Anal. Calcd. for $C_{11}H_{20}N_2O_5$: C, 50.75; H, 7.75; N, 10.76. Found: C, 50.55; H, 7.38; N, 10.41.

Diethyl 4-Isohexyl-3,4,5,6-tetrahydro-1,2-pyridazinedicarboxylate.—The Diels–Alder adduct from myrcene and diethyl azodicarboxylate[2] was catalytically reduced to the saturated diester in alcohol solution with 5% palladium-on-charcoal catalyst (1 g./10 g. ester) in yields of 88–90%. The product boiled at 148–149°(0.8 mm.); $n^{26.3}_D$ 1.45973.

Anal. Calcd. for $C_{16}H_{30}N_2O_4$: C, 61.1; H, 9.62. Found: C, 61.1; H, 9.32.

Lithium Aluminum Hydride Reduction of Tetrahydropyridazine Esters.—A solution of the tetrahydropyridazinedicarboxylic ester in ether was added slowly, without cooling, to a threefold molar excess of lithium aluminum hydride in ether. After stirring for 1.5–2 hr. and treating with a minimum amount of water, the solids were filtered and washed with ether. The ether solution was dried over magnesium sulfate, the ether carefully distilled through a column and the residue distilled. Because of their volatility, most of these compounds were converted to their methiodides for analysis. All of these compounds are listed in Table I.

6*H*,13*H*-Octahydrodipyridazino[1,2-*a*:1′,2′-*d*]-s-tetrazines.—Hexahydropyridazine,[7] 4-methylhexahydropyridazine[7] and 3,6-dimethylhexahydropyridazine[12] have been previously reported. 4-Isohexylhexahydropyridazine [b.p. 84–84.5°(0.125 mm.)] was prepared by hydrolysis of the corresponding 1,2-dicarboxylic ester with 25% methanolic potassium hydroxide. The condensation of these hexahydropyridazines with formaldehyde was effected by adding the free bases slowly with cooling to one molar equivalent of 37% formalin solution. After standing at room temperature for 3 hr., the mixture was chilled and the product filtered off. Evaporation and chilling of the mother liquor gave a second crop of product. The recrystallization solvent was hexane. Physical constants are given in Table II.

A small amount (about 2%) of compound III crystallized in the lithium aluminum hydride reduction of diethyl tetrahydropyridazine-1,2-dicarboxylate when the ether solution was concentrated just prior to distillation (see above).

Bis(3,6-dimethyl-1,4,5,6-tetrahydro-1-pyradazyl)methane.—To 72.3 g. (0.645 mole) of 3,6-dimethyltetrahydropyradazine[12] was added slowly and with cooling 26 cc. (0.32 mole) of 37% formalin solution. After standing overnight, the water was distilled under reduced pressure and the residue vacuum distilled. There was collected 70.6 g. (93.5%) of the name compound boiling at 99–102° (0.6 mm.). The distillate crystallized in the receiver. It was quite soluble in many organic solvents and was recrystallized from petroleum ether only at great loss. The product melted at 58–62°. This compound was unstable on standing.

Anal. Calcd. for $C_{13}H_{24}N_4$: C, 66.06; H, 10.23; N, 23.7. Found: C, 66.20; H, 9.72; N, 23.7.

Condensation of Hydroxynitroacetophenones with Aromatic Aldehydes in the Presence of Hydrogen Chloride

T. Széll and Rauscher É. M. Unyi

Department of Applied Chemistry, University of Szeged, Szeged, Hungary

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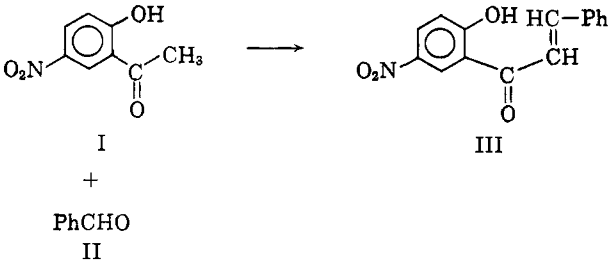
Acid catalysts ($AlCl_3$, BF_3, $ZnCl_2$, HF, HCl, H_2SO_4, AcOH, etc.) have long been used in the Claisen-Schmidt condensation of ketones and aldehydes.[1] Hydrogen chloride has been suggested by Wurtz,[2] Russel, and Lyle.[3] Schraufstätter and Deutsch state that this catalyst does not produce hydroxychalcones.[4] We have already shown that both basic and acidic catalysts can bring about the condensation of hydroxynitroacetophenones with aromatic aldehydes; the bases are the reagents of choice.[5,6]

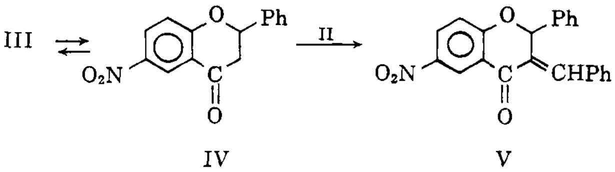
It has now been found that hydroxynitroacetophenones condense rapidly with aldehydes in alcoholic hydrogen chloride to form chalcones in satisfactory yield.



With an excess of aldehyde at higher temperature the condensation of 2-hydroxychalcones continues[7] and gives new products[5,8] which are formed also when the chalcone is employed as starting materials.

These compounds are regarded as 3-arylideneflavanones since they do not contain a hydroxyl group and are not identical with a number of other possible products. There is little likelihood of a Michael condensation between nitrochalcone and flavanone[9,10] and structural alternatives such as arylidenedi- and triacetophenones or dypnones can be excluded.[11]

The formation of V is believed to occur by cyclization of III in acidic medium and condensation of the flavanone (IV) with II. The cyclization is a known reaction and flavanones contain an active methylene group which can undergo aldol-type condensations.[9,12] In the case of nitroflavanones the conversion to benzylidene derivatives has been realized experimentally in 80% yield. An alternative route involving the direct condensation of chalcones with aldehydes is considered unlikely since 3- or 4-hydroxynitroacetophenones, nitroacetophenones or benzoyloxynitrochalcone without free hydroxyl do not condense with II. Chalcones, unlike flavanones, do not contain an active methylene group which can undergo an aldol-type condensation.



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[1] L. Claisen, *Ber.*, **20**, 657 (1887); Durga Nath Dhar, *J. Proc. Inst. Chem.*, **31**, 297 (1959).

[2] A. Wurtz, *J. prakt. Chem.*, II, **5**, 457 (1872).

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[7] With 5-nitro-2-hydroxyacetophenone this phenomenon has already been mentioned[5,8] but the structure of the compound formed was not satisfactorily determined.

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[9] B. N. Kaplash, R. C. Shah, and T. S. Wheeler, *J. Indian Chem. Soc.*, **19**, 117 (1942).

[10] Durga Nath Dhar, *Agra Univ. J. Res.* **10**, 75 (1961).

[11] Gy. Sipos and T. Széll, *Naturwiss.*, **46**, 532 (1959).

[12] H. de Diesbach and H. Kramer, *Helv. Chim. Acta*, **179**, 1400 (1945); H. Kramer, thesis, University of Fribourg, 1944; Durga Nath Dhar, *J. Proc. Inst. Chem.*, **31**, 297 (1959).

The separation of the chalcone and arylidene flavanone is not easy.

The product from the reaction of 2-hydroxy-5-nitroacetophenone with benzaldehyde (V) is not 6-nitroflavanone, 5-nitroflavanol, 6-nitro-flavanone, 2-benzoyl-6-nitro-flavone, nor 2′-benzoyloxy-5′-nitrochalcone (m.p. of a mixture). The compoud is insoluble in cold ethanolic sodium hydroxyde (absence of hydroxyl groups) and does not contain halogen.

Analyses are additional proof of the structure as 3-benzylidene-6-nitroflavanone. It is similar to 3-benzylideneflavanone[12] in that the double bond is not sensitive to bromine.

Experimental[13]

Materials.—Benzaldehyde was 4-chloro-benzaldehyde, commercial grade. 5-nitro-2-hydroxyacetophenone, 4-nitro-2-hydroxy-acetophenone, and 3-nitro-4-hydroxyacetophenone were prepared by Fries reaction[14,15]; 6-nitro-3-hydroxyacetophenone was obtained by Klinke's method.[6] The preparation of the chalcones used has been described in earlier papers.[5,6,16]

Condensation of 5-Nitro-2-hydroxyacetophenone with Benzaldehyde. 3-Benzylidene-6-nitroflavanone (V).—A mixture of 5-nitro-2-hydroxyacetophenone (0.37 g.; 2 mmoles), benzaldehyde (1 ml.; 9.9 mmoles) and anhydrous ethanol (15 ml.) was saturated with hydrogen chloride at 0°. The mixture was kept at room temperature for 30 min., refluxed for 25 min., poured into water (40 ml.) and evaporated. A hot saturated solution of the residue in ethyl acetate was diluted with aqueous ethanol (60%) to turbidity and cooled. The crystals formed were collected in the cold and shaken with aqueous ethanolic sodium hydroxide (25 ml. of ethanol; 2 ml. of 2 *N* sodium hydroxide) for 3 min. The solid V, 3-benzylidene-6-nitroflavanone, was filtered (0.29 g.), washed with ethanol and subsequently with dilute acetic acid, and finally it was twice crystallized from ethanol–ethyl acetate–water (1:1:2), to give pure V (20% yield) m.p. 158°.

Anal. Calcd. for $C_{22}H_{15}NO_4$: C, 73.9; H, 4.2; N, 3.9; O, 17.9. Found: C, 73.9; H, 4.5; N, 3.9; O, 17.9.

Acidification of the alkaline filtrate gave the chalcone in 60% yield.

Only the chalcone was formed at room temperature even with a 20-fold excess of aldehyde, or if a mixture of reactants not containing an excess of aldehyde was refluxed.

If in the above experiment ketone was replaced by chalcone or flavanone the benzylidene compound was obtained in yields of 30% and 80%, respectively.

Condensation of 3-Nitro-4-hydroxyacetophenone with Benzaldehyde.—The yield of chalcone under the experimental conditions already described was 90%. Only tarry products could be isolated even when a large excess of benzaldehyde was used under refluxing conditions for 5 hr. No identifiable result was obtained in attempts to condense the 3′-nitro-4′-hydroxychalcone with benzaldehyde.

Condensation of 4-Nitro-2-hydroxyacetophenone with Benzaldehyde. 3-Benzylidene-7-nitro-flavanone.—The benzylidene flavanone and the chalcone were formed as described in experiment 1 with a refluxing time of 5 min. (25%). The benzylidene flavanone was also rapidly produced from the chalcone and aldehyde in aqueous ethanol. (30% yield). A 1.5-mmole sample of chalcone was suspended in 15 ml. 96% ethanol. The mixture of chalcone and benzylideneflavanone was separated by treatment with aqueous ethanolic sodium hydroxyde as previously described. (20 ml. of ethanol and 20 ml. of 1 *N* sodium hydroxide), m.p. 156–157°.

Anal. Calcd. for $C_{22}H_{15}NO_4$: C, 73.9; H, 4.2; N, 3.9; O, 17.9. Found: C, 73.7; H, 4.4; N, 4.1; O, 17.8.

If the refluxing period was longer than 5 min., tarry materials were formed.

Condensation of 5′-Nitro-2′-hydroxychalcone with 4-Chlorobenzaldehyde. 3-*p*-Chlorobenzylidene-6-nitroflavanone.—The chalcone (1.35 g.; 5 mmoles) and 4-chlorobenzaldehyde (1.45 g.; 10 mmoles) in ethanol (65 ml.) were saturated under cooling in an ice bath with dry hydrogen chloride. After standing for an hour, the mixture was refluxed for 5 hr. The unchanged chalcone (0.7 g.) separated from the solution on cooling in a refrigerator. After mixing the mother liquor with 30 ml. of water a pale yellow solid (0.6 g.) melting at 98° separated. After recrystallizing from carbon tetrachloride 6-nitroflavanone (0.4 g.) melting at 112° was obtained. The mother liquor of the recrystallization was evaporated to dryness and the residue obtained in this way was boiled with a small amount of methanol and filtered. The substance insoluble in methanol gave after recrystallization from ethyl acetate 3-*p*-chlorobenzylidene-6-nitroflavanone melting at 175–176°.

Anal. Calcd. for $C_{22}H_{14}NO_4Cl$: C, 67.4; H, 3.6; N, 3.6; Cl, 9.0. Found: C, 67.2; H, 4.0; N, 3.8; Cl, 8.6.

Starting from 4′-nitro-2′-hydroxychalcone in this experiment a yellow crystalline substance melting at 221–222° (N, 4.7; Cl, 10.6) was obtained, which was not the expected benzylidene compound and gave a melting point depression with the 4′-nitro-2′-hydroxy-4′-chlorochalcone.

Condensation of 6-Nitro-3-hydroxyacetophenone with Benzaldehyde. 6′-Nitro-3′-hydroxychalcone.—The ketone (0.28 g.; 1.5 mmoles) was dissolved in 13 ml. of anhydrous ethanol, then saturated for half an hour under cooling in ice with hydrogen chloride, kept standing for half an hour, and finally boiled under reflux for an other half hour. After distilling the solvent the dry residue was recrystallized from benzene to give 6′-nitro-3′-hydroxychalcone melting at 177–81° (75% yield). After a repeated recrystallization the melting point rose to 185°.[17]

Condensation of 5′-Nitro-2′-hydroxy-4-chlorochalcone with Benzaldehyde. 3-Benzylidene-6-nitro-4′-chloroflavanone.—A mixture of the chalcone (0.2 g.; 0.66 mmole) and benzaldehyde (0.72 ml.; 7 mmoles) in 30 ml. of 96% ethanol was saturated with hydrogen chloride in the manner described above and after standing for half an hour refluxed for 2.5 hr. The unchanged chalcone, which separated on cooling was removed by filtration. On mixing the filtrate with water (15 ml.) the crude 2-benzylidene-6-nitro-4′-chloroflavanone melting at 130° separated (40% yield).

This product was recrystallized three times from a mixture of ethyl acetate–ethanol and 1–2 drops of water so that in every case the first fraction of crystals separating from the lukewarm ethyl acetate–ethanol solution was filtered off and 1–2 drops of water added to the filtrate just after this operation. In this way ivory-colored leaflets insoluble in alkali were obtained; m.p. 165°. The mixture of chalcone and benzylideneflavanone could be separated also with the aid of an alkaline methanolic solution.

Anal. Calcd. for $C_{22}H_{14}NO_4Cl$: C, 67.4; H, 3.6; N, 3.6. Found: C, 67.0; H, 3.7; N, 3.9.

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(13) The melting points are uncorrected.

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(17) Sipos and Széll also have found this melting point.[5]

The Pyrolysis of 3-Acetoxytetrahydrofuran

C. H. DEPUY AND C. N. GOEDERS[1]

Department of Chemistry, Iowa State University, Ames, Iowa

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There are very few examples of the effect of an adjacent hetero atom on the direction of pyrolysis of esters.

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