

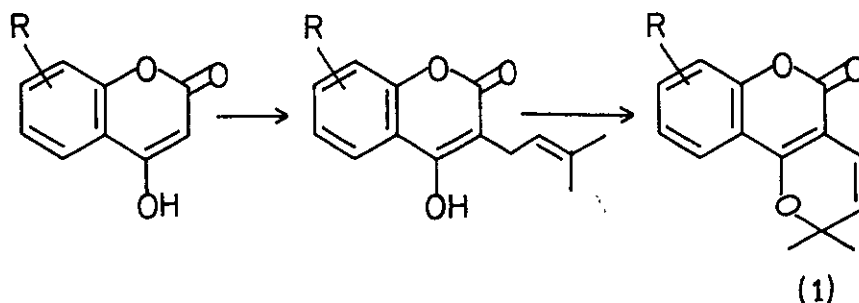
AN ELEGANT SYNTHESIS OF 2,2-DIMETHYL-2H,5H-PYRANO[3,2-C][1]
BENZOPYRAN-5-ONES

V.K.Ahluwalia*, K.K.Arora and Irani Mukherjee

Department of Chemistry, University of Delhi, Delhi-110007,
India

Abstract - Title compounds have been synthesised by the condensation of 4-hydroxycoumarins with isoprene followed by dehydrogenation with DDQ.

2,2-Dimethyl-2H,5H-pyrano[3,2-C][1]benzopyran-5-ones (1) (coumarins having a 2,2-dimethylpyran ring attached at 3,4-position) are natural compounds¹ of very recent origin. The structures of all such compounds have been assigned, only on the basis of spectral studies and no synthetic evidence has been provided so far. Bohlmann et al.¹ describe that biogenetically, these coumarins can arise by C-prenylation of appropriate 4-hydroxycoumarin to give corresponding 3-(3,3-dimethylallyl)-4-hydroxycoumarins followed by oxidative ring closure (Chart-I). In this context the co-occurrence of corresponding 3-(3,3-dimethylallyl)-4-hydroxycoumarins in the same plant is of significance¹.



(Chart-I)

A convenient route for the synthesis of these compounds may also involve the same approach i.e. C-prenylation of 4-hydroxycoumarins and then conversion to 2,2-dimethylpyrano compounds. Earlier attempts towards C-prenylation of 4-hydroxycoumarins^{2,3} led to cyclised products having a five membered ring at 3,4-position.

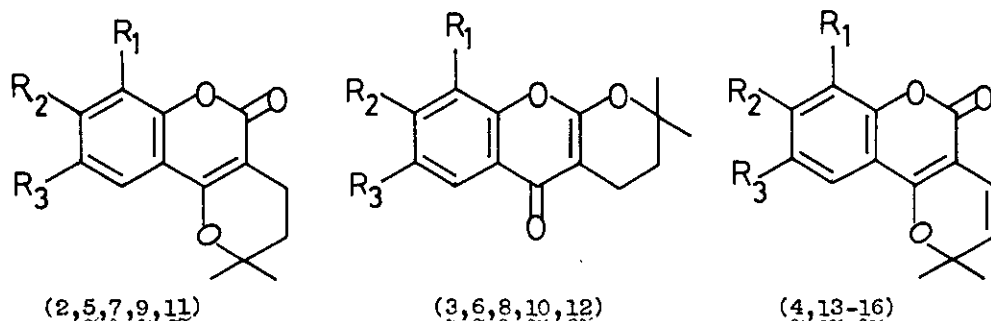
Only in one case, 2,2-dimethyl-2H,5H-pyrano[3,2-C][1]benzopyran-5-one was obtained in 10% yield, when 4-hydroxycoumarin was condensed with 3-chloro-3-methylbut-1-yne in presence of sodium hydride in inert atmosphere of nitrogen using dimethylformamide as the solvent². Recently, we have developed a very convenient method of C-prenylation^{4,5} which involves the direct condensation of phenolic compounds with isoprene in presence of orthophosphoric acid (85%). To check the versatility of this reaction, we have carried out the C-prenylation of 4-hydroxycoumarins under identical conditions. The resulting 3,4-dihydro-2,2-dimethyl-2H,5H-pyrano[3,2-C][1]benzopyran-5-ones are dehydrogenated with DDQ to give the title compounds in good yield.

Thus, the condensation of 4-hydroxy-7-methoxycoumarin with isoprene in presence of orthophosphoric acid (85%) at 35-40°C gave a mixture of two products A & B (ratio 4:3; overall yield 85%) which were separated by column chromatography over silica gel. Compound (A) obtained on elution with benzene-petroleum ether (1:1), showed the absence of a free hydroxy group at 4-position (insoluble in 5% aq. sodium carbonate solution) and its elemental analysis indicated the introduction of one isoprene unit. In its IR spectrum a strong band at 1710 cm^{-1} indicated that the >C=O of coumarin is intact. Its $^1\text{H-NMR}$ spectrum showed the presence of a chroman ring [δ 1.41(6H, s); 1.82 and 2.53 (each 2H, each t, $J=7\text{Hz}$)] along with a singlet of three protons at 3.81 for $-\text{OCH}_3$ and the aromatic protons appeared at 6.72(1H, d, $J=2\text{Hz}$); 6.78(1H, dd, $J=8\text{Hz}$, 2Hz) and 7.63(1H, d, $J=8\text{Hz}$). On this basis it was assigned the structure 3,4-dihydro-8-methoxy-2,2-dimethyl-2H,5H-pyrano[3,2-C][1]benzopyran-5-one (2).

The second compound (B) obtained on elution with benzene, was found to be isomeric with compound A on the basis of elemental analysis. Its IR showed a strong peak at 1620 cm^{-1} indicating the presence of >C=O of γ -pyrone. Its $^1\text{H-NMR}$ also showed the presence of one chroman ring [δ 1.44(6H, s); 1.83 and 2.62 (each 2H, each t, $J=7\text{Hz}$)]. The signal for one aromatic proton was shifted downfield to 8.06 as compared to that at 7.63 in compound A. So it was assigned the alternate structure, 3,4-dihydro-8-methoxy-2,2-dimethyl-2H,5H-pyrano[2,3-b]-[1]benzopyran-5-one (3).

The compound (2) on dehydrogenation with DDQ in refluxing benzene gave a product (C) in 70% yield. Its IR showed absorption at 1710 cm^{-1} and $^1\text{H-NMR}$ indicated the presence of a chromene ring [δ 1.51(6H, s); 5.38 and 6.44 (each 1H,

each d, $J=10\text{Hz}$) along with other signals. So it was assigned the structure 8-methoxy-2,2-dimethyl-2H,5H-pyrano[3,2-c][1]benzopyran-5-one (4).



	R_1	R_2	R_3
<u>2,3,4</u>	H	OCH_3	H
<u>5,6,13</u>	H	H	H
<u>7,8,14</u>	OCH_3	OCH_3	H
<u>9,10,15</u>	CH_3	OCH_3	H
<u>11,12,16</u>	H	OCH_3	OCH_3

Similar results were obtained when the reaction was extended to other 4-hydroxycoumarins. Thus 4-hydroxycoumarin gave a mixture of two products 5 and 6. 4-Hydroxy-7,8-dimethoxycoumarin afforded 7 and 8, and 4-hydroxy-7-methoxy-8-methylcoumarin afforded 9 and 10. Similarly 4-hydroxy-6,7-dimethoxycoumarin yielded a mixture of 11 and 12. All these products were separated by column chromatography over silica gel and characterised on the basis of elemental analysis, IR and $^1\text{H-NMR}$ spectral data. Dehydrogenation of 5, 7, 9 and 11 with DDQ gave 13, 14, 15 and 16 respectively. Table-1 summarises the yield, mp and spectral data of all these compounds.

Table-1: Compounds 2-16 prepared

Compound ^a	Yield ^b (%)	mp ^c (°C)	IR $\nu_{\text{max}}^{\text{KBr}}$ cm^{-1}	$^1\text{H-NMR}$ (CDCl_3/TMS) δ (ppm)
<u>2</u>	48.0	99-101	1710	1.41(s, 6H); 1.82 and 2.53(each t, $J=7\text{Hz}$, each 2H); 3.81(s, 3H); 6.72(d, $J=2\text{Hz}$, 1H, H-7); 6.78(dd, $J=8\text{Hz}$, 2Hz, 1H) and 7.63(d, $J=8\text{Hz}$, 1H).

<u>3</u>	37.0	176-177	1620	1.44(s,6H); 1.83 and 2.62(each t, J=7Hz, each 2H); 3.84(s, 3H); 6.74(d, J=2Hz, 1H); 6.86(dd, J=8Hz, 2Hz, 1H) and 8.06(d, J=8Hz, 1H).
<u>5</u>	42.5	125 (lit. ² 123-124)	1710	1.41(s,6H); 1.84 and 2.55(each t, J=7Hz, each 2H); 7.06-7.42(m, 3H) and 7.66(dd, J=8Hz, 2Hz, 1H).
<u>6</u>	32.0	107 (lit. ² 106-107)	1640	1.46(s,6H); 1.83 and 2.61(each t, J=7Hz, each 2H); 7.25-7.60(m,3H) and 8.16(dd, J=8Hz, 2Hz, 1H).
<u>7</u>	46.0	179-180	1705	1.41(s,6H); 1.82 and 2.53(each t, J=7Hz, each 2H); 3.90 and 3.93(each s, each 3H); 6.79 and 7.41(each d, J=8Hz, each 1H).
<u>8</u>	38.5	87-88	1640	1.44(s,6H); 1.82 and 2.61(each t, J=7Hz, each 2H); 3.94(s, 6H); 6.94 and 7.86(each d, J=8Hz, each 1H).
<u>9</u>	52.5	157-158	1690	1.41(s,6H); 1.83(t, J=7Hz, 2H); 2.25(s, 3H); 2.54(t, J=7Hz, 2H); 3.81(s, 3H); 6.70 and 7.50(each d, J=8Hz, each 1H).
<u>10</u>	26.0	146-147	1620	1.42(s, 6H); 1.82(t, J=7Hz, 2H); 2.27(s, 3H); 2.62(t, J=7Hz, 2H); 3.92(s, 3H); 7.25 and 8.00(each d, J=8Hz, each 1H).
<u>11</u>	46.0	109-110	1695	1.45(s, 6H); 1.84 and 2.56(each t, J=7Hz, each 2H); 3.85(s, 6H); 6.71 and 7.02(each s, each 1H).
<u>12</u>	15.0	165-166	1620	1.45(s,6H); 1.83 and 2.61(each t, J=7Hz, each 2H); 3.92 and 3.94(each s, each 3H); 6.84 and 7.59(each s, each 1H).
<u>4</u>	70.0	85-86	1710	1.51(s, 6H); 3.81(s, 3H); 5.38 and 6.44(each d, J=10Hz, each 1H); 6.70(d, J=2Hz, 1H); 6.76(dd, J=8Hz, 2Hz, 1H) and 7.58(d, J=8Hz, 1H).
<u>13</u>	40.0	92-93 (lit. ² oil)	1700	1.52(s, 6H); 5.41 and 6.47(each d, J=10Hz, each 1H); 7.08-7.38(m, 3H) and 7.69(dd, J=8Hz, 2Hz, 1H).
<u>14</u>	70.0	102-103	1710	1.51(s,6H); 3.94 and 3.96(each s, each 3H); 5.46 and 6.52(each d, J=10Hz, each

				1H); 6.86 and 7.48(each d, J=8Hz, each 1H)
<u>15</u>	80.0	161-162	1700	1.53(s,6H); 2.29(s,3H); 3.90(s,3H); 5.44 and 6.49(each d, J=10Hz, each 1H); 6.79 and 7.58(each d, J=9Hz, each 1H).
<u>16</u>	70.0	135-136	1695	1.51(s,6H); 3.89(s,6H); 5.40 and 6.46 (each d, J=10Hz, each 1H); 6.73 and 7.05(each s, each 1H).

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- a. Satisfactory microanalysis obtained for all the products.
- b. Yields for the compounds 2, 3, 5-12 are based on corresponding 4-hydroxy-coumarin whereas for 4, 13-16 are w.r.t. 2, 5, 7, 9 and 11, respectively.
- c. Not corrected.

ACKNOWLEDGEMENTS We acknowledge the financial assistance provided by C.S.I.R., New Delhi, India.

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Received, 11th July, 1983