von 3-*meta*-substituierten Aryloxymethylcumarinen

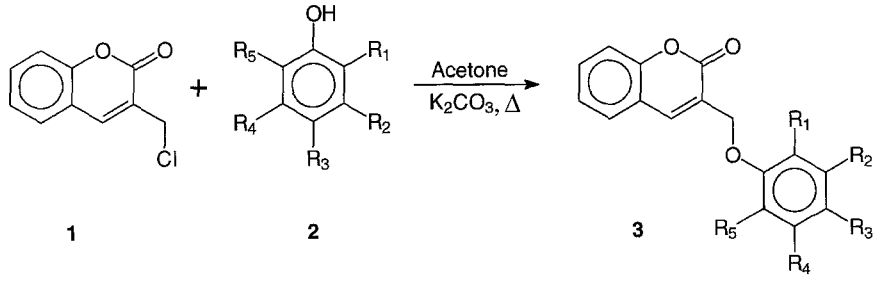
Zusammenfassung. Bei erhöhter Temperatur reagieren die 3-*meta*-substituierten Aryloxymethylcumarine **3a–e** und **3g–k** über eine sigmatrope Umlagerung zu den hydroxylierten 3-Benzylcumarinen **4a–e** und **4g–k**. Methylierung der 3-chlorsubstituierten Benzoylcumarine **4a**, **4m** und **4n**, gefolgt von Oxidation mit N-Bromsuccinimid, ergibt die 3-chlorsubstituierten Benzoylcumarine **8a**, **8m** und **8n**.

Introduction

Recently we have reported that the thermal sigmatropic rearrangement of 3-aryloxymethylcoumarins affords hydroxylated 3-benzylcoumarins [1]. We have then studied the rearrangement of substrates containing *ortho*- and *para*-substituted aryloxy groups, observing exclusively [1s, 5s]- and [1s, 3a]-sigmatropic rearrangements, respectivly. So far, no substrates containing *meta*-substituted aryloxy groups have been considered. In the context of [3s, 3s]-sigmatropic rearrangements of *meta*-substituted allyl phenyl ethers [2] it has been shown that if the *meta*-substituent is electron accepting, the rearrangement occurs predominantly *ortho* to the substituent. If the substituent is electron donating, however, the major product obtained is that in which the allyl group migrates *para* to the substituent. It occurred to us that the study would remain incomplete without considering the thermal rearrangement of 3-(*meta*-substituted aryloxymethyl) coumarins. Therefore, we have now investigated substrates containing *meta*-substituted aryloxy

groups in order to study the regiochemical outcome of the rearrangement. In addition, we have also studied the rearrangement of a number of substrates containing disubstituted aryloxy groups (**3g–l**). Among these substrates, **3g**, **3h**, and **3l** also contain a *meta*-substituted aryloxy group. We have also attempted the conversion of the hydroxylated 3-(chlorosubstituted benzyl) coumarins **4a**, **4m**, and **4n**.

The 3-aryloxymethyl[1]benzopyran-2-ones (**3**) required for this study were synthesized by reacting 3-chloromethylcoumarin (**1**) with an appropriate phenol (**2**) in refluxing acetone in the presence of anhydrous potassium carbonate (Scheme 1).



	R^1	R^2	R^3	R^4	R^5		R^1	R^2	R^3	R^4	R^5
3a	H	Cl	H	H	H	**3g**	H	CH_3	H	CH_3	H
3b	H	CH_3	H	H	H	**3h**	CH_3	H	H	CH_3	H
3c	H	OCH_3	H	H	H	**3i**	CH_3	CH_3	H	H	H
3d	H	CN	H	H	H	**3j**	CH_3	H	H	H	CH_3
3e	H	OCH_2Ph	H	H	H	**3k**	CH_3	H	CH_3	H	H
3f	H	NO_2	H	H	H	**3l**	Cl	H	Cl	H	H

Scheme 1

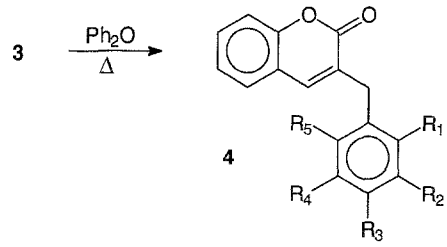
Results and Discussion

Recent work in our laboratory has proved diphenyl ether and quinoline to be effective solvents for the rearrangement of 3-aryloxymethyl coumarins. We therefore used these solvents for the present study. Heating compound **3a** in diphenyl ether at 240°C for 4 h gave a single product (m.p.: 190°C, yield: 77%). Elemental analysis and spectroscopic data corroborated structure **4a** for this product. Each of the remaining substrates **3b–l** except **3f** and **3l** rearranged in the same way, giving rise to a single hydroxylated benzyl derivative (**4b–e**, **4g–k**) (Scheme 2).

3f and **3l** decomposed completly to give tarry materials from which no tractable product could be obtained. Nitroaryloxy substituted substrates usually need a higher activation energy for thermal rearrangement; they are, however, known to decompose at elevated temperatures [3]. The decomposition of **3l** might in addition be due to the presence of the 2,4-dichlorophenoxy moiety.

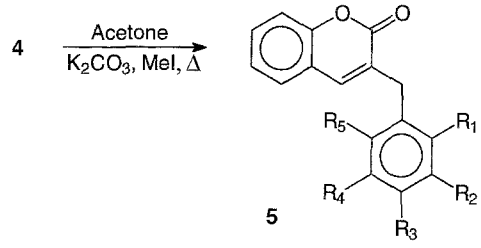
The hydroxylated 3-benzylcoumarins are converted to either the methoxy derivatives **5a–d** and **5m–o** with methyl iodide/potassium carbonate in acetone (Scheme 3) or to the acetoxy derivatives **6g–k** with acetic anhydride and freshly fused sodium acetate (Scheme 4).

3a–l were also heated in refluxing quinoline for 5 h to explore any occurrence of [3s, 3s]-sigmatropic rearrangements in these substrates. All compounds except



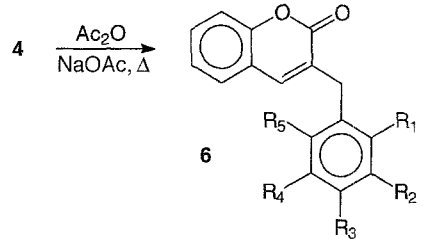
	R_1	R_2	R_3	R_4	R_5		R_1	R_2	R_3	R_4	R_5
4a	Cl	H	OH	H	H	**4g**	CH_3	H	OH	H	CH_3
4b	CH_3	H	OH	H	H	**4h**	H	CH_3	OH	H	CH_3
4c	OCH_3	H	OH	H	H	**4i**	CH_3	CH_3	OH	H	H
4d	CN	H	OH	H	H	**4j**	H	CH_3	OH	CH_3	H
4e	OCH_2Ph	H	OH	H	H	**4k**	OH	CH_3	H	CH_3	H

Scheme 2



	R_1	R_2	R_3	R_4	R_5		R_1	R_2	R_3	R_4	R_5
5a	Cl	H	OCH_3	H	H	**5m**	H	Cl	OCH_3	H	H
5b	CH_3	H	OCH_3	H	H	**5n**	OCH_3	H	H	Cl	H
5c	OCH_3	H	OCH_3	H	H	**5o**	H	H	OCH_3	H	H
5d	CN	H	OCH_3	H	H						

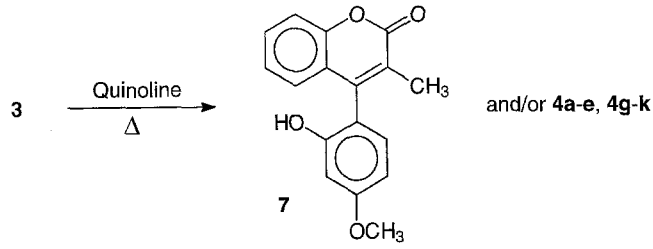
Scheme 3



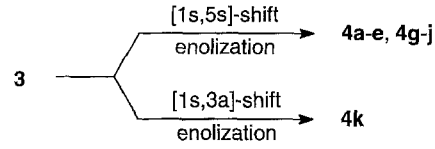
	R_1	R_2	R_3	R_4	R_5		R_1	R_2	R_3	R_4	R_5
6g	CH_3	H	OAc	H	CH_3	**6j**	H	CH_3	OAc	CH_3	H
6h	H	CH_3	OAc	H	CH_3	**6k**	OAc	CH_3	H	CH_3	H
6i	CH_3	CH_3	OAc	H	H						

Scheme 4

3c gave the same products **4a–e** and **4g–k** as obtained when heated in diphenyl ether. **3c** furnished a mixture of **4c** and a new product **7** arising from an initial [3s, 3s]-sigmatropic rearrangement (Scheme 5). **3f** and **3l** decomposed completely on heating; no product could be obtained as in the case of diphenyl ether. Earlier it has been observed that substrates containing *ortho*-substituted aryloxy groups furnish products arising from an initial *Claisen* rearrangement [1]. In our case, **3k** and **3l** contain *ortho*-substituted aryloxy groups in addition to a substituent in the *para*-position. Formation of products **4a–e**, **4g–j** and **4k** from **3a–e**, **3g–j** and **3k** may be explained *via* [1s, 5s]- and [1s, 3a]-sigmatropic shifts respectively, followed by enolization (Scheme 6).



Scheme 5

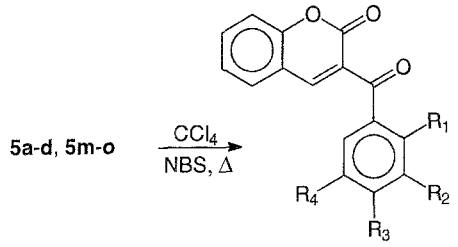


Scheme 6

The aryloxymethyl group of **3g**, containing two methyl groups positioned *meta* to each other, furnished a product the ^{1}H NMR spectrum of which clearly indicates the occurrence of a [1s, 5s]-shift in preference to a [1s, 3a]-shift. [1s, 3a]-sigmatropic rearrangements in other substrates containing *m*-substituted aryloxy groups (**3a–l**) with a theoretical possibility of formation of two products have also been considered. This pathway, however, could be ruled out on the basis of the ^{1}H NMR spectra of the products, comparing them with those of disubstitued phenols [4]. The present study reaffirms our earlier proposal that thermal [1s, 5s]-sigmatropic shifts take place in case of substrates where the *para*-position of the aryloxy group is free [1]. Our present observation in quinoline also complements the alternative mechanism proposed by us earlier [1]. It was then observed that substrates containing *ortho*-substituted aryloxy group furnished the *Claisen* product. In the present study, **3k** did not give any *Claisen* product; only a single product arising from a [1s, 3a]-shift (**4k**) was obtained. **3c**, containing a *m*-methoxyphenoxy group, gave a mixture of *Claisen* product **7** and **4c**.

We have also examined the reactions of compound **4** with N-bromosuccinimide (*NBS*) in tetrachloromethane to oxidize the benzyl methylene group to obtain 3-benzoylcoumarins. Earlier, we have observed that *NBS* effects nuclear bromination of the phenyl moiety in compounds **4** in preference to bromination/oxidation of the

methylene function which is benzylic with respect to the phenyl ring as well as allylic with respect to the coumarin ring. We have deactivated the phenol ring by converting compounds **4** to the corresponding methoxy derivatives **5a–d** and **5m–o**. The methoxy derivatives were then refluxed in tetrachloromethane with *NBS* for 4 h. The substrates containing chloro substituted aryloxy groups smoothly furnished the benzoylcoumarin derivatives, **8a**, **8m** and **8n** (Scheme 7). Substrates containing methyl substituted methoxy phenyl groups expectedly gave a mixture which could not be effectively separated to give any pure product.



8

	R_1	R_2	R_3	R_4
8a	Cl	H	OCH_3	H
8m	H	Cl	OCH_3	H
8n	OCH_3	H	H	Cl

Scheme 7

From the present study it may be concluded that with sigmatropic rearrangements of 3-aryloxymethylcoumarins the preferred reaction path is a [1s, 5s]-sigmatropic shift when the *para*-position of the aryloxy group of **3** is vacant, but a [1s, 3a]-shift takes places when the *para*-position of the aryloxy group of **3** is occupied. *m*-Substituted aryloxymethylcoumarins follow the same pattern. 3-(Chloro substituted) methoxybenzylcoumarins give 3-(chlorosubstituted benzoyl) coumarins when treated with N-bromosuccinimide in tetrachloromethane.

Experimental

Melting points are uncorrected. UV absorption spectra were recorded on a Hitachi 200–20 spectrometer (absolute ethanol). IR spectra were run as KBr discs on a Perkin-Elmer 1330 apparatus. NMR specta were determined on a Jeol FX100 (100 MHz) spectromter ($CDCl_3$, internal *TMS*) at the IICB, Calcutta, and a Bruker AC-400 (250 MHz) spectrometer at the University of Konstanz, Germany. Coupling constants are given in Hz. Elemental analyses and mass spectra were carried out by RSIC (CDRI), Lucknow. *PE* refers to petroleum ether of boling range 60–80°C.

General procedure for the preparation of 3-(aryloxymethyl)[1]benzopyran-2-ones (**3a-l**)

3-Chloromethyl coumarin (**1**, 2.3 g, 1.2 mmol) was refluxed with the corresponding phenol (**2**, 1.5 mmol) in dry acetone (100 ml) in the presence of anhydrous potassium carbonate (3 g) for 10 h.

After cooling the solvent was removed from the filtrate. The residual mass was taken up in chloroform (3 × 25 ml), and the extract was washed with saturated brine and dried over Na_2SO_4. Removal of chloroform gave the crude solid which was purified by column chromatography over silica gel using benzene-*PE* (1:3) as eluent.

3a: 68%; m.p.: 146°C; UV (EtOH): $\lambda_{max}(\log \varepsilon) = 312$ (4.28), 273 (4.02), 260 (3.91) nm; IR (KBr): $\nu_{max} = 1700$ (CO), 1235 cm^{-1}; ^1H NMR (250 MHz, $CDCl_3$, *TMS*): $\delta = 5.00$ (s, 2H), 6.90 – 7.90 (m, 9H) ppm; MS: $m/z = 286$, 288 (M^+); $C_{16}H_{11}ClO_3$; calc.: C 67.01, H 3.83%; found: C 67.11, H 3.58%.

3b: 70%; m.p.: 118°C; UV (EtOH): $\lambda_{max}(\log \varepsilon) = 310$ (4.25), 260 (3.90) nm; IR (KBr): $\nu_{max} = 1700$, 1240 cm^{-1}; ^1H NMR (100 MHz, $CDCl_3$, *TMS*): $\delta = 2.28$ (s, 3H), 4.96 (s, 2H), 6.72 – 7.92 (m, 9H) ppm; MS: $m/z = 226$ (M^+); $C_{17}H_{14}O_3$; calc.: C 76.70; H 5.26%; found: C 76.52, H 5.01%.

3c: 65%; m.p.: 140°C; UV (EtOH): $\lambda_{max}(\log \varepsilon) = 372$ (4.01), 273 (4.05) nm; IR (KBr): $\nu_{max} = 1720$, 1240 cm^{-1}; ^1H NMR (100 MHz, $CDCl_3$, *TMS*): $\delta = 3.76$ (s, 3H), 4.96 (s, 2H), 6.80 – 7.92 (m, 9H) ppm; MS: $m/z = 282$ (M^+); $C_{17}H_{14}O_4$; calc.: C 72.34, H 4.96%; found: C 72.02, H 5.12%.

3d: 67%; m.p.: 126°C; UV (EtOH): $\lambda_{max}(\log \varepsilon) = 313$ (4.23), 274 (3.95) nm; IR (KRr): $\nu_{max} = 1700$, 1250 cm^{-1}; ^1H NMR (100 MHz, $CDCl_3$, *TMS*): $\delta = 5.00$ (s, 2H), 6.80 – 7.92 (m, 9H) ppm; MS: $m/z = 277$ (M^+); $C_{17}H_{11}NO_3$; calc.: C 73.64, H 3.97, N 5.05%; found: C 73.36, H 3.71, N 5.31%.

3e: 60%; m.p.: 128°C; UV (EtOH): $\lambda_{max}(\log \varepsilon) = 312$ (4.40), 278 (4.12), 226 (4.81) nm; IR (KBr): $\nu_{max} = 1705$, 1255 cm^{-1}; ^1H NMR (100 MHz, $CDCl_3$ *TMS*): $\delta = 5.00$ (s, 2H), 5.04 (s, 2H), 6.60 – 7.90 (m, 14H) ppm; MS: $m/z = 358$ (M^+); $C_{23}H_{18}O_4$; calc.: C 77.09, H 5.02%, found: C 76.80, H 5.32%.

3f: 68%; m.p.: 130°C; UV (EtOH): $\lambda_{max}(\log \varepsilon) = 312$ (4.31), 274 (3.99) nm; IR (KBr): $\nu_{max} = 1690$, 1250 cm^{-1}; ^1H NMR (100 MHz, $CDCl_3$, *TMS*): $\delta = 5.12$ (s, 2H), 7.20 – 7.92 (m, 9H) ppm; MS: $m/z = 297$ (M^+); $C_{16}H_{11}NO_5$; calc.: C 64.65, H 3.70, N 4.71%; found: C 64.90, H 4.00, N 5.00%.

3g: 62%; m.p.: 140°C; UV (EtOH): $\lambda_{max}(\log \varepsilon) = 312$ (4.16), 274 (3.86) nm; IR (KBr): $\nu_{max} = 1690$, 1245 cm^{-1}; ^1H NMR (100 MHz, $CDCl_3$, *TMS*): $\delta = 2.24$ (s, 6H), 4.96 (s, 2H), 6.60 – 7.62 (m, 8H) ppm; MS: $m/z = 280$ (M^+); $C_{18}H_{16}O_3$; calc.: C 77.14, H 5.71%; found: C 77.10, H 5.70%.

3h: 61%; m.p.: 148°C; UV (EtOH): $\lambda_{max}(\log \varepsilon) = 311$ (4.40), 278 (4.10) nm; IR (KBr): $\nu_{max} = 1725$, 1250 cm^{-1}; ^1H NMR (250 MHz, $CDCl_3$, *TMS*): $\delta = 2.30$ (s, 6H), 5.00 (s, 2H), 6.70 – 7.90 (m, 8H) ppm; MS: $m/z = 280$ (M^+); $C_{18}H_{16}O_3$; calc.: C 77.14, H 5.71%; found: C 77.35, H 5.59%.

3i: 63%; m.p.: 138°C; UV (EtOH): $\lambda_{max}(\log \varepsilon) = 312$ (4.22), 278 (3.91) nm; IR (KBr): $\nu_{max} = 1710$, 1230 cm^{-1}; ^1H NMR (100 MHz, $CDCl_3$, *TMS*): $\delta = 2.28$ (brs, 6H), 5.00 (s, 2H), 6.72 – 7.92 (m, 8H) ppm; MS: $m/z = 280$ (M^+); $C_{18}H_{16}O_3$; calc.: C 77.14, H 5.71%; found: C 77.31, H 6.02%.

3j: 68%; m.p.: 110°C; UV (EtOH): $\lambda_{max}(\log \varepsilon) = 310$ (4.23), 275 (4.98) nm; IR (KBr): $\nu_{max} = 1720$, 1200 cm^{-1}; ^1H NMR (250 MHz, $CDCl_3$, *TMS*): $\delta = 2.30$ (s, 6H), 4.80 (s, 2H), 6.90 – 8.00 (m, 8H) ppm; MS: $m/z = 280$ (M^+); $C_{18}H_{16}O_3$; calc.: C 77.14, H 5.71%; found: C 77.32, H 5.52%.

3k: 60%; m.p.: 116°C; UV (EtOH): $\lambda_{max}(\log \varepsilon) = 313$ (4.32), 278 (3.92) nm; IR (KBr): $\nu_{max} = 1710$, 1250 cm^{-1}; ^1H NMR (100 MHz, $CDCl_3$, *TMS*): $\delta = 2.20 - 2.30$ (brs, 6H), 5.10 (s, 2H), 6.80 – 7.96 (m, 8H) ppm; MS: $m/z = 280$ (M^+); $C_{18}H_{16}O_3$; calc.: C 77.14, H 5.71%; found: C 77.33, H 5.97%.

3l: 66%; m.p.: 132°C; UV (EtOH): $\lambda_{max}(\log \varepsilon) = 313$ (4.01), 276 (4.28) nm; IR (KBr): $\nu_{max} = 1705$, 1265 cm^{-1}; ^1H NMR (250 MHz, $CDCl_3$, *TMS*): $\delta = 5.03$ (s, 2H), 6.93 – 8.00 (m, 8H) ppm; MS: $m/z = 320$, 324 (M^+); $C_{16}H_{10}Cl_2O_3$; calc.: C 59.81, H 3.11%; found: C 60.10, H 2.91%.

General procedure for the synthesis of hydroxylated 3-benzyl[1]benzopyrano-2-ones (**4a–k**)

3-Aryloxymethyl coumarin (**3**, 0.4 g) was heated for 4 h in diphenyl ether (5 cm^3) on an oil bath at 240°C. The reaction mixture was chromatographed over silica gel (benzene) to give solid product **4**.

4a: 77%; m.p.: 190°C; UV (EtOH): $\lambda_{max}(\log \varepsilon) = 308$ (4.81), 277 (4.02) nm; IR (KBr): $\nu_{max} = 3330$, 1690 cm^{-1}; ^1H NMR (250 MHz, $CDCl_3$, *TMS*): $\delta = 2.92$ (s, 2H), 5.24 (s, 1H, D_2O exchangable), 6.74 (dd, $J = 8.3$, 2.5 Hz, 1H, 14-H), 6.97 (d, $J = 2.5$ Hz, 1H, 12-H) 7.20 – 7.22 (m, 2H, 6-H, 15-H), 7.28 – 7.36 (m, 2H, 5-H, 4-H), 7.41 – 7.48 (m, 2H, 7-H, 8-H) ppm; MS: $m/z = 288$, 286 (M^+); $C_{16}H_{11}ClO_3$; calc.: C 67.01, H 3.83%; found: C 67.12, H 3.59%.

4b: 70%, m.p.: 162°C; UV (EtOH): $\lambda_{max}(\log \varepsilon) = 310$ (4.72), 281 (3.85) nm; IR (KBr): $\nu_{max} = 3300$, 1700 cm^{-1}; ^1H NMR (250 MHz, $CDCl_3$, *TMS*): $\delta = 2.23$ (s, 3H), 3.80 (s, 2H), 6.82 (d, $J = 8$ Hz, 1H, 14-H), 6.91 – 6.97 (m, 2H, 12-H, 15-H), 7.23 – 7.52 (m, 5H), 7.68 (s, 1H, D_2O exchangable) ppm; MS: $m/z = 266$ (M^+); $C_{17}H_{14}O_3$; calc.: C 76.70, H 5.26%; found: C 77.00, H 5.02%.

4c: 72%, m.p.: 190°C; UV (EtOH): $\lambda_{max}(\log \varepsilon) = 308$ (4.62), 277 (3.92) nm; IR (KBr): $\nu_{max} = 3420$, 1700 cm^{-1}; ^1H NMR (100 MHz, $CDCl_3$ *TMS*): $\delta = 3.72$ (s, 3H), 3.81 (s, 2H), 6.68 – 6.72 (m, 2H, 12-H, 14-H), 6.87 (d, $J = 8.5$ Hz, 1H, 15-H), 7.24 – 7.51 (m, 5H), 7.68 (s, 1H, D_2O exchangable) ppm; MS: $m/z = 282$ (M^+); $C_{17}H_{14}O_4$; calc.: C 72.34, H 4.96%; found: C 72.07, H 5.13%.

4d: 60%, m.p.: 164°C; UV (EtOH): $\lambda_{max}(\log \varepsilon) = 308$ (4.88), 277 (3.82) nm; IR (KBr): $\nu_{max} = 3260$, 1670 cm^{-1}; ^1H NMR (250 MHz, $CDCl_3$, *TMS*): $\delta = 3.94$ (s, 2H), 5.49 (s, 1H, D_2O exchangable), 6.76 (dd, $J = 8.3$, 2.5 Hz, 1H, 14-H), 6.96 (d, $J = 2.4$ Hz, 1H, 12-H), 7.23 – 7.55 (m, 6H) ppm; MS.: $m/z = 277$ (M^+); $C_{17}H_{11}NO_3$; calc: C 73.64, H 3.97, N 5.05%; found: C 73.96, H 4.21, N 4.82%.

4e: 55%, m.p.: 160°C; UV (EtOH): $\lambda_{max}(\log \varepsilon) = 311$ (4.72), 275 (3.77) nm; IR (KBr): $\nu_{max} = 3310$, 1690 cm^{-1}; ^1H NMR (250 MHz, $CDCl_3$, *TMS*): $\delta = 3.80$ (s, 2H), 5.00 (s, 2H), 5.32 (s, 1H, D_2O exchangable), 6.32 – 6.56 (m, 2H), 7.08 – 7.56 (m, 11H) ppm; MS: $m/z = 358$ (M^+); $C_{23}H_{18}O_4$; calc: C 77.09, H 5.02%; found: C 77.18, H 4.71%.

4g: 62%, m.p.: 168°C; UV (EtOH): $\lambda_{max}(\log \varepsilon) = 308$ (4.56), 276 (4.02) nm; IR (KBr): $\nu_{max} = 3310$, 1690 cm^{-1}; ^1H NMR (250 MHz, $CDCl_3$, *TMS*): $\delta = 2.18$ (s, 6H), 3.76 (s, 2H), 5.02 (s, 1H, D_2O exchangable), 6.60 (s, 2H, 12-H, 14-H), 7.24 – 7.52 (m, 5H), ppm; MS: $m/z = 280$ (M^+); $C_{18}H_{16}O_3$; calc: C 77.14, H 5.71%; found: C 77.38, H 5.42%.

4h: 67%, m.p.: 156°C; UV (EtOH): $\lambda_{max}(\log \varepsilon) = 312$ (4.68), 278 (3.84) nm; IR (KBr): $\nu_{max} = 3300$, 1700 cm^{-1}; ^1H NMR (250 MHz, $CDCl_3$, *TMS*): $\delta = 2.16$ (s, 3H), 2.20 (s, 3H), 2.76 (s, 2H), 5.00 (s, 1H, D_2O exchangable), 6.67 (s, 1H, 12-H), 6.90 (s, 1H, 15-H), 6.98 (m, 1H), 7.15 – 7.43 (m, 4H), ppm; MS: $m/z = 280$ (M^+); $C_{18}H_{16}O_3$; calc: C 77.14, H 5.71%; found: C 76.90, H 6.00%.

4i: 59%, m.p.: 208°C; UV (EtOH): $\lambda_{max}(\log \varepsilon) = 312$ (4.74), 278 (3.82) nm; IR (KBr): $\nu_{max} = 3405$, 1680 cm^{-1}; ^1H NMR (250 MHz, $CDCl_3$, *TMS*): $\delta = 2.12$ (s, 3H), 2.24 (s, 3H) 3.80 (s, 2H), 4.80 (s, 1H, D_2O exchangable), 6.67 (d, $J = 8$ Hz, 1H, 14-H), 6.90 (d, $J = 8$ Hz, 1H, 15-H), 6.95 – 7.00 (m, 1H), 7.14 – 7.45 (m, 4H), ppm; MS: $m/z = 280$ (M^+); $C_{18}H_{16}O_3$; calc: C 77.14, H 5.71%; found: C 77.40, H 5.93%.

4j: 73%, m.p.: 159°C; UV (EtOH): $\lambda_{max}(\log \varepsilon) = 309$ (4.81), 277 (3.77) nm; IR (KBr): $\nu_{max} = 3440$, 1700 cm^{-1}; ^1H NMR (250 MHz, $CDCl_3$, *TMS*): $\delta = 2.22$ (s, 6H), 3.74 (s, 2H), 4.61 (s, 1H, D_2O exchangable), 6.87 (s, 2H), 7.20 – 7.34 (m, 5H), ppm; MS.: $m/z = 280$ (M^+); $C_{18}H_{16}O_3$; C 77.14, H 5.71%; found: C 76.91, H 5.44%.

4k: 56%, m.p.: 174°C; UV (EtOH): $\lambda_{max}(\log \varepsilon) = 312$ (4.75), 278 (3.70) nm; IR (KBr): $\nu_{max} = 3300$, 1700 cm^{-1}; ^1H NMR (250 MHz, $CDCl_3$, *TMS*): $\delta = 2.22$ (s, 6H), 3.74 (s, 2H) 4.61 (s, 1H, D_2O exchangable), 6.87 (s, 2H), 7.20 – 7.34 (m, 5H), ppm; MS.: $m/z = 280$ (M^+); $C_{18}H_{16}O_3$; C 77.14, H 5.71%; found: C 77.37, H 5.50%.

General procedure for the methylation of compounds **4**

A mixture of the appropriate phenolic compound (**4**, 1 mmol), methyl iodide (1.2 mmol), and potassium carbonate (1 g) in dry acetone (20 cm^3) was refluxed for 4 h. The reaction mixture was cooled and filtered, and the solvent was removed from the filtrate. The residual mass was extracted with chloroform, the extract was washed with saturated brine and dried (Na_2SO_4). Removal of solvent gave a crude solid which was purified by column chromatography over silica gel using benzene- *PE* (1:1) as eluent.

5a: 74%; m.p.: 114°C; UV (EtOH): $\lambda_{max}(\log \varepsilon) = 307$ (4.80), 275 (3.67) nm; IR (KBr): $\nu_{max} = 1700, 1520\,cm^{-1}$; ^1H NMR (100 MHz, $CDCl_3$, *TMS*): $\delta = 3.80$ (s, 2H), 3.84 (s, 3H), 6.88 – 7.60 (m, 8H) ppm; MS: $m/z = 300$, 302 (M^+); $C_{17}H_{13}ClO_3$; calc.: C 67.89, H 4.33%; found: C 67.61, H 4.62%.

5b: 80%; m.p.: 148°C; UV (EtOH): $\lambda_{max}(\log \varepsilon) = 308$ (4.78), 280 (3.82) nm; IR (KBr): $\nu_{max} = 1700, 1530\,cm^{-1}$; ^1H NMR (100 MHz, $CDCl_3$, *TMS*): $\delta = 2.12$ (s, 3H), 3.76 (s, 2H), 3.80 (s, 3H), 6.60 – 7.44 (m, 8H) ppm; MS: $m/z = 280$, (M^+); $C_{18}H_{16}O_3$; calc: C 77.14, H 5.71%; found: C 77.40, H 6.00%.

5c: 72%; m.p.: 101°C; UV (EtOH): $\lambda_{max}(\log \varepsilon) = 283$ (4.62), 274 (3.88) nm; IR (KBr): $\nu_{max} = 1700, 1520\,cm^{-1}$; ^1H NMR (100 MHz, $CDCl_3$, *TMS*): $\delta = 3.80$ (brs, 8H), 6.80 – 7.60 (m, 8H) ppm; MS: $m/z = 296$ (M^+); $C_{18}H_{16}O_4$; calc: C 72.97, H 5.40%; found: C 73.18, H 5.12%.

5d: 70%; m.p.: 124°C; UV (EtOH): $\lambda_{max}(\log \varepsilon) = 310$ (4.94), 275 (3.98) nm; IR (KBr): $\nu_{max} = 1700, 1520\,cm^{-1}$; ^1H NMR (100 MHz, $CDCl_3$, *TMS*): $\delta = 3.80$ (s, 3H), 3.94 (s, 2H), 6.80 – 7.56 (m, 8H) ppm; MS: $m/z = 291$ (M^+); $C_{18}H_{13}NO_3$; calc: C 74.23, H 4.47, N 4.81%; found: C 74.00, H 4.29, N 4.93%.

5m: 78%; m.p.: 141°C; UV (EtOH): $\lambda_{max}(\log \varepsilon) = 309$ (4.80), 280 (3.86) nm; IR (KBr): $\nu_{max} = 1710\,cm^{-1}$; ^1H NMR (100 MHz, $CDCl_3$, *TMS*): $\delta = 3.80$ (s, 2H), 3.88 (s, 3H), 6.86 – 7.60 (m, 8H) ppm; MS: $m/z = 300$, 302 (M^+); $C_{17}H_{13}ClO_3$; calc: C 67.89, H 4.33%; found; C 67.72, H 4.18%.

5n: 74%; m.p.: 130°C; UV (EtOH): $\lambda_{max}(\log \varepsilon) = 313$ (4.72), 275 (3.76) nm; IR (KBr): $\nu_{max} = 1700\,cm^{-1}$; ^1H NMR (100 MHz, $CDCl_3$, *TMS*): $\delta = 3.79$ (s, 2H), 3.88 (s, 3H), 6.80 – 7.50 (m, 8H) ppm; MS: $m/z = 300$, 302 (M^+); $C_{17}H_{13}ClO_3$; C 67.89, H 4.33%; found; C 67.59, H 4.04%.

5o: 66%; m.p.: 120°C; UV (EtOH): $\lambda_{max}(\log \varepsilon) = 308$ (4.82), 277 (3.94) nm; IR (KBr): $\nu_{max} = 1720\,cm^{-1}$; ^1H NMR (100 MHz, $CDCl_3$, *TMS*): $\delta = 3.72$ (s, 2H), 3.80 (s, 3H), 7.16 – 7.60 (m, 9H) ppm; MS: $m/z = 266$, (M^+); $C_{17}H_{14}O_3$; C 76.99, H 5.26%; found; C 76.67, H 5.56%.

Preparation of acetate derivatives of compounds **4g–k**

A mixture of phenolic compound (**4**, 0.2 g), anhydrous sodium acetate (0.2 g), and freshly distilled acetic anhydride (2 cm^3) was heated on a water bath for 6 h and left overnight. The reaction mixture was poured into ice-water, extracted with chloroform, and the extract was washed successively wih 5% aqueous sodium bicarbonate and saturated brine and dried (Na_2SO_4). Removal of solvent gave a crude mass which was then purified by column chromatography over silica gel. Elution of the column with benzene-*PE* (1:1) furnished the desired acetate derivatives **6g–k**.

6g: 82%; m.p.: 178°C; UV (EtOH): $\lambda_{max}(\log \varepsilon) = 309$ (4.22), 275 (3.98), 238 (3.66) nm; IR (KBr): $\nu_{max} = 1765, 1700\,cm^{-1}$; ^1H NMR (100 MHz, $CDCl_3$, *TMS*) $\delta = 2.16$ (s, 6H), 2.24 (s, 3H), 3.80 (s, 2H), 6.80–6.92 (m, 3H), 7.20–7.60 (m, 4H) ppm; MS: $m/z = 322$ (M^+); $C_{20}H_{18}O_4$; calcd.: C 74.53, H 5.59%; found: C 74.77, H 5.76%.

6h: 86%; m.p.: 108°C; UV (EtOH): $\lambda_{max}(\log \varepsilon) = 310$ (4.12), 277 (3.96), 240 (3.62) nm; IR (KBr): $\nu_{max} = 1735, 1720\,cm^{-1}$; ^1H NMR (100 MHz, $CDCl_3$, *TMS*): $\delta = 2.12$ (s, 3H), 2.18 (s, 3H), 2.36 (s, 3H), 3.80 (s, 2H), 6.82 – 7.66 (m, 7H) ppm; MS: $m/z = 322$ (M^+); $C_{20}H_{18}O_4$; calc.: C 74.53, H 5.59%; found: C 74.31, H 5.88%.

6i: 88%; m.p.: 110°C; UV (EtOH): $\lambda_{max}(\log\varepsilon) = 312$ (4.20), 274 (3.82), 240 (3.58) nm; IR (KBr): $\nu_{max} = 1755, 1700\,cm^{-1}$; ^1H NMR (100 MHz, $CDCl_3$, *TMS*): $\delta = 2.21$ (s, 3H), 2.24 (s, 3H), 2.36 (s, 3H), 3.84 (s, 2H), 7.00 – 7.66 (m, 7H) ppm; MS: $m/z = 322$ (M^+); $C_{20}H_{18}O_4$; calc.: C 74.53, H 5.59%; found: C 74.81, H 5.73%.

6j: 85%; m.p.: 136°C; UV (EtOH): $\lambda_{max}(\log\varepsilon) = 311$ (4.10), 276 (3.88), 241 (3.56) nm; IR (KBr): $\nu_{max} = 1745, 1705\,cm^{-1}$; ^1H NMR (100 MHz, $CDCl_3$, *TMS*): $\delta = 2.20$ (s, 6H), 2.30 (s, 3H), 3.90 (s, 2H), 6.80 – 6.90 (m, 3H), 7.20 – 7.50 (m, 4H) ppm; MS: $m/z = 322$ (M^+); $C_{20}H_{18}O_4$; C 74.53, H 5.59%; found: C 74.72, H 5.29%.

6k: 85%; m.p.: 134°C; UV (EtOH): $\lambda_{max}(\log\varepsilon) = 315$ (4.20), 278 (4.02), 241 (3.82) nm; IR (KBr): $\nu_{max} = 1750, 1700\,cm^{-1}$; ^1H NMR (100 MHz, $CDCl_3$, *TMS*): $\delta = 2.12$ (s, 3H), 2.20 – 2.28 (brs, 6H), 3.76 (s, 2H), 6.90 – 7.56 (m, 7H) ppm; MS: $m/z = 322$ (M^+); $C_{20}H_{18}O_4$; calc: C 74.53, H 5.59%; found: C 74.72, H 5.74%.

Rearrangement of **3a-l** *in quinoline*

Compound **3** (0.4 g) were refluxed in quinoline (5 cm^3) for 5 h. The reaction mixture was cooled and poured into ice-cold 6 *N* HCl (5 cm^3). The crude mass was extracted with chloroform (20 cm^3), and the extract was successively washed with dilute HCl, brine, and water and then dried (Na_2SO_4). The solvent was removed and the crude mass was purified by column chromatography over silica gel using benzene as eluent to furnish **4a–e** and **4g–k**. **3c** gave a mixture of **7** and **4c**, **3f** and **3l** decomposed upon heating.

7: 52%; m.p.: 166° C; UV (EtOH): $\lambda_{max}(\log\varepsilon) = 308$ (4.50), 277 (4.01) nm; IR (KBr): $\nu_{max} = 3430, 1700\,cm^{-1}$; ^1H NMR (100 MHz, $CDCl_3$, *TMS*): $\delta = 2.02$ (s, 3H), 3.66 (s, 3H), 5.02 (s, 1H, D_2O exchangable), 6.46 (d, $J = 2.5$ Hz, 1H), 6.92 – 7.45 (m, 6H) ppm; MS: $m/z = 282$ (M^+); $C_{17}H_{14}O_4$; C 72.34, H 4.96%; found: C 72.07, H 4.81%.

General procedure for the benzylic oxidation of **5a–d** and **5m–o**

A mixture of compound **5** (0.1 g, 0.3 mmol) and *NBS* (0.06 g, 0.3 mmol) was refluxed in CCl_4 for 4 h. The reaction mixture was filtered, and the filtrate was washed with brine and dried (Na_2SO_4). The solvent was removed and the residual mass was purified by column chromatography over silica gel using benzene-*PE* (1:1) as eluent.

8a: 63% m.p.: 130°C; UV (EtOH): $\lambda_{max}(\log\varepsilon) = 290$ (4.50), 213 (5.16) nm; IR (KBr): $\nu_{max} = 1700, 1640\,cm^{-1}$; ^1H NMR (100 MHz, $CDCl_3$, *TMS*): $\delta = 4.00$ (s, 3H), 6.90 – 8.20 (m, 8H) ppm; MS: $m/z = 314, 316$ (M^+); $C_{17}H_{11}ClO_4$; calc.: C 64.86, H 3.50%; found: C 64.64, H 3.42%.

8m: 66% m.p.: 185°C; UV (EtOH): $\lambda_{max}(\log\varepsilon) = 290$ (4.58), 213 (5.12) nm; IR (KBr): $\nu_{max} = 1700, 1640\,cm^{-1}$; ^1H NMR (100 MHz, $CDCl_3$, *TMS*): $\delta = 4.00$ (s, 3H), 6.96 – 8.08 (m, 8H) ppm; MS: $m/z = 314, 316$ (M^+); $C_{17}H_{11}ClO_4$; calc.: C 64.86, H 3.50%; found: C 64.81, H 3.68%.

8n: 60% m.p.: 142°C; UV (EtOH): $\lambda_{max}(\log\varepsilon) = 290$ (4.62), 213 (5.12) nm; IR (KBr): $\nu_{max} = 1700, 1640\,cm^{-1}$; ^1H NMR (100 MHz, $CDCl_3$, *TMS*): $\delta = 4.00$ (s, 3H), 6.80 – 8.20 (m, 8H) ppm; MS: $m/z = 314, 316$ (M^+); $C_{17}H_{11}ClO_4$; calc.: C 64.86, H 3.50%; found: C 64.83, H 3.42%.

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