

## NEW NITROCHALCONES. XII<sup>1</sup>

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Some new chalcones (5'-nitro-2'-hydroxy-3-methoxy-; 4'-nitro-2'-hydroxy-3-methoxy-; 3'-nitro-4'-hydroxy-3-methoxy-; 6'-nitro-3'-hydroxy-3-methoxy-; 3,5-dimethoxy-; 5'-nitro-2'-hydroxy-2,4-dichloro-chalcone) and 3-arylidene-6-nitroflavanones (3-*p*-bromobenzylidene-; 3-naphthylidene-; 3-phenanthrylidene-6-nitroflavanone) have been prepared. The synthesis of 3'-nitrochalcone has been improved and the known 3'-methoxychalcone, mostly obtainable as an oil, has been synthesized as a crystalline compound of high purity, melting at 46–47°.

A number of new chalcones [1], [2] and 3-arylidene-6-nitroflavanones [3] have been recently reported. In this paper we complement these series with some new compounds. Characteristic data of the compounds are listed in Table I.

3'-methoxychalcone, a known compound, has been described by several authors as an oily material [2], [5], [6], [7], although AUWERS reported this chalcone to have m.p. 41–3° [8]. In the course of our work 3'-methoxychalcone could be prepared as a well defined crystalline substance of high purity, melting at 46–7°.

According to the literature, 3'-nitrochalcone could only be prepared, in the presence of sodiummethoxide in methanol, as a dark coloured, contaminated material [9], [10], [11], [12]. DAVEY and TIVEY reported that a tar was obtained in a similar experiment [13]. An improved and shorter way of preparation is now described for this chalcone, involving the precipitation of the product in fairly high purity and in better yields than those given in the literature [4]. LYLE and PARADIS alone [14] reported practically 100% yield, but they applied hydrogen chloride as condensing agent and their procedure lasted several days, while that suggested by us can be carried out within half an hour.

### Experimental<sup>2</sup>

#### 5'-NO<sub>2</sub>-2'-OH-3-MeO-chalcone

a) A saturated ethanolic solution of 3-OMe-benzaldehyde (0,41 g; 3 mmoles) was added to a solution of 5-NO<sub>2</sub>-2-OH-acetophenone (0,37 g; 2 mmoles) in hot 1 N NaOH (35 ml), and the mixture was shaken for 30 min. Precipitation of the

<sup>1</sup> For part X. see. ref [2].

Part XI. Sohár, P., T. Széll, T. Dudás: Acta Chim. Acad. Sci. Hung. in press (1970).

<sup>2</sup> All melting points were determined with a Franz Küstner microscope, and they are uncorrected.

Table I

No.	Name, formula and mol. wt.	Analysis, %						M. p., °C
		Calcd.			Found			
		C	H	N	C	H	N	
1	5'-NO <sub>2</sub> -2'-OH-3-OMe-chalcone C <sub>16</sub> H <sub>13</sub> NO <sub>5</sub> (299,3)	64,2	4,4	4,6	64,6	4,7	—	128-9
2	4'-NO <sub>2</sub> -2'-OH-3-OMe-chalcone C <sub>16</sub> H <sub>13</sub> NO <sub>5</sub> (299,3)	64,2	4,4	4,6	64,0	4,4	4,5	176-8
3	3'-NO <sub>2</sub> -4'-OH-3-OMe-chalcone C <sub>16</sub> H <sub>13</sub> NO <sub>5</sub> (299,3)	64,2	4,4	4,6	63,9	4,2	4,7	130-1
4	6'-NO <sub>2</sub> -3'-OH-3-OMe-chalcone C <sub>16</sub> H <sub>13</sub> NO <sub>5</sub> (299,3)	64,2	4,4	4,6	64,5	4,6	4,6	136-8
5	3,5-diMeO-chalcone C <sub>17</sub> H <sub>16</sub> O <sub>3</sub> (268,3)	76,1	6,0	—	75,9	6,2	—	77-8
6	5'-NO <sub>2</sub> -2'-OH-2,4-diCl-chalcone C <sub>15</sub> H <sub>9</sub> NO <sub>4</sub> Cl <sub>2</sub> (338,1)	—	—	4,1	—	—	4,2	219-21 *
7	3-( <i>p</i> -Br-benzylidene)-6-NO <sub>2</sub> - flavanone C <sub>22</sub> H <sub>14</sub> NO <sub>4</sub> Br (436,1)	60,6	3,2	—	60,4	3,1	—	195-6
8	3-naphtylidene-6-NO <sub>2</sub> -flavanone C <sub>26</sub> H <sub>17</sub> NO <sub>4</sub> (407,4)	76,6	4,2	—	76,5	4,1	—	208-9
9	3-phenanthrylidene-6-NO <sub>2</sub> -flava- none C <sub>30</sub> H <sub>19</sub> NO <sub>4</sub> (457,5)	78,8	4,2	—	78,9	4,1	—	235-7

\* About one third of the chalcone did not melt below 245°; at this temperature molten material became clear. The IR spectrum corresponds to the structure assumed. Such melting may be due to *cis-trans* isomerism.

sodium salt of the chalcone began after a few minutes. The mixture was allowed to stand for a day, the salt of the chalcone filtered off and treated with 2 N HCl (15 ml) on a water bath for 20 min. The chalcone was filtered, washed with 2 × 2 ml of water and 2 × 2 ml of ethanol, and dried to obtain 0,6 g (99%) of the product. Recrystallization from ethanol gave yellow needles.

b) 5-NO<sub>2</sub>-2-OH-acetophenone (0,55 g; 3 mmoles) was dissolved in 20% aqueous NaOH (36 ml) and mixed with a solution of 3-MeO-benzaldehyde (0,41 g; 3 mmoles) in methanol (13 ml). The mixture was kept at room temperature for 30 min., then cc. HCl (20 ml) was added and the precipitated chalcone filtered off. The yield was 0,56 g (62%).

#### 4'-NO<sub>2</sub>-2'-OH-3-MeO-chalcone

A solution of 4-NO<sub>2</sub>-2-OH-acetophenone (0,46 g; 2,5 mmoles) in ethanol (20 ml) was mixed to 3-MeO-benzaldehyde (0,41 g; 3 mmoles) dissolved in ethanol

(20 ml); an aqueous solution of NaOH (0,96 g NaOH in 10 ml) was added to this mixture. The solution was allowed to stand at 30° for 4 hours, and acidified with 4% aqueous acetic acid (50 ml). The reaction mixture was cooled in a refrigerator, then the yellow chalcone was filtered off, washed as above, and dried to obtain 0,57 g (75%) of the product, which was recrystallized from EtOAc-EtOH-H<sub>2</sub>O (1:0,8:0,2).

#### *3'-NO<sub>2</sub>-4'-OH-3-OMe-chalcone*

The synthesis was achieved in the same way as described for the preparation of 5'-NO<sub>2</sub>-2'-OH-3-MeO-chalcone under *a*), using 3-NO<sub>2</sub>-4-OH-acetophenone, which was dissolved in the NaOH solution at 80°. Yield: 0,56 g (92%); yellow needles.

#### *6'-NO<sub>2</sub>-3'-OH-3-OMe-chalcone*

This compound was prepared analogously to 4'-NO<sub>2</sub>-2'-OH-3-MeO-chalcone in 74% yield (0,56 g). The chalcone was recrystallized from 75% aqueous ethanol; pale yellow needles.

#### *3,5-diMeO-chalcone*

This chalcone was prepared in a similar way as described for 3,4-diOMe-chalcone by DICKINSON et al. [15]. The chalcone was obtained as an almost white, slightly butter-coloured substance. It was recrystallized from ethanol. The yield for the crude product was 33%.

#### *5'-NO<sub>2</sub>-2'-OH-2,4-diCl-chalcone*

This chalcone was synthesized according to a method described earlier [1]. The product, however, had no definite melting point. It seemed as if the chalcone had consisted of two isomers. Even after six recrystallizations, this behavior did not change. The IR spectrum detected the presence of a carbonyl group, a chelate ring, a nitro group and two trisubstituted aromatic rings confirming the structure of the chalcone. *Cis-trans* isomerism may be responsible for the melting characteristics observed.

#### *3-arylidene-6-NO<sub>2</sub>-flavanones*

6-NO<sub>2</sub>-flavanone [3] (0,04 g; 0,15 mmoles) and the appropriate aldehyde (0,56 g of *p*-Br-benzaldehyde; 0,47 g of 1-naphthaldehyde; or 0,62 g of phenathrene-9-aldehyde, 3 mmoles each) were dissolved in dry ethanol (3,2 and 8 ml, respectively). (With the last aldehyde 5 ml of benzene was also added, since it was not soluble enough in ethanol.) The solutions thus obtained were saturated with dry hydrogen chloride at 0° and allowed to stand for 3 days at room temperature.

When using *p*-Br-benzaldehyde, the saturation was then repeated, the solution kept for another day, refluxed for 10 min. and allowed to stand at room temperature for further 3 days to give the crude product.

With 1-naphthaldehyde, crystals appeared after 3 days.

In case of phenanthrene-9-aldehyde, the solution obtained on standing for 3 days was refluxed for 10 min., and kept at room temperature for another day. It was then evaporated in vacuum, and the residue crystallized from EtOAc to give crude phenanthrylidene-6-NO<sub>2</sub>-flavanone. The crude products were recrystallized from EtOAc-EtOH (1:1); EtOAc-EtOH (2:1) and EtOAc, respectively.

### 3'-OMe-chalcone

This chalcone was prepared as described in a patent of the Upjohn Co. [6b]. The resulting oil was distilled under reduced pressure. The distillate was seeded with pumice stone and stored overnight in a refrigerator when it crystallized. The yield of the crude product was 78%. It was recrystallized from 96% ethanol to give yellow needles melting at 46-7°. Anal.: Calc.: C<sub>16</sub>H<sub>14</sub>O<sub>2</sub>; C 80,65; H 5,9. Found: C 80,5; H 5,9%.

### 3'-NO<sub>2</sub>-chalcone

3-NO<sub>2</sub>-acetophenone (2,47 g; 15 mmoles) was dissolved in methanol (40 ml) and benzaldehyde (1,59 g; 15 mmoles) was added to the solution at room temperature. It was then cooled to 10° and a solution of sodium methoxide (0,3 g sodium metal in 3,5 ml of methanol) was added by drops, with stirring, within 10 min. Crude chalcone precipitated during the addition of the catalyst. Stirring was continued for 20 min., then the product was filtered off, washed with 2×2 ml of water and 2×2 ml of ethanol, and dried. The filtrate, after standing overnight in a refrigerator, gave a further small crop of the chalcone. The combined crude products weighed 2,16 g (57%). Recrystallization from ethanol gave white crystals melting at 131°. Anal.: Calc.: C<sub>15</sub>H<sub>11</sub>NO<sub>3</sub>; C 71,1; H 4,4; N 5,5. Found: C 71,1; H 4,6; N 5,5%.

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### НОВЫЕ НИТРО-ХАЛКОНЫ. XI

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Были созданы несколько новых халконов и 3-арилиден -6-нитрофлаванон. Синтез 3'-нитро-халкона был улучшен. Авторы приготовили 3'-метокси-халкон в кристаллической форме известный главным образом в виде масла - с большой чистотой. Точка плавления полученного материала 46—47 °С.