

## Kostanecki-Robinson Acylation of Methyl-2:4-Dihydroxy-5-Butyryl and 5-Propionylbenzoates

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Kostanecki-Robinson Reaction of methyl-2:4-dihydroxy-5-butyryl and 5-propionylbenzoate has been described. The various chromone and flavone derivatives were obtained. The chromone structure was assigned to these products on the basis of the results of hydrolysis of the hydroxycarboxy chromone derivatives to known *o*-hydroxybenzoic acid derivatives, Kostanecki-Robinson acetylation of methyl 2:4-dihydroxy-5-butyrylbenzoate during the present work and Kostanecki-Robinson acetylation of methyl-2:4-dihydroxy-5-propionylbenzoate by Desai, Desai and Desai.

Naik and Thakore<sup>1</sup>, Thanawala, Seshadri and Trivedi<sup>2</sup> have carried out Kostanecki-Robinson reaction using nitroketones. They have obtained nitro chromone derivatives. Parkhi and Sethna<sup>3</sup> have observed that Kostanecki-Robinson acetylation of methyl-2:4-dihydroxy-5-acetylbenzoate yielded diacetoxy derivative and not the expected coumarin or chromone. Few reactions have been carried out by Desai, Desai and Desai<sup>4</sup> on methyl-2:4-dihydroxy-5-acyl and 3-acylbenzoates using sodium acetate and acetic anhydride. They have obtained carbmethoxy and carboxychromone derivatives. In the present work Kostanecki-Robinson acylation of methyl-2:4-dihydroxy-5-butyryl and 5-propionylbenzoates has been studied.

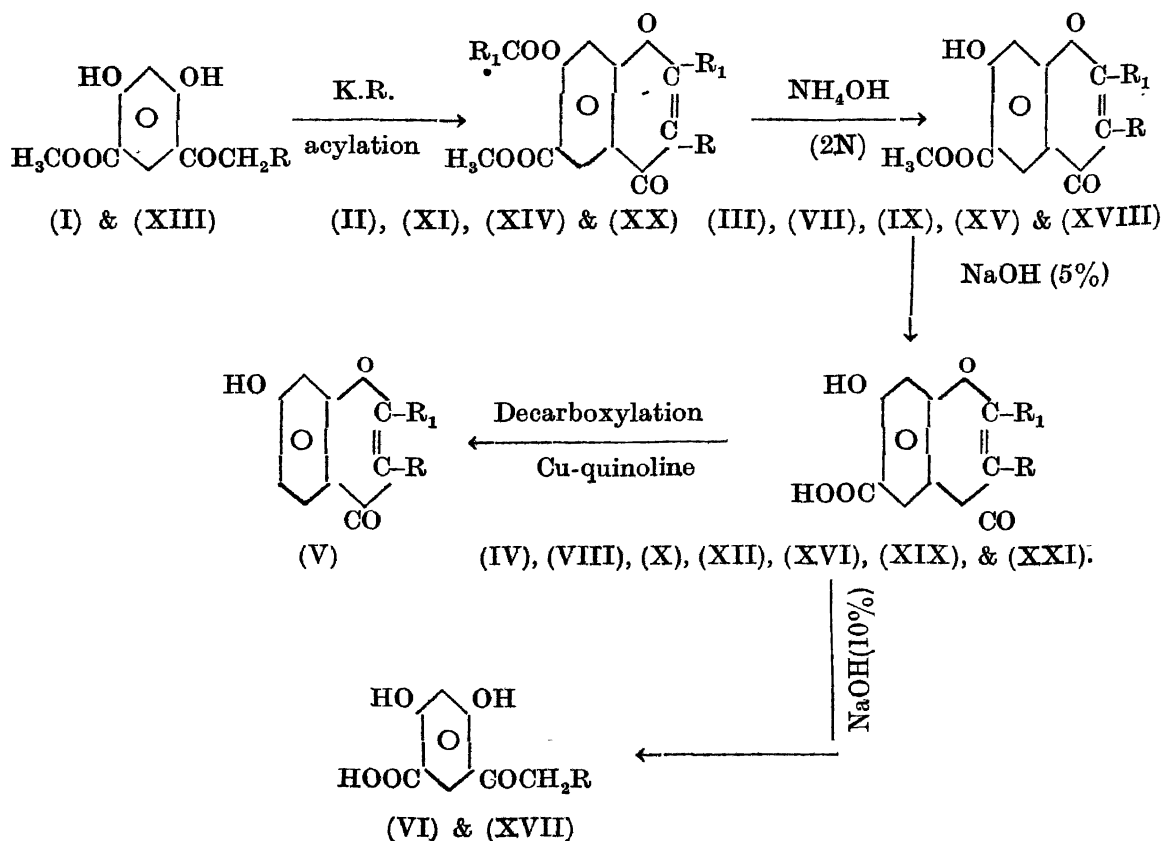
Methyl-2:4-dihydroxy-5-butyrylbenzoate (I) when refluxed with fused sodium acetate and acetic anhydride at 150–60° for sixteen hours, furnished 7-acetoxy-6-carbmethoxy-2-methyl-3-ethylchromone (II). Hydrolysis of the above chromone with ammonium hydroxide (2*N*) afforded 7-Hydroxy-6-carbmethoxy-2-methyl-3-ethylchromone (III), while 7-hydroxy-6-carboxy-2-methyl-3-ethylchromone (IV) was obtained on alkali hydrolysis (NaOH 5%) in cold. In order to confirm the chromone structure 7-Hydroxy-6-carboxy-2-methyl-3-ethylchromone was decarboxylated with copper in quinoline to the known 7-Hydroxy-2-methyl-3-ethylchromone (V)<sup>5</sup>. The known 2:4-dihydroxy-5-butyrylbenzoic acid (VI) was obtained when sodium hydroxide (10%) in cold was used for hydrolysis of (IV) suggesting the rupture of  $\gamma$ -pyrone ring of the chromone<sup>6</sup>.

\* Since deceased.

1. R. M. Naik and V. M. Thakor, *Proc. Ind. Acad. Sci.*, 1953, **37A**, 774.
2. C. B. Thanawala, S. Seshadri and P. L. Trivedi, *J. Indian Chem. Soc.*, 1959, **36**, 674.
3. S. Parkhi and S. M. Sethna, *Proc. Ind. Sci. Cong.*, 1955, **Part III**, 115.
4. R. D. Desai, B. M. Desai and J. I. Desai, *J. Indian Chem. Soc.*, 1960, **37**, 491.
5. F. W. Canter, F. H. Curd and A. Robertson, *J. Chem. Soc.*, 1931, **trans Part I**, 1255.
6. A. S. Gupta, (unpublished work).

Similarly, methyl-2 : 4-dihydroxy-5-butyrylbenzoate, on Kostanecki-Robinson propionylation and butyrylation at 170–80° for nine hours, furnished crude propionoxy and butyryloxy chromone derivatives, which on treatment with ammonium hydroxide (2*N*) yielded 7-Hydroxy-6-carbmethoxy-2 : 3-diethylchromone (VII) and 7-Hydroxy-6-carbmethoxy-2-propyl-3-ethylchromone (IX) respectively. Hydrolysis of the above chromone derivatives with sodium hydroxide (5%) afforded 7-Hydroxy-6-carboxy-2 : 3-diethylchromone (VIII) and 7-Hydroxy-6-carboxy-2-propyl-3-ethylchromone (X) respectively, which on further hydrolysis with sodium hydroxide (10%) gave the known 2 : 4-dihydroxy-5-butyrylbenzoic acid (VI).

On similar Kostanecki-Robinson benzylation of methyl-2 : 4-dihydroxy-5-butyrylbenzoate at 170–80° for twelve hours, yielded 7-benzoyloxy-6-carbmethoxy-3-ethylflavone (XI). As the treatment of this flavone with ammonium hydroxide (2*N*) or sodium hydroxide



I to VI  
VII to VIII  
IX to X  
XI to XII  
XIII to XVII  
XVIII to XIX  
XX to XXI

$\text{R} = \text{C}_2\text{H}_5$   
 $\text{R} = \text{C}_2\text{H}_5$   
 $\text{R} = \text{C}_2\text{H}_5$   
 $\text{R} = \text{C}_2\text{H}_5$   
 $\text{R} = \text{CH}_3$   
 $\text{R} = \text{CH}_3$   
 $\text{R} = \text{CH}_3$

$\text{R}_1 = \text{CH}_3$   
 $\text{R}_1 = \text{R} = \text{C}_2\text{H}_5$   
 $\text{R}_1 = \text{C}_3\text{H}_7$   
 $\text{R}_1 = \text{C}_6\text{H}_5$   
 $\text{R}_1 = \text{C}_2\text{H}_5$   
 $\text{R}_1 = \text{C}_3\text{H}_7$   
 $\text{R}_1 = \text{C}_6\text{H}_5$

(5%) did not give any definite product it was hydrolysed with concentrated sulphuric acid when 7-Hydroxy-6-carboxy-3-ethylflavone (XII) was obtained. On hydrolysis with sodium hydroxide (10%) hot it gave the known 2 : 4-dihydroxy-5-butyrylbenzoic acid (VI).

TABLE I

*Kostanecki-Robinson Reaction Product*

Ketone	K.R. Reaction	Product obtained	M.P. °C	Yield (g.)	FeCl <sub>3</sub> Test	Mol.For.	% of C and H
Methyl-2 : 4-dihydroxy-5-butyrylbenzoate.	Acetylation	7-Acetoxy-6-carb-methoxy-2-methyl-3-ethylchromone.	141-42	1.1	No. colour	C <sub>16</sub> H <sub>16</sub> O <sub>6</sub>	Reqd. C—63.15 Found C—63.08 Reqd. H— 5.26 Found H— 5.19
	Propionylation	Crude product	—	—	—	—	—
	Butyrylation	Crude product	—	—	—	—	—
	Benzoylation	7-Benzoyloxy-6-carbmethoxy-3-ethylflavone.	175-76	1.0	No colour	C <sub>26</sub> H <sub>20</sub> O <sub>6</sub>	Reqd. C—72.89 Found C—
	Propionylation*	7-Propionoxy-6-carbmethoxy-2-ethyl-3-methylchromone.	110-12	0.85	No colour	C <sub>17</sub> H <sub>18</sub> O <sub>6</sub>	Reqd. C—64.16 Found C—64.00 Reqd. H— 5.66 Found H— 5.62
Methyl-2 : 4-dihydroxy-5-propionylbenzoate.	Butyrylation	Crude product	—	—	—	—	—
	Benzoylation	7-Benzoyloxy-6-carbmethoxy-3-methylflavone.	155-56	1.2	No colour	C <sub>25</sub> H <sub>18</sub> O <sub>6</sub>	Reqd. C—72.46 Found C—72.40 Reqd. H— 4.34 Found H— 4.30

\* I.R. (Nujal) 1770 cm<sup>-1</sup> (—OCOC<sub>2</sub>H<sub>5</sub>), 1720 cm<sup>-1</sup> (—COOCH<sub>3</sub>), 1655 cm<sup>-1</sup> (Chromone C = O).

Similarly, methyl-2 : 4-dihydroxy-5-propionylbenzoate (XIII) on Kostanecki-Robinson propionylation and butyrylation furnished 7-propionoxy-6-carbmethoxy-2-ethyl-3-methylchromone (XIV) and crude butyryloxy product respectively. Hydrolysis of the above chromone derivatives with ammonium hydroxide (2*N*) afforded 7-Hydroxy-6-carbmethoxy-2-ethyl-3-methylchromone (XV) and 7-Hydroxy-6-carbmethoxy-2-propyl-3-methylchromone (XVIII) respectively, which on further hydrolysis with sodium hydroxide (5%) yielded 7-Hydroxy-6-carboxy-2-ethyl-3-methylchromone (XVI) and 7-Hydroxy-6-carboxy-2-propyl-3-methylchromone (XIX) respectively. The known 2 : 4-dihydroxy-5-propionylbenzoic acid (XVII) was obtained, when sodium hydroxide (10%) in cold was used for hydrolysis of (XVI) and (XIX) suggesting the rupture of  $\gamma$ -pyrone ring of the chromone<sup>7</sup>. The chromone structure was assigned the compounds (II), (III), (IV), (V), (VII), (VIII), (IX), (X), (XIV),

7. P. L. Trivedi and S. M. Sethna, *J. Indian Chem. Soc.*, 1952, **29**, 141.

(XV), (XVI), (XVIII) and (XIX) by analogy with the results obtained in the Kostanecki-Robinson acetylation of methyl-2 : 4-dihydroxy-5-butyrylbenzoate during the present work, Kostanecki-Robinson acetylation of methyl-2 : 4-dihydroxy-5-propionylbenzoate by Desai, Desai and Desai (loc. cit.) and on the basis of formation of the known *o*-hydroxy benzoic acid derivative when hydroxy-carboxychromone was hydrolysed with sodium hydroxide (10%).

TABLE II

*Hydrolysis of 7-Acyloxy-6-carb-methoxychromone derivatives with NH<sub>4</sub>OH (2N)*

Acyloxy carb-methoxy chromone derivative	Chromone obtained on hydrolysis	M.P. °C	Yield (g.)	FeCl <sub>3</sub> Test	Mol. For.	% of C and H
7-Acetoxy-6-carb-methoxy-2-methyl-3-ethylchromone.	7-Hydroxy-6-carb-methoxy-2-methyl-3-ethylchromone.	140	0.55	Red colour	C <sub>14</sub> H <sub>14</sub> O <sub>5</sub>	Reqd. C—64.12 Found C—64.25 Reqd. H— 5.34 Found H— 5.20
Crude Acyloxy product from propionylation.	7-Hydroxy-6-carb-methoxy-2 : 3-diethyl-chromone.	105-08	0.8	Red colour	C <sub>16</sub> H <sub>16</sub> O <sub>5</sub>	Reqd. C—65.21 Found C—65.15 Reqd. H— 5.79 Found H— 5.67
Crude Acyloxy product from butyrylation.	7-Hydroxy-6-carb-methoxy-2-propyl-3-ethylchromone.	79-80	0.5	Red colour	C <sub>18</sub> H <sub>18</sub> O <sub>5</sub>	Reqd. C—66.20 Found C—66.15 Reqd. H— 6.20 Found H— 6.10
7-Propionoxy-6-carb-methoxy-2-ethyl-3-methylchromone.	*7-Hydroxy-6-carb-methoxy-2-ethyl-3-methylchromone.	124-25	0.6	Red colour	C <sub>14</sub> H <sub>14</sub> O <sub>5</sub>	Reqd. C—64.12 Found C—64.14 Reqd. H— 5.34 Found H— 5.32
Crude Acyloxy product from butyrylation.	7-Hydroxy-6-carb-methoxy-2-propyl-3-methylchromone.	98-100	0.75	Red colour	C <sub>15</sub> H <sub>16</sub> O <sub>5</sub>	Reqd. C—65.21 Found C—65.05 Reqd. H— 5.79 Found H— 5.65

\* I.R. (Nujol) 1697 cm<sup>-1</sup> (—COOCH<sub>3</sub>), 1660 cm<sup>-1</sup> (Chromone C = O).

On similar Kostanecki-Robinson benzoylation of methyl-2 : 4-dihydroxy-5-propionylbenzoate yielded 7-benzoyloxy-6-carb-methoxy-3-methylflavone (XX). As the treatment of this flavone with ammonium hydroxide (2N) or sodium hydroxide (5%) did not give any definite product, it was hydrolysed with concentrated sulphuric acid when 7-Hydroxy-6-carboxy-3-methylflavone (XXI) was obtained. On hydrolysis with sodium hydroxide (10%) hot it gave the known 2 : 4-dihydroxy-5-propionylbenzoic acid (XVII).

Details regarding the above mentioned compounds are given in the Tables I to V.

TABLE III

*Hydrolysis of 7-Hydroxy-6-carbomethoxychromone derivatives with NaOH (5%)*

Hydroxy-Carbomethoxy-chromone derivative	Chromone obtained on hydrolysis	M.P. °C	Yield (g.)	FeCl <sub>3</sub> Test	Mol.For.	% of C and H
7-Hydroxy-6-carbomethoxy-2-methyl-3-ethylchromone.	*7-Hydroxy-6-carboxy-2-methyl-3-ethylchromone.	285	0.45	Red colour	C <sub>13</sub> H <sub>12</sub> O <sub>5</sub>	Reqd. C—62.90 Found C—63.00 Reqd. H— 4.83 Found H— 4.90
7-Hydroxy-6-carbomethoxy-2 : 3-diethylchromone	7-Hydroxy-6-carboxy-2 : 3-diethylchromone.	218-20	0.45	Red colour	C <sub>14</sub> H <sub>14</sub> O <sub>5</sub>	Reqd. C—64.12 Found C—64.05 Reqd. H— 5.34 Found H— 5.38
7-Hydroxy-6-carbomethoxy-2-propyl-3-ethylchromone.	7-Hydroxy-6-carboxy-2-propyl-3-ethylchromone.	198-99	0.22	Red colour	C <sub>15</sub> H <sub>16</sub> O <sub>5</sub>	Reqd. C—65.21 Found C—65.17 Reqd. H— 5.79 Found H— 5.61
7-Hydroxy-6-carbomethoxy-2-ethyl-3-methylchromone.	7-Hydroxy-6-carboxy-2-ethyl-3-methylchromone.	270-72	0.55	Red colour	C <sub>15</sub> H <sub>12</sub> O <sub>5</sub>	Reqd. C—62.90 Found C—62.85 Reqd. H— 4.83 Found H— 4.75
7-Hydroxy-6-carbomethoxy-2-propyl-3-methylchromone.	7-Hydroxy-6-carboxy-2-propyl-3-methylchromone.	245-47	0.4	Red colour	C <sub>14</sub> H <sub>14</sub> O <sub>5</sub>	Reqd. C—64.12 Found C—64.10 Reqd. H— 5.34 Found H— 5.29

\* I.R. (Nujol) 1690 cm<sup>-1</sup> (—COOH), 1635 cm<sup>-1</sup> (Chromone C = O).

TABLE IV

*Hydrolysis of Hydroxy-Carboxychromone derivative with NaOH (10%)*

Hydroxy-carboxychromone derivative	Formation of o-hydroxy benzoic acid derivative	M.P. °C
7-Hydroxy-6-carboxy-2-methyl-3-ethylchromone		
7-Hydroxy-6-carboxy-2 : 3-diethylchromone	2 : 4-Dihydroxy-5-butyryl benzoic acid	186-87
7-Hydroxy-6-carboxy-2-propyl-3-ethylchromone		
7-Hydroxy-6-carboxy-2-ethyl-3-methylchromone	2 : 4-Dihydroxy-5-propionyl benzoic acid	232-34
7-Hydroxy-6-carboxy-2-propyl-3-methylchromone		

TABLE V

*Hydrolysis of 7-benzoyloxy-6-carbmethoxyflavone derivatives with conc.  $H_2SO_4$* 

Benzoyloxy-carb-methoxy-flavone derivative	Flavone obtained on hydrolysis	M.P. °C	Yield (g.)	FeCl <sub>3</sub> Test	Mol.For.	% of C and H
7-Benzoyloxy-6-carb-methoxy-3-ethyl-flavone.	7-Hydroxy-6-carboxy-3-ethylflavone.	205-06	0.2	Red colour	C <sub>18</sub> H <sub>14</sub> O <sub>5</sub>	Reqd. C—69.67 Found C—69.55 Reqd. H— 4.51 Found H— 4.48
7-Benzoyloxy-6-carb-methoxy-3-methyl-flavone.	7-Hydroxy-6-carboxy-3-methylflavone.	194-95	0.35	Red colour	C <sub>17</sub> H <sub>12</sub> O <sub>5</sub>	Reqd. C—68.91 Found C—68.85 Reqd. H— 4.05 Found H— 4.01

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