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1-(1-PHTHALAZINYL)- AND 1-(4-METHOXYPHENYL)-6,6-DIMETHYL-4-OXO-4,5,6,7-TETRAHYDROINDAZOLE

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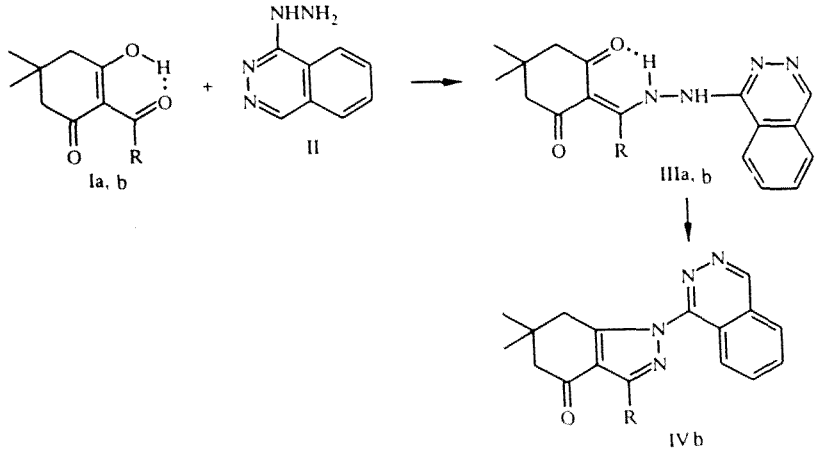
2-(1-Phthalazinylhydrazino)methylene-(IIIa) or 2-(1-phthalazinylhydrazino)ethylidene-5,5-dimethyl-1,3-cyclohexanediones (IIIb) were prepared from 1-hydrazinophthalazine and 2-formyl- or 2-acetyldimedone. Cyclization of IIIb in the presence of p-*TsOH gave 1-(1-phthalazinyl)3,6,6-trimethyl-4-oxo-4,5,6,7-tetrahydroindazole. Reaction of 4-methoxyphenylhydrazine with 2-formyl- and 2-acetyldimedone gave the corresponding 1-(4-methoxyphenyl)-4-oxo-4,5,6,7-tetrahydroindazole. In the case of 2-formyldimedone the intermediate 2-(4-methoxyphenylhydrazinomethylene)-5,5-dimethyl-1,3-cyclohexanedione was isolated.*

In continuation of work on the synthesis of 4-oxo-4,5,6,7-tetrahydroindazoles with heterocyclic substituents in position 1 [1-3] we have prepared the corresponding 2-hydrazinoalkylidene derivatives (IIIa and b) by the reaction of 2-formyl-(Ia) and 2-acetyldimedone (Ib) with hydrazinophthalazine (II). However, only 2-(1-phthalazinylhydrazino)ethylidene-5,5-dimethyl-1,3-cyclohexanedione (IIIb) gave the corresponding indazole (IVa) on cyclizing in the presence of *p*-TsOH.

The corresponding indazoles (VIIa and b) were obtained considerably more easily by the reaction of 4-methoxyphenylhydrazine (I) and the 2-acyldimedones, Ia and b. For example, 1-(4-methoxyphenyl)-3,6,6-trimethyl-4-oxo-4,5,6,7-tetrahydroindazole (VIb) was formed directly by boiling for 2 h equimolar quantities of 2-acetyldimedone (Ib), 4-methoxyphenylhydrazine hydrochloride and sodium bicarbonate.

Under the same conditions, the potassium salt of 2-formyldimedone and 4-methoxyphenylhydrazine hydrochloride gave 2-(4-phenoxyphenylhydrazinomethylene)-5,5-dimethyl-1,3-cyclohexanedione (VIIa) which cyclized to the indazole VIa on boiling in ethanol in the presence of HCl.



The structures of the hydrazinoalkylidene derivatives IIIa, IIIb, VIIa and the indazoles IVb, VIa and VIb were confirmed by IR and ^{1}H NMR spectroscopy. Intense carbonyl bands occur at 1670 (IVb), 1678 (VIa) and 1666 cm^{-1} (VIb) for the indazoles, whereas for the enehydrazines IIIa, IIIb and VIIa this group is characterized by a low intensity band at 1655-1630 and a more intense band at 1610-1550 cm^{-1}. The intensities were noticeably weaker for the enamines and enehydrazines

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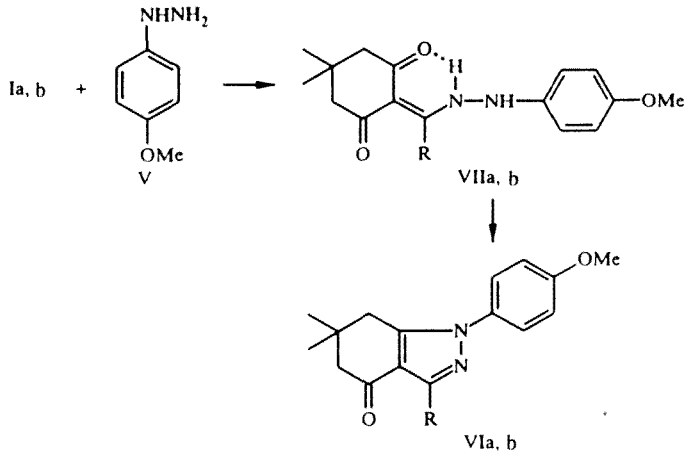
of 2-formyl-1,3-cyclohexanedione than for the corresponding compounds of 2-acetyl-1,3-cyclohexanedione [4-6]. Differences for similar structures were also observed in the ^{1}H NMR spectra. For example, the chelated hydrogens of the enehydrazines IIIa and VIIa have chemical shifts of 13.81 (IIIa) and 11.94 (VIIa) whereas for IIIb (the methyl substituted analog of IIIa) the signal appears at 16.16 ppm. Hydrogen signals for the indazoles appear in the expected positions, the signals of the 5- and 7-methylene groups differing by 0.3-0.6 ppm, whereas in the 2-substituted 1,3-cyclohexanediones they appear as a single four hydrogen singlet (IIIb) or the signals differ by 0.05-0.07 ppm (IIIa and VIIa).



I, IV—VII a R = H, b R = Me

EXPERIMENTAL

IR spectra of Nujol (1800-1500 cm^{-1}) and hexachlorobutadiene (3600-2000 cm^{-1}) suspensions were recorded with a Specord 75-IR spectrometer, but the C–H vibrations in the 3050-2800 cm^{-1} region are not reported. ^{1}H NMR spectra of $CDCl_3$ solutions with TMS as internal standard were recorded with a Bruker WH-90/DS (90 MHz) spectrometer.

2-(1-Phthalazinohydrazinomethylene)-5,5-dimethyl-1,3-cyclohexanedione (IIIa). Boiling solutions of the potassium salt of 2-formyldimedone (0.41 g, 2 mmol) in distilled water (10 cm^3) and 1-hydrazinophthalazine hydrochloride (0.39 g, 2 mmol) in distilled water (10 cm^3) were mixed together and the precipitate was recrystallized from ethanol. Yield 0.46 g (74%). M.p. 222-224°C. IR spectrum: 1657, 1633, 1597, 1551; 3145 cm^{-1}. ^{1}H NMR Spectrum: 1.06 (6H, s, *gem*-Me_2), 2.36 (2H, s, CH_2), 2.41 (2H, s, CH_2), 7.67 (3H, m, 5-, 6-, 7-$H_{phthalazinyl}$ [H_{pt}]), 8.00 (1H, s, 4-H_{pt}), 8.36 (1H, m, 8-H_{pt}), 8.61 (1H, d, J = 10 Hz, H_R), 10.81 (1H, s, NH), 13.81 ppm (1H, d, J = 10 Hz, NH...O). Found, %: C 65.60, H 5.96, N 18.00. Calc. for $C_{17}H_{18}N_4O_2$, %: C 65.79, H 5.85, N 18.05.

2-[1-(1-Phthalazinohydrazino)ethylidene]-5,5-dimethyl-1,3-cyclohexanedione(IIIb). 1-Hydrazinophthalazinehydrochloride (II) (0.39 g, 2 mmol) in distilled water (10 cm^3), heated to 70-75°C, was added to a boiling solution of 2-acetyldimedone (Ib) (0.36 g, 2 mmol) in ethanol (5 cm^3) and then a solution of sodium acetate (0.16 g, 2 mmol) in water (2 cm^3) was added. A yellow precipitate of the product was formed slowly. It was filtered off after a day and recrystallized from ethanol. Yield 0.35 g (56%). M.p. 229-231°C. IR spectrum: 1630, 1614, 1596, 1558: 3300, 3060 cm^{-1}. ^{1}H NMR spectrum: 1.00 (6H, s, *gem*-Me_2), 2.37 (4H, s, CH_2), 2.83 (3H, s Me_R), 7.53 (3H, m, 5-,6-,7-H_{pt}), 7.90 (1H, s, 4-H_{pt}), 8.33 (1H, m, 8-H_{pt}), 10.26 (1H, br. s, NH), 16.16 ppm (1H, br. s, NH...O). Found, %, C 66.45, H 6.65, N 17.40. Calc. for $C_{18}H_{20}N_4O_2$, %: C 66.65, H 6.22, N 17.27.

1-(1-Phthalazinyl)-3,6,6-trimethyl-4-oxo-4,5,6,7-tetrahydroindazole (IVb). Hydrazine IIIb (0.32 g, 1 mmol) in ethanol (20 cm^3) was boiled in the presence of a catalytic amount of *p*-toluenesulfonic acid for 30 min. The ethanol was removed on a rotary evaporator, the residue was triturated with a mixture of benzene and hexane and the colorless solid product (IVb) was purified by reprecipitation from ethanol solution (3-5 cm^3) with water. Yield 0.18 g (72%). M.p. 136-137°C. IR spectrum: 1670, 1618, 1578, 1558, 1546, 1505 cm^{-1}. ^{1}H NMR spectrum: 1.26 (6H, s, *gem*-Me), 2.49 (2H, s, CH_2), 2.67 (3H, s, Me_R), 3.13 (2H, s, CH_2), 8.09 (3H, m, 5-, 6-,7-H_{pt}), 8.69 (1H, m, 8-H_{pt}), 9.06 ppm (1H, s, 4-H_{pt}). Found, %: C 70.71, H 5.82, N 18.40. Calc. for $C_{18}H_{18}N_4O$, %: C 70.57, H 5.92, N 18.29.

2-(4-Methoxyphenylhydrazinomethylene)-5,5-dimethyl-1,3-cyclohexanedione (VIIa). The potassium salt of 2-formyldimedone (1.03 g, 5 mmol) and 4-methoxyphenylhydrazine hydrochloride (0.88 g, 5 mmol) were boiled in ethanol (50 cm^3) for 1 h and the hot solution was then decanted from the precipitated KCl. The product (VIIa) which precipitated over 24 h was filtered off and recrystallized from ethanol. Yield 1.10 g (76%). M.p. 164-166°C. IR spectrum: 3220, 3090, 1650, 1625, 1605, 1570, 1540, 1515 cm^{-1}. ^1H NMR spectrum: 0.98 (6H, s, *gem*-Me), 2.24 (2H, s, CH_2), 2.31 (2H, s, CH_2), 3.67 (3H, s, OMe), 6.68 (4H, m, H_{Ar}), 7.69 (1H, br. s, NH), 8.82 (1H, d, J = 11 Hz, H_R), 11.94 (1H, d, J = 11 Hz, NH...O). Found, %: C 66.48, H 6.80, N 9.60. Calc. for $C_{16}H_{20}N_2O_3$, %: C 66.64, H 6.99, N 9.71.

1-(4-Methoxyphenyl)-6,6-dimethyl-4-oxo-4,5,6,7-tetrahydroindazole (VIa). Hydrazine VIIa (0.72 g, 2.5 mmol) was boiled in ethanol (20 cm^3) in the presence of concentrated hydrochloric acid (1 cm^3) for 3 h. The ethanol was then removed on a rotary evaporator. White crystals of VIa were filtered off after 24 h. Yield 0.42 g (63 %). M.p. 110-112°C. IR spectrum: 1678, 1620, 1545, 1520 cm^{-1}. ^1H NMR spectrum: 1.07 (6H, s, *gem*-Me_2), 2.40 (2H, s, CH_2), 2.76 (2H, s, CH_2), 3.87 (3H, s, OMe), 7.02 (2H, m, H_{Ar}), 7.38 (2H, m, H_{Ar}), 8.02 (1H, s, H_R). Found, %: C 70.92, H 6.66, N 10.19. Calc. for $C_{16}H_{18}N_2O_2$, %: C 71.09, H 6.71, N 10.36.

1-(4-Methoxyphenyl)-3,6,6-trimethyl-4-oxo-4,5,6,7-tetrahydroindazole (VIb). 2-Acetyldimedone (0.91 g, 5 mmol), 4-methoxyphenylhydrazine hydrochloride (0.87 g, 5 mmol) and sodium bicarbonate (0.42 g, 5 mmol) were boiled in ethanol (30 cm^3) for 2 h after which the hot solution was filtered. Ethanol (20 cm^3) was removed on the rotary evaporator and hot water (20 cm^3) was then added. Colorless crystals of VIb separated on cooling. Yield 0.85 g (60%). M.p. 98-101°C. IR spectrum: 1666, 1620, 1545, 1530 cm^{-1}. ^1H NMR spectrum: 1.09 (6H, s, *gem*-Me), 2.38 (2H, s, CH_2), 2.53 (3H, s, Me_R), 2.71 (2H, s, CH_2), 3.84 (3H, s, OMe), 6.96 (2H, m, H_{Ar}), 7.38 ppm (2H, m, H_{Ar}). Found, %: C 71.61, H 7.00, N 9.99. Calc. for $C_{17}H_{20}N_2O_2$, %: C 71.80, H 7.09, N 9.85.

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