NITROGEN-CONTAINING HETEROCYCLES DERIVED FROM TETRACARBONYL COMPOUNDS AND THEIR ANALOGS. SYNTHESIS OF 2-(4,4-DIMETHYL-2,6-DIOXOCYCLOHEXYL)-1,4-DIPHENYLBUTANE-1,4-DIONE AND ITS REACTION WITH N-NUCLEOPHILES

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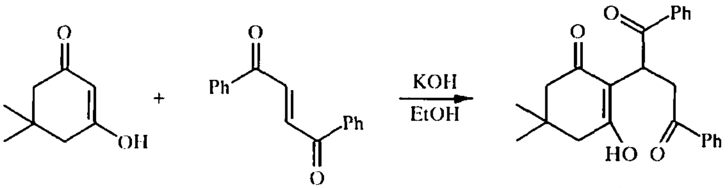
Condensation of dimedone with 1,2-dibenzoylethylene in the presence of base gave 2-(4,4-dimethyl-2,6-dioxocyclohexyl)-1,4-diphenylbutane-1,4-dione. Its reaction with amines gives the corresponding pyrrole derivatives.

An extremely promising basis for building up the pyrrolo[4,3,2-*d,e*]quinoline system (which appears in the structure of many natural alkaloids) are tetracarbonyl compounds in which two carbonyl groups are situated in 1,4 positions to one another and the other two in a 1,5 position. As a model compound we chose the Michael adduct of dimedone with *trans*-3-benzoylacrylic acid. With this adduct the synthesis of the novel pyrrolo[4,3,2-*d,e*]quinoline structure was successfully carried out by use of ammonia [1].

With the aim to explore the range for use of the given scheme we have carried out the synthesis of novel tetracarbonyl compounds by condensation of dimedone with *trans*-1,2-dibenzoylethylene and studied its reaction with N-nucleophiles.

Reaction of dimedone with 1,2-dibenzoylethylene proceeded in alcoholic solution in the presence of KOH.



I

Formation of compound I was confirmed by the presence of an AMX spin system ($COCH_2CR_2$) in its PMR spectrum.

We have carried out the reaction of tetraketone I with ammonia, methylamine, benzylamine, *o*-phenylenediamine, and aniline. The involvement of the dimedone fragment was assumed with the formation if not of the pyrrolo[4,3,2-*d*,*e*]quinoline system II, then at least of a tetrahydroindole structure. However, in all cases, pyrrole derivatives were obtained.

Reaction with ammonia, methylamine, and benzylamine in aqueous alcohol solution in an autoclave led to formation of compounds IIIa-c. Formation of the pyrroles IIIa-c was confirmed by the presence in their PMR spectra of 4-H pyrrole proton signals in the region 6.2-6.8 ppm and enamine fragment NH protons at 4.5-5.4 ppm (as well as in the case of compound IIIa the signal for the pyrrole NH proton at 8.5 ppm). IR absorption bands in the region 3400-3370 cm^{-1} are characteristic of NH stretching vibrations for the NH groups of the enamines. In the spectrum of compound IIIa there appears a band at 3270 cm^{-1} (pyrrole NH).

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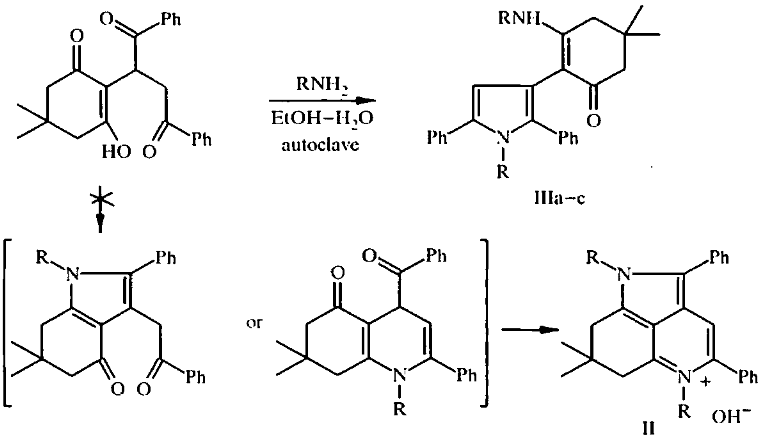
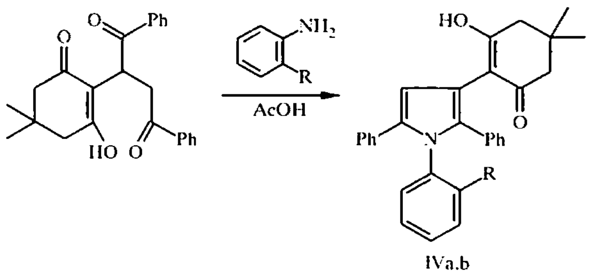


III a R = H; b R = Me; c R = $PhCH_2$

Reaction of tetraketone I with *o*-phenylenediamine and aniline in acetic acid leaves the dimedone fraction unchanged overall.



IV a R = H; b R = NH_2

The proposed structures for compounds IVa,b are supported by the PMR spectral data in which there appear signals for the 4-H pyrrole protons at 6.2 ppm. The IR spectra show a broad absorption at 2630-2600 cm^{-1} (enolic OH) and two bands in the region 3480 and 3380 cm^{-1} (NH_2) for compound IVb.

EXPERIMENTAL

IR spectra were taken on a Specord IR-75 spectrophotometer in vaseline oil and methylene chloride. Mass spectra were determined on an HP 5972 MSD/HP chromatographic mass spectrometer at an electron ionization energy of 70 eV. PMR spectra were taken on a Bruker WM-250 spectrometer using $CDCl_3$ and DMSO-d_6 solutions (internal standard TMS). Monitoring of the reaction course and the purity of the individual materials was carried out using TLC on Silufol UV-254 and Sorbfil.

2-(4,4-Dimethyl-2,6-dioxocyclohexyl)-1,4-diphenylbutane-1,4-dione (I). A mixture of dimedone (2.80 g, 0.02 mol) and 1,2-dibenzoylethylene (4.72 g, 0.02 mol) was dissolved in ethanol (50 ml) at 70°C. Aqueous alcoholic KOH solution (4 N, 1.5 ml) was added to the stirred hot solution and the mixture was refluxed for 3 h, neutralized with acetic acid, and progressively diluted with water to 500 ml. The precipitate was filtered off and dried to give 6.17 g (82%) of product with mp 184-185°C (ethanol-water, 4:1). IR spectrum (vaseline): 1692, 1680 cm^{-1}. PMR spectrum ($CDCl_3$): 10.19 (1H, s, OH); 8.09 (2H, d, H_{arom}); 7.97 (2H, d, H_{arom}); 7.53-7.62 (2H, m, H_{arom}); 7.41-7.50 (4H, m, H_{arom}); 5.47 (1H, dd, J_1 = 6.0, J_2 =9.0 Hz, 2-H); 4.15 (1H, dd, J_1 = 9.0, J_2 = 20.0 Hz, 3-H); 3.33 (1H, dd, J_1 = 6.0, J_2 = 20.0 Hz, 3-H); 2.35 (2H, s, CH_2); 2.18 (2H, s, CH_2); 0.98 (3H, s, CH_3); 0.92 ppm (3H, s, CH_3). Found, %: C 76.70; H 6.38. $C_{24}H_{24}O_4$. Calculated, %: C 76.57; H 6.43.

3-(2-Amino-4,4-dimethyl-6-oxocyclohexen-1-yl)-2,5-diphenylpyrrole (IIIa). A solution of compound I (0.38 g, 1 mmol) in a mixture of ethanol (2.5 ml) and ammonia (25%, 2 ml) was heated in an autoclave of volume 5 ml for 5 h at 150°C. The mixture was cooled and the precipitate was filtered off and dried. Yield 0.27 g (75%); mp 134-137°C (aqueous alcohol). IR spectrum (vaseline): 3400, 3270, 3128, 1634 cm^{-1}. PMR spectrum (CDCl$_3$): 8.54 (1H, s, NH); 7.15-7.54 (10H, m, 2Ph); 6.39 (1H, s, 4-H); 4.50 (2H, s, NH$_2$); 2.37 (2H, s, CH$_2$); 2.18-2.35 (2H, m, CH$_2$); 1.13 ppm (6H, s, 2CH$_3$). M$^+$ 356. Found, %: C 80.96; H 6.73; N 7.93. C$_{24}$H$_{24}$N$_2$O. Calculated, %: C 80.87; H 6.79; N 7.86.

1-Methyl-3-(2-methylamino-4,4-dimethyl-6-oxocyclohexen-1-yl)-2,5-diphenylpyrrole (IIIb). A solution of compound I (0.40 g, 1.1 mmol) in a mixture of ethanol (2 ml) and aqueous methylamine (25%, 2 ml) was heated in an autoclave of volume 5 ml for 3.5 h at 150°C. The mixture was cooled and the precipitated oil was triturated with ice to give 0.30 g (73%) of product with mp 80-83°C (aqueous alcohol). IR spectrum (CH$_2$Cl$_2$): 3370, 1700, 1646 cm^{-1}. PMR spectrum (CDCl$_3$); 7.28-7.56 (10H, m, 2 Ph); 6.78 (1H, d, J = 5.5 Hz, 4-H); 4.91 (1H, q, NH); 3.54 (3H, s, CH$_3$); 3.38 (3H, s, CH$_3$); 2.64 (2H, s, J = 5.5 Hz, CH$_2$); 2.15-2.44 (2H, m, CH$_2$); 1.07 ppm (6H, br s, 2CH$_3$). Found, %: C 81.02; H 7.54; N 7.17. C$_{26}$H$_{28}$N$_2$O. Calculated, %: C 81.21; H 7.34; N 7.29.

1-Benzyl-3-(2-benzylamino-4,4-dimethyl-6-oxocyclohexen-1-yl)-2,5-diphenylpyrrole (IIIc). A solution of compound I (0.40 g, 1.1 mmol) in a mixture of ethanol (3 ml) and benzylamine (1 ml) was heated in an autoclave of volume 5 ml for 3.5 h at 150°C. The mixture was cooled and the precipitated oil triturated with ice to give 0.42 g (74%) of product with mp 58-60°C (aqueous alcohol). IR spectrum (CH$_2$Cl$_2$): 3366 cm^{-1}. PMR spectrum (CDCl$_3$): 7.05-7.40 (18H, m, H$_{arom}$); 6.82 (1H, t, H$_{arom}$); 6.69 (1H, t, H$_{arom}$); 6.24 (1H, s, 4-H); 5.36 (1H, t, J = 7.0 Hz, NH); 5.15 (2H, s, CH$_2$–N); 4.25 (2H, d, J = 7.0 Hz, CH$_2$–NH); 2.30 (2H, br. s, CH$_2$); 2.25 (2H, br. s, CH$_2$); 1.02 (3H, br. s, CH$_3$); 0.83 ppm (3H, br. s, CH$_3$). M$^+$ 537; [PhCH$_2$]$^+$ 91, Found, %: C 85.19; H 6.64; N 5.05. C$_{38}$H$_{36}$N$_2$O. Calculated, %: C 85.04; H 6.76; N 5.22.

3-(4,4-Dimethyl-2,6-dioxocyclohexyl)-1,2,5-triphenylpyrrole (IVa). A mixture of compound I (0.20 g, 0.5 mmol) and aniline (0.05 g, 0.5 mmol) in acetic acid (5 ml) was refluxed for 10 min. The contents crystallized upon cooling. The crystals were filtered off and washed with water and then acetone. Yield 0.14 g (61%); mp 292°C (with decomp.). IR spectrum (vaseline): 2600 cm^{-1}. PMR spectrum (DMSO-d$_6$): 9.70 (1H, s, OH); 6.88-7.28 (15H, m, 3 Ph); 6.20 (1H, s, 4-H); 2.45 (2H, s, CH$_2$); 2.08-2.30 (2H, m, CH$_2$); 0.95 ppm (6H, s, 2 CH$_3$). Found, %: C 83.28; H 6.36; N 3.13. C$_{30}$H$_{27}$NO$_2$. Calculated, %: C 83.11; H 6.28; N 3.23.

1-(2-Aminophenyl)-3-(4,4-dimethyl-2,6-dioxocyclohexyl)-2,5-diphenylpyrrole (IVb). A mixture of compound I (0.40 g, 1.1 mmol) and o-phenylenediamine (0.12 g, 1.1 mmol) in acetic acid (7 ml) was refluxed for 2 h. The mixture was decomposed with icy water and the precipitated crystals were filtered off, washed with water, then alcohol, and dried to give 0.13 g (27%) of product with mp 210-213°C. IR spectrum (vaseline): 3476, 3384, 2630 cm^{-1}. PMR spectrum (DMSO-d$_6$): 9.61 (1H, s, OH); 7.00-7.24 (10H m, 2 Ph); 6.97 (1H, t, H$_{arom}$); 6.86 (2H, d, H$_{arom}$); 6.58 (1H, d, H$_{arom}$); 6.40 (1H, t, H$_{arom}$); 6.24 (1H, s, 4-H); 5.02 (2H, s, NH$_2$); 2.23 (2H, s, CH$_2$); 2.17 (2H, s, CH$_2$); 0.98 (3H, br. s, CH$_3$); 0.90 ppm (3H, br. s, CH$_3$). Found, %: C 80.12; H 6.46; N 6.41. C$_{30}$H$_{28}$N$_2$O$_2$. Calculated, %: C 80.33; H 6.29; N 6.25.

REFERENCES

1. S. V. Dubovitskii and V. A. Kaminskii, *Zh. Org. Khim.*, **33**, 1118 (1997).