Identification of Phenyl Vinyl Ketone and Related Compounds as 2,4-Dinitrophenylhydrazones and Pyrazolines

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Received September 23, 1974

C. F. H. ALLEN. Can. J. Chem. **53**, 865 (1975).

The closely interrelated, titled compounds, which have similar physical properties and which form mixtures difficult to separate, are best characterized by instrumental methods.

All α,β-unsaturated aldehydes and methyl ketones gave open-chain dinitrophenylhydrazones directly, whereas the arylated ketones form pyrazolines, as is well known.

C. F. H. ALLEN. Can. J. Chem. **53**, 865 (1975).

La façon la plus simple de caractérisé les composés mentionnés dans le titre qui sont intimement reliés entre eux, qui ont des propriétés physiques similaires et qui forment des mélanges difficiles à séparer fait appel à des méthodes instrumentales.

Tous les aldéhydes et toutes les méthyles cétones non-saturés en position α,β donnent directement des dinitrophénylhydrazones en chaîne ouverte alors que les cétones portant un groupe aryle forment, comme il est bien connu, des pyrazolines. [Traduit par le journal]

During our earlier work (1) it was found that phenyl vinyl ketone (PVK, **1**) could be isolated in quantity by chloroform extraction of an alcoholic solution of 3-chloro- or 3-dimethylaminopropiophenone containing potassium acetate (1,2), thus avoiding the many tedious, recorded methods (3–13). The usual, characteristic solid derivative, now employed for identification of isolated PVK, is 1,3-diphenyl-2-pyrazoline **9** (2, 3, 15, 16, 20).

Because PVK is such a reactive substance, mixtures, difficult to separate, are formed in alcoholic and acidic solutions of 2,4-dinitrophenylhydrazine by all usual procedures. Furthermore, the solubilities, colors, and melting points of closely related compounds, including dinitrophenylhydrazine itself, are very similar, so they are not readily separated and identified; an example is the derivative of dinitrophenylhydrazone of 3-dimethylaminopropiophenone (**4**), probably the preferable source of PVK in solution, and 1-(2,4-dinitrophenyl)-3-phenylpyrazoline (**5**).

Anticipating that 3-chloropropiophenone-DNPH (**6**) could be dehydrohalogenated to PVK-DNPH (**2**), an alcoholic solution was treated with the reagent (14). The mixture formed consisted of a small amount of the desired derivative **6**, considerable 3-ethoxypropiophenone-DNPH (**3**), and, as the main product, the bis-DNPH of 2′,2′-di-(2-benzoylethyl)-2,4-dinitrophenyl-1-hydrazine (**7**); a propoxy derivative of the latter has been previously described (18).

When **6** was dissolved in warm pyridine it at once lost hydrogen chloride, with consequent formation of the known pyrazoline **5** (19). The formation of **3** suggests that there has been a partial dehydrohalogenation of 3-chloropropiophenone to give **1**, which preferentially adds alcohol (3).

Experimental

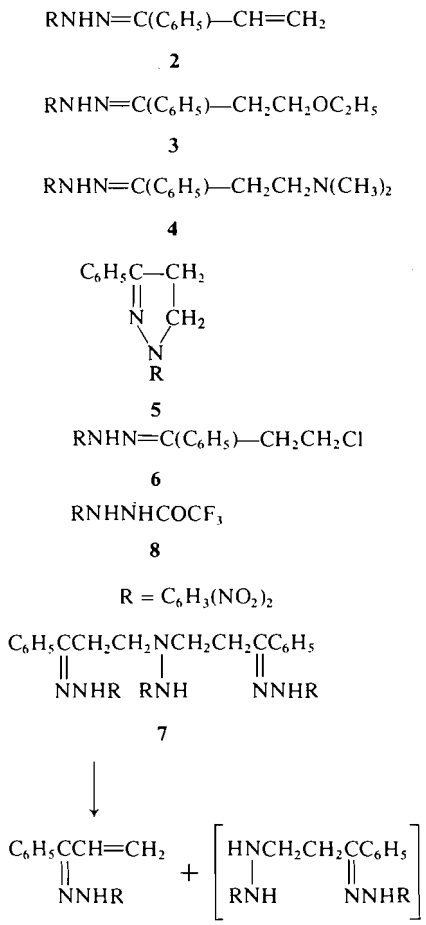
Preparation of Compounds

3-Dimethylaminopropiophenone-DNPH (4)

A mixture of the free base from 2.2 g of the hydrochloride (17) and 25 ml of alcohol was added to a hot, previously prepared dinitrophenylhydrazinium chloride solution (14). There was no visible change but small orange-yellow crystals began to separate in 3–4 min. After 1 h in the refrigerator, 1 g of the derivative was collected on a filter; successive crops made the yield practically quantitative. The same derivative (**4**) is directly obtainable from the hydrochloride. It is also formed on employing DMF as a solvent and evaporating all the latter in a current of air on the steam bath. The substance is very slightly soluble in alcohol, ethyl acetate, and chloroform, moderately soluble in hot acetic acid (unsuitable for recrystallization), but very soluble in hot pyridine, hot DMF, Diglyme, and DMSO.

When the usual procedure for preparing dinitrophenylhydrazones was employed with **1** the product was **3**. An attempted use of trifluoroacetic acid gave 2′-trifluoroacetyl-2,4-dinitrophenylhydrazine (**8**) almost instantly; off-white needles, m.p. 163–164°.

Because DNPH is moderately soluble in cold DMF, this solvent was examined. The deep red solution of 0.2 g of the hydrazine in 1.4 ml of DMF was unchanged after addition of 1 g of PVK but the color was at once lightened on adding 3 drops of concentrated hydrochloric acid. After removal of all the solvent in a current of air, on the steam bath, a gummy mixture remained; less than



1 mg of fine red material was isolated from two runs by triturating with ethyl acetate or formate, chloroform, or ether. It melted at 188–189° (lit. (9) m.p. 195–196°). It seems obvious that PVK-DNPH (**2**) is not a suitable reference compound.

3-Chloropropiophenone (6)

To a hot suspension of 0.8 g of dinitrophenylhydrazine in 25 ml of boiling alcohol, 4 ml of concentrated hydrochloric acid was added, followed by 0.8 g of the 3-chloro ketone in 15 ml of hot alcohol; shortly, a crystalline mixture began to separate. After 4 h it was collected on a filter. Separation of the mixture was tedious. The chloro derivative **6** was always formed in a very low yield. As it was more soluble in alcohol it could be separated from **3**; the latter crystallized well from ethyl acetate or propyl alcohol. Although it was difficult to remove traces of these low-melting components, the main product was always the bishydrazone **7**. The latter is sparingly soluble in the usual solvents but dissolves easily in warm pyridine, 1-methylpyrrolidone, Diglyme, and DMF. It is best purified by dissolving in a little hot pyridine and adding an equal volume of water. The pure product melts at 243–244°, with preliminary shrinking at about 225–226°.

Occasionally the crude chloro derivative (m.p. 139–140°), which contains considerable ethoxy-DNPH (**3**), separated in a few hours. Purification was then accomplished by suspending in hot alcohol and adding sufficient ethyl acetate to give a clear solution. After several recrystallizations the analytical sample had m.p. 131°. Small amounts were purified by chromatography (45 g of Al_2O_3 in 42 ml of hexane, using a 50 ml burette). A benzene suspension was added at the top and eluted with this solvent, collecting the deep orange-red effluent. The separation was discontinued when the color became yellow (due to **3**). The reddish product that separated on evaporation of the solvent was suitable for conversion to the dinitropyrazoline **5**. The crude, chlorinated hydrazone **6** dissolved readily in warm pyridine; upon the addition of water the known (19) pyrazoline **5** separated in shiny, yellow flakes, suggestive of 'gold dust.' This pyrazoline was also identified in the colored mixtures that resulted from the interaction of **1** and dinitrophenylhydrazinium chloride in methyl and ethyl alcohols; only the pyrazoline and unchanged DNPH could be isolated from the red tar that was formed in Diglyme (24).

1,3-Diphenylpyrazoline (9)

This compound (m.p. 151–152°) is obtainable reproducibly by mixing 3 drops each of isolated **1** and phenylhydrazine in 5 ml of alcohol, and adding a trace of acetic acid (3). More recently this pyrazoline has been obtained from the Mannich salt (16) and from 3-chloropropiophenone; the literature (15) gives no details but it "is easier to get than phenyl vinyl ketone." This pyrazoline and its benzene solution show a striking brilliant blue fluorescence in u.v. light; invisible spots that may get on the skin, not removable by washing, are readily detected in this way.

Physical Properties

The remainder of this section is concerned with the characterization of PVK and closely related compounds by instrumental methods. Although none of the latter is universally applicable, mass spectroscopy appears to be the most useful. In all but one instance **7** it gave the molecular ion and characteristic fragmentation pattern. These spectra were determined by the use of a Hitachi RMS-4.

Mass Spectroscopy

2,4-Dinitrophenylhydrazine has a molecular ion at *m/e* 198 (74% M) and fragment ions at *m/e* 180 (8.5), 122 (28), 92 (16), 79 (100), 76 (44), 75 (44), and 51 (89).

Phenyl vinyl ketone-DNPH (2) has a molecular ion at *m/e* 312 (70% M) and fragment ions at *m/e* 265 (41), 264 (13), 218 (15), 189 (14), 115 (74), 105 (100), and 77 (100).

3-Ethoxypropiophenone-DNPH (3) has a molecular ion at *m/e* 358 (84% M) and fragment ions at *m/e* 329 (6.3), 312 (27), 311 (16), 295 (16), 265 (46), 119 (65), 104 (41), 103 (100), 59 (70), and 29 (75). The fragmentation pattern is very similar to that of **5**.

3-Chloropropiophenone-DNPH (6) has a molecular ion at *m/e* 348 (13% M) and fragment ions at *m/e* 312 (50), 295 (5), 265 (40), 219 (24), 218 (33), 117 (25), 116 (25), 115 (65), 104 (37), 103 (30), and 77 (100). The fragmentation pattern is very similar to that of **5**.

3-Dimethylaminopropiophenone-DNPH (4) has a molecular ion at *m/e* 357 (12% M) and fragment ions at *m/e* 355 (2), 312 (0.8), 310 (0.1), 265 (2), 115 (4), 103 (22),

TABLE 1. Analyses

Compound No.	Empirical Formula	Molecular weight	Calculated (%) C	H	N	Found (%) C	H	N
4	$C_{17}H_{20}N_5O_4Cl$	393	51.9	5.1	17.8	51.5	4.9	17.5
						51.4	4.9	17.7
3	$C_{17}H_{18}N_4O_5$	358	57.1	5.0	15.6	57.1	4.8	15.2
6	$C_{15}H_{13}ClN_4O_4$*	348	51.7	3.8	16.0	51.7	3.9	16.0
5	$C_{15}H_{12}N_4O_4$	312	57.7	3.8	17.6	57.6	3.9	17.3
7	$C_{36}H_{30}N_{12}O_{12}$	822	52.6	3.6	20.0	52.4	3.6	20.2
8	$C_8H_5F_3N_4O_5$	294	32.7	1.7		32.4	1.8	

*Calculated: Cl, 10.1. Found: 9.8.

77 (14), and 58 (100), the last attributed to $—CH_2N(CH_3)_2$.

3-Methoxypropiophenone-DNPH (26) has a molecular ion at *m/e* 344 and fragment ions comparable to the ethoxy homolog, as well as the significant one at 45 (100%) attributed to $—CH_2OCH_3$.

1,3-Diphenyl-2-pyrazoline (9) has a molecular ion at *m/e* 222 (100% M) and fragment ions at *m/e* 221 (27), 117 (8), with small amounts at 115, 111, 104, 103, 91, 75.

1-(2,4-Dinitrophenyl)-3-phenyl-2-pyrazoline (5) has a molecular ion at *m/e* 312 (100% M) and fragment ions at *m/e* 295 (23), 265 (91) plus smaller amounts at 220 (20), 219 (23), 218 (6), 165 (19), 117 (22), 116 (6), 103 (50), and 77 (36).

The pyrazoline from chalcone (25) has a molecular ion at *m/e* 388 (70% M), 386 (15), 371 (30), 356 (10), 353 (31), 340 (100), 294 (46), and small values down to 103 (13), and 77 (32).

The bishydrazone 7 decomposed in the mass spectrometer, leaving a brownish residue; because the peak intensity ratios changed during the analysis, thermal decomposition is suggested. Scale divisions (in parentheses) were measured. Found: *m/e* 329 (7), 328 (9), 325 (10), *312* (70), 298 (19), 279 (41), *265* (65), 264 (22), ***218*** (70), *217* (30), *183* (55), *115* (63), *105* (80), 104 (90), ***103*** (210), *77* (190). The values in italics are those characteristic of **2**. The value at 312 has the same *m/e* as **2** (70% M) and the isomeric dinitropyrazoline **5** (100% M); the latter also has values (bold face italic) *not found* in the above, at 295, 220, 219, 165, 117, 116, hence both **2** and **5** may be present. Although the peaks fit better for the PVK-DNPH, its presence is not unequivocally certain. However, on inspection of the structures involved it is seen that a cleavage of 7 to give this DNPH **2** is essentially a reverse Michael addition (21–23), consistent with and analogous to the formation of phenyl vinyl ketone from 3-dimethylaminopropiophenone (7). Its presence is a reasonable conclusion.

$$C_6H_5COCH_2CH_2N(CH_3)_2 \rightarrow C_6H_5COCH{=}CH_2 + HN(CH_3)_2$$

Nuclear Magnetic Resonance

These spectra were measured on a Varian A spectrometer. The chemical shifts are reported in ppm downfield from tetramethylsilane. The solvents were $CDCl_3$ and DMSO-d_6.

Compound 3: δ 1.15 (t, J = 7 Hz, 3H, O—C—CH_3), 3.20 (t, J = 5.5 Hz, 2H, N = C—CH_2), 3.85 (t, J = 5.5 Hz, N = C—C—CH_2—O—), 7.4 (m, 3H, ArH), 7.9 (m, 2H, ArH), 8.03 (d, $J_{AB} \simeq$ 9 Hz, 1H, A of ABX of 2,4-DNP), 8.31 (dd, $J_{AB} \simeq$ 9 Hz, $J_{BX} \simeq$ 2.5 Hz, 1H, B of ABX), 9.13 (d, $J_{BX} \simeq$ 2.5 Hz, 1H, X of ABX), 11.9 (broad s, 1H NH).

Compound 4: δ 2.85 (s, 6H, NMe_2), 3.3 (broad m, area uncertain since H_2O peak superimposed, =C—CH_2CH_2—N—), 7.5 (m, 3H, *m, p*-Hs of phenyl), 8.0 (m, 2H, *o*-Hs of phenyl), 8.05 (d, J_{AM} = 9 Hz, 1H, A of AMX of 2,4-DNP), 8.37 (dd, J_{AM} = 9 Hz, J_{MX} = 3 Hz, 1H, M of AMX), 8.83 (d, J_{MX} = 3 Hz, 1H, X of AMX), and 11.3 (broad s, 1H, NH).

Compound 6: ABX for dinitrophenyl at 9.12 (J = 2.5 Hz), 8.34 (J = 9 Hz, 2.5 Hz), the remaining H of this pattern is obscured by the other aromatic absorption: C_6H_5 at 7.76 (m, 2H) and 7.43 (m, 4H); AA′BB′ pattern at 3.42 (t, 2H) and 3.83 (t, 2H, NH at 11.7).

Compound 2: δ 5.86 (dd, J_{AM} = 2 Hz, J_{MX} = 17 Hz, 1H, =CH_2), 6.18 (dd, J_{AM} = 2 Hz, J_{AX} = 11 Hz, 1H, =CH_2), 6.75 (dd, J_{MX} = 1 Hz, J_{AX} = 11 Hz, 1H, =CH), 7.5 (m, 3H, *m*- and *p*-H of C_6H_5), 7.8 (m, 2H, *o*-H of C_6H_5), 8.14 (d, J_{AM} = 9 Hz, 1H, A of AMX of 2,4-DNP), 8.38 (dd, J_{AM} = 9 Hz, J_{MX} = 3 Hz, 1H, M of AMX of 2,4-DNP), 9.18 (d, J_{MX} = 3 Hz, 1H, X of AMX of 2,4-DNP), 13.0 (broad s, 1H, NH).

Compound 9: this showed a typical symmetrical AA′BB′ pattern, the two halves being centered at ~3.2 and 3.8 p.p.m. for the N—$CH_ACH_{A'}$—$CH_BCH_{B'}$—C= N moiety. The aromatic H appeared in a complex multiplet from 6.7–7.8 p.p.m.

Compound 5: ABX for DNP at 7.09 (J = 9 Hz), 8.27 (J = 9 Hz, 2.5 Hz), 8.45 (J = 2.5 Hz), phenyl at 7.44 (m, 3H), 7.67 (m, 2H), AA′BB′ at 3.43 (t, 2H) and 4.07 (t, 2H).

Ultraviolet Spectroscope

Ultraviolet absorption appears to be of less use for the identification of closely related 2,4-dinitrophenylhydrazones because, as will be noticed on inspection of the earlier literature (9), the wavelengths and extinctions of many of the derivatives are very close. This may be attributed to the fact that the major part of the molecule is the aromatic chromophore, $—C_6H_3(NO_2)_2$. In the data for the following compounds the first figure is wavelength and the second is log ε_{max}: 7, 368, 5.62; **3**, 380, 2.51; **6**, 372, 1.30; **4**, 368, 2.26; **2**, 383, 2.78 (9); **9**, 354, 1.87; **5**, 4.2, 4.52 (19); 2,4-dinitrophenylhydraz*ine*, 348, 4.12 (20), and 352, 4.17 (18).

Infrared Spectroscope

Examination of the i.r. absorption of the representative 2,4-dinitrophenylhydrazones of α,β-carbonyl compounds, $CH_2C{=}CHCHO$, $CH_2C{=}CHCOCH_3$, $C_6H_{13}CH{=}CHCOCH_3$, and $C_6H_5CH{=}CHCOCH_3$ revealed the presence of the typical NH band at 3.0–3.1 μ in each instance. The dinitrophenylhydrazone of chalcone (25) is now shown to be the lower melting isomer, m.p. 178°.

We are pleased to have had the invaluable assistance of Miss T. J. Davis for the i.r., D. Maier for the m.s., T. H. Regan for the n.m.r., D. Bush and D. Wall for the u.v. spectra, and D. Ketchum for the microanalyses, all of the Eastman Kodak Company Research Laboratory.

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