# HYDROBORATIONS: NEW SYNTHESES OF PSEUDO-BAPTIGENIN, O-METHYL PSEUDO-BAPTIGENIN AND CABREUVIN.

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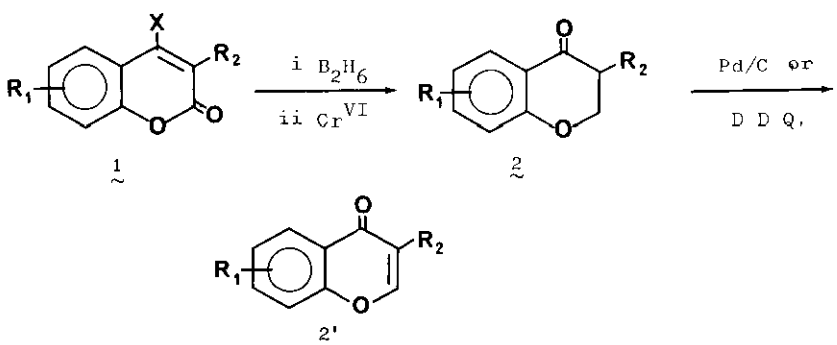
Abstract ——— Application of hydroboration followed by chromic acid oxydation to 4-hydroxy 7-methoxy 3-(3',4'-methylenedioxyphenyl) coumarin and 4-hydroxy 7-benzyloxy 3-(3',4'-methylenedioxyphenyl) coumarin forms the corresponding isoflavanones which are dehydrogenated into isoflavones.

We have previously reported that hydroboration followed by chromic oxydation of coumarin (1, X = H) and 4-hydroxy coumarins (1, X = OH) substitued at the 3-position led in straightforward fashion to the corresponding 4-chromanones (2), which were dehydrogenated further to 4-chromones (2')[1,2]. The application of these reactions to 3-phenyl coumarins (1, X = H, $R_2 = C_6H_5$) and to 4-hydroxy 3-phenyl coumarins (1, X = OH, $R_2 = C_6H_5$) gave isoflavanones (2) and isoflavones (2') (Scheme I) [3].



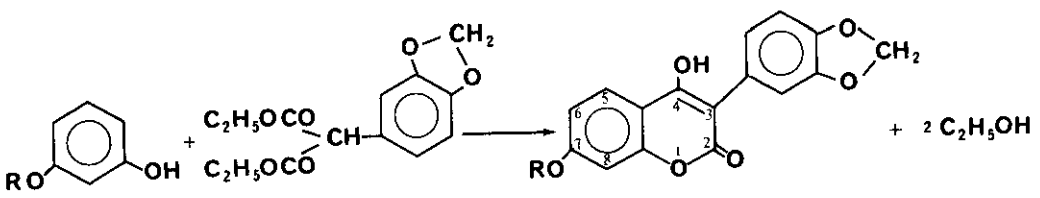

1 2 2'

X = H, OH
$R_1$ = H, $OCH_3$
$R_2$ = alkyl, aryl, arylalkyl.

Scheme I

The present work points out the generality of this method and describes the syntheses of ψ-baptigenin, O-methyl ψ-baptigenin and cabreuvin. Besides chemical interest, this work agrees with phytopharmaceutical studies about phytoalexin derivatives [4,5].

The 4-hydroxy 3-phenyl coumarins (5a and 5b) were prepared, according to Mentzer[6], by a thermal condensation of diethyl 3,4-methylenedioxyphenyl malonate (4) and the 3-substitued phenols. Thus, reaction of (4) with O-methyl resorcinol (3, R = $CH_3$) and O-benzyl resorcinol (3, R = $CH_2C_6H_5$) afforded respectively 4-hydroxy 7-methoxy 3-(3',4'-methylenedioxyphenyl) coumarin (5a, R = $CH_3$) and 4-hydroxy 7-benzyloxy 3-(3',4'-methylenedioxyphenyl) coumarin (5b, R = $CH_2C_6H_5$) (Yield, about 50%) (Scheme II).




3 4

3a: R = $CH_3$,
3b: R = $CH_2C_6H_5$.

5a: R = $CH_3$,
5b: R = $CH_2C_6H_5$.

Scheme II

These structures were proved by elemental and spectral analyses (ir bands at 1670 ( $\nu_{C=O}$ lactone) and 3200 $cm^{-1}$ ( $\nu_{OH}$); $^1H$ nmr data listed in Table I).

Table I. 7-alkoxy 4-hydroxy 3-phenyl coumarins 5

| Coumarine | R | Analyses | mp, °C | $^1H$ nmr δ, J in Hz |
|---|---|---|---|---|
| 5a | $CH_3$ | $C_{17}H_{12}O_6$ | 254* | DMSO $d_6$: 3.9 (s, 3H, $OCH_3$), 6.05 (s, 2H, $OCH_2O$), 6.8-7.1 (m, 5H ar. and OH), 7.9 (d, J=10, H5). |
| 5b | $CH_2C_6H_5$ | $C_{23}H_{16}O_6$ | 197** | $CDCl_3$: 5.2 (s, 2H, $PhCH_2$), 6.0 (s, 2H, $OCH_2O$) 6.8-7.1 (m, 5H ar.), 7.45 (s, 5H ar, $PhCH_2$), 7.8 (d, J=10, 1H, H5), under the operative conditions, no signal for OH was seen, but a strong chloroform peak appeared at 7.25 by exchange. |

* recrystallized from THF-ethanol-water;
** recrystallized from petroleum ether-chloroform.

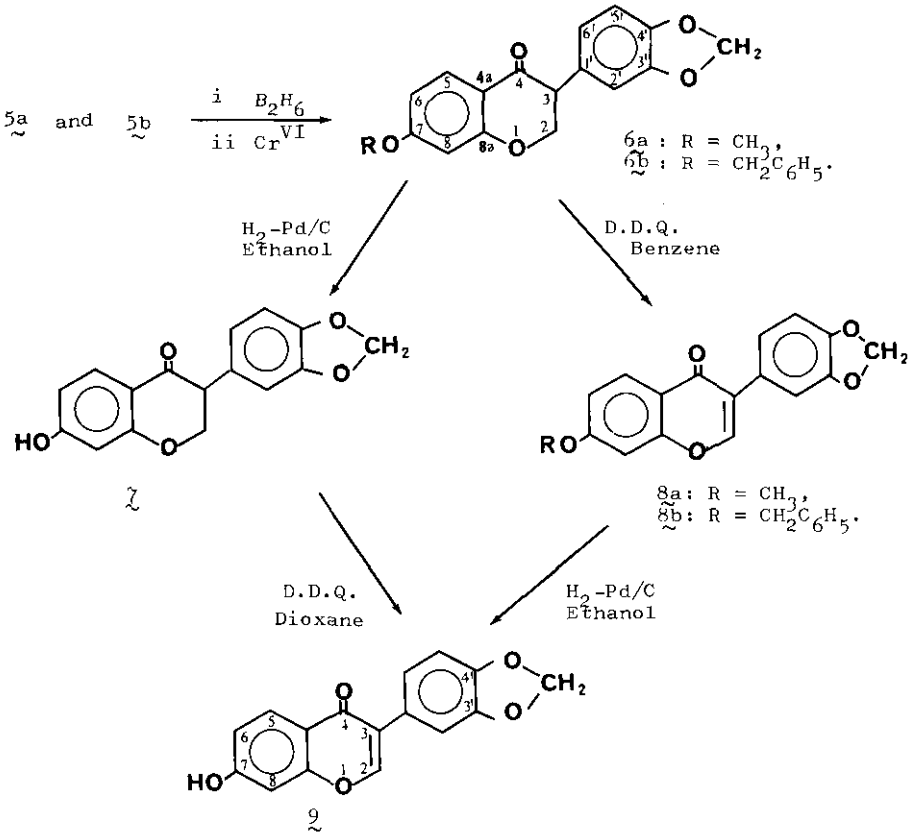
The reaction of hydroboration followed by chromic oxydation (pyridinium dichromate in methylene chloride at 0°C for 3hr) of (5a and 5b), yielded about 15% of 7-methoxy 3-(3',4'-methylenedioxy) isoflavanone (6a) and 7-benzyloxy 3-(3',4'-methylenedioxy) isoflavanone (6b). These structures were confirmed by spectral and elemental analyses. The ir spectra show a band at 1675 $cm^{-1}$ ( $\nu_{C=O}$) and the absence of a $\nu_{OH}$ vibration. The $^{1}H$ and $^{13}C$ chemical shifts are listed in Tables II and III.

The dehydrogenation of (6a) by 2,3-dichloro 5,6-dicyano benzoquinone (D.D.Q.) afforded 0-methyl ψ-baptigenin (8a) (Yield, 40%).

The synthesis of ψ-baptigenin (9) was performed according to two pathways:

1.- hydrogenolysis of (6b) to 7-hydroxy isoflavanone (7) by palladium (10%) on charcoal, followed by dehydrogenation of (7) with D.D.Q. .

2.- dehydrogenation of (6b) to 0-benzyl ψ-baptigenin (8b), followed by hydrogenolysis of the benzyl group. These reactions are displayed in Scheme III.




Scheme III

Table II. Isoflavanones

| Compound* | R | Analyses | mp, °C | $^1$H nmr δ, J in Hz |
|---|---|---|---|---|
| 6a | $CH_3$ | $C_{17}H_{14}O_5$ | 108<br>109 | $CDCl_3$: 3.8 (t, J=6, H3), 3.85 (s, $OCH_3$) 4.6 (d, J=6, H2α and H2β), 5.9 (s, $OCH_2O$) 6.45 (d, J=3, H8), 6.5 (q, J=10 J=3, H6), 6.65-6.85 (m, H2', H5', H6'), 7.85 (d, J=10, H5). |
| 6b | $CH_2C_6H_5$ | $C_{23}H_{18}O_5$ | 122 | $CDCl_3$: 3.8 (t, J=6, H3), 4.6 (d, J=6, H2α and H2β), 5.1 (s, $PhCH_2$), 5.95 (s, $OCH_2O$) 6.60 (d, J=3, H8), 6.65 (q, J=10 J=3, H6), 6.70-6.80 (m, H2', H5', H6'), 7.45 (s, $PhCH_2$), 7.95 (d, J=10, H5). |
| 7 | H | $C_{16}H_{12}O_5$ | 190 | $CD_3OD$: 3.85 (t, J=6, H3), 4.6 (d, J =6, H2α and H2β), 5.95 (s, $OCH_2O$), 6.4 (d, J=3,H8), 6.45 (q, J=10, J=3, H6), 6.6-6.8 (m, H2', H5', H6'), 7.8 (d, J=10, H5) no signal for OH was seen, but a strong methanol $CD_3OH$ peak appeared at 4.8 by exchange. |

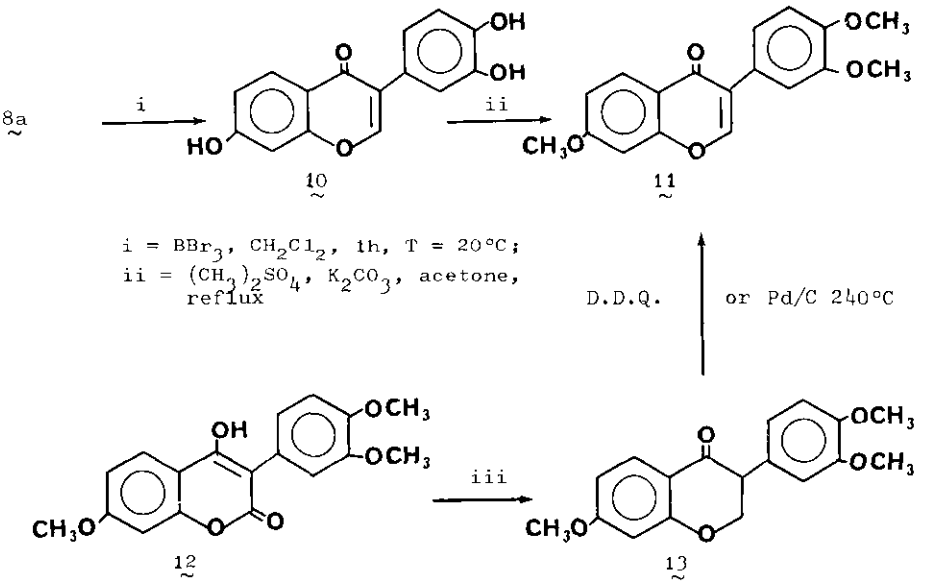
* recrystallized from petroleum ether-ethanol.

Table III. Isoflavanones: $^{13}$C chemical shifts ($CDCl_3$)

| | C2 | C3 | C4 | C4a | C5 | C6 | C7 | C8 | C8a |
|---|---|---|---|---|---|---|---|---|---|
| 6a | 71.8 | 51.4 | 190.65 | 114.75 | 129.4 | 110.1 | 166 | 100.6 | 163.4 |
| 6b | 71.8 | 51.4 | 190.6 | 114.85 | 129.4 | 110.6 | 165 | 101.6 | 163.25 |

| | C1' | C2' | C3' | C4' | C5' | C6' | $OCH_2O$ | $OCH_3$ | $OCH_2C_6H_5$ |
|---|---|---|---|---|---|---|---|---|---|
| 6a | 128.95 | 108.9 | 147.9 | 147.05 | 108.5 | 121.8 | 100.95 | 55,5 | - |
| 6b | 128.8 | 108.8 | 147.8 | 147.0 | 108.45 | 121.8 | 100.95 | - | 70.2 ($CH_2$), 143.3 135.75, 128.6, 128 |

The reaction of boron tribromide with (8a) led to 3',4',7-trihydroxy isoflavone (10), which was directly methylated (without separation, by *dimethyl sulfate* anhydrous potassium carbonate and acetone) to cabreuvin (11). This compound was identical (ir spectrum, elemental analysis, mixed melting point test) with a cabreuvin referee sample, which was previously prepared according to the route [3] 4-hydroxy coumarin (12) ⟶ isoflavanone (13) ⟶ (11) (Scheme IV).




Scheme IV

Tables II and V display the physico-chemical data of the isoflavanones and isoflavones obtained in these reactions. The $^{13}C$ chemical shifts of the isoflavanones (Table III) agree with those found for 4-chromanones [11]. The $^{13}C$ nmr data of the isoflavones agree also with the published values [11].

More work is now performed for the preparation of compounds which are structural analogous to phytoalexines.

Table IV. Isoflavones

| Compound | Analyses | mp*, °C | $^1$H nmr , J in Hz |
|---|---|---|---|
| O-methyl ψ-baptigenin | $C_{17}H_{12}O_5$ | 178 | $CDCl_3$: 3.95 (s, $OCH_3$), 6.0 (s, $OCH_2O$), 6.75-7.35 (m, 5H ar.), 7.75 (s, H2), 8.2 (d, J=8, H5). |
| O-benzyl ψ-baptigenin | $C_{23}H_{16}O_5$ | 164 | $CDCl_3$: 5.15 (s, $PhCH_2$), 5.9 (s, $OCH_2O$) 6.8-7.5 (m, 10H ar.), 7.9 (s, H2), 8.2 (d, J=8, H5). |
| ψ-baptigenin | $C_{16}H_{10}O_5$ | 296 | DMSO $d_6$: 6.1 (s, $OCH_2O$), 6.85-7.2 (m, 5H ar.), 7.4 (s, H2), 8.05 (d, J=8, H5) 8,35 (OH). |

* Melting points agree with the published values (8a [8,9,10]; 8b [10]; 9 [8])

REFERENCES


1. B.S. Kirkiacharian, G.H. Elia and G. Mahuzier, Compt. rend. (France), (C), 1974, 279, 151.
2. B.S. Kirkiacharian, Chem. Comm., 1975, 162.
3. B.S. Kirkiacharian and H.Chidiac, Compt. rend. (France), 1975, 280, 775.
4. A. Ravisé and B.S. Kirkiacharian, Phytopathologische Zeitschrift, 1976, 85, 74; 1976, 86, 314; 1978, 92, 36; 1980, 97, 219.
5. B.S. Kirkiacharian and A. Ravisé, Phytochemistry, 1976, 15, 907.
6. C. Mentzer and G. Urbain, Bull. Soc. chim. France, 1943, 404; 1944, 305.
7. H.C. Brown and C.P. Garg, J. Amer. Chem. Soc., 1961, 83, 2951.
8. E. Spath and E. Lederer, Chem. Ber., 1930, 63B, 743.
9. L. Farkas, A. Major, L. Pallos and J. Varady, Chem. Ber., 1958, 91, 2858.
10. W. Baker, R. Robinson and N.M. Simpson, J. Chem. Soc., 1937, 805.
11. A. Pelter, R.S. Ward and T.I. Gray, J. Chem. Soc. Perkin, 1976, 23, 2475.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