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Synthesis of 4-Substituted 1,5-Diaryl-3-diphenylmethoxy-3-pyrrolin-2-ones and Their [1,5]-Sigmatropic Rearrangement

V. L. Gein[a], L. F. Gein[b], and V. S. Platonov[a]

[a] *Perm State Pharmaceutical Academy, ul. Polevaya 2, Perm, 614990 Russia*
e-mail: geinvl48@mail.ru
[b] *Perm State Medical Academy, Perm, Russia*

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Abstract—Reactions of 1,4,5-trisubstituted 3-hydroxy-3-pyrrolin-2-ones with diphenyldiazomethane yield the *O*-alkylation products. Thermolysis of 1,5-diaryl-4-heteroyl-3-hydroxy-3-pyrrolin-2-ones is accompanied with suprafacial [1,5]-sigmatropic rearrangement.

Keywords: diphenyldiazomethane, [1,5]-sigmatropic rearrangement, 3-hydroxy-3-pyrrolin-2-one

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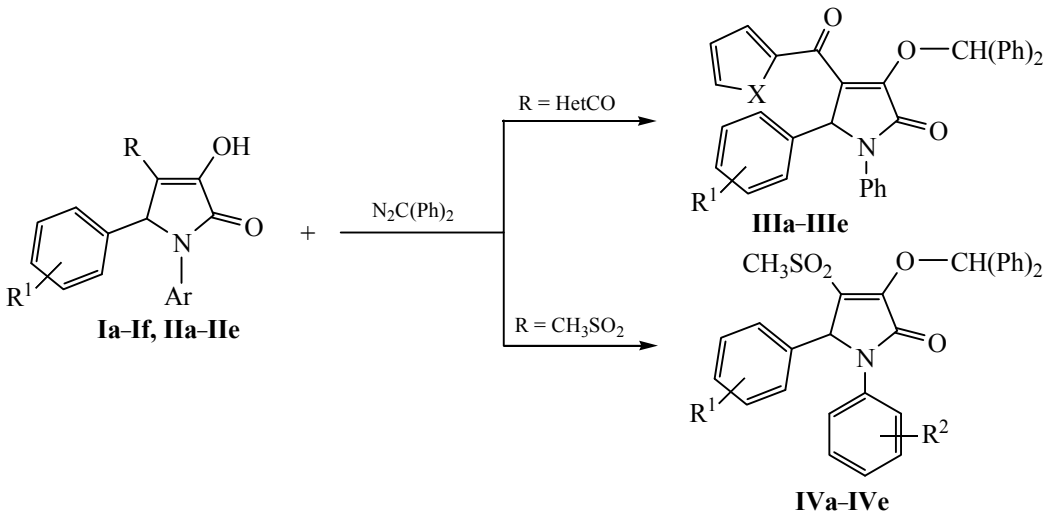
We have recently found that, depending on the nature of the substituent at position 4, the *O*-alkylated 4-acyl-1,5-diphenyl-3-hydroxy-3-pyrrolin-2-ones [1], 4-bromo-1,5-diphenyl-3-hydroxy-3-pyrrolin-2-ones [2], 1,5-diaryl-4-alkoxycarbonyl-3-hydroxy-3-pyrrolin-2-ones [3] and *N*-aryl-1,5-diaryl-3-hydroxy-3-pyrrolin-2-one-4-carboxamides [4] as well as 4-methylsulfonyl-5-aryl-2,5-dihydrofuran-2-ones [5] undergo suprafacial [1,5]- [1] or [1,3]-sigmatropic rearrangement [2–4] in the course of the thermolysis process.

Extending the knowledge in this area, herein we considered [1,5]- and [1,3]-sigmatropic rearrangements in the series 4-heteroyl- or 4-methylsulfonyl-substituted *O*-alkylated 3-hydroxy-3-pyrrolin-2-ones.

Starting compounds **Ia**–**If** and **IIa**–**IIe** were prepared according to the known methods [6–10].

Reactions of 1,5-diaryl-4-heteroyl(methylsulfonyl)-3-hydroxy-3-pyrrolin-2-ones **I** and **II** with diphenyldiazomethane proceeded in dioxane at room tempera-

Scheme 1.



I, **III**, R^1 =H (**a**, **d**), 4-CH_3 (**b**, **e**), 4-Br (**c**), 4-NO_2 (**f**); X = O (**a**–**c**), S (**d**–**f**); **II**, **IV**, R^1 = H (**a**–**c**), 4-Cl (**d**), 4-Br (**e**); R^2 = H (**a**, **d**), 4-NH_2SO_2 (**b**), 4-I (**c**), 4-Br (**e**).

ture within 1 d to give 1-phenyl-5-aryl-4-heteroyl-3-diphenylmethoxy-3-pyrrolin-2-ones **IIIa–IIIf** and 1-phenyl-5-aryl-4-methylsulfonyl-3-diphenylmethoxy-3-pyrrolin-2-ones **IVa–IVe** with fairly good yields (Scheme 1).

The obtained compounds were colorless or pale-yellow crystalline solids soluble in DMSO, DMF, and most common organic solvents.

The ^{1}H NMR spectra of **IIIa–IIIf** contained signals of aromatic and heterocyclic protons in the region of 7.39–7.61 ppm, singlet of 5-methine proton of pyrrolinone ring at 6.29–6.57 ppm, and singlet of methine proton of benzhydryl moiety at 7.14–7.26 ppm.

IR spectra of **IIIa–IIIf** contained strong absorption bands assigned to the carbonyl group conjugated with the double bond (1609–1623 cm^{-1}) and to the lactam carbonyl group (1689–1707 cm^{-1}).

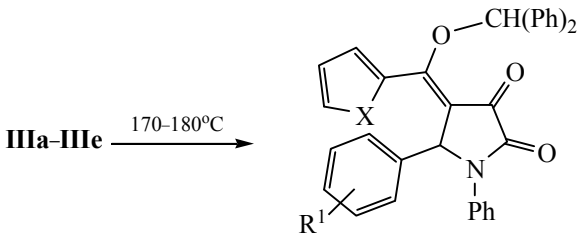
Mass spectrum of **IIIb** contained the molecular ion peak $[M]^+$ with *m*/*z* 525 and the fragmentation peaks with *m*/*z* 358 $[M - CHPh_2]^+$, 167 $[CHPh_2]^+$, 95 [furanoyl]$^+$, and 77 $[C_6H_5]^+$, coinciding with the proposed structure.

In ^{1}H NMR spectra of **IVa–IVe**, signals characteristic of original pyrrolinones **II** as well as singlet of the methine proton of benzhydryl moiety (7.53–7.81 ppm) were observed.

IR spectra of **IVa–IVe** contained absorption bands due to stretching of sulfonyl group (1138–1150 and 1309–1321 cm^{-1}), double bond (1633–1648 cm^{-1}), and lactam carbonyl (1702–1711 cm^{-1}).

The obtained compounds **III** and **IV** did not give a positive reaction for the enol hydroxyl group, which also confirmed the proposed structure.

Pyrrolinones **IIIa–IIIe** were found to undergo rearrangement into 5-aryl-4-[heteryl(diphenylmethoxy)-methylene]-1-phenylpyrrolidine-2,3-diones **Va–Ve** when heated at 170–180°C during 5–10 min.



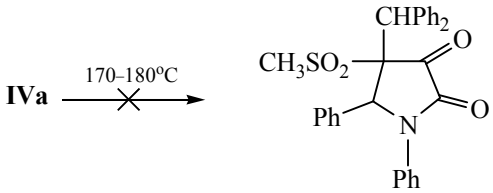
Va–Ve

III, **V**, R = H (**a**, **d**), 4-CH_3 (**b**, **e**), 4-Br (**c**); X = O (**a–c**), S (**d**, **e**).

In the ^{1}H NMR spectra of compounds **Va–Ve**, aromatic and heterocyclic protons resonated in the region of 6.90–7.38 ppm. Singlet at 5.77–5.83 ppm corresponded to the 5-methine proton of the ring. The methine proton of diphenylmethoxy group manifested at 7.88–7.91 ppm.

In IR spectra of compounds **Va–Ve,** the absorption band of lactam carbonyl group was shifted towards higher frequency as compared to the spectra of to **Ia–Ie** (to 1751–1765 cm^{-1}), apparently, due to the increased strain in the tetrahydropyrrolidine-2,3-dione ring resulting from formation of the exocyclic double bond. Furthermore, the IR spectra contained the absorption bands assigned to ketone carbonyl (1710–1718 cm^{-1}) and exocyclic double bond (1640–1650 cm^{-1}). Hence, in this case the suprafacial [1,5]-sigmatropic rearrangement took place, similar to the case of 4-acyl-1,5-diphenyl-3-diphenylmethoxy-3-pyrrolin-2-ones [1]. Some decrease in the yields of **Va–Ve** as compared with those of the compounds described previously [1] was apparently caused by a different structure of the transition state. In the studied case it was less favorable due to the presence of five-membered heterocyclic residue, less aromatic than the aroyl substituent.

In addition, it was found that 4-methylsulfonyl-substituted pyrrolinones did not undergo [1,3]-sigmatropic rearrangement: after heating of **IVa** in a metal bath at 170–180°C only the starting pyrrolinone was isolated.



Probably, that fact could be explained by the steric hindrance due to the bulky methylsulfonyl moiety.

EXPERIMENTAL

IR spectra (mineral oil) were obtained with the Specord UR-20 spectrophotometer. ^{1}H NMR spectra (in DMSO-d_6) were registered on a Bruker DRX 500 spectrometer (500.13 MHz) relative to internal TMS reference. Mass spectra (CI, 70 eV) were recorded with the Finnigan MAT INCOS 50 instrument. Elemental analysis was performed using the Perkin Elmer 2400 unit. Melting points were measured with the Melting Point M-565 apparatus.

1,5-Diphenyl-3-diphenylmethoxy-4-(2-furanoyl)-3-pyrrolin-2-one (IIIa). 1.95 g (0.01 mol) of diphenyldiazomethane was added to a solution of 3.45 g (0.01 mol) of 1,5-diphenyl-4-(2-furanoyl)-3-hydroxy-3-pyrrolin-2-one **Ia** in 10 mL of dioxane. The mixture was incubated at room temperature during 1 day. Then the solvent was removed, and the residue was recrystallized. Yield 4.33 g (84.6%), mp 231–232°C (toluene). ^{1}H NMR spectrum, δ, ppm: 6.36 s (1H, 5-CH), 7.17 s (1H, $CHPh_2$), 7.39 m (23H, H_{arom}). Found, %: C 79.72, 79.67; H 5.01, 5.08; N 2.62, 2.57. $C_{34}H_{25}NO_4$. Calculated, %: C 79.82; H 4.92; N 2.74.

Compounds **IIIb–IIIf** were obtained similarly.

5-(4-Tolyl)-1-phenyl-3-diphenylmethoxy-4-(2-furanoyl)-3-pyrrolin-2-one (IIIb). Yield 4.77 g (90.7%), mp 230–231°C (toluene). IR spectrum, ν, cm^{-1}: 1622 (C=O), 1700 (CON). ^{1}H NMR spectrum, δ, ppm: 2.10 s (3H, CH_3), 6.31 s (1H, 5-CH), 7.16 s (1H, $CHPh_2$), 7.39 m (22H, H_{arom}). Found, %: C 80.23, 80.17; H 5.08, 5.03; N 2.59, 2.51. $C_{35}H_{27}NO_4$. Calculated, %: C 79.98; H 5.18; N 2.66. Mass spectrum, *m*/*z* (I_{rel}, %): 525 $[M]^+$, 358 $[M - CHPh_2]^+$, 167 $[CHPh_2]^+$, 95 [furanoyl]$^+$, 77 $[C_6H_5]^+$.

5-(4-Bromophenyl)-1-phenyl-3-diphenylmethoxy-4-(2-furanoyl)-3-pyrrolin-2-one (IIIc). Yield 4.68 g (79.3%), mp 224–226°C (toluene). IR spectrum, ν, cm^{-1}: 1623 (C=O), 1720 (CON). ^{1}H NMR spectrum, δ, ppm: 6.38 s (1H, 5-CH), 7.26 s (1H, $CHPh_2$), 7.41 m (22H, H_{arom}). Found, %: C 69.03, 68.96; H 4.01, 4.08; N 2.29, 2.33. $C_{34}H_{24}BrNO_4$. Calculated, %: C 69.16; H 4.09; N 2.37.

4-(2-Thienoyl)-1,5-diphenyl-3-diphenylmethoxy-3-pyrrolin-2-one (IIId). Yield 4.39 g (83.2%), mp 230–231°C (toluene). ^{1}H NMR spectrum, δ, ppm: 6.34 s (1H, 5-CH), 7.18 s (1H, $CHPh_2$), 7.60 m (23H, H_{arom}). Found, %: C 77.53, 77.57; H 4.68, 4.61; N 2.71, 2.75; S 5.97, 5.89. $C_{34}H_{25}NO_3S$. Calculated, %: C 77.40; H 4.77; N 2.65; S 6.08.

4-(2-Thienoyl)-5-(4-tolyl)-1-phenyl-3-diphenylmethoxy-3-pyrrolin-2-one (IIIe). Yield 3.55 g (65.6%), mp 185–187°C (toluene). IR spectrum, ν, cm^{-1}: 1609 (C=O), 1707 (CON). ^{1}H NMR spectrum, δ, ppm: 2.09 s (3H, CH_3), 6.29 s (1H, 5-CH), 7.14 s (1H, $CHPh_2$), 7.52 m (22H, H_{arom}). Found, %: C 77.53, 77.46; H 5.08, 5.13; N 2.69. 2.74; S 6.05, 5.97. $C_{35}H_{27}NO_3S$. Calculated, %: C 77.61; H 5.02; N 2.59; S 5.92.

4-Methylsulfonyl-1,5-diphenyl-3-diphenylmethoxy-3-pyrrolin-2-one (IVa). 1.07 g (0.005 mol) (10% excess) of diphenyldiazomethane was added to a solution of 1.65 g (0.005 mol) of 1,5-diphenyl-4-methylsulfonyl-3-hydroxy-3-pyrrolin-2-one **IIa** in 10 mL of dioxane. The mixture was incubated at room temperature during 1 day. Then the solvent was evaporated, and the residue was recrystallized from ethanol. Yield 2.30 g (93%), mp 176–178°C. IR spectrum, ν, cm^{-1}: 1138, 1312 (SO_2), 1648 (C=C), 1702 (CON). ^{1}H NMR spectrum, δ, ppm: 2.63 s (3H, CH_3SO_2), 6.18 s (1H, 5-CH), 7.81 s (1H, $CHPh_2$), 6.90–7.63 m (23H, H_{arom}). Found, %: C 72.93, 72.89; H 4.89, 4.95; N 2.76, 2.71; S 6.34, 6.38. $C_{30}H_{25}NO_4S$. Calculated, %: C 72.70; H 5.08; N 2.83; S 6.47.

Compounds **IVb–IVd** were obtained similarly.

1-(4-Aminosulfonylphenyl)-4-methylsulfonyl-5-phenyl-3-diphenylmethoxy-3-pyrrolin-2-one (IVb). Yield 1.79 g (61%), mp 173–175°C (ethanol). IR spectrum, ν, cm^{-1}: 1150, 1321 (SO_2); 1633 (C=C), 1711 (CON); 3232, 3336 (NH_2). ^{1}H NMR spectrum, δ, ppm: 2.69 s (3H, CH_3SO_2), 6.28 s (1H, 5-CH), 697 s (2H, NH_2), 7.76 s (1H, $CHPh_2$), 7.33–7.54 m (22H, H_{arom}). Found, %: C 62.63, 62.59; H 4.39, 4.45; N 4.76, 4.82; S 11.04, 10.98. $C_{30}H_{26}N_2O_6S_2$. Calculated, %: C 62.70; H 4.56; N 4.87; S 11.16.

1-(4-Iodophenyl)-4-methylsulfonyl-5-phenyl-3-diphenylmethoxy-3-pyrrolin-2-one (IVc). Yield 1.80 g (58%), mp 143–146°C (ethanol). IR spectrum, ν, cm^{-1}: 1132, 1309 (SO_2); 1642 (C=C), 1705 (CON). ^{1}H NMR spectrum, δ, ppm: 2.65 s (3H, CH_3SO_2), 6.32 s (1H, 5-CH), 7.53 s (1H, $CHPh_2$), 6.80–7.75 m (22H, H_{arom}). Found, %: C 57.83, 57.88; H 3.73, 3.69; N 2.16, 2.21; S 5.30, 5.26. $C_{30}H_{24}INO_4S$. Calculated, %: C 57.98; H 3.89; N 2.25; S 5.16.

4-Methylsulfonyl-1-phenyl-3-diphenylmethoxy-5-(4-chlorophenyl)-3-pyrrolin-2-one (IVd). Yield 2.04 g (77%), mp 164–166°C (ethanol). IR spectrum, ν, cm^{-1}: 1138, 1315 (SO_2); 1648 (C=C), 1708 (CON). ^{1}H NMR spectrum, δ, ppm: 2.56 s (3H, CH_3SO_2), 6.40 s (1H, 5-CH), 7.59 s (1H, $CHPh_2$), 6.79–7.70 m (22H, H_{arom}). Found, %: C 72.93, 72.85; H 4.89, 4.95; N 2.76, 2.72; S 6.34, 6.39. $C_{30}H_{25}NO_4S$. Calculated, %: C 72.70; H 5.08; N 2.83; S 6.47.

1,5-Diphenyl-4-[(fur-2-yl)diphenylmethoxymethylene]pyrrolidine-2,3-dione (Va). 5.11 g (0.01 mol) of 1,5-diphenyl-4-(2-furanoyl)-3-diphenylmethoxy-3-pyrrolin-2-one **IIIa** was heated (metal bath) at 170–180°C during 5–10 min. Then the residue was treated with ethanol, filtered off, and recrystallized. Yield 1.66 g (32.4%), mp 241–243°C (ethanol). IR spectrum, ν, cm^{-1}:

1650 (C=C), 1715 (C=O), 1751 (CON). ^{1}H NMR spectrum, δ, ppm: 5.80 s (1H, 5-CH), 7.88 s (1H, $CHPh_2$), 7.29 m (23H, H_{arom}). Mass spectrum, *m*/*z* (I_{rel}, %): 358 $[M]^+$. Found, %: C 79.79, 79.72; H 4.83, 4.81; N 2.69, 2.63. $C_{34}H_{25}NO_4$. Calculated, %: C 79.82; H 4.92; N 2.74.

Compounds **Vb–Ve** were obtained similarly.

5-(4-Tolyl)-1-phenyl-4-[(fur-2-yl)diphenylmethoxy]-pyrrolidine-2,3-dione (Vb). Yield 3.00 g (57.1%), mp 241–243°C (ethanol). IR spectrum, ν, cm^{-1}: 1640 (C=C), 1710 (C=O), 1760 (CON). ^{1}H NMR spectrum, δ, ppm: 2.05 s (3H, CH_3), 5.77 s (1H, 5-CH), 7.89 s (1H, $CHPh_2$), 6.98 m (22H, H_{arom}). Found, %: C 79.82, 79.86; H 5.27, 5.21; N 2.51, 2.47. $C_{35}H_{27}NO_4$. Calculated, %: C 79.98; H 5.18; N 2.66.

5-(4-Bromophenyl)-1-phenyl-4-[(fur-2-yl)-3-diphenylmethoxy]pyrrolidine-2,3-dione (Vc). Yield 4.90 g (83.1%), mp 235–237°C (ethanol). IR spectrum, ν, cm^{-1}: 1645 (C=C), 1711 (C=O), 1762 (CON). ^{1}H NMR spectrum, δ, ppm: 5.79 s (1H, 5-CH), 7.89 s (1H, $CHPh_2$), 7.21 m (22H, H_{arom}). Found, %: C 68.93, 69.03; H 3.91, 3.98; N 2.46, 2.40. $C_{34}H_{24}BrNO_4$. Calculated, %: C 69.16; H 4.09; N 2.37.

1,5-Diphenyl-4-[(thien-2-yl)diphenylmethoxymethylene]pyrrolidine-2,3-dione (Vd). Yield 4.18 g (79.2%), mp 229–230°C (ethanol). IR spectrum, ν, cm^{-1}: 1648 (C=C), 1714 (C=O), 1763 (CON). ^{1}H NMR spectrum, δ, ppm: 5.79 s (1H, 5-CH), 7.91 s (1H, $CHPh_2$), 7.38 m (23H, H_{arom}). Found, %: C 77.27, 77.32; H 4.60, 4.66; N 2.58, 2.53; S 5.87, 5.91. $C_{34}H_{25}NO_3S$. Calculated, %: C 77.40; H 4.77; N 2.65; S 6.08.

5-(4-Tolyl)-1-phenyl-4-[(thien-2-yl)diphenylmethoxymethylene]pyrrolidine-2,3-dione (Ve). Yield 4.90 g (83.1%), mp 235–237°C (ethanol). IR spectrum, ν, cm^{-1}: 1645 (C=C), 1711 (C=O), 1762 (CON). ^{1}H NMR spectrum, δ, ppm: 5.79 s (1H, 5-CH), 7.89 s (1H, $CHPh_2$), 7.21 m (22H, H_{arom}). Found, %: C 68.93, 68.99; H 3.91, 4.02; N 2.46, 2.42. $C_{34}H_{24}BrNO_4$. Calculated, %: C 69.16; H 4.09; N 2.37.

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