

SYNTHESIS OF 2-AROYLMETHYLQUINOLIN-4-ONES VIA THE ADDITION REACTION OF *ORTHO*-NITROBENZOYLKETENE TO 1-ARYL-1-TRIMETHYLSILYLOXYETHYLENES

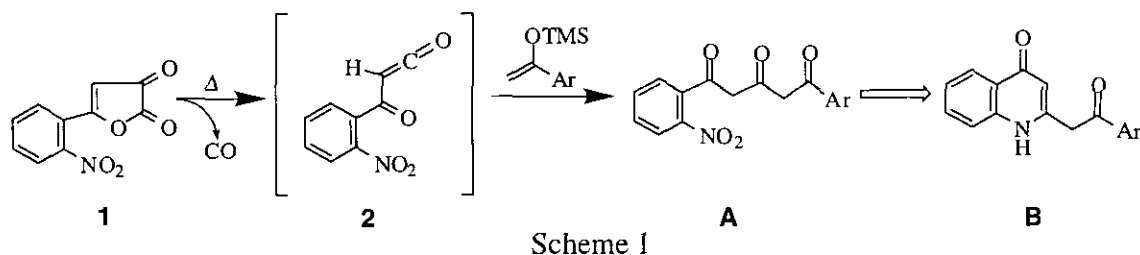
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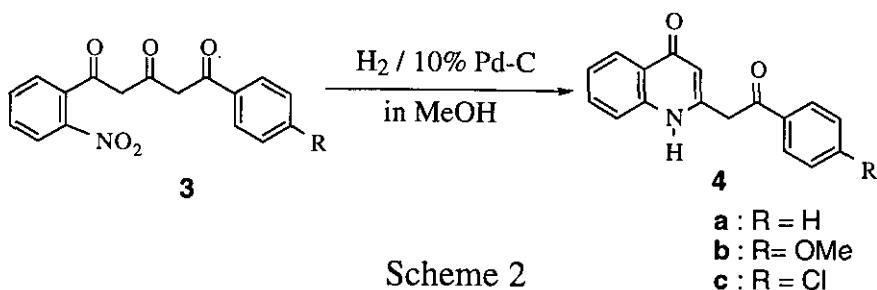
Abstracts—Catalytic hydrogenation of 1-aryl-5-(2-nitrophenyl)pentane-1,3,5-triones **A** over 10% Pd-C caused selective reduction of the nitro group with concomitant cyclization to give 2-aroilmethylquinolin-4-ones **B**. This provides a simple method of quinolin-4-one synthesis.

Recently, we have reported that aroylketene generated from 5-aryl-2,3-dihydrofuran-2,3-dione (dioxofuran) reacted with 1-aryl-1-trimethylsilyloxyethylenes to give various 1,5-diarylpentane-1,3,5-triones and 2,6-diaryl-4*H*-pyran-4-ones.¹ The aroylketene also reacted with cyclic enol ethers to give analogous compounds.² In these papers we demonstrated that introduction of electron withdrawing substituents into the aromatic part of the aroylketene enhanced ketene reactivity for the addition reaction.

In this paper we show that 1-aryl-5-(2-nitrophenyl)pentane-1,3,5-triones **A** obtained by the addition reaction of 2-nitrobenzoylketene (**2**) to 1-aryl-1-trimethylsilyloxyethylenes^{1,2} can be converted into 2-aroilmethyl-4-quinolones **B** which provides a simple method of quinolin-4-one synthesis.

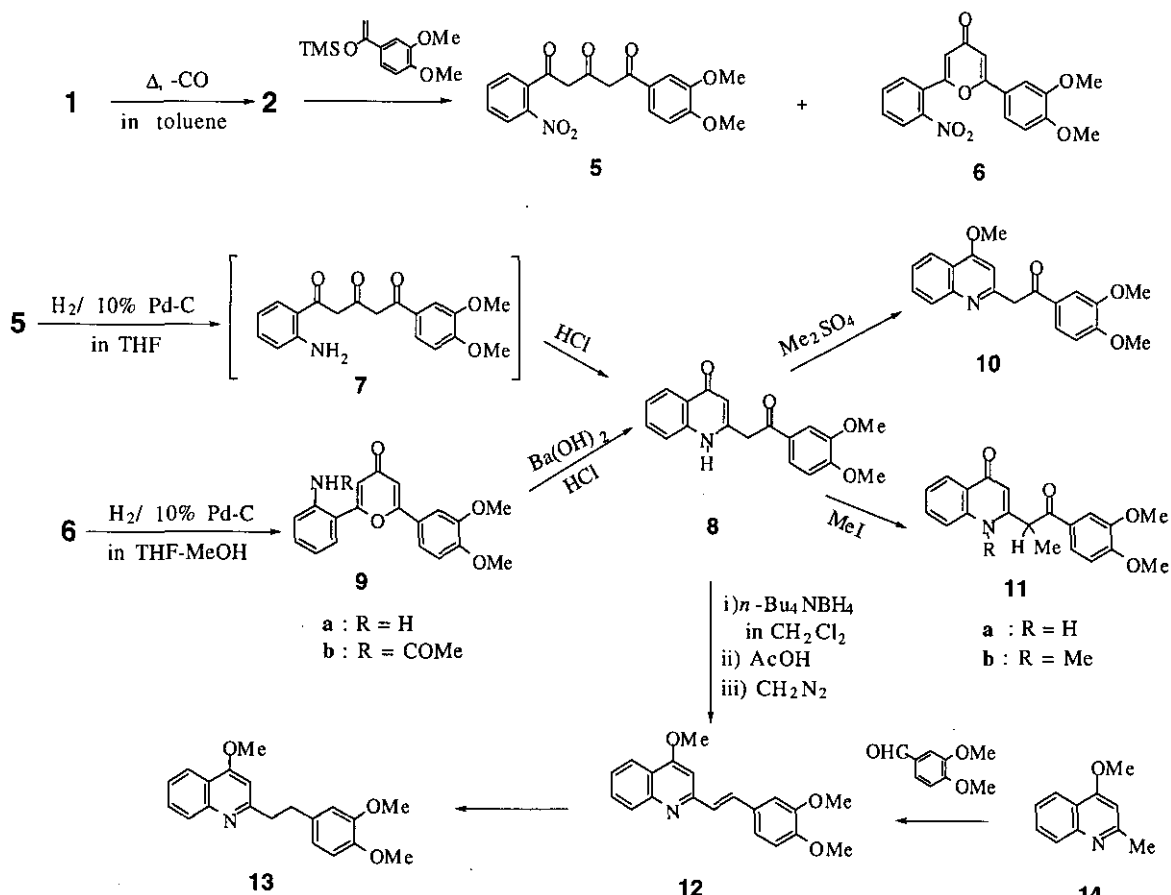


When the triones (**3a-c**)¹ were subjected to catalytic hydrogenation over 10% Pd-C, the nitro group was selectively reduced with concomitant ring formation to give 2-aroilmethylquinolin-4-ones (**4a**) in 37%, (**4b**) in 41%, and (**4c**) in 94% yields, respectively. Although the products were characterized by MS, IR, and UV spectra, their NMR spectral data were not obtained because of their insolubility for organic solvents, thus preventing the full structural assignment. The low yields observed in the cases of **3a** and **3b** seemed to be attributable to the extreme insolubility which makes difficult to elute the products (**4a** and **4b**) from the catalyst.



Scheme 2

In order to prove chemically the structures of the quinolin-4-ones, we carried out a synthesis of galipin (13), a quinoline alkaloid from *Galipea longiflora krause*.^{3,4} *o*-Nitrobenzoylketene (2) generated *in situ* by pyrolysis of the dioxofuran (1) at 100 °C in toluene reacted with 1-(3,4-dimethoxyphenyl)-1-trimethylsilyloxyethylene to give a triketone (5) in 59% yield and a pyrone (6) in 21% yield. Catalytic hydrogenation of 5 over 10% Pd-C gave an amine (7) in 53% yield and a quinolone (8) in 45% yield. The amine (7) seemed to be an uncyclized anilino derivative shown by its MS spectrum. In fact, treatment of 7 with 10% hydrochloric acid at room temperature slowly caused cyclization to give 8 in 30% yield (recovery of 7; 65%). The structural evidences of 8 were obtained by the spectral data of its methyl derivatives.



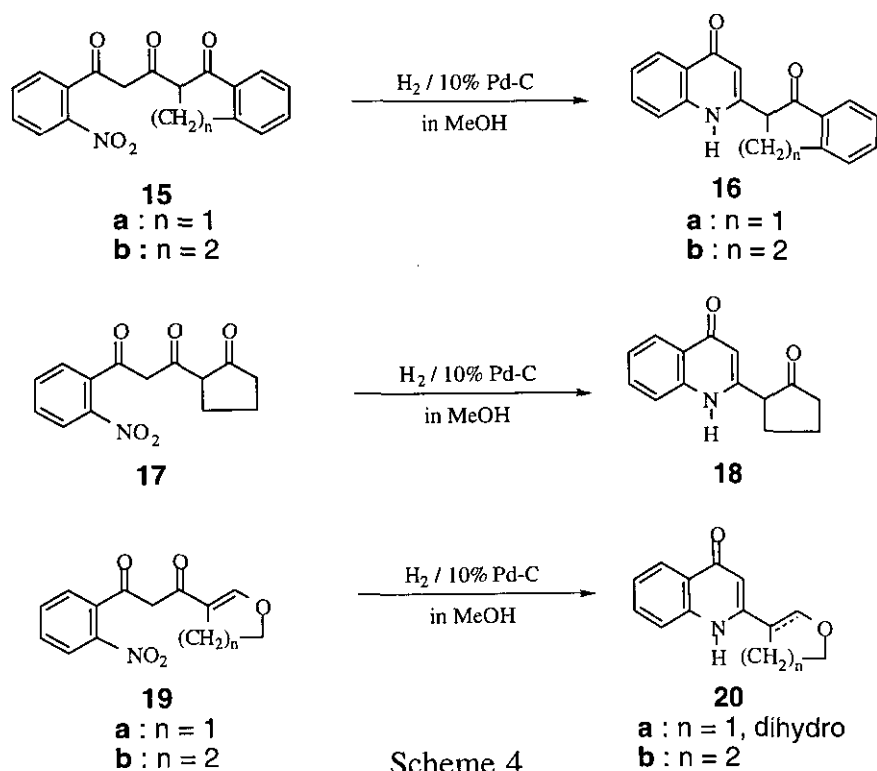
Scheme 3

Methylation of **8** with dimethyl sulfate and 1% KOH gave *O*-methyl derivative (**10**), with methyl iodide and K_2CO_3 in DMF gave *C*-monomethyl (**11a**) and *C,N*-dimethyl derivatives (**11b**). The 1H -NMR spectra of **10**, and **11a, b** (see Experimental) were well consistent with the assigned 2-arylmethylquinolin-4-one structure. The structure was also supported by the ^{13}C -NMR spectra which clearly revealed the presence of a ketone carbonyl group (191.9 for **10** and 197.7 ppm for **11a**) and of a lactam (178.9 ppm for **11a**).

The pyrone (**6**), a minor product of the ketene addition reaction, was also converted to the quinolone (**8**) as follows. The nitro group of **6** was similarly hydrogenated with 10% Pd-C to give the aniline (**9a**) in 96% yield, which was fully characterized as the acetamide (**9b**). Hydrolysis of **9a** with barium hydroxide in methanol under reflux for 5.5 h followed by treatment with hydrochloric acid, gave **8** in 44% yield.

The conversion of **8** into galipin (**13**), on the contrary of our expectation, was fairly difficult. For examples, on Clemmensen reduction or Wolff-Kishner reduction, **8** extensively decomposed to give no characterizable products. Furthermore, reduction of **8** with sodium borohydride in ethanol or with lithium aluminum hydride in tetrahydrofuran was failed because of its insolubility for these solvents. However, we found that reduction of **8** with tetra-*n*-butylammonium borohydride in dichloromethane followed by dehydration of the resulting crude alcohol with acetic acid and by *O*-methylation with diazomethane gave the 4-methoxyquinoline **12** (total yield from **8**: 14%). Catalytic hydrogenation of **12** over 10% Pd-C gave galipin (**13**) in quantitative yield. Structures of **12** and **13** were confirmed by direct comparison with the samples prepared from 4-methoxy-2-methylquinoline (**14**) by the known method which was applied for synthesis of galipin⁴ and of its methylenedioxy analog (*cusparin*).⁵

From our biological interests, several analogous quinolones were prepared. 2-Indanoyl- (**16a**), 2-tetraoyl-



Scheme 4

(**16b**), and 2-cyclopentanoylquinolin-4-ones (**18**) were readily obtained by similar catalytic hydrogenation of the corresponding triketones (**15a-b**) and (**17**)² in yields of 99%, 35%, and 61%, respectively. As further examples, we applied the similar catalytic reduction for the diketofuryl- (**19a**) and the diketopyranyl (**19b**) derivatives² to give 2-tetrahydrofuryl- (**20a**) and 2-dihydropyranylquinolin-4-ones (**20b**) in yields of 88% and 98%, respectively. In the case of **20a**, the double bond of dihydrofuran ring was concomitantly reduced.

EXPERIMENTAL

Unless otherwise stated, following procedure were adopted. Melting points (mp) were determined with YANACO MP-S1 melting point apparatus and are uncorrected. IR spectra were measured with JASCO FT/IR-5000 Fourier transform infrared spectrometer using KBr and are given as cm^{-1} . UV spectra were recorded on Hitachi U-3200 spectrophotometer, and are given as nm (e). ¹H-NMR and ¹³C-NMR spectra were obtained with a JEOL JNM-EX90 (¹H; 90 MHz), ¹³C; 22.5 MHz) in CDCl₃ using tetramethylsilane as an internal standard. HRMS and LRMS spectra were obtained on JEOL JMS-D300 or JMS-HX110A spectrometer at 30 eV by the direct inlet system. CIMS was measured with JMS-D300 spectrometer at 150 eV by direct inlet system. Elemental analysis were recorded on YANACO CHN-corder MT-3.

Catalytic Hydrogenation of **3a-c**, **15a-b**, **17**, and **19a-b** over Pd-C.

The ketones (**3c**) (20 mg, 0.064 mmol), **15a** (100 mg, 0.31 mmol), **15b** (100 mg, 0.30 mmol), **17** (100 mg, 0.36 mmol), **19a** (100 mg, 0.38 mmol), and **19b** (124 mg, 0.45 mmol) in MeOH (each 50 mL), and **3a** (500 mg, 1.60 mmol) in MeOH-THF (1:1) (80 mL) and **3b** (20 mg, 0.059 mmol) in THF (50 mL) were hydrogenated for 3-5 h over 10% Pd-C (10-20 w/w % of the ketone) at rt under atmospheric pressure. The products were obtained by either following procedure. i) The reaction mixture was filtrated and the residual catalyst was washed with the solvents used. The combined filtrate was concentrated to dryness to give the crystalline residue which was recrystallized from CHCl₃-MeOH to give the quinolin-4-ones **4a** (158 mg, 37%), **4c** (16 mg, 94%), **16a** (85mg, 99.8%), **18** (56 mg, 61%), **20a** (72 mg, 88%), and **20b** (110 mg, 99%). ii) The reaction mixture obtained from **3b** or **15b** was diluted with 10% NaOH solution (20 mL) and then after removal of the catalyst by filtration, the filtrate was acidified with 10% HCl and extracted with CH₂Cl₂. The products were recrystallized with CHCl₃-MeOH to give the quinolin-4-ones **4b** (7 mg, 41%) or, **16b** (30 mg, 35%).

2-(2-Oxo-2-phenylethyl)quinolin-4-one (**4a**): colorless needles, mp 200 °C (decomp). IR: 1688, 1601. UV: 245 (10900), 254 (10200), 316 (6700), 402 (3900). ¹H-NMR (CDCl₃-CD₃OD=1:10): 6.48 (1H, s), 7.4-7.9 (5H, m), 8.0-8.2 (3H, m), 8.30 (1H, dd, *J*=2, 8 Hz). ¹³C-NMR(CDCl₃-CD₃OD=1:10, enol form): 115.7 (d), 123.6 (s), 124.3 (d), 125.0 (d), 125.1 (d), 127.9(dx2), 128.1 (d), 128.5 (dx2), 131.9 (s), 132.0 (d), 133.4 (d)135.7 (s), 140.1 (s), 147.2 (s), 181.5 (s). LRMS *m/z*: 263 (M⁺).

2-(2-(4-Methoxyphenyl)-2-oxoethyl)quinolin-4-one (**4b**): colorless needles, mp 250-253 °C. IR: 1673, 1636, 1599, 1549, 1508. UV: 250 (10400), 277 (14500), 320 (7300), 331 (8000), 417 (2200), 439 (1700). CIMS *m/z*: 294 (MH⁺).

2-(2-(4-Chlorophenyl)-2-oxoethyl)quinolin-4-one (**4c**): colorless needles, mp 253 °C (decomp). IR: 1684, 1593. UV: 319 (2900), 414 (1800). CIMS *m/z*: 298 (MH⁺).

2-(2,3-Dihydroinden-1-on-2-yl)quinolin-4-one (**16a**): colorless needles, mp 150-152 °C. IR: 1658, 1605, 1549. UV: 230 (4700), 327 (3700), 365 (1500), 438 (3300). CIMS m/z : 276 (MH⁺).

2-(2,3-Dihydro-1-(2*H*)-naphthalenon-2-yl)quinolin-4-one (**16b**): colorless needles, mp 216-219 °C. IR: 1682, 1599, 1551. UV: 247 (20300), 254 (21100), 326 (9200), 342 (7900), 389 (4000). CIMS m/z : 290 (MH⁺).

2-(Cyclopentanon-2-yl)quinoline (**18**): colorless needles, mp 128-130 °C. IR: 1740, 1638, 1601, 1564, 1551. UV: 213 (25100), 241 (10900), 256 (8700), 309 (5400), 333 (5000), 343 (5000). CIMS m/z : 228 (MH⁺).

2-(2,3,4,5-Tetrahydrofuran-3-yl)quinolin-4-one (**20a**): colorless needles, mp 179-181 °C. IR: 1638, 1597, 1547, 1508. UV: 240 (12200), 286 (2100), 318 (6100), 330 (6800). ¹H-NMR: 2.0-2.7 (3H, m), 3.5-4.2 (4H, m), 6.34 (1H, s), 7.3-7.8 (3H, m), 8.34 (1H, dd, $J = 1, 8$ Hz). ¹³C-NMR: 32.7 (t), 43.1 (d), 67.9 (t), 72.7 (t), 107.2 (d), 118.1 (d), 123.8 (d), 125.2 (s), 125.6 (d), 132.1 (d), 140.2 (s), 154.4 (s), 179.0 (s). HRMS m/z (M⁺): Calcd for C₁₃H₁₃NO₂: 215.0944, Found: 215.0931.

2-(3,4-Dihydro-2*H*-pyran-5-yl)quinolin-4-one (**20b**): colorless needles, mp 288-290 °C. IR: 1638, 1593, 1535. UV: 241 (12300), 269 (16300), 305 (7700), 331 (9000). ¹H-NMR: 2.01 (2H, quintet, $J = 6$ Hz), 2.39 (2H, t, $J = 6$ Hz), 4.09 (2H, t, $J = 6$ Hz), 6.21 (1H, d, $J = 3$ Hz), 7.2-7.4 (2H, m), 7.33 (1H, s), 7.5-7.6 (2H, m), 8.22 (1H, dt, $J = 1, 8$ Hz). ¹³C-NMR: 19.8 (t), 20.6 (t), 65.3 (t), 103.8 (d), 106.9 (s), 116.9 (d), 122.6 (d), 123.5 (s), 124.1 (d), 131.0 (d), 139.2 (s), 149.8 (d), 153.4 (s), 178.0 (s). HRMS m/z (M⁺): Calcd for C₁₄H₁₃NO₂: 227.0947, Found: 227.0949.

Addition Reaction of **2** to 1-(3,4-Dimethoxyphenyl)-1-trimethylsilyloxyethylene

The dioxofuran (**1**, 10 g, 45.7 mmol) and the olefin (23 g, 91.4 mmol) in toluene (500 mL) was heated at 100 °C under stirring for 1 h under argon atmosphere. After evaporation of the solvent *in vacuo*, the residue was crystallized from CH₂Cl₂-Et₂O to give **5** (10 g, 59%). The mother liquor was subjected to flash chromatography over silica gel. Elution with AcOEt-hexane (1:1) and recrystallization from CH₂Cl₂-Et₂O gave **6** (3.3 g, 21%).

1-(3,4-Dimethoxyphenyl)-5-(2-nitrophenyl)pentane-1,3,5-trione (**5**): orange plates, mp 113-115 °C. IR: 1572, 1520. UV: 391 (17000). *Anal.* Calcd for C₁₉H₁₇NO₇: C, 61.45; H, 4.64; N, 3.77, Found C, 4.64; H, 61.30; N, 3.94.

2-(3,4-Dimethoxyphenyl)-6-(2-nitrophenyl)-4*H*-pyran-4-one (**6**): pale yellow needles, mp 172-175 °C. IR: 1659, 1613, 1599, 1526. UV: 212 (29600), 227 (28100), 269 (17400), 309 (17200). ¹H-NMR: 3.93 (3H, s), 3.95 (3H, s), 6.64 (1H, d, $J = 2$ Hz), 6.74 (1H, d, $J = 2$ Hz), 6.9-7.3 (3H, m), 7.6-8.1 (4H, m). ¹³C-NMR: 56.0 (qx2), 108.4 (d), 109.7 (d), 111.3 (d), 113.9 (d), 116.6 (s), 117.0 (d), 118.4 (d), 119.3 (d), 123.7 (s), 129.3 (d), 132.0 (d), 144.9 (s), 149.4 (s), 151.9 (s), 163.8 (s), 164.0 (s), 180.1 (s). HRMS m/z (M⁺): Calcd for C₁₉H₁₅NO₆: 353.0924, Found: 353.0899.

Catalytic Hydrogenation of the Nitro Group of **5** over Pd-C

A solution of triketone (**5**) (500 mg, 1.35 mmol) in dry THF (200 mL) was hydrogenated over 10% Pd-C (50 mg) for 5 h under atmospheric pressure. The reaction mixture was diluted with 10% NaOH, and after removal of the catalyst by filtration the filtrate was acidified with 10% HCl. The resulting precipitates were collected by filtration and recrystallization from CHCl₃-MeOH gave **7** (243 mg, 53%). The filtrate was ex-

tracted with CH_2Cl_2 . The organic layer was concentrated *in vacuo* and purified by recrystallizations from CHCl_3 -MeOH to give **8** (195 mg, 45%).

1-(2-Aminophenyl)-5-(3,4-dimethoxyphenyl)pentane-1,3,5-trione (**7**): colorless prisms, mp 265-267 °C. IR: 1669, 1599, 1518. CIMS m/z : 341 (M^+).

2-[2-(3,4-Dimethoxyphenyl)-2-oxoethyl]quinolin-4-one (**8**): colorless prisms, mp 278-280 °C. IR: 1669, 1640, 1599, 1553, 1510. UV: 232 (21400), 278 (9600), 317 (10700), 419 (2200). $^1\text{H-NMR}$ (CDCl_3 - CD_3OD): 3.95 (3H, s), 3.98 (3H, s), 4.26 (2H, s), 6.25 (1H, s), 6.94 (1H, d, $J=8$ Hz), 7.3-7.4 (2H, m), 7.55 (1H, d, $J=2$ Hz), 7.6 (1H, m), 7.71 (1H, dd, $J=2, 8$ Hz), 8.33 (1H, dd, $J=1, 8$ Hz), 9.74 (1H, br s). LRMS m/z : 323 (M^+).

Acid Catalyzed Cyclization of **7** to **8**

A suspension of **7** (100 mg, 0.29 mmol) in 10% HCl (30 mL) was stirred vigorously at rt for 22 h, and after removal of the unreacted starting material by filtration (65 mg, 65 %), the filtrate was extracted with CH_2Cl_2 . The extract was dried over Na_2SO_4 and evaporated *in vacuo* to give a crystalline residue. Recrystallization from CHCl_3 -MeOH gave **8** (28 mg, 30%), which was identical with that obtained from the above reaction by comparison of its IR spectrum.

Catalytic Hydrogenation of the Nitro Group of **6** over Pd-C

A solution of pyrone (**6**) (100 mg, 0.28 mmol) in MeOH (50 mL) was hydrogenated over 10% Pd-C as described above to give 2-(2-aminophenyl)-6-(3,4-dimethoxyphenyl)-4H-pyran-4-one (**9a**) (88 mg, 96%): colorless needles from CH_2Cl_2 - Et_2O , mp 190 °C. IR: 1644, 1601, 1516. UV: 227 (35300), 313 (20900). $^1\text{H-NMR}$: 3.43 (3H, s), 3.95 (3H, s), 4.31 (2H, br s), 6.63 (1H, d, $J=2$ Hz), 6.73 (1H, d, $J=2$ Hz), 6.8-6.9 (3H, m), 7.2-7.5 (4H, m). $^{13}\text{C-NMR}$: 56.1 (q), 108.4 (d), 109.9 (d), 111.3 (d), 114.1 (d), 116.7 (s), 117.1 (d), 118.7 (d), 119.4 (d), 123.8 (d), 129.5 (d), 132.1 (d), 144.9 (s), 149.4 (s), 151.9 (s), 163.5 (s), 164.1 (s), 180.2 (s). HRMS m/z (M^+): Calcd for $\text{C}_{19}\text{H}_{17}\text{NO}_4$: 323.1158, Found: 323.1194.

Acetylation of **9a** (200 mg, 0.62 mmol) with acetic anhydride (2 mL) and pyridine (4 mL) as usual manner gave the acetate, 2-(acetylamino-phenyl)-6-(3,4-dimethoxyphenyl)-4H-pyran-4-one (**9b**) (183 mg, 81%): colorless needles CH_2Cl_2 - Et_2O , mp 152-154 °C. UV: 230 (30000), 264 (18400), 314 (18000). $^1\text{H-NMR}$: 2.07 (3H, s), 3.82 (3H, s), 3.89 (3H, s), 6.40, 6.56 (each 1H, d, $J=2$ Hz), 6.9-8.0 (7H, m), 8.67 (1H, br s). CIMS m/z : 366 (MH^+).

Conversion of Pyrone (**9a**) into Quinolone (**8**)

A solution of **9a** (500 mg, 1.42 mmol) in combination solvent MeOH (60 mL) and saturated $\text{Ba}(\text{OH})_2$ solution (60 mL) was refluxed for 5.5 h under argon atmosphere. After acidification with 10% HCl, extraction of the mixture with CH_2Cl_2 and recrystallization of the extract from CHCl_3 gave **8** (219 mg, 44%).

Methylation of **8** with Dimethyl Sulfate

Dimethyl sulfate (0.2 mL) was slowly added to a 1% KOH aqueous solution (50 mL) of **8** (500 mg, 1.55 mmol) at rt and the whole was stirred for 5.5 h. The reaction mixture was extracted with CH_2Cl_2 , dried over Na_2SO_4 , and evaporated *in vacuo* to dryness. The residue was recrystallized from CH_2Cl_2 -ether to give 2-(3,4-dimethoxybenzoylmethyl)-4-methoxyquinoline (**10**), colorless needles, mp 150-153 °C. IR: 1678, 1622, 1601, 1562, 1516. $^1\text{H-NMR}$: 3.94 (3H, s), 3.97 (3H, s), 4.02 (3H, s), 4.40 (2H, s), 6.12 (1H, s), 6.93 (1H, d, $J=8$ Hz), 7.3-7.8 (5H, m), 8.3-8.4 (1H, m). $^{13}\text{C-NMR}$: 40.8 (t), 56.0 (q), 56.2 (q), 64.7 (q),

110.2 (d), 110.3 (d), 110.9 (d), 113.4 (d), 123.2 (d), 124.1 (d), 126.0 (s), 126.9 (d), 129.0 (s), 132.6 (d), 138.1 (s), 146.3 (s), 149.4 (s), 154.1 (s), 176.9 (s), 191.9 (s). CIMS m/z : 338 (MH⁺).

Methylation of **8** with Methyl Iodide

A mixture of **8** (400 mg, 1.24 mmol), K₂CO₃ (205 mg, 1.49 mmol) and methyl iodide (2.1 g, 12.4 mmol) in DMF (50 mL) was stirred for 3 h at rt. The product was purified by MPLC (elution with 5% MeOH-CH₂Cl₂) and by PTLC (developed by CH₂Cl₂-5%MeOH) to give **11a** (38 mg, 9%) and **11b** (25 mg, 6%).

2-[1-(3,4-Dimethoxybenzoyl)ethyl]quinolin-4-one (**11a**): colorless gum. IR: 1676, 1634, 1595, 1551, 1506. UV: 234 (26000), 280 (11200), 317 (13700). ¹H-NMR: 1.63 (3H, d, $J=7$ Hz), 3.88 (3H, s), 3.90 (3H, s), 4.83 (1H, q, $J=7$ Hz), 6.31 (1H, s), 6.80 (1H, d, $J=9$ Hz), 7.2-7.4 (2H, m), 7.5-7.7 (3H, m), 8.32 (1H, d, $J=9$ Hz). ¹³C-NMR: 19.3 (q), 44.2 (d), 56.0 (q), 56.1 (q), 108.5 (d), 110.2 (d), 110.5 (d), 118.2 (d), 123.7 (d), 123.9 (d), 125.1 (s), 125.6 (d), 128.3 (s), 132.1 (d), 140.0 (s), 149.3 (s), 152.4 (s), 154.2 (s), 178.9 (s), 197.7 (s). LRMS m/z : 337 (M⁺).

2-[1-(3,4-Dimethoxybenzoyl)ethyl]-1-methylquinolin-4-one (**11b**): colorless gum. IR: 1676, 1622, 1599, 1562, 1518. UV: 235 (24700), 277 (10400), 316 (10500), 326 (10800), 342 (10000). ¹H-NMR: 1.68 (3H, d, $J=7$ Hz), 3.90 (3H, s), 3.92 (3H, s), 4.09 (3H, s), 4.95 (1H, q, $J=7$ Hz), 6.19 (1H, s), 6.87 (1H, d, $J=9$ Hz), 7.32 (1H, dd, $J=2, 9$ Hz), 7.42 (1H, dd, $J=2, 8$ Hz), 7.5-7.6 (2H, m), 7.75 (1H, dd, $J=2, 9$ Hz), 8.36 (1H, d, $J=9$ Hz). CIMS m/z : 352 (MH⁺).

Conversion of **8** into Dehydrogalipin (**12**)

A suspension of **8** (195 mg, 0.60 mmol) in CH₂Cl₂ (100 mL) was treated with tetra-*n*-butylammonium borohydride (370 mg, 1.44 mmol) at rt for 1 h under argon atmosphere. After decomposition of excess hydride by adding 5% HCl, the mixture was extracted with CH₂Cl₂, then the organic layer was dried over Na₂SO₄, and concentrated *in vacuo* to dryness. The residue (245 mg) in AcOH (30 mL) was refluxed for 1 h. After evaporation of the solvent *in vacuo* to dryness, the residue in CH₂Cl₂ (50 mL) was treated with ethereal solution of dia-zomethane (20 mL) for 17 h at rt. The reaction mixture was concentrated *in vacuo* and then the residue was purified by recrystallization from CH₂Cl₂-Et₂O to give 2-(2-(3,4-dimethoxyphenyl)vinyl)-4-methoxyquino-line (**12**) (27 mg, 14% based on **8**), colorless needles, mp 133-135 °C. IR: 1613, 1591, 1555, 1512. UV: 237 (18200), 258 (16200), 288 (16700), 344 (29000). ¹H-NMR: 3.91 (3H, s), 3.95 (3H, s), 4.11 (3H, s), 7.03 (1H, d, $J=15$ Hz), 7.43 (1H, d, $J=15$ Hz), 6.8-7.8 (6H, m), 8.0-8.2 (2H, m). ¹³C-NMR: 55.3 (q), 55.6 (q), 55.7 (q), 97.2 (d), 108.8 (d), 111.0 (d), 120.4 (s), 121.0 (d), 121.5 (d), 124.8 (d), 127.4 (d), 128.3 (d), 129.3 (d), 129.7 (s), 133.5 (d), 148.9 (s), 149.0 (s), 149.5 (s), 157.1 (s), 162.1 (s).

Synthesis of Galipin (**13**)

A solution of **12** (100 mg, 0.31 mmol)⁵ in MeOH (20 mL) was hydrogenated over 10% Pd-C (10 mg) for 5 h. After removal of the catalyst by filtration, the filtrate was concentrated *in vacuo* to give **13** (100 mg, 99%), color-less needles from CH₂Cl₂-Et₂O, mp 109-112 °C [*lit.*,⁴ mp 113.5 °C]. IR: 1620, 1599, 1564, 1516. UV: 228 (33600), 312 (8300). ¹H-NMR: 3.1-3.2 (4H, m), 3.81 (3H, s), 3.86 (3H, s), 3.97 (3H, s), 6.53 (1H, s), 6.79 (3H, s), 7.47 (1H, ddd, $J=1, 7, 8$ Hz), 7.67 (1H, ddd, $J=1, 7, 8$ Hz), 8.00 (1H, dd, $J=1, 7$ Hz), 8.15 (1H, dd, $J=1, 8$ Hz). ¹³C-NMR: 35.7 (t), 41.9 (t), 55.6 (q), 55.8 (q), 55.9 (q), 100.3 (d), 111.2 (d), 112.0 (d), 120.1 (s), 120.4 (d), 121.6 (d), 124.9 (d), 128.3 (d), 129.8 (d), 134.2 (s), 147.3 (s),

148.8 (sx2), 162.3 (s), 163.0 (s). HRMS m/z (M^+): Calcd for $C_{20}H_{21}NO_3$: 323.1519, Found: 323.1506.

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