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Substituted 1-Nitro-2-phenylethenes in Reaction with *N*-Phenacyl- and *N*-Acetonylisoquinolinium Bromides

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The information on reactions of nitrophenylethenes with azomethine ylides is very limited. It is only known that 1-nitro-2-phenylethene reacted with *N*-(2-methyl-5-methoxycarbonylfur-3-yl)methyl-isoquinolinium bromide giving a product of 1,3-dipolar cycloaddition, 1-nitro-2-phenyl-3-R-2,3-dihydrobenzo[*g*]indolizine in a low yield [1].

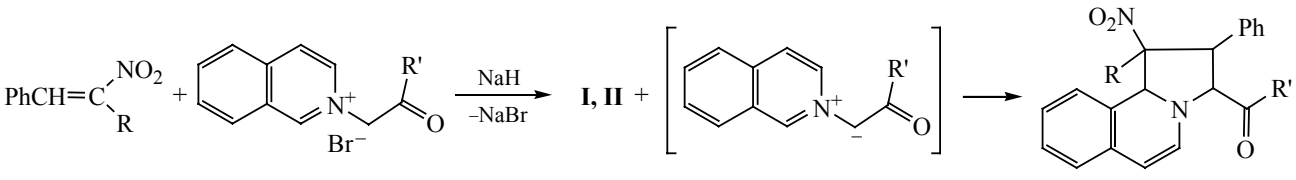
In order to test the general character of this reaction we attempted to extend it to a new type of dipolarophile, 1-nitro-2-phenyl-1-cyano-ethene (**I**), and its analog, 1-bromo-1-nitro-2-phenylethene (**II**).

It was established that phenylethenes **I** and **II** reacted with the precursors of azomethine ylides, N-phenacyl- (**III**) or N-acetonylisoquinolinium bromides (**IV**), giving 1-nitro-2-phenyl-1,2,3,10*b*-tetrahydropyrrolo[2,1-*a*] isoquinolines **V–VIII**. It is presumable that at treating the N-onium salts **III** and **IV** with sodium hydride in dry dioxane active azomethine ylides **A** are generated [2] which as a result of 1,3-dipolar cycloaddition to molecules of dipolarophiles **I** or **II** are stabilized in the form of substituted tetrahydropyrroloisoquinolines **V–VIII** in 55–62% yield. The structure of compounds was confirmed by IR and ^{1}H NMR spectra, and the composition, by elemental analysis data. The IR spectra contain strong absorption bands of the stretching vibrations of the NO_2 group at 1555 (ν_{as}), 1380 cm^{-1} (ν_s), and of C=O group at 1710 cm^{-1}. In cycloadducts **V** and **VI** in contrast to initial phenylethene **I** (2225 cm^{-1}) the absorption bands of the CN group are shifted in the longwave direction (2250 cm^{-1}) with decrease in the intensity, apparently due to the stronger steric hindrances in the final products. The parameters of the ^{1}H NMR spectra are consistent with the assumed structures and are close to those of model compounds of similar structures from the series of pyrrolidine and isoquinoline [3, 4]. For instance, the protons of the pyrrolidine ring appear in the region 4.35–5.67 ppm, and the signals of protons H^5 and H^6 of the isoquinoline ring, at 6.57 and 6.35 ppm respectively (Scheme 1).

The presence of a carbonyl group in the cycloadducts **V–VIII** provided a possibility to carry out a heterocyclization involving hydrazine hydrate to obtain previously unknown substituted 1-nitro-2-phenyl-2,2*a*,5,5*a*,6,10*b*-hexahydrotriazinoindolizine **IX–XII** (Scheme 2).

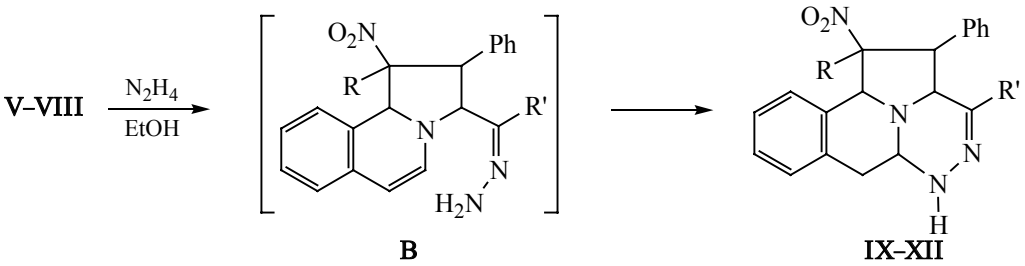
It is presumable that the reaction proceeds through the formation of intermediate hydrazone derivatives of pyrrolidine **B** which undergo a spontaneous heterocyclization

Scheme 1.



R = CN (**I**), Br (**II**); R' = Ph (**III**), Me (**IV**); R = CN, R' = Ph (**V**), Me (**VI**); R = Br, R' = Ph (**VII**), Me (**VIII**).

Scheme 2.



R = CN (**IX, X**), Br (**XI, XII**); R' = Ph (**IX, XI**), Me (**X, XII**).

into compounds **IX–XII**. The structure of compounds was established from IR and ^{1}H NMR spectra. In the IR spectra alongside the absorption bands of groups NO_2 and CN (for compounds **IX, X**) an absorption band of NH group was also observed at 3350 cm^{-1}, and in the ^{1}H NMR spectrum this group appeared as a broadened singlet at 5.98 ppm. The signals of protons H^{5a} and H^6 because of the reduction of this fragment in the isoquinoline ring give rise to signals in the region 3.85 and 2.70 ppm respectively.

Therefore that reactions described permit the preparation of a number of difficultly accessible by the other methods pyrrolizine derivatives of isoquinoline and the fusion to the principal part of the molecule of the 1,2,4-triazine ring.

1-Nitro-2-phenyl-1-cyanoethene was obtained by the method [5], 1-bromo-1-nitro-2-phenylethene, by the procedure [6], *N*-phenacyl- and *N*-acetonylisoquinolinium bromides, as described in [7].

Reaction of substituted 1-nitro-2-phenylethenes I, II with N-phenacyl- (III) or N-acetonylisoquinolinium bromides (IV). To a solution of 5 mmol of phenylethene **I** or **II** in 80 ml of dry dioxane was added at 0 ± 5°C while stirring 5 mmol of isoquinolinium bromide **III** or **IV** and 1 min later, 7 mmol of sodium hydride. The reaction mixture was stirred at room temperature for 3 days, the precipitate was filtered off, washed with 15 ml of dioxane, the solvent was evaporated from the combined organic solution, and the residue was subjected to chromatography on a column (250 ×10 mm) packed with the activated Silicagel 100/400 μ eluting with Trappe solvents. The eluent for compounds **V–VIII** was benzene.

3-Benzoyl-1-nitro-2-phenyl-1,2,3,10*b*-tetrahydropyrrolo[2,1-*a*]isoquinoline-1-carbonitrile (V). Yield 60%, mp 125–126°C. IR spectrum, ν, cm^{-1}: 2250 (CN), 1555, 1380 (NO_2), 1710 (C=O). ^{1}H NMR spectrum, δ, ppm: 4.43 d (1H, H^2), 4.61 s (1H, H^{10b}), 5.67 d (1H, H^3), 6.36 d (1H, H^6), 6.57 d (1H, H^5), 7.78–7.74 m (10H, $2C_6H_5$), 7.85–7.51 m ($4H_{isoquin}$). Found, %: C 73.94; H 4.33; N 9.83. $C_{26}H_{19}N_3O_3$. Calculated, %: C 74.11; H 4.51; N 9.98.

3-Acetyl-1-nitro-2-phenyl-1,2,3,10*b*-tetrahydropyrrolo[2,1-*a*]isoquinoline-1-carbonitrile (VI). Yield 62%, mp 105–106°C. IR spectrum, ν, cm^{-1}: 2250 (CN), 1555, 1380 (NO_2), 1710 (C=O). ^{1}H NMR spectrum, δ, ppm: 2.12 s (3H, CH_3), 4.37 s (1H, H^{10b}), 4.38 d (1H, H^2), 4.94 d (1H, H^3), 6.35 d (1H, H^6), 6.59 d (1H, H^5), 7.75 m (5H, C_6H_5), 7.84–7.50 m ($4H_{isoquin}$). Found, %: C 70.02; H 4.58; N 11.53. $C_{21}H_{17}N_3O_3$. Calculated, %: C 70.19; H 4.74; N 11.70.

3-Benzoyl-1-bromo-1-nitro-2-phenyl-1,2,3,10*b*-tetrahydropyrrolo[2,1-*a*]isoquinoline (VII). Yield 57%, mp 152°C. IR spectrum, ν, cm^{-1}: 1555, 1380 (NO_2), 1710 (C=O). ^{1}H NMR spectrum, δ, ppm: 4.43 d (1H, H^2), 4.60 s (1H, H^{10b}), 5.67 d (1H, H^3), 6.36 d (1H, H^6), 6.56 d (1H, H^5), 7.76–7.73 m (10H, $2C_6H_5$), 7.85–7.53 m ($4H_{isoquin}$). Found, %: C 63.01; H 3.84; N 5.73. $C_{25}H_{19}BrN_2O_3$. Calculated, %: C 63.16; H 4.00; N 5.89.

3-Acetyl-1-bromo-1-nitro-2-phenyl-1,2,3,10*b*-tetrahydropyrrolo[2,1-*a*]isoquinoline (VIII). Yield 55%, mp 140°C. IR spectrum, ν, cm^{-1}: 1555, 1380 (NO_2), 1710 (C=O). ^{1}H NMR spectrum, δ, ppm: 2.13 s (3H, CH_3), 4.35 s (1H, H^{10b}), 4.37 d (1H, H^2), 4.95 d (1H, H^3), 6.45 d (1H, H^6), 6.60 d (1H, H^5), 7.74 m (5H, C_6H_5), 7.84–7.52 m ($4H_{isoquin}$). Found, %: C 57.96; H 3.97; N 6.62. $C_{20}H_{17}BrN_2O_3$. Calculated, %: C 58.11; H 4.12; N 6.78.

Reaction of substituted tetrahydropyrroloisoquinolines V–VIII with hydrazine hydrate. To a solution of 2 mmol of compounds **V–VIII** in 20 ml of ethanol at cooling to 5°C was added while stirring 2.5 mmol of hydrazine hydrate in 5 ml of ethanol. The reaction mix-

ture was stirred at room temperature for 6 h. The reaction mixture of compounds **VI** or **VIII** with hydrazine hydrate was stirred for 12 h at 40°C. The solvent was evaporated at reduced pressure, the residue was diluted with 20 ml of ice water, the water layer was extracted with ethyl ether (2×20 ml), the extract was dried with $MgSO_4$. The solvent was evaporated, the residue was subjected to chromatography as described above, eluent for compounds **IX–XII** was chloroform.

1-Nitro-2,3-diphenyl-2,2*a*,5,5*a*,6,10*b*-hexahydro-1*H*-benzo[*g*][1,2,4]triazino[5,4,3-*cd*]indolizine-1-carbonitrile (IX). Yield 41%, mp 168°C. IR spectrum, ν, cm^{-1}: 3350 (NH), 2250 (CN), 1555, 1380 (NO_2). ^1H NMR spectrum, δ, ppm: 2.70 d (2H, C^6H_2), 3.86 q (1H, H^{5a}), 4.48 s (1H, H^{10b}), 4.57 d (1H, H^2), 4.86 d (1H, H^{2a}), 5.98 br.s (1H, NH), 7.62–7.25 m (10H, $2C_6H_5$), 7.75–7.50 m ($4H_{isoquin.}$). Found, %: C 71.56; H 4.64; N 15.92. $C_{26}H_{21}N_5O_2$. Calculated, %: C 71.72; H 4.83; N 16.09.

3-Methyl-1-nitro-2-phenyl-2,2*a*,5,5*a*,6,10*b*-hexahydro-1*H*-benzo[*g*][1,2,4]triazino[5,4,3-*cd*]indolizine-1-carbonitrile (X). Yield 30%, mp 110°C. IR spectrum, ν, cm^{-1}: 3350 (NH), 2250 (CN), 1555, 1380 (NO_2). ^1H NMR spectrum, δ, ppm: 2.13 s (3H, CH_3), 2.70 d (2H, C^6H_2), 3.85 q (1H, H^{5a}), 4.47 s (1H, H^{10b}), 4.56 d (1H, H^2), 4.84 d (1H, H^{2a}), 5.97 br.s (1H, NH), 7.45 m (5H, C_6H_5), 7.74–7.50 m ($4H_{isoquin.}$). Found, %: C 67.38; H 4.94; N 18.62. $C_{21}H_{19}N_5O_2$. Calculated, %: C 67.56; H 5.09; N 18.77.

1-Bromo-1-nitro-2,3-diphenyl-2,2*a*,5,5*a*,6,10*b*-hexahydro-1*H*-benzo[*g*][1,2,4]triazino[5,4,3-*cd*]-indolizine (XI). Yield 40%, mp 144°C. IR spectrum, ν, cm^{-1}: 3350 (NH), 1555, 1380 (NO_2). ^1H NMR spectrum, δ, ppm: 2.70 d (2H, C^6H_2), 3.86 q (1H, H^{5a}), 4.47 s (1H, H^{10b}), 4.55 d (1H, H^2), 4.85 d (1H, H^{2a}), 5.98 br.s (1H, NH), 7.61–7.24 m (10H, $2C_6H_5$), 7.75–7.51 m ($4H_{isoquin.}$). Found, %: C 61.19; H 4.06; N 11.28. $C_{25}H_{21}BrN_4O_2$. Calculated, %: C 61.35; H 4.29; N 11.45.

1-Bromo-3-methyl-1-nitro-2-phenyl-2,2*a*,5,5*a*,6,10*b*-hexahydro-1*H*-benzo[*g*][1,2,4]triazino-[5,4,3-*cd*]indolizine (XII). Yield 28%, mp 115°C. IR spectrum, ν, cm^{-1}: 3350 (NH), 1555, 1380 (NO_2). ^1H NMR spectrum, δ, ppm: 2.13 s (3H, CH_3), 2.70 d (2H, C^6H_2), 3.85 q (1H, H^{5a}), 4.46 C (1H, H^{10b}), 4.55 d (1H, H^2), 4.83 d (1H, H^{2a}), 5.98 br.s (1H, NH), 7.47 m (5H, C_6H_5), 7.74–7.51 m ($4H_{isoquin.}$). Calculated, %: C 56.04; H 4.28; N 12.97. $C_{20}H_{19}BrN_4O_2$. Found, %: C 56.21; H 4.45; N 13.11.

IR spectra were recorded on a spectrophotometer ANDQC-29 from solutions in chloroform, concentration 40 mg/ml, *l* 0.1 mm. ^1H NMR spectra were registered on a spectrometer Tesla BS-487C (80 MHz) in acetone-d_6, internal reference HMDS. The reaction progress was monitored and the homogeneity of compounds obtained was checked by ascending TLC on Silufol UV-254 plates in the solvent mixture acetone–hexane, 2 : 3, development in iodine vapor.

REFERENCES

1. Baran'ski, A. and Kelarev, V.I., *Khim. Geterotsikl. Soedin*., 1990, p. 435.
2. Štetinova, J., Jurašek, A., Kovač, J., and Dandarova, M., *Coll. Czech. Chem. Commun.,* 1986, vol. 51, p. 412.
3. Gordon, A.J. and Ford, R.A., *The Chemist's Companion*, New York: Wiley, 1972.
4. Pretsch, E., Buhlmann, P., and Affolter, C., *Structure Determination of Organic Compounds*, Springer-Verlag, 2000.
5. Ried, W. and Kőhler, E., *Lieb. Ann*., 1956, *598*, 145.
6. Priebs, B., *Ann*. 1884, vol. 225, p. 319.
7. Štetinova, J., Dandarova, M., Knoppova, V., and Kovač, J., *Coll. Czech. Chem. Commun.,* 1978, vol. 43, p. 2041.