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SHORT COMMUNICATIONS

Reaction of α-Nitrocinnamic Acid Esters with Pyrrole

L. V. Baichurina, R. I. Baichurin, N. I. Aboskalova, G. A. Berkova, and V. M. Berestovitskaya

Hertzen Russian State Pedagogical University, nab. r. Moiki 48, St. Petersburg, 191186 Russia
e-mail: kohrgpu@yandex.ru

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Synthetically accessible α-nitrocinnamic acid esters may be regarded as promising precursors of β-phenylalanine and its substituted derivatives [1–4]. Undoubtedly, introduction into their molecules of pharmacophoric structural fragments, e.g., pyrrole ring, attracts interest. Pyrrole ring constitutes the key fragment of porphyrin macroring which is the base of a number of important natural compounds, such as hemoglobin, chlorophyll, and cytochrome. Some medical agents, e.g., Ketorolac (analgesic and antiinflammatory drug), Atorvastatin (cholesterol-lowering agent) [5, 6], etc., contain a pyrrole ring in their molecules.

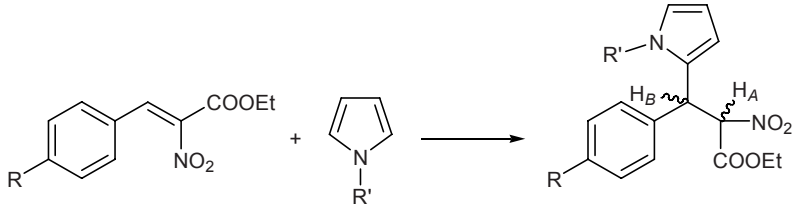
We were the first to react α-nitrocinnamic acid esters **Ia** and **Ib** with pyrrole and *N*-methylpyrrole. The reactions were carried out with excess pyrrole reagent at room temperature under solvent-free conditions in the absence of catalyst, and the yields of the corresponding addition products were 48–52%. Ethyl 3-aryl-2-nitro-3-(1*H*-pyrrol-2-yl)propanoates **IIa**–**IIc** were isolated as slightly colored crystalline substances. Compound **IIa** was isolated as a single diastereoisomer, while esters **IIb** and **IIc** were mixtures of *erythro* and *threo* isomers.

The structure of the products was confirmed by spectral data. The IR spectra of **IIa**–**IIc** contained strong absorption bands due to stretching vibrations of nonconjugated nitro (1565–1570, 1370–1375 cm^{-1}) and carbonyl groups (1750 cm^{-1}); in addition, compounds **IIa** and **IIc** displayed absorption at 3450–3465 cm^{-1} due to stretching vibrations of the pyrrole N–H group.

In the ^{1}H NMR spectrum of compound **IIa** we observed two well-resolved doublets at δ 5.76 and 5.06 ppm, which belong to the H_A and H_B protons ($^3J_{AB}$ = 11.03 Hz); protons of the ethoxy group resonated as a triplet and quartet at δ 0.88 and 3.96 ppm, respectively. Signals in the regions δ 7.20–7.40 and 6.10–6.63 ppm were assigned to protons in the benzene and pyrrole rings, and the NH proton gave a downfield signal at δ 8.61 ppm. The ^{1}H NMR spectra of esters **IIb** and **IIc** contained doubled sets of signals, indicating the presence of two diastereoisomers.

Initial ethyl α-nitrocinnamates **Ia** and **Ib** were synthesized by reactions of ethyl nitroacetate [7] with the corresponding Schiff bases or diacetals according to the procedures described in [8–10] or by direct acid-catalyzed alkenylation of ethyl nitroacetate with aromatic aldehydes according to the procedure proposed previously for the preparation of geminal acylnitroethenes [11–13].

Ethyl 2-nitro-3-phenyl-3-(1*H*-pyrrol-2-yl)propanoate (IIa). Pyrrole, 0.67 g (10 mmol), was added to 0.22 g (1 mmol) of ethyl 2-nitro-3-phenylprop-2-enoate (**Ia**), and the mixture was left to stand at room temperature in the dark. After 48 h, ethyl acetate and water (4 : 1) were added to the mixture, the aqueous



Ia, **Ib** **IIa–IIc**

I, R = H (**a**), MeO (**b**); **II**, R = R′ = H (**a**), R = H, R′ = Me (**b**), R = MeO, R′ = H (**c**).

phase was separated in a separatory funnel, the organic phase was washed with two portions of a saturated solution of sodium chloride and dried over calcined magnesium sulfate, the solvent was evaporated in air, and the residue was treated with ethanol. Yield 0.139 g (48%), off-white crystals, mp 128–130°C (from EtOH). IR spectrum, ν, cm^{-1}: 1570, 1370 (NO_2); 1750 (C=O); 3450 (NH). ^1H NMR spectrum, δ, ppm: 0.88 t (3H, CH_3); 3.96 q (2H, OCH_2); 5.76 d (1H, H_A, $^3J_{AB}$ = 11.03 Hz); 5.06 d (1H, H_B, $^3J_{AB}$ = 11.03 Hz); 6.10, 6.12, and 6.63 (3H, pyrrole); 7.20–7.40 m (5H, H_{arom}); 8.61 s (1H, NH). Found, %: N 9.92. $C_{15}H_{16}N_2O_4$. Calculated, %: N 9.72.

Compounds **IIb** and **IIc** were synthesized in a similar way; in the synthesis of **IIc**, the mixture was kept for 72 h.

Ethyl 3-(1-methyl-1*H*-pyrrol-2-yl)-2-nitro-3-phenylpropanoate (IIb). Yield 51%, colorless crystals, mp 104–106°C (from hexane). IR spectrum, ν, cm^{-1}: 1565, 1375 (NO_2); 1750 (C=O). ^1H NMR spectrum, δ, ppm: 6.04, 6.17, and 6.51 (3H, pyrrole); 7.20–7.30 m (5H, H_{arom}); diastereoisomer **A**: 0.89 t (CH_3), 3.39 s (NCH_3), 3.87 q (OCH_2), 5.64 d (H_A, $^3J_{AB}$ = 11.77 Hz), 5.03 d (H_B, $^3J_{AB}$ = 11.77 Hz); diastereoisomer **B**: 1.15 t (CH_3), 3.44 s (NCH_3), 4.16 q (OCH_2), 5.67 d (H_A, $^3J_{AB}$ = 11.03 Hz), 4.97 d (H_B, $^3J_{AB}$ = 11.03 Hz); ratio **A**:**B** = 1:2. Found, %: N 9.53. $C_{16}H_{18}N_2O_4$. Calculated, %: N 9.27.

Ethyl 3-(4-methoxyphenyl)-2-nitro-3-(1*H*-pyrrol-2-yl)propanoate (IIc). Yield 52%, colorless crystals, mp 106–108°C (from hexane). IR spectrum, ν, cm^{-1}: 1565, 1375 (NO_2); 1750 (C=O); 3465 (NH). ^1H NMR spectrum, δ, ppm: 5.99, 6.10, and 6.68 (3H, pyrrole); 6.80–7.30 m (4H, H_{arom}); diastereoisomer **A**: 1.00 t (CH_3), 3.77 s (OCH_3), 3.99 q (OCH_2), 5.70 d (H_A, $^3J_{AB}$ = 10.90 Hz), 5.05 d (H_B, $^3J_{AB}$ = 10.90 Hz), 8.42 s (NH); diastereoisomer **B**: 1.18 t (CH_3), 3.77 s (OCH_3), 4.19 q (OCH_2), 5.67 d (H_A, $^3J_{AB}$ = 11.03 Hz), 5.04 d (H_B, $^3J_{AB}$ = 11.03 Hz), 8.52 s (NH); ratio **A**:**B** = 1:2. Found, %: N 8.84. $C_{16}H_{18}N_2O_5$. Calculated, %: N 8.81.

The IR spectra were recorded on a InfraLYuM FT-02 spectrometer with Fourier transform using $CHCl_3$ as solvent (concentration 40 mg/ml). The ^1H NMR spectra were measured on a Bruker WM-400 spectrometer from solutions in chloroform-*d* using hexamethyldisiloxane as internal reference.

REFERENCES

1. Dauzonne, D. and Royer, R., *Synthesis*, 1987, no. 4, p. 399.
2. Perekalin, V.V. and Temp, A.A., USSR Inventor's Certificate no. 209465, 1968; *Byull. Izobret*., 1968, vol. 45, no. 5, p. 33.
3. Babievskii, K.K., Belikov, V.M., Filatova, I.M., and Garbalinskaya, N.S., *Izv. Akad. Nauk SSSR, Ser. Khim*, 1973, p. 1608.
4. Kaji, E. and Zen, S., *Bull. Chem. Soc. Jpn*., 1973, vol. 46, p. 337.
5. Joule, J.A. and Mills, K., *Heterocyclic Chemistry*, Malden, MA: Blackwell Science, 2000, 4th ed. Translated under the title *Khimiya geterotsiklicheskikh soedinenii*, Moscow: Mir, 2004, p. 309.
6. Soldatenkov, A.T., Kolyadina, N.M., and Shendrik, I.V., *Osnovy organicheskoi khimii lekarstvennykh veshchestv* (Principles of Organic Chemistry of Drugs), Moscow: Khimiya, 2001, p. 94.
7. Radionov, V.M., Machinskaya, I.V., and Belikov, V.M., *Sintez Org. Soedin.*, 1950, vol. 1, p. 117.
8. Kochetkov, K.A., Babievskii, K.K., Belikov, V.M., Garbalinskaya, M.S., and Bakhmutov, V.I., *Izv. Akad. Nauk SSSR. Ser. Khim*., 1980, p. 639.
9. Babievskii, K.K., Belikov, V.M., Vinogradova, A.I., and Latov, V.K., *Zh. Org. Khim*., 1973, vol. 9, p. 1700.
10. Dornow, A. and Menzel, H., *Justus Liebigs Ann. Chem*., 1954, vol. 588, p. 40.
11. Sokolov, N.A., Tishchenko, I.G., Karpitskaya, N.V., and Grinkevich, V.G., *Vestn. Belorus. Gos. Univ*., 1978, no. 3, p. 29.
12. Bakhareva, S.V., *Cand. Sci. (Chem.) Dissertation*, St. Petersburg, 2001.
13. Velezheva, V.S., Erofeev, Yu.V., and Suvorov, N.N., *Zh. Org. Khim*., 1980, vol. 16, p. 2157.