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ONE-STEP SYNTHESIS OF A NOVEL HETEROCYCLIC SYSTEM: SPIRO[[1,4]THIAZINO-[4,3-*a*]QUINOLINE-5,5'-PYRIMIDINE]

I. V. Paramonov, N. A. Belyaev, T. V. Glukhareva, A. S. Volkov, E. V. Deeva, and Yu. Yu. Morzherin

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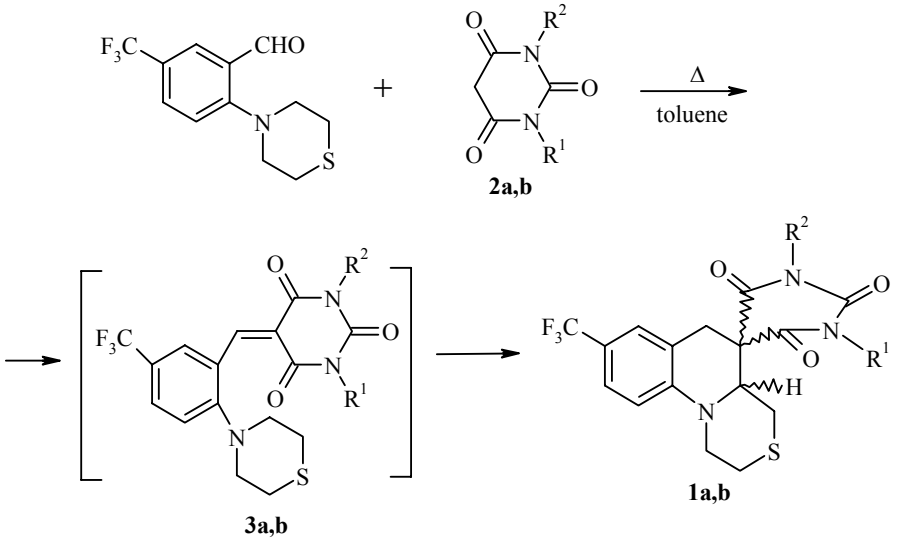
We have observed that when 2-thiomorpholino-5-trifluoromethylbenzaldehyde is reacted with barbituric acids under Knoevenagel condensation conditions, a novel heterocyclic system is formed: 1,2,4,4*a*,5,6-hexahydrospiro[[1,4]thiazino[4,3-*a*]quinoline-5,5'-pyrimidine]-2',4',6'-triones **1a,b**, i.e., two new C–C bonds are formed during the reaction. The reaction occurs through the *o*-vinyl derivatives **3** [1, 2] followed by their cyclization according to a *tert*-amino effect mechanism [3, 4]. When monosubstituted barbituric acids were used, two isomers could be formed. We have shown that with monosubstituted barbituric acid **2b**, a 1:1 mixture of spiro-linked condensed [1,2-*a*]quinolines **1b** is formed in 78% yield. One of the isomers can be isolated in 33% yield by fractional crystallization from aqueous alcohol.



1–3 **a** $R^1 = R^2 = Me$, **b** $R^1 = H$, $R^2 = C_6H_4CF_3$-4

Urals State Technical University/Urals Polytechnical Institute, Ekaterinburg 620002, Russia; e-mail: morzherin@htf.ustu.ru. Translated from Khimiya Geterotsiklicheskikh Soedinenii, No. 1, pp. 141-142, January, 2006. Original article submitted August 24, 2005.

The ^{1}H NMR spectra were taken on a Bruker 250 (250 MHz) in DMSO-d_6, internal standard TMS.

1',3'-Dimethyl-8-(trifluoromethyl)-1,2,4,4*a*,5,6-hexahydrospiro[[1,4]thiazino[4,3-*a*]quinoline-5,5'-pyrimidine]-2',4',6'-trione (1a). A solution of 2-thiomorpholino-5-trifluoromethylbenzaldehyde (0.275 g, 1.00 mmol) and N,N'-dimethylbarbituric acid (0.156 g, 1.00 mmol) in toluene (10 ml) was refluxed. After 3 h, the solvent was evaporated under vacuum to dryness, and the residue was recrystallized from aqueous alcohol. Yield 0.175 g (72%); mp 222°C. ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 7.33 (1H, s, ArH); 7.30 (1H, d, *J* = 8.5, ArH); 6.90 (1H, d, *J* = 8.5, ArH); 4.44 (1H, d, *J* = 14.7, CH); 4.13 (1H, d, *J* = 10.3, CH); 3.54 (1H, dd, *J* = 11.9, *J* = 13.1, CH); 3.47 and 2.87 (2H, AB, *J* = 17.7, $ArCH_2$); 3.20 (3H, s, CH_3); 3.12 (3H, s, CH_3); 2.85 (1H, dd, *J* = 13.1, *J* = 10.3, CH); 2.54 (1H, dd, *J* = 14.7, *J* = 10.3, CH); 2.17 (1H, d, *J* = 13.4, CH); 2.08 (1H, d, *J* = 13.4, CH). Mass spectrum, *m*/*z* (I_{rel}, %): 413 [$M^{+\cdot}$] (92). Found, %: N 10.28. $C_{18}H_{18}F_3N_3O_3S$. Calculated, %: N 10.16.

1'-(4-Trifluoromethylphenyl)-8-(trifluoromethyl)-1,2,4,4a,5,6-hexahydrospiro[[1,4]-thiazino[4,3-*a*]-quinoline-5,5'-pyrimidine]-2',4',6'-trione (1b). A solution of 2-thiomorpholino-5-trifluoromethyl-benzaldehyde (0.275 g, 1.00 mmol) and N-*p*-trifluoromethylphenylbarbituric acid (0.272 g, 1.00 mmol) in DMF (2.0 ml) was refluxed for 3 min; then water (100 ml) was added and the precipitate was filtered out and recrystallized from aqueous alcohol. Yield 0.175 g (33%); mp 167-168°C. ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 11.51 (1H, s, NH); 7.77 (2H, d, *J* = 8.5, ArH); 7.49 (2H, d, *J* = 8.5, ArH); 7.36 (1H, s, ArH); 7.31 (1H, d, *J* = 8.8, ArH); 6.94 (1H, d, *J* = 8.8, ArH); 4.51 (1H, d, *J* = 14.3, CH); 4.41 (1H, d, *J* = 10.6, CH); 3.60 (1H, dd, *J* = 12.5, *J* = 13.1, CH); 3.47 and 2.97 (2H, AB, *J* = 17.4, $ArCH_2$); 2.89 (1H, dd, *J* = 13.1, *J* = 11.6, CH); 2.63 (1H, dd, *J* = 11.6, *J* = 10.6, CH); 2.24 (1H, d, *J* = 13.7, CH); 2.14 (1H, d, *J* = 13.7, CH). Mass spectrum, *m*/*z* (I_{rel}, %); 529 [$M^{+\cdot}$] (89). Found, %: N 8.08. $C_{23}H_{17}F_6N_3O_3S$. Calculated, %: N 7.94.

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