Chemistry of Heterocyclic Compounds, Vol. 39, No. 1, 2003

SYNTHESIS OF SPIRANES BY CYCLOCONDENSATION OF 2-PHENACYLBENZOTHIAZOLE WITH HYDRAZINES AND *o*-HYDROXY-BENZALDEHYDES

A. V. Vypirailenko, I. B. Dzvinchuk, and M. O. Lozinskii

2-Phenacylbenzothiazole reacts with hydrazines and o-hydroxybenzaldehydes to give hydrazones and chalcones. These compounds tend to isomerize to benzothiazole-2-spiro-3'-pyrazoles and benzo[b]-pyran-2-spiro-2'-benzothiazoles, respectively.

Keywords: benzopyrans, benzothiazoles, hydrazones, pyrazoles, spiranes, isomerism.

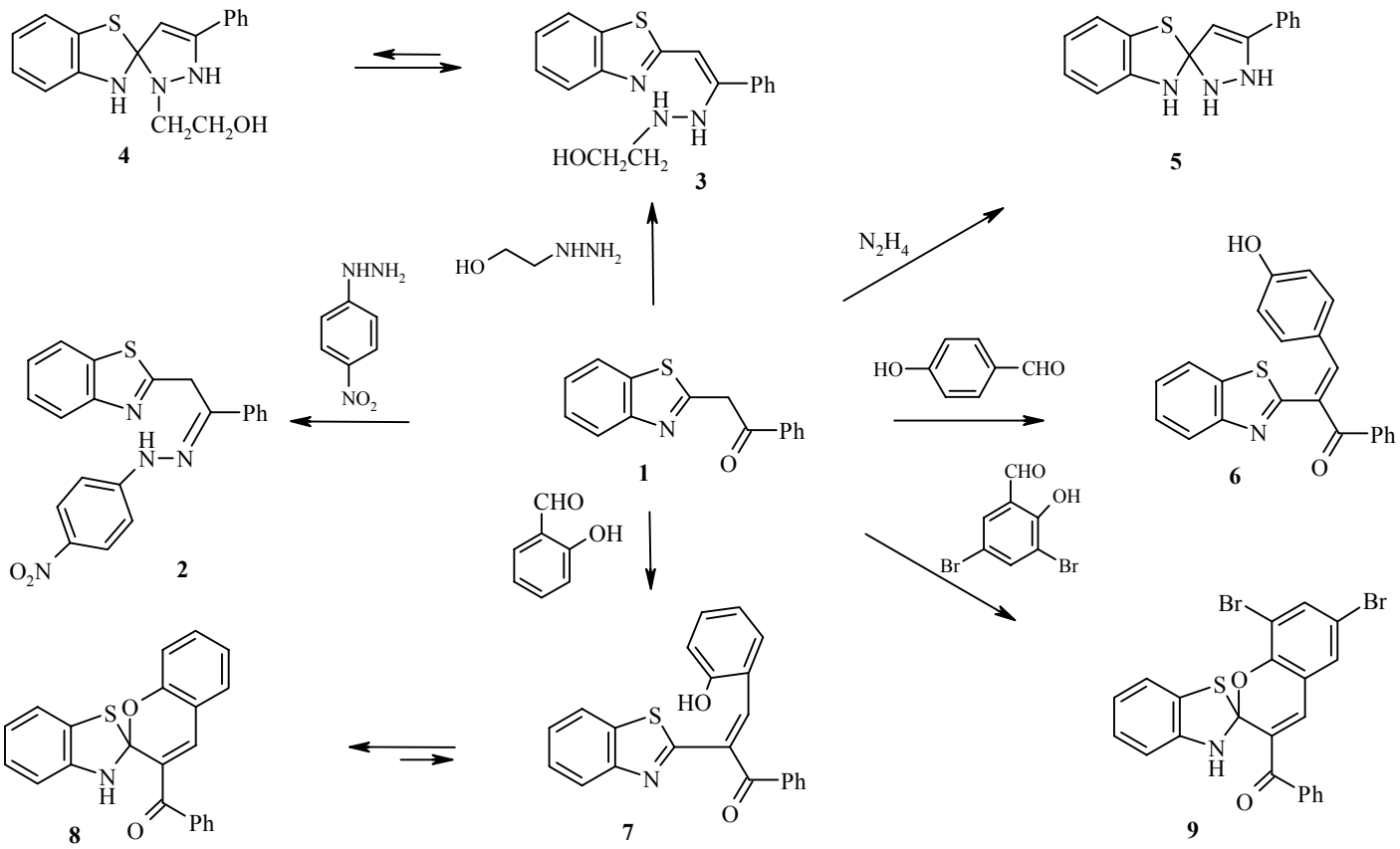
We have already shown that 2-phenacylbenzimidazole condenses with hydrazines and aldehydes in the usual manner to give the corresponding hydrazones [1] and chalcones [2]. In a study of the analogous transformations of 2-phenacylbenzothiazole (**1**), we discovered cases of isomerization caused by intramolecular condensation at the C=N bond of the benzothiazole system, which would have been difficult to predict theoretically.

Thus, a rather stable hydrazone **2** was obtained only in the case of *p*-nitrophenylhydrazine. The reaction with hydroxyethylhydrazine led to enehydrazine **3**, which exists in solution as an equilibrium mixture with tautomeric spiran form **4**. Spiran **5**, which does not undergo tautomerization, was obtained with hydrazine.

Condensation with *p*-hydroxybenzaldehyde gave expected chalcone **6**. The reaction with salicylaldehyde does not stop at the formation of chalcone **7**, but rather leads to spiran **8**. This product in solution displays tautomerism with chalcone form **7**. Condensation with 3,5-dibromosalicylaldehyde gave stable spiran **9**.

The structures of the products were established by ^{1}H NMR spectroscopy using solutions in DMSO-d_6 at 300 MHz. The signals for the NH group protons of spiran forms **8** and **9** at 8.56 and 8.98 ppm and of the phenolic hydroxyl proton of tautomer **7** and **6** at 10.29 and 10.07 ppm provide the most information in the spectra of the products of the condensation with aldehydes. The signals of the benzoyl group protons corresponding to structures **6-9** are characteristic: *o*-protons at 7.95-7.98 ppm, *p*-protons at 7.45-7.65 ppm, and *m*-protons at 7.33-7.51 ppm. Thus, the ketol–lactol isomerism characteristic for *o*-hydroxystyryl ketones [3] may be excluded. According to the integral intensities, the equilibrium solutions of **3** and **8** were found to contain 20 and 78% spiran form, respectively.

Institute of Organic Chemistry, National Academy of Sciences of Ukraine, 02094 Kiev, Ukraine; e-mail: avpr@i.com.ua. Translated from Khimiya Geterotsiklicheskikh Soedinenii, No. 1, pp. 131-133, January, 2003. Original article submitted May 8, 2002.


Ph
S
N
N
NH
H
CH2CH2OH
4
HOCH2CH2
3
5
HO
NHNH2
N2H4
NHNH2
NO2
HO
CHO
1
2
O2N
6
CHO
OH
Br
Br
8
7
9

EXPERIMENTAL

***p*-Nitrophenylhydrazone of 2-Phenacylbenzothiazole (2).** A mixture of **1** (10 mmol), *p*-nitrophenylhydrazine (10 mmol), and acetic acid (10 ml) was stirred at 55°C for 5 min. After cooling, the precipitate was filtered off and washed with 2-propanol and ether to give **2** in 79% yield; mp 171-173.5°C (dec.). ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 4.88 (2H, s, CH_2); 7.34-8.05 (9H, m, C_6H_5 + 4-H, 5-H, 6-H, 7-H); 7.92, 8.18 (2×2H, 2d, *J* = 9.0, *p*-C_6H_4); 10.86 (1H, s, NH). Found, %: C 64.75; H 4.18; N 14.50. $C_{21}H_{16}N_4O_2S$. Calculated, %: C 64.93; H 4.15; N 14.42.

2-[β-(2-Hydroxyethylhydrazino)styryl]benzothiazole (3). A mixture of **1** (5 mmol), hydroxyethylhydrazine (7.5 mmol), acetic acid (0.1 ml), and 2-propanol (5 ml) was heated at reflux for 1 h. After cooling, the precipitate was filtered off and washed with 2-propanol to give **3** in 82% yield; mp 135-136°C. ^{1}H NMR spectrum, δ, ppm (*J*, Hz): signals common for forms **3** and **4**: 3.77 (2H, m, CH_2N); 4.14 (2H, m, CH_2O); 5.40 (1H, br. s, OH); 7.28 (1H, t, *J* = 7.5, *p*-H_{Ph}); 7.36-7.42 (2H, m, *m*-H_{Ph} + 4-H); signals for form **3**: 4.99 (1H, br. s, NH–CH_2); 6.47 (1H, s, –CH=); 6.79, 6.97, 7.13 (3×1H, 3 m, 5-H, 7-H, 6-H); 7.66 (1H, br. s, NH–C=CH); 7.79 (2H, d, *J* = 7.8, *o*-H_{Ph}); signals for form **4**: 6.59 (1H, s, –CH=); 6.72, 7.08 (3×1H, 3 m, 5-H, 7-H, 6-H); 7.60 (2H, d, *J* = 7.8, *o*-H_{Ph}); 8.11, 8.60 (2×1H, 2 br. s, 2NH). Found, %: C 65.76; H 5.52; N 13.55. $C_{17}H_{17}N_3OS$. Calculated, %: C 65.57; H 5.50; N 13.49.

2,3-Dihydrobenzothiazole-2-spiro-3'-(2',3'-dihydro-5'-phenylpyrazole) (5) was obtained analogously to **2**. Yield of **5** 99%; mp 110-115°C. Mass spectrum, *m/z* (I_{rel}, %): 267 [M^+] (100). ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 6.32 (1H, s, –CH=); 6.39 (1H, m, 6-H); 6.67 (1H, m, 5-H); 7.16 (1H, d, *J* = 7.8, 7-H); 7.31 (1H, t, *J* = 6.9, *p*-H_{Ph}); 7.38-7.44 (3H, m, 4-H + *m*-H_{Ph}); 7.75 (2H, d, *J* = 8.4, *o*-H_{Ph}); 8.64 (2H, br. s, 2NH). Found, %: C 67.20; H 4.98; N 15.75. $C_{15}H_{13}N_3S$. Calculated, %: C 67.39; H 4.90; N 15.72.

2-(α-Benzoyl-4-hydroxystyryl)benzothiazole (6) was obtained in 70% yield according to our previous procedure [2]; mp 186-187°C. ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 6.70, 7.29 (2×2H, 2 d, *J* = 8.7, *p*-C_6H_4); 7.41-7.47 (2H, m, 5-H, 6-H); 7.51 (2H, dd, $J_1 = J_2$ = 7.2, *m*-H_{Ph}); 7.65 (1H, t, *J* = 7.2, *p*-H_{Ph}); 7.76 (1H, s, –CH=); 7.84 (1H, m, 7-H); 7.98 (2H, d, *J* = 7.2, *o*-H_{Ph}); 8.10 (1H, m, 4-H); 10.07 (1H, br. s, OH). Found, %: C 74.10; H 4.33; N 3.97. $C_{22}H_{15}NO_2S$. Calculated, %: C 73.93; H 4.23; N 3.92.

4-Benzoyl-2H-benzo[*b*]pyran-2-spiro-2'-(2',3'-dihydrobenzothiazole) (8) was obtained in 70% yield according to our previous procedure [2]; mp 222-223°C. ^{1}H NMR spectrum, δ, ppm (*J*, Hz): signals of form **7**: 6.61-7.16 (4H, m, C_6H_4O); 7.87 (1H, d, *J* = 7.2, 7-H); 8.08 (1H, s, –CH=); 8.10 (1H, s, *J* = 7.2, 4-H); 10.29 (1H, s, OH); the remaining signals are overlapped by the signals of the predominant spirane isomer **8**; signals of form **8**: 6.88 (1H, d, *J* = 8.4, 8-H); 7.02 (1H, m, 6-H); 7.27-7.36 (4H, m, 5'-H, 6'-H + *m*-H_{Ph}); 7.43-7.61 (5H, m, 5-H, 7-H, 4'-H, 7'-H + *p*-H_{Ph}); 7.94 (2H, d, *J* = 9.0, *o*-H_{Ph}); 7.98 (1H, s, 4-H); 8.56 (1H, s, NH). Found, %: C 73.95; H 4.25; N 3.92. $C_{22}H_{15}NO_2S$. Calculated, %: C 73.93; H 4.23; N 3.92.

4-Benzoyl-6,8-dibromo-2H-dihydrobenzo[*b*]pyran-2-spiro-2'-(2',3'-dihydrobenzothiazole) (9) was obtained in 87% yield according to our previous procedure [2]; mp 221-223°C. ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 7.34-7.39 (4H, m, 5'-H, 6'-H+*m*-H_{Ph}); 7.48 (1H, t, *J* = 8.1, *p*-H_{Ph}); 7.59-7.63 (2H, m, 4'-H, 7'-H); 7.77 (1H, s, 7-H); 7.87 (1H, s, 5-H); 7.96 (2H, d, *J* = 8.1, *o*-H_{Ph}); 7.99 (1H, s, 4-H); 8.98 (1H, br. s, NH). Found, %: C 51.21; H 2.55; N 2.68. $C_{22}H_{13}Br_2NO_2S$. Calculated, %: C 51.29; H 2.54; N 2.72.

REFERENCES

1. I. B. Dzvinchuk, A. V. Vypirailenko, and M. O. Lozinskii, *Khim. Geterotsikl. Soedin.*, 1195 (2001).
2. I. B. Dzvinchuk, A. V. Vypirailenko, M. O. Lozinskii, and T. V. Makitruk, *Ukr. Khim. Zh.*, **65**, 111 (1999).
3. R. E. Valter, *Ring–Chain Isomerism in Organic Chemistry* [in Russian], Zinatne, Riga (1978), p. 93.