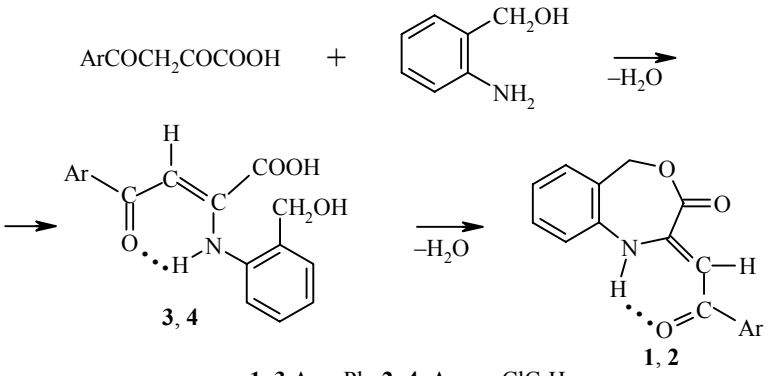
4-ARYL-2-(*o*-HYDROXYMETHYLPHENYLAMINO)-4-OXO-*Z*-2-BUTENOIC ACIDS AS INTERMEDIATES IN THE SYNTHESIS OF *Z*-2-PHENACYLIDENE-1,2,3,5-TETRAHYDRO-4,1-BENZOXAZEPIN-3-ONES

A. N. Maslivets, N. S. Kistanova, K. S. Bozdyreva, and O. A. Maslivets

Keywords: *o*-aminobenzyl alcohol, 4-aryl-2-(*o*-hydroxymethylphenylamino)-4-oxo-2-butenoic acids, aroylpyruvic acids, 2-phenacylidene-1,2,3,5-tetrahydro-4,1-benzoxazepin-3-ones.

Andreichikov et al. [1] described a synthesis of 2-phenacylidene-1,2,3,5-tetrahydro-4,1-benzoxazepin-3-one (**1**) and 2-*p*-chlorophenacylidene-1,2,3,5-tetrahydro-4,1-benzoxazepin-3-one (**2**) by heating aroylpyruvic acids with *o*-aminobenzyl alcohol in toluene at reflux for 2 h with 70-76% yields.

We have isolated intermediate 2-(*o*-hydroxymethylphenylamino)-4-oxo-4-phenyl-butenoic acid (**3**) and 2-(*o*-hydroxymethylphenylamino)-4-oxo-4-*p*-chlorophenyl-*Z*-2-butenoic acid (**4**) by carrying out this reaction in benzene at reflux for 10-15 sec. Acids **3** and **4** smoothly cyclize to the corresponding benzoxazepinones **1** and **2** upon heating in decane at reflux for 4-5 min.



1, **3** Ar = Ph, **2**, **4** Ar = *p*-ClC_6H_4

Regioselective nucleophilic attack of the amino group of the reagent by the ketonic carbonyl group at $C_{(2)}$ of the acids probably occurs in the first step of the reaction of *o*-aminobenzyl alcohol and the aroylpyruvic acids. Intermediates **3** and **4** exist in the enaminoketone form with an H-chelate intramolecular hydrogen bond (IHB) between the NH group and carbonyl group at $C_{(4)}$, i.e., in the form of *Z*-isomers. Upon heating, **3** and **4** undergo regioselective cyclodehydration to give benzoxazepinones **1** and **2**, which also exist in the enaminoketone form with an intramolecular hydrogen bond between the NH group and carbonyl group of the phenacylidene substituent, i.e., in the form of *Z*-isomers.

Perm State University, 614990 Perm, Russia; e-mail: koh@psu.ru. Translated from Khimiya Geterotsiklicheskikh Soedinenii, No. 2, pp. 302-303, February, 2003. Original article submitted December 27, 2002.

2-(*o*-Hydroxymethylphenylamino)-4-oxo-4-phenyl-*Z*-2-butenoic Acid (3). A solution of benzoylpyruvic acid (0.01 mol) and *o*-aminobenzyl alcohol (0.01 mol) in benzene (10 ml) was heated at reflux for 15 sec and cooled. The precipitate formed was filtered off to give 2.55 g (86%) of compound **3**; mp 103-104°C (dec., from benzene). IR spectrum (vaseline), ν, cm^{-1}: 3200 br (OH, NH in IHB), 1660 (C=O in CO_2H), 1605 br ($C_{(4)}$=O in IHB). ^1H NMR spectrum (400 MHz, DMSO-d_6, HMDS as the internal standard), δ, ppm (*J*, Hz): 4.56 (2H, s, CH_2); 5.48 (1H, br. s, OH); 6.43 (1H, s, CH=); 6.97-7.61 (7H, m, *o*-C_6H_4 + C_6H_3); 7.98 (2H, d, *J* = 6.91, 2 *o*-CH in COC_6H_5); 12.01 (1H, s, NH), 13.70 (1H, br. s, CO_2H). Found, %: C 68.72; H 5.11; N 4.66. $C_{17}H_{15}NO_4$. Calculated, %: C 68.68; H 5.09; N 4.71.

4-*p*-Chlorophenyl-2-(*o*-hydroxymethylphenylamino)-4-oxo-*Z*-2-butenoic Acid (4) was obtained analogously in 88% yield (2.92 g); mp 152-153°C (benzene). IR spectrum (vaseline), ν, cm^{-1}: 3310 br, 3120 br (OH, NH in IHB), 1670 (C=O in CO_2H), 1610 br ($C_{(4)}$=O in IHB). ^1H NMR spectrum (400 MHz, DMSO-d_6, HMDS as the internal standard), δ, ppm (*J*, Hz): 4.55 (2H, s, CH_2); 5.41 (1H, br. s, OH); 6.38 (1H, s, CH=); 6.97-7.67 (6H, m, C_6H_4 + 2 *m*-CH in COC_6H_4Cl-*p*); 7.98 (2H, d, *J* = 8.85, 2 *o*-CH in COC_6H_4Cl-*p*); 12.01 (1H, s, NH); 14.00 (1H, br. s, CO_2H). Found, %: C 61.59; H 4.33; Cl 10.71; N 4.20. $C_{17}H_{14}ClNO_4$. Calculated, %: C 61.55; H 4.25; Cl 10.69; N 4.22.

***Z*-2-Phenacylidene-1,2,3,5-tetrahydro-4,1-benzoxazepin-3-one (1).** A solution of **3** (0.01 mol) in decane (5 ml) was heated at reflux for 5 min and cooled. The precipitate formed was filtered off to give 2.32 g (83%) of compound **1**; mp 152-154°C (hexane). IR spectrum (vaseline), ν, cm^{-1}: 3085 br ($N_{(1)}H$ in IHB), 1732 ($C_{(3)}$=O), 1604 br (COC_6H_5 in IHB). ^1H NMR spectrum (400 MHz, DMSO-d_6, HMDS as the internal standard), δ, ppm (*J*, Hz): 5.21 (2H, s, CH_2); 6.62 (1H, s, CH=); 7.18-7.58 (7H, m, $C_{(6-9)}H$ + C_6H_3); 7.98 (2H, d, *J* = 7.00, 2 *o*-CH in COC_6H_5); 13.01 (1H, s, NH). Found, %: C 73.09; H 4.77; N 5.12. $C_{17}H_{13}NO_3$. Calculated, %: C 73.11; H 4.69; N 5.01.

***Z*-2-*p*-Chlorophenacylidene-1,2,3,5-tetrahydro-4,1-benzoxazepin-3-one (2)** was synthesized analogously in 84% yield (2.64 g); mp 165-167°C (hexane). IR spectrum (vaseline), ν, cm^{-1}: 3080 br ($N_{(1)}H$ in IHB), 1740 ($C_{(3)}$=O), 16.08 br (COC_6H_4Cl-*p* in IHB). ^1H NMR spectrum (400 MHz, DMSO-d_6, HMDS as the internal standard), δ, ppm (*J*, Hz): 5.20 (2H, s, CH_2); 6.55 (1H, s, CH=); 7.17-7.47 (6H, m, $C_{(6-9)}H$ + 2 *m*-CH in COC_6H_4Cl-*p*); 7.92 (2H, d, *J* = 8.58, 2 *o*-CH in COC_6H_4Cl-*p*); 12.99 (1H, s, NH). Found, %: C 65.09; H 3.88; Cl 11.43; N 4.39. $C_{17}H_{12}ClNO_3$. Calculated, %: C 65.08; H 3.86; Cl 11.30; N 4.46.

This work was carried out with the financial support of the Russian Basic Research Fund (Grants Nos. 01-03-32641 and 02-03-96411) and the NMR spectra were taken at the Urals NMR Center (Russian Basic Research Fund Grant No. 00-03-40139).

REFERENCES

1. Yu. S. Andreichikov, L. A. Voronova, Z. D. Belykh, and A. N. Plaksina, USSR Inventor's Certificate 666799; *Byul. Izobr.*, No. 21 (1979).