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Reactions of 7-Methoxyimino-4-methylchromene-2,8-dione with Phosphines. Preparation of *N*-substituted 7-Amino-8-hydroxy-4-methyl-2*H*-[1]-benzopyran-2-ones.

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Abstract: 7-Methoxyimino-4-methylchromene-2,8-dione **2** reacts with triarylphosphines **1(a-d)** to give the unexpected 7-arylamino-8-hydroxy-4-methyl-2*H*-[1]-benzopyran-2-ones **7(a-d)** and methyl diarylphosphinates **8(a-d)** in high yields. The reaction of **2** with trialkylphosphines **1(e,f)** as well as with diphenylphosphine **15** leads to the formation of the *N*-dialkylphosphinoyl derivatives **11, 12, 14** and the *N*-diphenylphosphinoyl derivative **19**, along with compounds **7(e,f)**. The methylation of compounds **7a, 7f, 11** and **19** is also studied and reaction mechanisms to explain the formation of the products obtained are suggested.

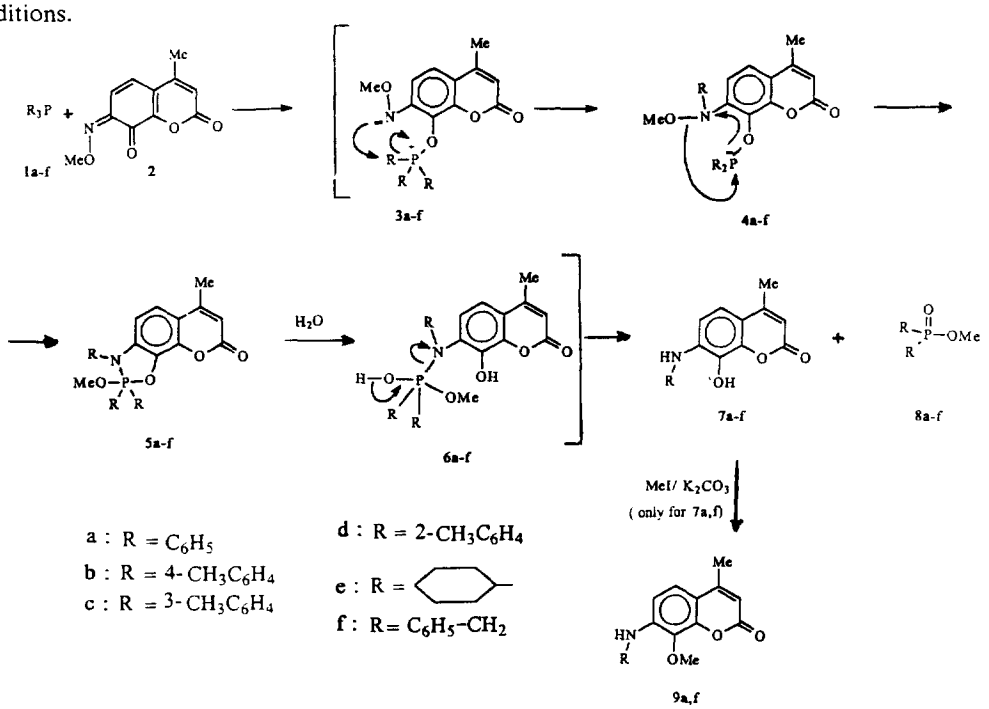
We have recently[1] reported on reactions of 7-methoxyimino-4-methyl-chromene-2,8-dione **2** with several phosphorus ylides, which led mainly into the formation of 2-substituted 6-methyl-8*H*-[1]benzopyrano-[7,8-d]-oxazol-8-ones, instead of the expected Wittig reaction products. In addition to the above products, in almost all the reactions studied we also obtained the unexpected 8-hydroxy-4-methyl-7-(phenylamino)-2*H*-[1]-benzopyran-2-one **7a** (6-15% yield). In a preliminary control experiment we found that compound **7a** is formed from the reaction of **2** with triphenylphosphine **1a**, generated *in situ* during the synthesis of the above benzopyranoxazoles. This result prompted us to study systematically the reaction of **2** with a variety of phosphines in order to prepare *N*-substituted 7-amino-8-hydroxy coumarin derivatives and to shed more light into the reaction mechanism.

N-(2,4-Dichloro-6-oxo-2,4-cyclohexadien-1-ylidene)-4-nitrobenzamide (an *o*-quinone monoimide) reacts with **1a** to give[2] 2,6-dichloro-2-(4-nitrophenyl)benzoxazole (72%), while 9,10-phenanthrenequinone monoimine or 3,5-di-*tert*-butyl-*o*-benzoquinone in the presence of ammonia undergoes cycloaddition with **1a** to give the corresponding 2,3-dihydro-1,3,2-λ^5-benzoxazaphospholes in good yields.[3] The same phenanthrene monoimine reacts in boiling benzene with trialkyl phosphites to give 2,2,2,3-tetrahydro-2,2,2-trialkoxy-phenanthro[9,10-d]-1,3,2-oxazaphospholes, stable only for a few days.[4]

The work detailed here involves the study of the reactions of compound **2** with triarylphosphines **1a-d**, trialkylphosphines **1e,f** and diphenylphosphine **15,** depicted in Schemes 1-4.

Treatment of monoxime **2** with an equimolar amount of **1a** in boiling dichloromethane for 75 min and separation of the reaction mixture by column chromatography gave compound **7a** and methyl diphenylphosphinate **8a**[5] in 93% and 91% yield respectively. By a similar treatment of compound **2** with tri-*p*-tolylphosphine **1b** or tri-*o*-tolylphosphine **1d,** the corresponding 7-tolylaminocoumarins **7b** (68%) or **7d** (56%) and the methyl ditolylphosphinates **8b**[5] (84%) or **8d**[6] (55%) were respectively obtained. The

reaction of **2** with phosphine **1b** or **1c**, at room temperature for 5 min gave compounds **7b** (85%), **8b** (75%) or **7c** (83%), **8c** (48%) respectively, while phosphine **1d** did not react with **2** under these conditions.



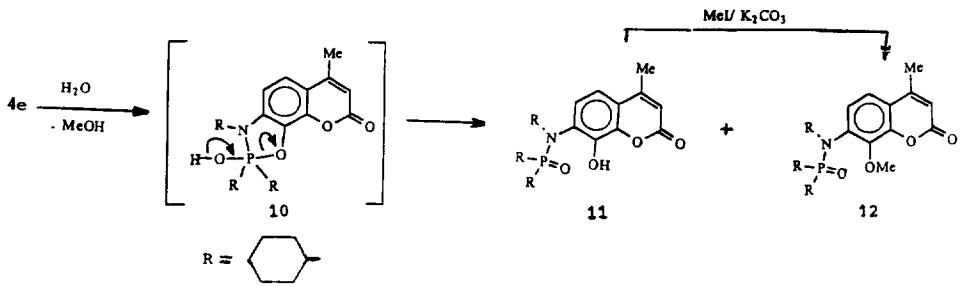
Scheme 1

The analytical and spectral data of the new coumarins **7b-d** and phosphinate **8c** resemble well the structures proposed as well as the spectral data of the known compounds **7a** and **8a,b,d** respectively. Treatment of compound **7a** with an excess of methyl iodide and potassium carbonate in DMF gave the *O*-methyl derivative **9a** in 97% yield. The ^{1}H-NMR spectrum of **9a** exhibits a singlet at δ 4.06 for the methoxy protons, a fact which further supports the *N*-phenyl structure **7a** previously suggested by us, as well as the structures **7b-d**.

These interesting and easy preparations of coumarins **7a-d** and of phosphinates **8a-d** can be explained by the mechanism suggested in Scheme 1. Nucleophilic attack of the phosphine **1** to the carbonyl oxygen of the quinoid part of compound **2** could give the corresponding betaine intermediate **3**, as in the case of the reaction of trimethylphosphite with *N*-(phenylsulfonyl)-1,4-benzoquinone monoimine.[7] Intramolecular nucleophilic attack of the nitrogen anion to the aryl- substituent of the phosphonium group of **3** with formation of the intermediate **4**, followed by formation of the 1,3,2-oxazaphosphole ring and migration of the methoxy group from nitrogen to phosphorus atom of **4**. Further hydrolysis of the resulting intermediate **5**, can afford the products **7** and **8** *via* the intermediate

6. The intramolecular migration of the methoxy-group from the N to P atom in the suggested reaction sequence is further supported by the fact, that, when in a control experiment the reaction between **1a** and **2** was carried out in the presence of ethanol, only products **7a** and **8a** were obtained again.

Treatment of **2** with tricyclohexylphosphine **1e** in boiling dichloromethane for 20 min gave 7-(cyclohexylamino)-8-hydroxy-4-methyl-2*H*-[1]-benzopyran-2-one **7e** (37%), methyl phosphinate **8e** (23%), 7-(*N*-cyclohexyl-*N*-dicyclohexylphosphinoylamino)-8-hydroxy-4-methyl-2*H*-[1]benzopyran-2-one **11** (41%) and the 8-methoxy-derivative **12** (3%) (Scheme 2).



Scheme 2

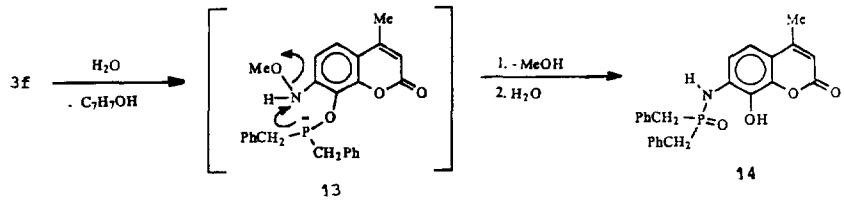
In this case it is believed that the reaction proceeds again *via* the intermediates **3e**, **4e** depicted in Scheme 1, but the bulky cyclohexyl substituents in **4e** also favour the partial formation of the intermediate **10** and finally the formation of **11** (Scheme 2), *via* an intermolecular nucleophilic attack of water and methanol elimination, along with the formation of **7e**, **8e** (*via* the intermediates **5e**, **6e**). Intramolecular nucleophilic attack[8] of hydroxyl to the methyl substituent Me-O-P< in the case of **6e** accompanied by dehydration can account for the low yield formation of compound **12** (Scheme 2).

Methylation of **11** with methyl iodide, as described for **7a**, gave compound **12** (70%). The analytical and spectral data of **11** and **12** are in good agreement with the structures proposed for them. The ^{1}H-NMR spectrum of **12** shows a singlet at δ 4.13 for the $\underline{CH_3}O$- proton.

When compound **2** was treated with tribenzylphosphine **1f** for 30 min, *N*-benzyl-derivative **7f** (11%), the methyl phosphinate **8f** (12%) and *N*-dibenzylphosphinoyl-derivative **14** (29%) (Scheme 3) were obtained.

Probably an abstraction of a proton from a water molecule present, by the anionic nitrogen atom of **3f**, accompanied by elimination of C_7H_7OH, to give the intermediate **13** and further closure of an oxazaphosphole ring with elimination of methanol, followed by hydrolytic opening of the latter heterocyclic ring, can account for the formation of compound **14** (Scheme 3), along with the formation of **7f** in low yield. The predominant transformation of **3f** to **13**, instead of **4f**, can be attributed to the

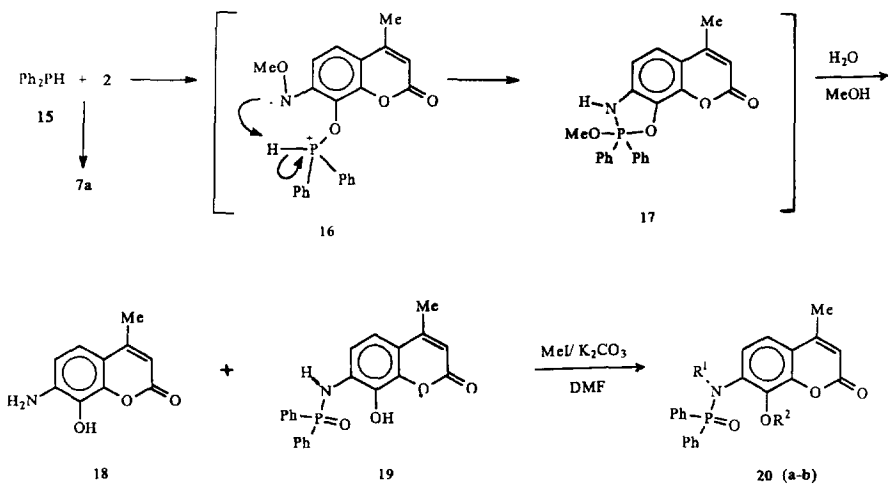
strained conformation of **3f**, because its bulky benzyl substituents do not favour the intramolecular attack of N-atom at the carbon atom α to P.



Scheme 3

Methylation of compound **7f** with methyl iodide (Scheme 1) gave the methoxy derivative **9f** (79%) very similar to **9a** with a singlet at δ 3.99 in its ^{1}H-NMR spectrum. The *N*-phosphinoyl structure of **14** is well established by its spectral data and mainly by the NH doublet (δ 5.52, J=12.6) in its ^{1}H-NMR spectrum, which is in good agreement with the NH resonances in analogous known systems[9].

8-Hydroxy-4-methyl-7-(diphenylphosphinoylamino)coumarin **19,** similar to coumarin **14,** was obtained in 96% yield by treatment of **2** with diphenylphosphine **15** (Scheme 4). Compounds **7a** and **18**[10] were also obtained in very low yields (~1% and ~1.5% respectively).



a : R^1 = H, R^2 = Me

b : R^1 = R^2 = Me

Scheme 4

A formation of the betaine intermediate **16** analogous to **3** (Scheme 4) can explain the formation of product **19** *via* the intermediate **17**, which is produced through an intramolecular proton abstraction by the anionic nitrogen atom from the phosphonium group of **16** and rearrangement of the methoxy group, like that in sequence **3** → **4** → **5** (Scheme 1). Subsequent hydrolysis and methanol elimination can then account for the formation of the main product **19** in this reaction. Further hydrolysis of **19** can lead to the aminophenol derivative **18**.

By treatment of compound **19** with methyl iodide the *O*-methyl derivative **20a** (19%) and the *N,O*-dimethyl derivative **20b** (72%) were obtained. The analytical and spectral data of these compounds support the structures proposed for them. The ^{1}H-NMR spectrum of **20b** exhibits two absorptions for the methyl protons at δ 4.17 (3 H, s, CH_3O-) and 3.07 [3 H, d, J=11.5, $CH_3NP(O)<$], while the ^{1}H-NMR spectrum of compounds **20a** shows singlet at δ 4.05 for CH_3O- protons.

The formation of products **9a, 9f, 12, 20a, 20b** proves beyond any doubt that the phenyl, benzyl, cyclohexyl or phosphinoyl group in the corresponding parent coumarins **7a, 7f, 11, 19** is attached to the amino- and not to the hydroxy- substituent of **18**.

In conclusion the reactions studied result to the high to moderate yield formation of the unexpected title coumarin derivatives through an unusual final interchange of their initial *N*-methoxy and *P*-aryl (or alkyl or hydrogen) substituents. A resembling base induced analogous rearrangement of *O*-alkylsulfonyl group of *N*-(diphenylphosphinoyl)tosylhydroxylamines to a P atom has been reported recently[11], with formation of the corresponding phosphonamidic sulfonic mixed anhydride.

EXPERIMENTAL

General. Mps are uncorrected and were determined on a Kofler hot-stage apparatus. Ir spectra were obtained with a Perkin-Elmer 297 spectrophotometer. ^{1}H-NMR spectra were recorded with $CDCl_3$ as a solvent on a Bruker AW 80 (80 MHz) or 300 AM (300 MHz) spectrometer with $SiMe_4$ as the internal standard. ^{13}C NMR spectra were obtained at 75.5 MHz on a Bruker 300 AM spectrometer for $CDCl_3$ solutions with $SiMe_4$ as internal reference. Mass Spectra were determined on a VG-250 spectrometer with ionization energy maintained at 70 eV.

General Procedure for Reactions of Phosphines 1a-f with Compound 2. Reaction of 1a with 2. A solution of **1a** (0.105 g, 0.4 mmol) and monoxime **2** (88 mg, 0.4 mmol) in dichloromethane (4 mL) was refluxed for 75 min. The solvent was evaporated and the residue was chromatographed (silica gel, hexane/ethyl acetate 3:2) to give compound **7a** (100 mg, 93%): mp 213-215 °C (lit.[1] mp 214-216 °C). Compound **8a** was eluted second (85 mg, 91%): oil [lit.[5] bp 165-169 °C (0.8 mm Hg)]. When the above reaction was repeated with **1a** (53 mg, 0.2 mmol) and **2** (44 mg, 0.2 mmol) in dichloromethane (2 mL)

containing ethanol (19 mg, 0.4 mmol) at rt for 5 min only compounds **7a** (40 mg, 75%) and **8a** (32 mg, 68%) were obtained again.

Reaction of 1b with 2. The reaction of **1b** (0.122 g, 0.4 mmol) with **2** (88 mg, 0.4 mmol) was carried out for 35 min. *8-Hydroxy-4-methyl-7-(4-methylphenylamino)-2H-[1]-benzopyran-2-one* **7b** was eluted first (76 mg, 68%): mp 209-211 °C (from dichloromethane) (Found:C, 72.7; N, 5.1; H, 5.4. $C_{17}H_{15}NO_3$ requires C, 72.6; N, 5.0; H, 5.4%); IR (Nujol) 3430, 3300 and 1710 cm^{-1}; ^1H NMR (300 MHz) δ 2.34 (3 H, s), 2.37 (3 H, s), 6.05 (1 H, s) and 6.98-7.22 (6 H, m); ^{13}C NMR δ 18.7, 20.8, 109.0, 109.9, 112.0, 116.3, 121.3, 130.0, 130.1, 133.1, 136.3, 137.9, 141.8, 153.9 and 160.9; mass spectrum m/z 281 (M^+, 100%), 253 (21), 106 (5), 91 (18) and 77 (9). Compound **8b** was eluted second (88 mg, 84%): oil [lit.[5] bp 174 °C (0.5 mm Hg)]. When the reaction between **1b** (0.122 g, 0.4 mmol) and **2** (88 mg, 0.4 mmol) was repeated at rt for 5 min, compounds **7b** (96 mg, 85%) and **8b** (79 mg, 76%) were obtained.

Reaction of 1c with 2. The reaction of **1c** (0.122 g, 0.4 mmol) with **2** (88 mg, 0.4 mmol) was carried out at rt for 5 min. *8-Hydroxy-4-methyl-7-(3-methylphenylamino)-2H-[1]-benzopyran-2-one* **7c** was eluted first (94 mg, 83%): mp 183-185 °C (from dichloromethane) (Found: C, 72.7; N, 4.95; H, 5.5. $C_{17}H_{15}NO_3$ requires C, 72.6; N, 5.0; H, 5.4%); IR (Nujol) 3410, 3320 and 1690 cm^{-1}; ^1H NMR (300 MHz) δ 2.35 (3 H, s), 2.39 (3 H, s), 6.07 (1 H, s), 6.94 (1 H, d, J=7.5 Hz), 7.01-7.13 (3 H, m) and 7.16-7.3 (2 H, m); mass spectrum m/z 281 (M^+, 62%), 253 (13), 106 (14), 104 (15), 91 (83), 77 (63) and 65 (100). Compound **8c** was eluted second (50 mg, 48%), oil (Found: C, 69.0; H, 6.8. $C_{15}H_{17}O_2P$ requires C, 69.2; H, 6.6%); IR (Neat) 1590, 1230, 1113 and 1026 cm^{-1}; ^1H NMR (300 MHz) δ 2.38 (6 H, s), 3.76 (3 H, d, J=11.2 Hz), 7.32-7.36 (4 H, m), 7.53-7.63 (2 H, m) and 7.65 (2 H, d, J=12.7 Hz); ^{13}C NMR δ 21.3, 51.4, 51.5, 128.3, 128.5, 128.6, 128.7, 132.0, 132.1, 132.56, 132.61, 132.91, 132.95, 138.3 and 138.4; mass spectrum m/z 260 (M^+, 51%), 259 (34), 258 (39), 245 (4), 229 (9), 228 (6), 227 (12), 183 (5), 169 (12), 91 (91) and 65 (100).

Reaction of 1d with 2. The reaction of **1d** (0.122 g, 0.4 mmol) with **2** (88 mg, 0.4 mmol) was carried out at reflux for 18 h. *8-Hydroxy-4-methyl-7-(2-methylphenylamino)-2H-[1]-benzopyran-2-one* **7d** was eluted first (63 mg, 56%), mp 194-196 °C (dichloromethane/benzene) (Found: C, 72.9; N, 5.1; H, 5.4. $C_{17}H_{15}NO_3$ requires C, 72.6; N, 5.0; H, 5.4%); IR (Nujol) 3410, 3300 and 1685 cm^{-1}; ^1H NMR (300 MHz) δ 2.29 (3 H, s), 2.38 (3 H, s), 6.07 (1 H, s), 6.18 (1 H, s, D_2O exchangeable), 6.68 (1 H, br s, D_2O exchangeable), 6.83 (1 H, d, J=8.7 Hz), 6.99-7.12 (2 H, m) and 7.18-7.36 (3 H, m); ^{13}C NMR 17.8, 18.6, 109.3, 109.9, 112.0, 116.2, 122.5, 124.4, 126.8, 130.2, 131.2, 131.6, 136.7, 138.7, 141.8, 154.0 and 161.0; mass spectrum m/z 281 (M^+, 100%), 253 (6), 93 (7), 91 (4), 78 (74) and 77 (14). Compound **8d** was eluted second (57 mg, 55%): oil (lit.[6] oil).

Reaction of 1e with 2. The reaction of **1e** (0.126 g, 0.45 mmol) with **2** (99 mg, 0.45 mmol) was carried out at reflux for 20 min. *7-(Cyclohexyl-amino)-8-hydroxy-4-methyl-2H-[1]-benzopyran-2-one* **7e** was eluted first (40 mg, 37%), mp 181-183 °C (dichloromethane/n-hexane) (Found: C, 70.5; N, 5.3; H, 7.0. $C_{16}H_{19}NO_3$ requires C, 70.3; N, 5.1; H, 7.0%); IR (Nujol) 3400, 3300 and 1685 cm^{-1}; ^1H NMR (300

MHz) δ 1.20-2.20 (10 H, m), 2.34 (3 H, d, *J*=0.9 Hz),3.30-3.40 (1 H, m), 5.94 (1 H, q, *J*=0.9 Hz), 6.40 (1 H, br s, D_2O exchangeable), 6.59 (1 H, d, *J*=8.9 Hz) and 7.20 (1 H, d, *J*=8.9 Hz); mass spectrum m/z 274 (24%), 273 (M^+, 96), 231 (15), 230 (100), 202 (24), 192 (15), 191 (93), 163 (60), 162 (24) and 131 (16). *N-cyclohexyl-N-dicyclohexylphosphinoylamino)-8-hydroxy-4-methyl-2H-[1]-benzopyran-2-one* **11** was eluted second (90 mg, 41%), mp 139-141 °C (from ethyl acetate) (Found: C, 69.35; N, 2.9; H, 8.3. $C_{28}H_{40}NPO_4$ requires C, 69.3; N, 2.9; H, 8.3%); IR (Nujol) 3400 and 1715 cm^{-1}; ^1H NMR (300 MHz) δ 0.82-2.2 (32 H, m), 2.43 (3 H, s), 3.32-3.5 (1 H, m), 6.31 (1 H, s), 6.96 (1 H, d, *J*=8.6 Hz) and 7.03 (1 H, d, *J*=8.6 Hz), 10.9 (1 H, br s, D_2O exchangeable); mass spectrum m/z 486 (13%), 485 (M^+, 100), 442 (45), 272 (10), 255 (19), 238 (12), 214 (11), 191 (45), 163 (31), 131 (15), 83 (19) and 81 (21). *7-(N-cyclohexyl-N-dicyclohexylphosphinoylamino)-8-methoxy-4-methyl-2H-[1]-benzopyran-2-one* **12** was eluted next (6 mg, 3%), mp 219-221 °C (ethyl acetate/n-hexane) (Found: C, 69.9; N, 2.7; H, 8.8. $C_{29}H_{42}NPO_4$ requires C, 69.7; N, 2.8; H, 8.5%); IR (Nujol)1720 cm^{-1}; ^1H NMR (300 MHz) δ 0.8-2.17 (32 H, m), 2.44 (3 H, s), 3.48-3.60 (1 H, m), 4.13 (3 H, s), 6.29 (1 H, s), 7.19 (1 H, d, *J*=8.6 Hz) and 7.22 (1 H, d, *J*=8.6 Hz); ^{13}C NMR δ 19.0, 25.4, 26.1, 26.2, 26.3, 26.35, 26.4, 26.7, 26.8, 26.9, 26.95, 27.0, 27.1, 38.0, 39.0, 57.9, 58.0, 61.6, 114.7, 117.0, 120.3, 129.9, 130.0, 135.1, 147.1, 147.7, 147.8, 152.6 and 159.9; mass spectrum m/z 499 (M^+, 7%), 468 (6), 417 (7), 297 (22), 296 (20), 286 (25), 215 (20), 214 (100), 213 (20), 133 (23), 83 (16) and 81 (15). Compound **8e** was eluted at the end (25 mg, 23%), mp 57-58 °C (from ethanol) (lit.[12] mp 58-59 °C). In an attempted reaction between compounds **1e** (0.224 g, 0.7 mmol) and **2** (0.154 g, 0.7 mmol) at rt for 24 h 60 mg of **2** was recovered unchanged, while from the separation of the residue by column chromatography compounds **7e** (10 mg, 5%), **2** (20 mg, total yield 52%), **11**(74 mg, 22%) and **8e** (5 mg, 5%) were eluted.

Reaction of 1f with 2. The reaction of **1f** (0.152 g, 0.5 mmol) with **2** (0.110 g, 0.5 mmol) was carried out at reflux for 30 min. *7-(Benzylamino)-8-hydroxy-4-methyl-2H-[1]-benzopyran-2-one* **7f** was eluted first (16 mg, 11%), mp 201-203 °C (dichloromethane/n-hexane) (Found: C, 72.8; N, 4.9; H, 5.6. $C_{17}H_{15}NO_3$ requires C, 72.6: N, 5.0; H, 5.4%); IR (Nujol) 3410, 3340 and 1690 cm^{-1}; ^1H NMR (300 MHz) δ 2.35 (3 H, s), 3.40-3.60 (1 H, br s, D_2O exchangeable), 4.48 (2 H, s), 5.99 (1 H, s), 6.55 (1 H, d, *J*=8.7 Hz), 7.03 (1 H, d, *J*=8.7 Hz) and 7.24-7.38 (5 H, m); mass spectrum m/z 281 (M^+, 33%), 190 (19), 163 (13) and 91 (100). Compound **8f** was eluted second (15 mg, 12%), mp 74-76 °C (dichloromethane/n-hexane) (lit.[13] mp 75-76 °C); ^1H NMR (80 MHz) δ 3.07 (4 H, d, *J*=16 Hz), 3.54 (3 H, d, *J*=10 Hz), 7.1-7.5 (10 H, m). *7-(Dibenzylphospinoylamino)-8-hydroxy-4-methyl-2H-[1]-benzopyran-2-one* **14** was eluted then (60 mg, 29%), mp 108-110 °C (from dichloromethane) (Found: C, 68.7; N, 3.5; H, 5.1. $C_{24}H_{22}NPO_4$ requires C, 68.7; N, 3.3; H, 5.3%); IR (Nujol) 3410, 3220 and 1720 cm^{-1}; ^1H NMR (300 MHz) δ 2.35 (3 H, s), 3.30-3.40 (4 H, m), 5.52 (1 H, d, *J*= 12.6 Hz, D_2O exchangeable), 6.09 (1 H, s), 6.90 (1 H, d, *J*=8.7 Hz), 6.93 (1 H, d, *J*=8.7 Hz), 7.1-7.4 (10 H, m); mass spectrum m/z 420 (8%), 419 (M^+, 22), 328 (5), 265 (10), 191 (6), 92 (7), 91 (100).

Reaction of Diphenylphosphine 16 with 2. To a solution of **16** (0.130 g, 0.7 mmol, freshly distilled under nitrogen) in dichloromethane (4 mL) compound **2** (0.145 g, 0.7 mmol) was added at once under nitrogen atmosphere. A vigorous reaction took place and the reaction mixture was refluxed for further 2 h, until all the oxime was consumed. *8-Hydroxy-4-methyl-7-(diphenylphosphinoylamino)-2H-[1]-benzopyran-2-one* **19** was precipitated on cooling as white crystals (0.205 g, 79%), mp 232-235 °C (dec) (from methanol) (Found: C, 67.8; N, 3.5; H, 4.8. $C_{22}H_{18}NPO_4$ requires C, 67.5; N, 3.6; H, 4.6%); IR (Nujol) 3300 and 1715 cm^{-1}; ^1H NMR (300 MHz) δ 2.32 (3 H, s), 6.04 (1 H, d, *J*=9.5 Hz, exchangeable with D_2O), 6.10 (1 H, s), 6.55 (1 H, br s, exchangeable with D_2O), 6.91 (1 H, d, *J*=8.7 Hz), 7.14 (1 H, d, *J*=8.7 Hz) and 7.45-7.62 (6 H, m), 7.85-7.96 (4 H, m); mass spectrum m/z 391 (M^+, 100%), 374 (9), 201 (76) and 77 (15). The filtrate was concentrated and the residue was chromatographed [silica gel, n-hexane/ethyl acetate (1:1 up to 1:4) and then ethyl acetate/ methanol (95:5)]. Compound **7a** was eluted first (4 mg, 2%), mp 213-215 °C (lit.[1] 214-216 °C). Compound **18** was eluted second (4 mg, 3%), mp 222-225 °C (dec) (lit.[2] 223-225 °C). Compound **19** was eluted then (50 mg, total yield 98%).

Methylation of compound 7a. To a stirred solution of compound **7a** (40 mg, 0.15 mmol) in DMF (2 mL) anhydrous potassium carbonate (42 mg, 0.3 mmol) and methyl iodide (six drops) were added and the mixture stirred for 16 h. The solvent was evaporated in a rotary evaporator and the residue was extracted with dichloromethane (20 mL) and purified by column chromatography [silica gel, n-hexane/ethyl acetate (5:3)] to give *8-methoxy-4-methyl-7-(phenylamino)-2H-[1]benzopyran-2-one* **9a** (41 mg, 97%), mp 143-145 °C (ethyl acetate/n-hexane) (Found: C, 72.7; N, 4.95; H, 5.5. $C_{17}H_{15}NO_3$ requires C, 72.6; N, 4.95; H, 5.4%); IR (Nujol) 3309 and 1708 cm^{-1}; ^1H NMR (300 MHz) δ 2.37 (3 H, s), 4.06 (3 H, s), 6.06 (1 H, s), 6.64 (1 H, s, D_2O exchangeable) and 7.03-7.41 (7 H, m); mass spectrum m/z 281 (M^+, 42%), 266 (23), 238 (22), 210 (10), 196 (7), 167 (20) and 77 (100).

Methylation of compound 7f. To a stirred solution of compound **7f** (23 mg, 0.082 mmol) in DMF (2 mL) anhydrous potassium carbonate (28 mg, 0.2 mmol) and methyl iodide (four drops) were added and the mixture allowed under stirring for 24 h. The solvent was evaporated in a rotary evaporator, the residue extracted with CH_2Cl_2 (20 mL) and crystallized from dichloromethane/n-hexane to give *7-(benzylamino)-8-methoxy-4-methyl-2H-[1]benzopyrane-2-one* **9f** (19 mg, 79%), mp 191-193 °C (dichloromethane/n-hexane) (Found: C, 73.4: N, 4.6; H, 6.0. $C_{18}H_{17}NO_3$ requires C, 73.2; N, 4.7; H, 5.8%); IR (Nujol) 3340 and 1690 cm^{-1}; ^1H NMR (300 MHz) δ 2.32 (3 H, s), 3.99 (3 H, s), 4.46 (2 H, d, *J*=5.8 Hz), 5.26 (1 H, br t, *J*=5.8 Hz, exchangeable with D_2O), 5.99 (1 H, s), 6.53 (1 H, d, *J*=8.8 Hz), 7.16 (1 H, d, *J*=8.8 Hz) and 7.3-7.38 (5 H, m); mass spectrum m/z 295 (M^+, 5%), 266 (29), 265 (100), 264 (98), 238 (36), 237 (48), 204 (7), 160 (23), 91 (25) and 77 (15).

Methylation of compound 11. To a stirred solution of compound **11** (48.5 mg, 0.1 mmol) in DMF (2 mL) anhydrous potassium carbonate (14 mg, 0.1 mmol) and methyl iodide (four drops) were added and the mixture was allowed under stirring for 24 h. The solvent was evaporated in a rotary evaporator and the residue was extracted with dichloromethane (20 mL). The organic layer was concentrated and

separated by preparative tlc [ethyl acetate/n-hexane (9:5)] to give compound **12** (34 mg, 70%) identical to that described above.

Methylation of compound 19. Preparation of compounds 20a,b. The reaction of compound **20** (0.1 g, 0.25 mmol) with anhydrous potassium carbonate (70 mg, 0.7 mmol) and excess of methyl iodide (10 drops) in DMF (3 mL) was carried out at rt for 15 h like in the methylation of **11** and the reaction mixture was chromatographed [silica gel, n-hexane/ethyl acetate (1:2 up to 0:1)]. *8-Methoxy-4-methyl-7-(diphenylphosphinoylamino)-2H-[1]benzopyran-2-one* **20a** was eluted first (20 mg, 19%), oil (Found: C, 68.3; N, 3.25; H, 4.8. $C_{23}H_{20}NPO_4$ requires C, 68.1; N, 3.45; H, 5.0%); IR (Nujol) 3340 and 1715 cm^{-1}; ^1H NMR (300 MHz) δ 2.32 (3 H, d, *J*=1 Hz), 4.07 (3 H, s), 6.12 (1 H, q, *J*=1 Hz), 6.24 (1 H, d, *J*=11.6 Hz, exchangeable with D_2O), 7.06 (1 H, d, *J*=8.8 Hz), 7.13 (1 H, d, *J*=8.8 Hz), 7.48-7.64 (6 H, m) and 7.88-7.94 (4 H, m); ^{13}C NMR δ 18.8, 61.5, 112.1, 113.2, 113.3, 115.0, 119.7, 128.9, 129.1, 130.5, 131.7, 131.8, 132.2, 132.6, 137.3, 140.6, 146.9, 153.1 and 160.2; mass spectrum m/z 405 (M^+, 85%) 387 (13), 374 (5), 359 (6), 233 (27), 219 (18), 205 (45), 203 (54), 202 (55), 109 (22) and 77 (100). *8-Methoxy-4-methyl-7-(N-methyldiphenylphosphinoylamino)-2H-[1]-benzopyran-2-one* **20b** was eluted second (77 mg, 72%), mp 175-176 °C (dichloromethane/ether) (Found: C, 68.8; N, 3.5; H, 5,4. $C_{24}H_{22}NPO_4$ requires C, 68.7; N, 3.3; H, 5.3%); IR (Nujol) 1720 cm^{-1}; ^1H NMR (300 MHz) δ 2.32 (3 H, s), 3.08 (3 H, d, *J*=10.7 Hz), 4.21 (3 H, s), 6.20 (1 H, s), 7.04 (1 H, d, *J*=8.6 Hz), 7.36-7.48 (7 H, m) and 7.87-7.98 (4 H, m); ^{13}C NMR δ 18.9, 38.3, 38.4, 61.6, 114.2, 118.5, 119.3, 124.5, 124.6, 128.4, 128.6, 130.7, 131.8, 131.9, 132.3, 132.5, 140.9, 142.1, 143.6, 152.6 and 159.9; mass spectrum m/z 419 (M^+, 42%), 418 (51), 400 (25), 387 (61), 219 (34), 218 (97), 215 (58), 202 (51), 201 (48), 86 (100) and 77 (92).

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