

Five-Membered 2,3-Dioxo Heterocycles: LXIII.* Cascade Recyclization of Isopropyl 2-(1-Aryl-4,5-dioxo-2-phenyl-4,5-dihydro-1*H*-pyrrol-3-yl)-2-oxoacetates with Cyclic Enamines. Crystalline and Molecular Structure of 1'-Benzyl-6',6'-dimethyl-3-[*(Z*)-phenyl(phenylamino)methylidene]-6',7'-dihydro-3*H*-spiro[furan-2,3'-indole]-2',4,4',5(1'*H*,5'*H*)-tetraone

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Abstract—Isopropyl 2-(1-aryl-4,5-dioxo-2-phenyl-4,5-dihydro-1*H*-pyrrol-3-yl)-2-oxoacetates reacted with N-substituted 3-amino-5,5-dimethylcyclohex-2-en-1-ones to give the corresponding 1'-substituted (*Z*)-6',6'-dimethyl-3-[phenyl(aryl amino)methylidene]-6',7'-dihydro-3*H*-spiro[furan-2,3'-indole]-2',4,4',5(1'*H*,5'*H*)-tetraones. The structure of 1'-benzyl-6',6'-dimethyl-3-[*(Z*)-phenyl(phenylamino)methylidene]-6',7'-dihydro-3*H*-spiro[furan-2,3'-indole]-2',4,4',5(1'*H*,5'*H*)-tetraone was proved by X-ray analysis.

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We previously described reactions of new monocyclic 1*H*-pyrrole-2,3-diones [isopropyl 2-(4,5-dioxo-1,2-diphenyl-4,5-dihydro-1*H*-pyrrol-3-yl)-2-oxoacetates] with *o*-phenylenediamine and *o*-aminobenzene-thiol, which involved successive nucleophilic attacks on the C⁵ atom in the pyrrole ring and ketone carbonyl carbon atom in the substituent on C³ and resulted in the formation of substituted pyrrolo[2,3-*b*][1,5]benzodiazepines [2] and pyrrolo[2,3-*b*][1,5]benzothiazepines [3], respectively. Reactions of analogous 1*H*-pyrrole-2,3-diones with 1,3-binucleophiles were not studied.

In continuation of our studies on nucleophilic recyclizations of monocyclic 1*H*-pyrrole-2,3-diones, in the present work we examined reactions of isopropyl 2-(1-aryl-4,5-dioxo-2-phenyl-4,5-dihydro-1*H*-pyrrol-3-yl)-2-oxoacetates **Ia–Ic** with cyclic enamino ketones, N-substituted 3-amino-5,5-dimethylcyclohex-2-en-1-ones **IIa–IIf**. Substituent on the nitrogen atom in enamines **II** was varied over a wide range with a view to estimate its effect on the reaction course.

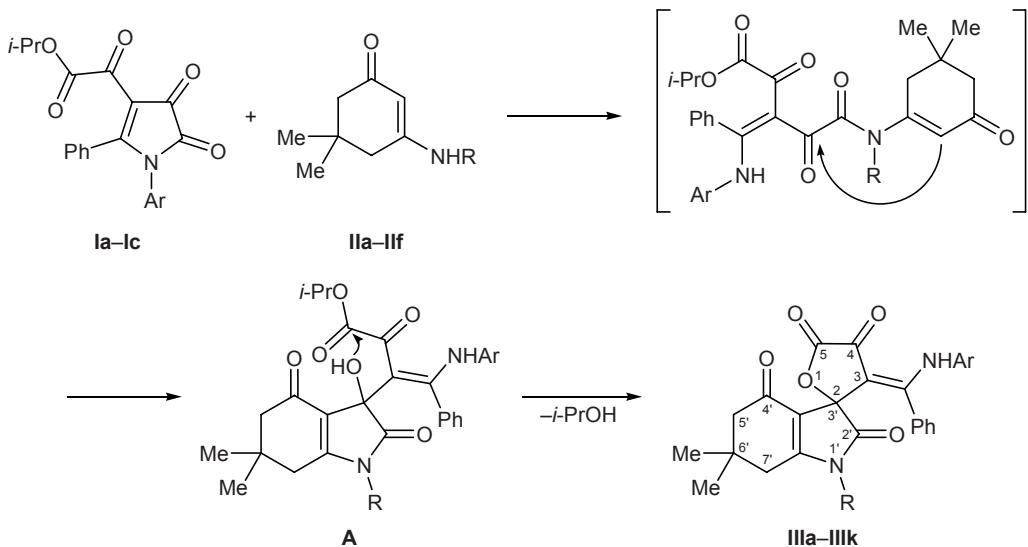
The reactions of compounds **Ia–Ic** with cyclic enamines **IIa–IIf** were carried out in anhydrous

chloroform using equimolar amounts of the reactants; the reaction mixtures were kept for 8–10 h at 20–22°C, the progress of the reaction being monitored by chromatography. As a result, we isolated in good yields the corresponding 1'-R-6',6'-dimethyl-3-[*(Z*)-phenyl(aryl amino)methylidene]-6',7'-dihydro-3*H*-spiro[furan-2,3'-indole]-2',4,4',5(1'*H*,5'*H*)-tetraones **IIIa–IIIk**. The structure of compound **IIIb** was proved by X-ray analysis.

Compounds **IIIa–IIIk** are bright yellow crystalline substances which are readily soluble in DMSO and DMF, poorly soluble in other common organic solvents, and insoluble in saturated hydrocarbons and water. They showed a negative test for enolic hydroxy group with an alcoholic solution of iron(III) chloride. The IR spectra of **IIIa–IIIk** contained absorption bands due to stretching vibrations of the NH group (a broad band at 3158–3183 cm^{−1}), lactone carbonyl group (C⁵=O, 1781–1793 cm^{−1}), lactam carbonyl group (C^{2'}=O, 1752–1764 cm^{−1}), and ketone carbonyl groups (C⁴=O, C^{4'}=O; one or two peaks in the region 1637–1660 cm^{−1}). In the ¹H NMR spectra of **IIIa–IIIk**, we observed signals from protons in the aliphatic substit-

* For communication LXII, see [1].

Scheme 1.



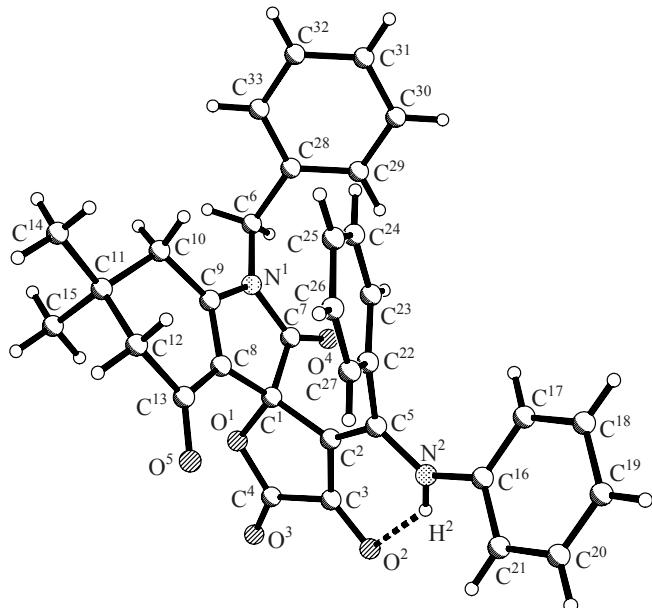
I, Ar = Ph (**a**), 4-MeOC₆H₄ (**b**), 4-MeC₆H₄ (**c**); **II**, R = CH₂=CHCH₂ (**a**), PhCH₂ (**b**), Ph (**c**), 4-MeC₆H₄ (**d**), 4-MeOC₆H₄ (**e**), 1-naphthyl (**f**); **III**, Ar = Ph, R = CH₂=CHCH₂ (**a**), PhCH₂ (**b**), Ph (**c**), 4-MeC₆H₄ (**d**), 4-MeOC₆H₄ (**e**), 1-naphthyl (**f**); Ar = 4-MeOC₆H₄, R = PhCH₂ (**g**), Ph (**h**), 4-MeOC₆H₄ (**i**), 1-naphthyl (**j**); Ar = 4-MeC₆H₄, R = PhCH₂ (**k**).

uents, aromatic rings, and substituents in the latter. Two methyl groups gave two singlets in the region δ 0.80–0.95 ppm, four nonequivalent protons in the C^{5'}H₂ and C^{7'}H₂ methylene groups resonated as doublets at δ 1.56–2.25 ppm with coupling constants *J* of 16.0–18.8 Hz, and the NH signal appeared as a broadened singlet in the region δ 12.65–12.78 ppm.

The structure of molecule **IIIb** is shown in figure. The configuration of the phenylamino group is fixed by strong intramolecular hydrogen bond N²—H²⋯O² with the following parameters: N²—H² 0.90(3), H²⋯O² 1.93(3), N²⋯O² 2.690(3) Å; ∠N²H²O² 141(3)°. The formation of intramolecular hydrogen bond affected the C³=O² bond length (1.236 Å). All other bond lengths and bond angles did not differ from the corresponding standard values. Neither intermolecular hydrogen bonds nor shortened contacts were found in crystal.

Presumably, compounds **IIIa–IIIk** are formed by initial addition of the activated NH group in enamines **IIa–IIIf** at the C⁵ carbon atom of pyrrolediones **Ia–Ic**. Next follows cleavage of the pyrrole ring at the N¹—C⁵ bond and closure of new pyrrole ring via intramolecular nucleophilic addition of the β-CH group in enamine **II** at the ketone carbonyl group in **I**. The hemiacetal hydroxy group thus formed (structure **A**) attacks the ester carbonyl carbon atom, leading to the formation of furan ring and elimination of propan-2-ol.

Variation of substituent on the nitrogen atom in enamines **IIa–IIIf** does not affect the direction of their reaction with pyrrolediones **Ia–Ic**, and the rate of the process also changes insignificantly. For example, we performed in parallel two control reactions of *N*-benzyl and *N*-phenyl enamino ketones **IIb** and **IIc** with the same pyrroledione **Ia** under similar conditions; accord-



Structure of the molecule of 1'-benzyl-6',6'-dimethyl-3-[(*Z*)-phenyl(phenylamino)methylidene]-6',7'-dihydro-3*H*-spiro-[furan-2,3'-indole]-2',4,4',5'(1*H*,5*H*)-tetraone (**IIIb**) according to the X-ray diffraction data.

ing to the TLC data, the reactions were complete almost simultaneously.

It should be noted that the described reaction is a rare example of cascade recyclization of monocyclic 1*H*-pyrrole-2,3-diones by the action of 1,3-difunctional nucleophiles, which gives rise to difficultly accessible spiro[furan-2,3'-indole] system with various substituents in several positions of both heterorings.

EXPERIMENTAL

The IR spectra were recorded on an FSM-1201 spectrophotometer from samples dispersed in mineral oil. The ¹H and ¹³C NMR spectra were measured on a Bruker AM-400 spectrometer (400 MHz for ¹H) using DMSO-*d*₆ as solvent and tetramethylsilane as internal reference. The purity of the isolated compounds was checked by TLC on Silufol plates using benzene–ethyl acetate (5:1) or ethyl acetate as eluent.

1'-Allyl-6',6'-dimethyl-3-[(Z)-phenyl(phenylamino)methylene]-6',7'-dihydro-3*H*-spiro[furan-2,3'-indole]-2',4,4',5(1'*H*,5'*H*)-tetraone (IIIa). A solution of 1.0 mmol of compound Ia and 1.0 mmol of enamine IIa in 15 ml of anhydrous chloroform was kept for 8 h at 20°C (until the initial pyrroledione disappeared according to the TLC data). The solvent was removed, and the residue was ground with hexane. Yield 72%, mp 148–149°C (from ethyl acetate). IR spectrum, ν , cm⁻¹: 3172 br (NH), 1788 (C⁵=O), 1753 (C²=O), 1649 (C⁴=O, C^{4'}=O). ¹H NMR spectrum, δ , ppm: 0.89 s and 0.95 s (3H each, Me), 1.77 d and 2.24 d (1H each, 7'-H, J = 18.4 Hz), 1.99 d and 2.01 d (1H each, 5'-H, J = 16.8 Hz), 3.66 d.d and 4.06 d.d (1H each, CH₂CH=CH₂, J = 16.8, J = 5.0 Hz), 5.01 d (1H, CH₂CH=CH₂, J = 17.6 Hz), 5.17 d (1H, CH₂CH=CH₂, J = 10.0 Hz), 5.74 m (1H, CH₂CH=CH₂), 6.95–7.44 m (10H, H_{arom}), 12.65 br.s (1H, NH). Found, %: C 74.13; H 5.41; N 5.77. C₂₉H₂₆N₂O₅. Calculated, %: C 74.18; H 5.43; N 5.81.

Compounds IIIb–IIIk were synthesized in a similar way.

1'-Benzyl-6',6'-dimethyl-3-[(Z)-phenyl(phenylamino)methylene]-6',7'-dihydro-3*H*-spiro[furan-2,3'-indole]-2',4,4',5(1'*H*,5'*H*)-tetraone (IIIb). Yield 77%, mp 152–153°C (from acetone–ethyl acetate–acetonitrile, 1:1:1). IR spectrum, ν , cm⁻¹: 3183 br (NH), 1781 (C⁵=O), 1751 (C²=O), 1651 (C⁴=O), 1637 (C⁴=O). ¹H NMR spectrum, δ , ppm: 0.81 s and 0.90 s (3H each, Me), 1.78 d and 2.25 d (1H each, 7'-H, J =

18.5 Hz), 1.89 d and 1.99 d (1H each, 5'-H, J = 16.0 Hz), 4.33 d and 4.70 d (1H each, CH₂Ph, J = 16.0 Hz), 6.97–7.43 m (15H, H_{arom}), 12.67 br.s (1H, NH). ¹³C NMR spectrum (DMSO-*d*₆), δ _C, ppm: 25.93 and 29.50 (Me), 32.82 (C^{6'}), 35.00 (C^{7'}), 43.24 (CH₂Ph), 49.99 (C^{5'}), 79.93 (C^{3'}), 110.64–135.54 (C_{arom}, C^{3a'}, C³=C), 162.18 (C^{7a'}), 164.23 (C⁵), 165.93 (C²), 174.65 (C⁴), 189.50 (C^{4'}). Found, %: C 74.36; H 5.27; N 5.23. C₃₃H₂₈N₂O₅. Calculated, %: C 74.42; H 5.30; N 5.26.

6',6'-Dimethyl-1'-(Z)-phenyl(phenylamino)methylenediene]-6',7'-dihydro-3*H*-spiro[furan-2,3'-indole]-2',4,4',5(1'*H*,5'*H*)-tetraone (IIIc). Yield 71%, mp 181–182°C (from ethyl acetate). IR spectrum, ν , cm⁻¹: 3158 br (NH), 1786 (C⁵=O), 1764 (C²=O), 1658 (C⁴=O), 1643 (C⁴=O). ¹H NMR spectrum, δ , ppm: 0.91 s (6H, Me), 1.81 d and 2.06 d (1H each, 7'-H, J = 18.8 Hz), 2.09 d and 2.11 d (1H each, 5'-H, J = 16.8 Hz), 6.96–7.56 m (15H, H_{arom}), 12.74 br.s (1H, NH). Found, %: C 74.05; H 5.03; N 5.36. C₃₂H₂₆N₂O₅. Calculated, %: C 74.12; H 5.05; N 5.40.

6',6'-Dimethyl-1'-(4-methylphenyl)-3-[(Z)-phenyl(phenylamino)methylene]-6',7'-dihydro-3*H*-spiro[furan-2,3'-indole]-2',4,4',5(1'*H*,5'*H*)-tetraone (IIId). Yield 74%, mp 168–170°C (from ethyl acetate). IR spectrum, ν , cm⁻¹: 3171 br (NH), 1788 (C⁵=O), 1752 (C²=O), 1660 (C⁴=O), 1641 (C⁴=O). ¹H NMR spectrum, δ , ppm: 0.90 s (6H, Me), 1.78 d and 2.04 d (1H each, 7'-H, J = 18.4 Hz), 2.08 d and 2.10 d (1H each, 5'-H, J = 16.8 Hz), 2.35 s (3H, Me), 6.91–7.54 m (14H, H_{arom}), 12.74 br.s (1H, NH). Found, %: C 74.37; H 5.26; N 5.24. C₃₃H₂₈N₂O₅. Calculated, %: C 74.42; H 5.30; N 5.26.

1'-(4-Methoxyphenyl)-6',6'-dimethyl-3-[(Z)-phenyl(phenylamino)methylene]-6',7'-dihydro-3*H*-spiro[furan-2,3'-indole]-2',4,4',5(1'*H*,5'*H*)-tetraone (IIIe). Yield 73%, mp 174–175°C (from chloroform–ethyl acetate, 1:3). IR spectrum, ν , cm⁻¹: 3160 br (NH), 1793 (C⁵=O), 1754 (C²=O), 1655 (C⁴=O), 1649 (C⁴=O). ¹H NMR spectrum, δ , ppm: 0.90 s and 0.91 s (3H each, Me), 1.76 d and 2.03 d (1H each, 7'-H, J = 18.3 Hz), 2.08 d and 2.11 d (1H each, 5'-H, J = 16.8 Hz), 3.80 s (3H, OMe), 6.95–7.22 m (14H, H_{arom}), 12.76 br.s (1H, NH). ¹³C NMR spectrum (DMSO-*d*₆), δ _C, ppm: 26.14 and 29.21 (Me), 33.04 (C^{6'}), 35.68 (C^{7'}), 50.29 (C^{5'}), 55.37 (OMe), 79.99 (C^{3'}), 111.08–130.77 (C_{arom}, C^{3a'}, C³=C), 159.27 (C^{4''}), 162.36 (C^{7a'}), 164.21 (C⁵), 165.49 (C²), 173.49 (C⁴), 190.11 (C⁴). Found, %: C 72.20; H 5.11; N 5.09. C₃₃H₂₈N₂O₆. Calculated, %: C 72.25; H 5.14; N 5.11.

6',6'-Dimethyl-1'-(1-naphthyl)-3-[(Z)-phenyl(phenylamino)methylidene]-6',7'-dihydro-3H-spiro[furan-2,3'-indole]-2',4,4',5(1'H,5'H)-tetraone (III f). Yield 68%, mp 185–186°C (from ethyl acetate). IR spectrum, ν , cm⁻¹: 3178 br (NH), 1793 (C⁵=O), 1759 (C^{2'}=O), 1656 (C^{4'}=O), 1651 (C⁴=O). ¹H NMR spectrum, δ , ppm: 0.85 s (6H, Me), 1.58 d and 1.78 d (1H each, 7'-H, J = 18.8 Hz), 2.11 d and 2.14 d (2H, 5'-H, J = 16.8 Hz), 7.03–8.17 m (17H, H_{arom}), 12.77 br.s (1H, NH). Found, %: C 76.00; H 4.94; N 4.90. C₃₆H₂₈N₂O₅. Calculated, %: C 76.04; H 4.96; N 4.93.

1'-Benzyl-3-[(Z)-(4-methoxyphenylamino)-(phenyl)methylidene]-6',6'-dimethyl-6',7'-dihydro-3H-spiro[furan-2,3'-indole]-2',4,4',5(1'H,5'H)-tetraone (III g). Yield 80%, mp 152–153°C (from ethyl acetate). IR spectrum, ν , cm⁻¹: 3174 br (NH), 1785 (C⁵=O), 1754 (C^{2'}=O), 1655 (C^{4'}=O), 1639 (C⁴=O). ¹H NMR spectrum, δ , ppm: 0.80 s and 0.90 s (3H each, Me), 1.76 d and 2.23 d (1H each, 7'-H, J = 18.8 Hz), 1.89 d and 1.97 d (1H each, 5'-H, J = 16.4 Hz), 3.65 s (3H, OMe), 4.31 d and 4.69 d (1H each, CH₂Ph, J = 16.0 Hz), 6.73–7.43 m (14H, H_{arom}), 12.67 br.s (1H, NH). Found, %: C 72.54; H 5.34; N 4.95. C₃₄H₃₀N₂O₆. Calculated, %: C 72.58; H 5.37; N 4.98.

3-[(Z)-(4-Methoxyphenylamino)(phenyl)methylidene]-6',6'-dimethyl-1'-phenyl-6',7'-dihydro-3H-spiro[furan-2,3'-indole]-2',4,4',5(1'H,5'H)-tetraone (III h). Yield 75%, mp 180–181°C (from ethyl acetate). IR spectrum, ν , cm⁻¹: 3168 br (NH), 1785 (C⁵=O), 1765 (C^{2'}=O), 1649 (C⁴=O, C^{4'}=O). ¹H NMR spectrum, δ , ppm: 0.91 s (6H, Me), 1.80 d and 2.03 d (1H each, 7'-H, J = 18.4 Hz), 2.07 d and 2.12 d (1H each, 5'-H, J = 16.4 Hz), 3.65 s (3H, OMe), 6.73–7.56 m (14H, H_{arom}), 12.76 br.s (1H, NH). Found, %: C 72.19; H 5.12; N 5.08. C₃₃H₂₈N₂O₆. Calculated, %: C 72.25; H 5.14; N 5.11.

1'-(4-Methoxyphenyl)-6',6'-dimethyl-6',7'-dihydro-3H-spiro[furan-2,3'-indole]-2',4,4',5(1'H,5'H)-tetraone (III i). Yield 72%, mp 163–164°C (from ethyl acetate). IR spectrum, ν , cm⁻¹: 3173 br (NH), 1785 (C⁵=O), 1758 (C^{2'}=O), 1660 (C^{4'}=O), 1649 (C⁴=O). ¹H NMR spectrum, δ , ppm: 0.90 s (6H, Me), 1.74 d and 2.00 d (1H each, 7'-H, J = 18.8 Hz), 2.06 d and 2.10 d (1H each, 5'-H, J = 16.4 Hz), 3.65 s and 3.80 s (3H each, OMe), 6.72–7.55 m (13H, H_{arom}), 12.76 br.s (1H, NH). Found, %: C 70.53; H 5.21; N 4.81. C₃₄H₃₀N₂O₇. Calculated, %: C 70.58; H 5.23; N 4.84.

3-[(Z)-(4-Methoxyphenylamino)(phenyl)methylidene]-6',6'-dimethyl-1'-(1-naphthyl)-6',7'-dihydro-3H-spiro[furan-2,3'-indole]-2',4,4',5(1'H,5'H)-

tetraone (III j). Yield 71%, mp 186–187°C (from ethyl acetate). IR spectrum, ν , cm⁻¹: 3173 br (NH), 1783 (C⁵=O), 1764 (C^{2'}=O), 1657 (C^{4'}=O), 1639 (C⁴=O). ¹H NMR spectrum, δ , ppm: 0.84 s (6H, Me), 1.56 d and 1.76 d (1H each, 7'-H, J = 18.4 Hz), 2.10 d and 2.14 d (1H each, 5'-H, J = 16.0 Hz), 3.67 s (3H, OMe), 6.75–8.17 m (16H, H_{arom}), 12.78 br.s (1H, NH). Found, %: C 74.18; H 5.03; N 4.67. C₃₇H₃₀N₂O₆. Calculated, %: C 74.23; H 5.05; N 4.68.

1'-Benzyl-6',6'-dimethyl-3-[(Z)-(4-methylphenyl)-(phenyl)methylidene]-6',7'-dihydro-3H-spiro[furan-2,3'-indole]-2',4,4',5(1'H,5'H)-tetraone (III k). Yield 76%, mp 152–153°C (from ethyl acetate). IR spectrum, ν , cm⁻¹: 3160 br (NH), 1781 (C⁵=O), 1753 (C^{2'}=O), 1650 (C⁴=O, C^{4'}=O). ¹H NMR spectrum, δ , ppm: 0.80 s and 0.90 s (3H each, Me), 1.77 d and 2.24 d (1H each, 7'-H, J = 18.4 Hz), 1.89 d and 1.97 d (1H each, 5'-H, J = 16.4 Hz), 2.17 s (3H, Me), 4.32 d and 4.69 d (1H each, CH₂Ph, J = 16.0 Hz), 6.87–7.43 m (14H, H_{arom}), 12.69 br.s (1H, NH). Found, %: C 74.66; H 5.51; N 5.09. C₃₄H₃₀N₂O₅. Calculated, %: C 74.71; H 5.53; N 5.12.

X-Ray diffraction data for compound III b . Yellow well-defined crystals, C₃₃H₂₈N₂O₈, rhombic crystal system; unit cell parameters: a = 9.890(2), b = 14.607(3), c = 18.947(4) Å; V = 2737.1(10) Å³; M 532.57; d_{calc} = 1.292 g/cm³; Z = 4; space group P2₁2₁2₁. The set of experimental reflections was acquired on a KM-4 (KUMA Diffraction) automatic four-circle diffractometer with χ -geometry (monochromatized MoK_α irradiation, $\omega/2\Theta$ scanning, $2\Theta \leq 50.5^\circ$). Total of 2559 independent reflections (91.1% of possible ones) were measured with no correction for absorption ($\mu = 0.087$ mm⁻¹). The structure was solved by the direct method using SIR92 program [4], followed by calculation of electron density maps. The positions of all hydrogen atoms (except for H²) were set on the basis of geometry considerations and were refined by the riding model. Full-matrix anisotropic approximation (for non-hydrogen atoms) by the least-squares procedure was performed using SHELXL-97 software [5] and was complete at R_1 = 0.0380, wR_2 = 0.1003 [for 2241 reflections with $I \geq 2\sigma(I)$] and R_1 = 0.0473, wR_2 = 0.1041 (for all reflections); number of refined parameters 364, goodness of fit 1.064. Friedel pairs of reflections were not measured, and the absolute structure of molecule III b was not determined.

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