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Aroylphenylacetylenes Ia-c react with *t*-butyl hydrazinecarboxylate (IIa) and 2-furylhydrazide (IIb) to give the corresponding hydroxydihydropyrazole derivatives IVa-f. This cyclic structure is supported by chemical transformations. Thus, when compounds IVa-c are heated with acetic anhydride, they yield the corresponding 5-aryl-1-(*t*-butoxycarbonyl)-3-phenylpyrazoles Va-c which, upon hydrolysis with methanolic potassium hydroxide, produce the corresponding 5(3)aryl-3(5)phenylpyrazoles VI. Spectroscopic data also confirm the suggested cyclic structure IV.

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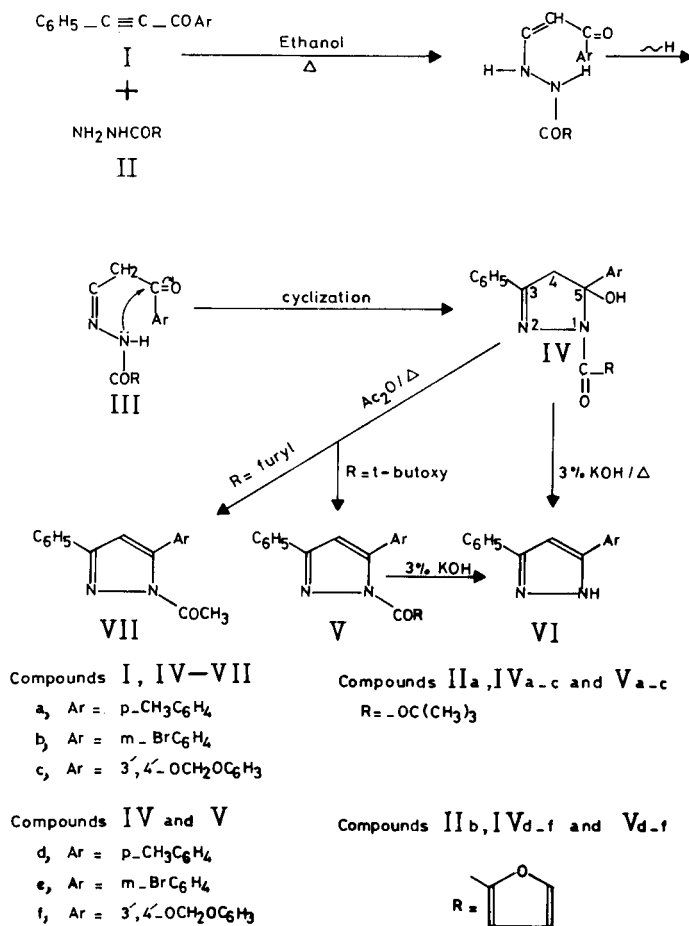
The reactions of aroylphenylacetylenes with ethyl and phenyl hydrazinecarboxylates have been reported to give ω -aroylacetophenone-*N*-ethoxycarbonyl- and *N*-phenoxy-carbonylhydrazones, respectively [1-5]. We believe now that the reaction products can exist in the cyclic hydroxydihydropyrazole form. This point prompted further investigation. The present work aims at preparing new substituted heterocycles of the same series *via* interaction of acetylenic ketones with *t*-butyl hydrazinecarboxylate and 2-furylhydrazides. Such study is expected to shed further light on the mechanism of this reaction, and on the structure of the products.

When aroylphenylacetylenes Ia-c are refluxed with hydrazine derivatives IIa,b in ethanol for 5 hours, they afford the corresponding 5-hydroxy-5-aryl-3-phenyl-4,5-dihydro-1*H*-pyrazole derivatives IVa-f, and not the open-chain form IIIa-f as suggested earlier [1-5] (Scheme 1). The heterocyclic structure IV is confirmed by spectroscopic data and is supported by chemical transformations. Thus the infrared spectra of compounds IVa-f show a broad band in the region 3200-3500 cm^{-1} (OH). The proposed new structure is also consistent with the presence of a strong band in the region 1630-1710 cm^{-1} attributed to a carbonyl group attached to nitrogen [6]. The ultraviolet spectra of these compounds show absorption maxima in the range 282-306 nm attributed to π - π^* transitions.

The ^1H -nmr spectra of these compounds in deuteriochloroform show an AB system ($J_{AB} = 18$ Hz) attributed to the prochiral methylene protons. When the nmr spectra of these compounds are obtained in hexadeuteriodimethylsulfoxide, the AB system collapses to an A_2 system in the region 3.41-3.55 ppm [4]. The nmr spectra also show a singlet, in the region 3.90-5.35 ppm which is exchangeable with deuterium oxide and is therefore assigned to an (OH) [7].

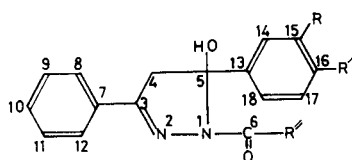
Further evidence for the cyclic form IV is gained from

Scheme 1

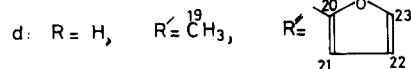
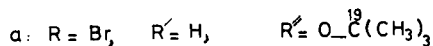


^{13}C -nmr spectra for compounds IVa,d (Table 1). These spectra lack signals in the region 195-210 ppm, characteristic of an aryl substituted ketonic carbon [8]. However, they exhibit signals corresponding to a quaternary carbon, C₅-OH (Table 1) for compounds IVa and IVd at 92.86 ppm

Table 1
¹³C-NMR Chemical Shifts of Compounds IVa,d



IV



Carbon No.	IVa	IVd
3	146.67	153.89
4	50.48	49.87
5	92.86	95.39
6	150.99	157.29
7	131.10	129.37
8	128.49	126.66
9	127.60	123.91
10	126.50	128.76
11	127.60	123.91
12	128.49	126.66
13	131.02	140.65
14	130.10	130.52
15	122.77	129.37
16	130.06	131.30
17	127.61	129.37
18	122.88	130.52
19	82.76	20.99
20	28.16	146.02
21	—	119.91
22	—	111.59
23	—	145.78

and 95.39 ppm, respectively. These data are in agreement with the cyclic structure IV, but not with the open form III. The ¹³C-nmr spectra also show signals at 146.67 ppm for compound IVa, and 153.89 ppm for compound IVd assigned to C₃=N. The methylene carbon (CH₂) shows signal at 50.48 ppm and 49.87 ppm in the spectra of compounds IVa and IVd, respectively.

The mass spectra of compounds IVa and IVd give further support for the cyclic assignment. They exhibit prominent peak corresponding to [M-OH]⁺ which is conceivable with structure IV, but not with III.

The chemical behavior of these compounds is also in agreement with the assigned structure. Thus, compounds IVa-c are easily dehydrated by refluxing with acetic anhydride to give the corresponding 5-aryl-1-(*t*-butoxycarbonyl)-3-phenyl-pyrazoles Va-c. The structure of these compounds is substantiated by their ¹H-nmr spectra which show a signal in the range 6.67-6.75 ppm attributed to the

olefinic proton [1,7]. Their infrared spectra show a strong band in the region 1768-1774 cm⁻¹ attributed to the carbonyl group [1]. The structure of the compounds Va-c is further confirmed by the fact that when refluxed with 3% methanolic potassium hydroxide, these compounds give the corresponding 5(3)-aryl-3(5)-phenylpyrazoles VI. The latter were also directly obtained from the respective hydroxydihydropyrazoles IVa-f by refluxing with 3% methanolic potassium hydroxide. Products VI are identical with authentic samples, obtained by reacting aroylphenylacetylenes Ia-c with hydrazine hydrate [1]. Refluxing of the compounds IVd-f with acetic anhydride gives the corresponding acetyl derivatives VIIa-c, which are identical with authentic samples obtained by reacting 5(3)-aryl-3(5)-pyrazoles with acetic anhydride.

EXPERIMENTAL

The infrared spectra were recorded using a Beckmann IR 4260 Research Infrared Spectrophotometer. The ultraviolet spectra were measured on a Beckmann Spectrophotometer ACTA using scan speed ¼ nm/second and 10 nm/inch. The ¹H-nmr spectra were recorded on JEOL JNM-PM spectrometer at 60 MHz using TMS as internal reference. The ¹³C-nmr spectra (FT-mode) were recorded on a Bruker WM-250 spectrometer at 62.97 MHz using DMSO-d₆ as the solvent and TMS as internal reference. Melting points are uncorrected. The purity of the analytical samples was checked by tlc (silica gel). Microanalyses (C, H, N, Br) were determined by the Central Analytical Laboratory at KISR, Kuwait.

Reaction of Aroylphenylacetylene (Ia-c) with *t*-Butyl Hydrazinecarboxylate (IIa) and 2-Furylhydrazide (IIb).

General Procedure.

A mixture of the appropriate aroylphenylacetylene I (0.01 mole) and IIa or IIb (0.01 mole) was refluxed in ethanol for 5 hours. The reaction product was then worked up as previously reported [1] to give a white material. Crystallization from ethanol yielded the corresponding hydroxydihydropyrazole derivatives IVa-f.

1-(*t*-Butoxycarbonyl)-5-hydroxy-5-(*p*-methylphenyl)-3-phenyl-4,5-dihydro-1H-pyrazole (IVa).

This compound was obtained in 95% yield, mp 151-152°; ir (potassium bromide): ν 3505-3200 br, 3405 s (OH), 1705 s, 1690 sh (COOR), 1600 m, 1570 m (C=N) cm⁻¹; uv (ethanol): λ max nm (log ε) 283 (4.39); uv (hexane): 283 (4.31); ¹H-nmr (deuteriochloroform): δ 1.37 (s, 6H, 2CH₃), 1.42 (s, 3H, CH₃), 2.33 (s, 3H, CH₃), 3.31, 3.65 (d, d, 2H, CH₂, J = 18 Hz), 3.90 (br, 1H, OH), 7.07-8.00 (m, 9H, ArH); ¹H-nmr (DMSO-d₆): δ 1.23 (s, 9H, -C(CH₃)₃), 2.31 (s, 3H, CH₃), 3.41 (s, 2H, CH₂), 6.98-7.80 (m, 9H, ArH).

Anal. Calcd. for C₂₁H₂₄N₂O₃: C, 71.59; H, 6.92; N, 7.95. Found: C, 71.50; H, 7.02; N, 7.78.

1-(*t*-Butoxycarbonyl)-5-hydroxy-5-(*m*-bromophenyl)-3-phenyl-4,5-dihydro-1H-pyrazole (IVb).

This compound was obtained in 94% yield, mp 159-160°; ir (potassium bromide): ν 3422-3200 br, 3270 m (OH), 1710 s, 1690 sh (COOR), 1600 m, 1590 m (C=N) cm⁻¹; uv (ethanol): λ max nm (log ε) 282 (4.40); uv (hexane): 284 (4.41); ¹H-nmr (deuteriochloroform): δ 1.37 (s, 9H, -C(CH₃)₃), 3.31, 3.64 (d, d, 2H, CH₂, J = 18 Hz), 4.23 (br, 1H, OH), 7.20-7.90 (m, 9H, ArH); ¹H-nmr (DMSO-d₆): δ 1.17 (s, 9H, -C(CH₃)₃), 3.52 (s, 2H, CH₂), 7.00-7.91 (m, 9H, ArH).

Anal. Calcd. for C₂₀H₂₁BrN₂O₃: C, 57.56; H, 5.07; N, 6.71; Br, 19.15. Found: C, 57.80; H, 5.13; N, 6.83; Br, 19.16.

1-(*t*-Butoxycarbonyl)-5-hydroxy-5-(3',4'-methylenedioxyphenyl)-3-phenyl-4,5-dihydro-1*H*-pyrazole (IVc).

This compound was obtained in 88% yield, mp 199-200°; ir (potassium bromide): ν 3400-3210 br, 3360 s, 3240 s (OH), 1690 s, 1675 s (COOR), 1600 m, 1570 m (C=N) cm^{-1} ; uv (ethanol): λ max nm (log ϵ) 286 (4.21), 266 (4.30); uv (hexane): 280 (4.40), 263 (4.44); ¹H-nmr (deuteriochloroform): δ 1.42 (s, 9H, -C(CH₃)₃), 3.29, 3.63 (d, d, 2H, CH₂, J = 18 Hz), 5.93 (s, 2H, OCH₂O), 4.82 (br, 1H, OH), 6.32-7.85 (m, 8H, ArH); ¹H-nmr (DMSO-d₆): δ 1.20 (s, 9H, -C(CH₃)₃), 3.45 (s, 2H, CH₂), 5.96 (s, 2H, OCH₂O), 6.50-7.90 (m, 8H, ArH).

Anal. Calcd. for C₂₁H₂₂N₂O₅: C, 65.97; H, 5.80; N, 7.33. Found: C, 66.11; H, 5.77; N, 7.44.

1-(2-Furoyl)-5-hydroxy-5-(*p*-methylphenyl)-3-phenyl-4,5-dihydro-1*H*-pyrazole (IVd).

This compound was obtained in 89% yield, mp 157-158°; ir (potassium bromide): ν 3500-3200 br, 3460 m (OH), 1640 s (COR), 1595 m, 1570 m (C=N) cm^{-1} ; uv (ethanol): λ max nm (log ϵ): 306 (4.25), 257 (4.18); uv (hexane): 306 (4.38), 256 (4.30); ¹H-nmr (deuteriochloroform): δ 2.33 (s, 3H, CH₃), 3.47, 3.78 (d, d, 2H, CH₂, J = 18 Hz), 5.28 (br, 1H, OH), 6.62-7.87 (m, 12H, Ar-H); ¹H-nmr (DMSO-d₆): δ 2.27 (s, 3H, CH₃), 3.50 (s, 2H, CH₂), 6.62-7.93 (m, 12H, Ar-H).

Anal. Calcd. for C₂₁H₁₈N₂O₃: C, 72.82; H, 5.24; N, 8.07. Found: C, 72.72; H, 5.23; N, 8.17.

1-(2-Furoyl)-5-hydroxy-5-(*m*-bromophenyl)-3-phenyl-4,5-dihydro-1*H*-pyrazole (IVe).

This compound was obtained in 91% yield, mp 193-194°; ir (potassium bromide): ν 3420-3200 br, 3280 s (OH), 1630 s (COR), 1595 m, 1570 m (C=N) cm^{-1} ; uv (ethanol): λ max nm (log ϵ) 305 (4.34), 258 (4.26); uv (hexane): 305 (4.20), 258 (4.15); ¹H-nmr (deuteriochloroform): δ 3.36, 3.71 (d, d, 2H, CH₂, J = 18 Hz), 5.33 (br, 1H, OH), 6.58-7.87 (m, 12H, ArH); ¹H-nmr (DMSO-d₆): δ 3.55 (s, 2H, CH₂), 6.65-7.92 (m, 12H, ArH).

Anal. Calcd. for C₂₀H₁₅BrN₂O₃: C, 58.41; H, 3.68; N, 6.81; Br, 19.43. Found: C, 58.48; H, 3.68; N, 6.99; Br, 19.44.

1-(2-Furoyl)-5-hydroxy-5-(3',4'-methylenedioxyphenyl)-3-phenyl-4,5-dihydro-1*H*-pyrazole (IVf).

This compound was obtained in 97% yield, mp 170-171°; ir (potassium bromide): ν 3500-3180 br, 3270 m (OH), 1630 s (COR), 1595 m, 1570 m (C=N) cm^{-1} ; uv (ethanol): λ max nm (log ϵ) 304 (4.41), 297 (4.42), 257 (4.21); uv (hexane): 306 (4.90), 295 (4.41), 257 (4.34); ¹H-nmr (deuteriochloroform): δ 3.36, 3.71 (d, d, 2H, CH₂, J = 18 Hz), 5.23 (s, 1H, OH), 5.83 (s, 2H, OCH₂O), 6.52-7.83 (m, 11H, ArH); ¹H-nmr (DMSO-d₆): δ 3.53 (s, 2H, CH₂), 5.98 (s, 2H, OCH₂O), 6.67-7.97 (m, 11H, ArH).

Anal. Calcd. for C₂₁H₁₆N₂O₅: C, 67.02; H, 4.29; N, 7.44. Found: C, 66.97; H, 4.34; N, 7.43.

Reaction of Acetic Anhydride with 1-(*t*-Butoxycarbonyl)-5-Hydroxy-5-Aryl-3-Phenyl-4,5-Dihydro-1*H*-Pyrazoles (IVa-c).

General Procedure.

A mixture of the hydroxydihydropyrazole derivative IVa-c (0.01 mole) and acetic anhydride (10 ml) was heated on a steam bath for 5 hours. The reaction mixture was then cooled and treated with cold 50% aqueous ethanol (100 ml), and the precipitated solid was crystallized from cyclohexane to give the corresponding 1-(*t*-butoxycarbonyl)-5-aryl-3-phenylpyrazoles Va-c. When compounds IVd-f were heated with acetic anhydride, under the same experimental conditions, they gave the corresponding *N*-acetyl derivatives VII identified by comparison with authentic samples prepared from the reaction of 3(5)-aryl-5(3)-phenylpyrazoles VI with acetic anhydride.

1-(*t*-Butoxycarbonyl)-5-(*p*-methylphenyl)-3-phenylpyrazole (Va).

This compound was obtained in 82% yield, mp 91-92°; ir (potassium bromide): ν 1771 s (C=O), 1565 s (C=N) cm^{-1} ; uv (ethanol): λ max nm (log ϵ) 258 (4.42); ¹H-nmr (deuteriochloroform): δ 1.24 (s, 9H, -C(CH₃)₃), 2.33 (s, 3H, CH₃), 6.71 (s, 1H, =CH-), 8.1-7.1 (m, 9H, ArH).

Anal. Calcd. for C₂₁H₂₂N₂O₂: C, 75.42; H, 6.63; N, 8.78. Found: C, 75.31; H, 6.59; N, 8.52.

1-(*t*-Butoxycarbonyl)-5-(*m*-bromophenyl)-3-phenylpyrazole (Vb).

This compound was obtained in 79% yield, mp 86-87°; ir (potassium bromide): ν 1768 s (C=O), 1560 s (C=N) cm^{-1} ; uv (ethanol): λ max nm (log ϵ) 262 (4.46); ¹H-nmr (deuteriochloroform): δ 1.15 (s, 9H, -C(CH₃)₃), 6.67 (s, 1H, =CH-), 7.9-7.1 (m, 9H, ArH).

Anal. Calcd. for C₂₀H₁₅BrN₂O₂: C, 60.16; H, 4.80; N, 7.20; Br, 20.02. Found: C, 60.21; H, 4.81; N, 6.90; Br, 19.74.

1-(*t*-Butoxycarbonyl)-5-(3',4'-methylenedioxyphenyl)-3-phenylpyrazole (Vc).

This compound was obtained in 85% yield, mp 101-102°; ir (potassium bromide): ν 1774 s (C=O), 1562 s (C=N) cm^{-1} ; uv (ethanol): λ max nm (log ϵ): 268 (4.51); ¹H-nmr (deuteriochloroform): δ 1.21 (s, 9H, -C(CH₃)₃), 5.92 (s, 2H, OCH₂O), 6.75 (s, 1H, =CH-), 7.92-6.90 (m, 8H, ArH).

Anal. Calcd. for C₂₁H₂₀N₂O₄: C, 69.22; H, 5.53; N, 7.69. Found: C, 68.92; H, 5.61; N, 7.74.

Action of Alcoholic Potassium Hydroxide on 1-(*t*-Butoxycarbonyl)- and 1-Furoyl-5-Hydroxy-5-Aryl-3-Phenyl-4,5-dihydro-1*H*-Pyrazoles IVa-f, and 1-(*t*-Butoxycarbonyl)-5-Aryl-3-Phenylpyrazoles Va-c.

General Procedure.

The pyrazole derivative IVa-f, Va-c (0.01 mole) was refluxed on a steam bath with 3% methanolic potassium hydroxide (20 ml) for 30 minutes. The reaction products were worked up as previously reported [1] to give almost quantitative yields of the corresponding 3(5)-aryl-5(3)-phenylpyrazole (VI) identical (mp, and mixed mp) with authentic samples prepared from aroylphenylacetylene and hydrazine hydrate [1].

3(5)-(*p*-Methylphenyl)-5(3)-phenylpyrazole (VIa).

This compound has mp 183-184° [1].

3(5)-(*m*-Bromophenyl)-5(3)-phenylpyrazole (VIb).

This compound has mp 182-183° [3].

3(5)-(3',4'-Methylenedioxyphenyl)-5(3)-phenylpyrazole (VIc).

This compound has mp 191-192° [1].

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