ISSN 1070-3632, Russian Journal of General Chemistry, 2008, Vol. 78, No. 3, pp. 442–445. © Pleiades Publishing, Ltd., 2008.
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Reaction of *N*-Methylsulfonyl- and *N*-(*p*-Tolylsulfonyl)-2-(Cyclopent-1-en-1-yl)anilines with Bromine in the Presence of Potassium Thiocyanate and in Methanol

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Received August 31, 2007

Abstract—The reactions of *N*-methylsulfonyl- and *N*-(*p*-tolylsulfonyl)-2-(cyclopent-1-en-1-yl)-6-methylaniline with molecular bromine in the presence of potassium thiocyanate gave *N*-methylsulfonyl- and *N*-(*p*-tolylsulfonyl)-2-(5-isothiocyanatocyclopent-1-en-1-yl)-6-methylanilines. *N*-Methylsulfonyl-2-(cyclopent-1-en-1-yl)-6-methylaniline reacted with bromine in methanol in the presence of $NaHCO_3$ or with $CuBr_2$ in MeOH to afford *N*-methylsulfonyl-2-(5-methoxycyclopent-1-en-1-yl)-6-methylaniline. The reaction of *N*-methylsulfonyl-2-(5-isothiocyanatocyclopent-1-en-1-yl)-6-methylaniline with diethylamine led to the formation of *N*-methylsulfonyl-2-{5-[diethylamino(thioxo)methyl]aminocyclopent-1-en-1-yl}-6-methylaniline which was converted into 5-methyl-4-methylsulfonyl-2,3,3a,4-tetrahydrocyclopenta[*b*]indole by heating with potassium hydroxide.

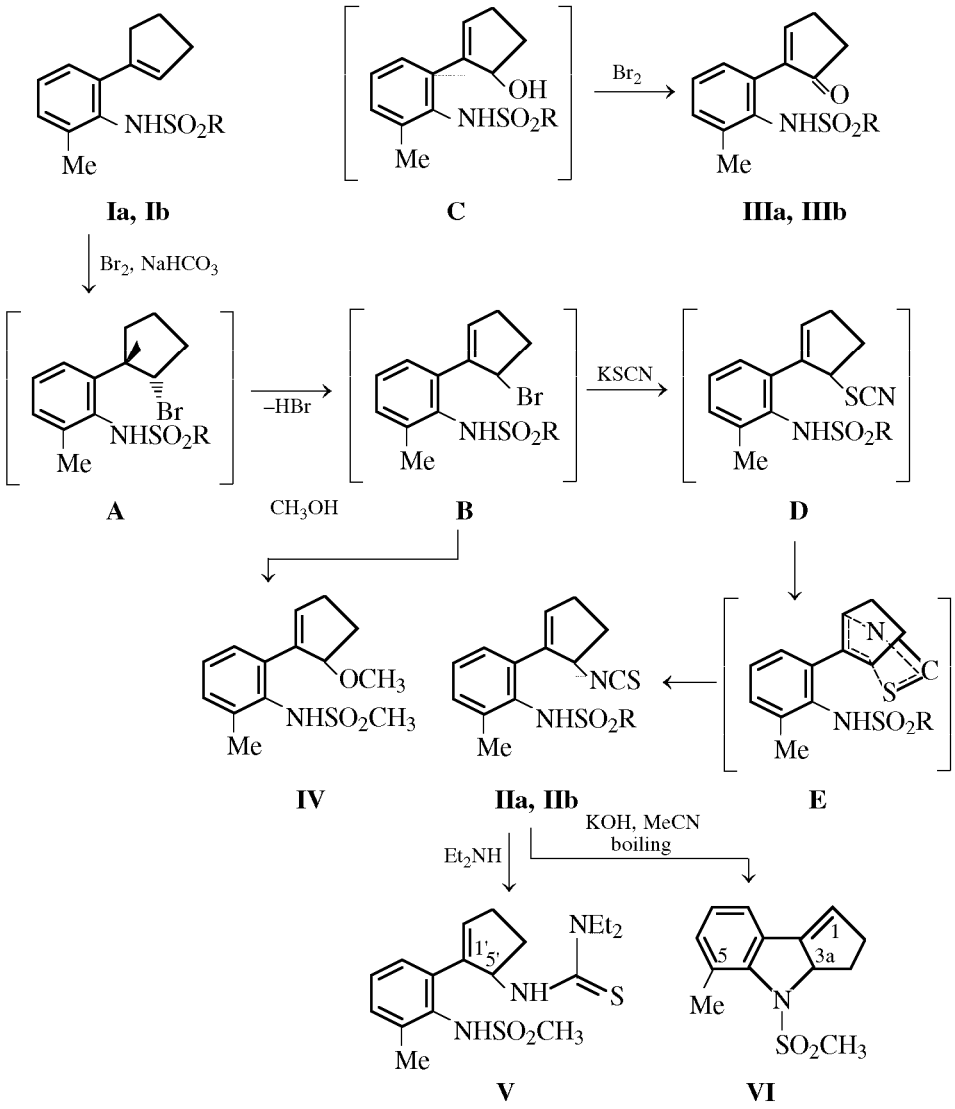
DOI: 10.1134/S1070363208030183

Derivatives of *ortho*-cycloalkenylanilines are used in the synthesis of biologically active compounds [1] and catalysts for olefin polymerization [2]. Some of these compounds exhibit local anesthetic effect [3]. Therefore, they attract interest of many researchers. In continuation of our studies on *ortho*-cycloalkenylanilines in the present work we examined reactions of *N*-methylsulfonyl- and *N*-(*p*-tolylsulfonyl)-2-(cyclopent-1-en-1-yl)-6-methylanilines **Ia** and **Ib** [4] with molecular bromine in the presence of potassium thiocyanate and in methanol.

The reactions of sulfonamides **Ia** and **Ib** with molecular bromine in acetonitrile in the presence of potassium thiocyanate gave compounds **IIa** and **IIb**, respectively, in high yields. Presumably, in the first step unstable vicinal dibromide **A** is formed via *trans*-addition of bromine at the double bond in the cyclopentene ring. Elimination of hydrogen bromide from intermediate **A** gives allylic bromide **B**. This reaction scheme is supported by the following. As we showed previously [4, 5], the reactions of cyclopentenylanilines **Ia** and **Ib** with 2 equiv of bromine in the presence of sodium hydrogen carbonate in acetonitrile or methylene chloride are accompanied by instantaneous disappearance of brown color, and the products are unsaturated ketones **IIIa** and **IIIb** (Scheme 1), which are likely to be formed via intermediate **B**. The presence of moisture in the reaction mixture promotes replacement of the labile bromine atom by hydroxy group, yielding allylic alcohol **C**, and oxidation of the latter gives ketone **IIIa** or **IIIb** [6]. The latter is also formed when the reaction is carried out under argon.

In the reaction of anilide **Ia** with bromine in methanol in the presence of $NaHCO_3$ at room temperature methyl ether **IV** is formed in high yield. Obviously, in this case the bromine atom in the allylic position is replaced ny methoxy group. Ether **IV** was also obtained when compound **Ia** in methanol was stirred in the presence of copper(II) bromide. The mechanisms of olefin transformation by the action of copper(II) bromide have been studied in sufficient detail for cyclopentadiene [7]. Taking into account published data on the behavior of stable allylic bromide (which is structurally related to bromide **B**) derived from cyclohexenylaniline [4] in methanol in

Scheme 1.



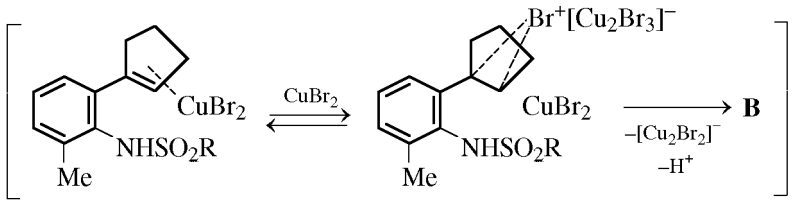
R = Me (**a**), 4-MeC_6H_4 (**b**).

the presence of $CuBr_2$, we presumed that the reaction involves intermediate formation of complex **G** which loses $[Cu_2Br_3]^-$ species and a proton (Scheme 2).

The reaction of sulfonamides **Ia** and **Ib** with bromine in the presence of potassium thiocyanate is likely to involve replacement of the bromine atom in intermediate **B** by thiocyanato group with formation of thiocyanate **D**, and its subsequent allylic isomerization gives isothiocyanate **IIa** or **IIb**. Also, alternative mechanisms proposed in [8–10] cannot be ruled out, but they seem to be less probable as applied to the reaction under study.

The condensation of isothiocyanate **IIa** with diethylamine occurs at the carbon atom of the NCS group with formation of compound **V** (Scheme 1). The reaction of **IIa** with potassium hydroxide in boiling acetonitrile is accompanied by elimination of the NCS group and cyclization to indole **VI** having unsaturated $C^{8b}=C^1$ bond.

Scheme 2.



F **G**

The structure of the isolated products was determined on the basis of analytical and spectral data. The ^{13}C NMR spectra (JMOD) of compounds **IIa** and **IIb** contained doublet signals at δ_C ~64 and ~131 ppm from the $C^{5'}$ atom and carbon atom in the N=C=S group. Compound **V** displayed in the ^{13}C NMR spectrum signals in the aliphatic region due to two methyl and two methylene groups and a signal at δ_C 178.5 ppm which is typical of thiourea fragment. The mass spectrum of **V** contained the molecular ion peak with *m*/*z* 381. Compound **VI** characteristically showed in the ^{13}C NMR spectrum (JMOD) a doublet at δ_C 74.8 from the bridgehead C^{3a} atom. The molecular ion peak with *m*/*z* 249 was present in the mass spectrum of **VI**.

EXPERIMENTAL

The ^1H and ^{13}C NMR spectra were recorded from solutions in $CDCl_3$ on a Bruker AM 300 instrument operating at 300.13 and 75.45 MHz, respectively. The chemical shifts were measured relative to tetramethylsilane as internal reference. The elemental compositions were determined on an M-185B CHN Analyzer. Qualitative TLC analysis was performed using Sorbfil plates (PTSKh-AF-V-UF, *Sorbpolimer* Ltd., Stavropol, Russia); spots were detected under UV light and by treatment with iodine vapor.

***N*-[2-(5-Isothiocyanatocyclopent-1-en-1-yl)-6-methylphenyl]methanesulfonamide (IIa).** A solution of 0.16 g of molecular bromine in 5 ml of acetonitrile was slowly added under stirring to a solution of 0.251 g of sulfonamide **Ia** and 0.97 g of potassium thiocyanate in 15 ml of acetonitrile. After 12 h, the mixture was filtered, and the filtrate was evaporated under reduced pressure. The residue was washed with water (2×50 ml), the organic phase was separated and dried over sodium sulfate, and the solvent was removed under reduced pressure. To remove tarry impurities, the residue was subjected to chromatography on a short column charged with 1 g of silica gel using benzene as eluent. Yield 0.3 g (97%), R_f 0.4 (C_6H_6–EtOAc, 85:15). ^1H NMR spectrum, ($CDCl_3$), δ, ppm: 1.90 s (3H, CH_3), 1.91–2.43 m (4H, CH_2), 3.02 s (3H, CH_3), 5.36 d.t (1H, 5′-H, J_1 = 2.5, J_2 = 7.5 Hz), 6.09 q (1H, 2′-H, J = 2.0 Hz), 6.28 br.s (1H, NH), 7.13 d (1H, H_{arom}, J = 8.0 Hz), 7.25 t (1H, H_{arom}, J = 8.0 Hz), 7.51 d (1H, H_{arom}, J = 8.0 Hz). ^{13}C NMR spectrum ($CDCl_3$), δ_C, ppm: 19.0 (CH_3), 30.6 ($C^{3'}$), 32.4 ($C^{4'}$), 41.4 (CH_3), 63.8 ($C^{5'}$), 127.9 (C^4), 128.3 ($C^{2'}$), 130.9 (C^3), 131.5 (C^6), 131.9 (NCS), 134.6 (C^2), 134.7 (C^5), 137.3 (C^1), 140.8 ($C^{1'}$). Found, %: C 54.35; H 5.08; N 8.91; S 20.58. $C_{14}H_{16}N_2O_2S_2$. Calculated, %: C 54.52; H 5.23; N 9.08; S 20.79.

***N*-[2-(5-Isothiocyanatocyclopent-1-en-1-yl)-6-methylphenyl]-4-toluenesulfonamide (IIb)** was synthesized in a similar way from 0.327 g of sulfonamide **Ib**. Yield 0.37 g (97%). ^1H NMR spectrum ($CDCl_3$), δ, ppm: 1.92 s (3H, CH_3), 1.95–2.39 m (4H, CH_2), 2.42 s (3H, CH_3), 5.32 d.t (1H, 5′-H, J_1 = 2.0, J_2 = 7.6 Hz), 6.04 q (1H, 2′-H, J = 4.0 Hz), 6.19 br.s (1H, NH), 7.11 d (1H, H_{arom}, J = 8.0 Hz), 7.23 t (1H, H_{arom}, J = 8.0 Hz), 7.37 d (2H, H_{arom}, J = 8.3 Hz), 7.51 d (1H, H_{arom}, J = 8.0 Hz), 7.62 d (2H, H_{arom}, J = 8.3 Hz). ^{13}C NMR spectrum ($CDCl_3$), δ_C, ppm: 18.2, 21.2 (CH_3); 30.2 ($C^{3'}$); 31.9 ($C^{3''}$); 63.1 ($C^{5'}$); 126.8, 127.7, 128.3, 129.2, 130.5, 133.8 ($C^{2''}$, $C^{6''}$, C^3, C^4, $C^{3''}$, $C^{5''}$, C^5, $C^{2'}$); 131.1, 134.5, 137.3, 137.5, 140.7, 143.4 (C^1, C^2, C^6, $C^{1''}$, $C^{4''}$, $C^{1'}$, $C^{5'}$); 131.7 (NCS). Found, %: C 62.36; H 5.18; N 7.11; S 16.42. $C_{20}H_{20}N_2O_2S_2$. Calculated, %: C 62.47; H 5.24; N 7.29; S 16.68.

***N*-[2-(5-Methoxycyclopent-1-en-1-yl)-6-methylphenyl]methanesulfonamide (IV).** A solution of 0.25 g of compound **Ia** in 5 ml of methanol was added dropwise under stirring to a solution of 0.45 g of $CuBr_2$ in 20 ml of methanol. After 12 h, the mixture was diluted with 25 ml of water and extracted with methylene chloride (30 ml), the organic phase was dried over Na_2SO_4, the solvent was removed under reduced pressure, and the residue was purified from tarry impurities by chromatography on a 2×20-cm

column charged with 0.5 g of silica gel using benzene as eluent. Yield 0.27 g (96%), viscous material, R_f 0.35 (C_6H_6–EtOAc, 9:1). IR spectrum: ν 3280 cm^{-1} (NH). ^1H NMR spectrum ($CDCl_3$), δ, ppm: 1.91–2.72 m (4H, CH_2), 2.54 s (3H, CH_3), 2.94 s (3H, CH_3), 3.41 s (3H, OCH_3), 4.62 m (1H, 5′-H), 5.97 m (1H, 2′-H), 6.93 d (1H, 3-H, J = 7.2 Hz), 7.08 t (1H, 4-H, J = 7.2 Hz), 7.22 d (1H, 5-H, J = 7.2 Hz), 8.30 s (1H, NH). ^{13}C NMR spectrum ($CDCl_3$), δ_C, ppm: 19.5, 40.5, 56.8 ($3CH_3$); 29.8 ($C^{3'}$), 30.4 ($C^{4'}$), 90.0 ($C^{5'}$), 126.7 (C^4), 128.0 ($C^{2'}$), 131.0 (C^3), 133.3 (C^6), 135.3 (C^2), 136.5 (C^5), 136.0 ($C^{1'}$), 142.5 (C^1). Found, %: C 59.45; H 6.43; N 4.67; S 11.02. $C_{14}H_{19}NO_3S$. Calculated, %: C 59.76; H 6.81; N 4.98; S 11.39.

***N*-(2-{5-[Diethylamino(thioxo)methylamino] cyclopent-1-en-1-yl}-6-methylphenyl)methanesulfonamide (V).** Diethylamine, 5 ml, was added to a solution of 0.308 g of compound **IIa** in 5 ml of chloroform. After 30 min, the mixture was diluted with 100 ml of chloroform and washed with 50 ml of water. The organic phase was dried over Na_2SO_4, the solvent was removed under reduced pressure, 5 ml of ethanol was added to the residue, and the mixture was heated for 10 min under reflux. After cooling, the solvent was separated by decanting from the oily residue, and the residue was dried under reduced pressure. Yield 0.354 g (93%), amorphous substance. ^1H NMR spectrum (DMSO-d_6), δ, ppm: 0.95 t (6H, CH_3, J = 7.0 Hz), 1.81–2.55 m (4H, CH_2), 2.18 s (3H, CH_3), 3.02 s (3H, CH_3), 3.50 q (4H, CH_2, J = 7.0 Hz), 5.32 d.d (1H, 5′-H, J_1 = 2.7, J_2 = 4.0 Hz), 5.90 s (1H, NH), 6.05 d.t (1H, 2′-H, J_1 = 2.4, J_2 = 4.6 Hz), 6.82 br.s (1H, NH), 7.11–7.28 m (3H, H_{arom}). ^{13}C NMR spectrum (DMSO-d_6), δ_C, ppm: 12.2 ($2CH_3$), 18.8 (CH_3), 30.5, 31.9 ($2CH_2$), 44.2 ($2CH_2$), 42.3 (CH_3), 63.3 ($C^{5'}$), 126.3 (C^4), 127.2 ($C^{2'}$), 129.5 (C^3), 132.3 (C^5), 132.4 (C^6), 136.5 (C^2), 137.8 (C^1), 141.0 ($C^{1'}$), 178.5 (C=C). Mass spectrum, *m*/*z*: 381 $[M]^+$, 308 $[M - HNC_4H_{10}]^+$, 302 $[M - SO_2Me]^+$, 265 $[M - CCHC_4H_{10}]^+$, 249 $[M - NH_2CCHC_4H_{10}]^+$, 229, 204, 170 (base peak) $[M - NH_2CCHC_4H_{10} - SO_2Me]^+$. Found, %: C 56.43; H 7.02; N 10.83; S 16.67. $C_{18}H_{27}N_3O_2S_2$. Calculated, %: C 56.66; H 7.13; N 11.01; S 16.81.

5-Methyl-4-methylsulfonil-2,3,3a,4-tetrahydrocyclopenta[*b*]indole (VI). Compound **IIa**, 0.308 g, was dissolved in 10 ml of acetonitrile, 0.28 g of potassium hydroxide was added to the solution, and the mixture was heated for 5 min under reflux. The solvent was evaporated under reduced pressure, the residue was dissolved in 30 ml of methylene chloride, and the solution was washed with water (2×50 ml), and dried over sodium sulfate. Removal of the solvent under reduced pressure gave 0.246 g (99%) of the crude product which was purified by chromatography on a short column charged with silica gel. Yield 0.2 g (80%), R_f 0.75 (C_6H_6–EtOAc, 85:15). ^1H NMR spectrum ($CDCl_3$), δ, ppm: 2.00–2.75 m (4H, $2CH_2$), 2.53 s (3H, CH_3), 2.94 s (3H, CH_3), 4.96 d.d.t (1H, 3a-H, J_1 = 2.5, J_2 = 3.5, J_3 = 6.0 Hz), 5.95 d.t (1H, 1-H, J_1 = 2.4, J_2 = 3.2 Hz), 7.05 d.t (1H, 7-H, J_1 = 6.1, J_2 = 6.8 Hz), 7.28 d (1H, 8-H, J = 6.8 Hz), 7.36 d (1H, 6-H, J = 6.1 Hz). ^{13}C NMR spectrum ($CDCl_3$), δ_C, ppm: 21.5 (CH_3), 34.7, 37.1 ($2CH_2$), 37.2 (CH_3), 74.8 (C^{3a}), 119.9 (C^7), 121.2 (C^8), 124.7 (C^1), 127.3 (C^{8a}), 127.4 (C^5), 133.4 (C^6), 142.4 (C^{8b}), 146.4 (C^{4a}). Mass spectrum, *m*/*z*: 249 $[M]^+$, 234 $[M - CH_3]^+$, 185 $[M - SO_2Me]^+$ (base peak). Found, %: C 62.39; H 5.48; N 5.46; S 12.65. $C_{13}H_{15}NO_2S$. Calculated, %: C 62.63; H 6.06; N 5.62; S 12.86.

REFERENCES

1. Mustafin, A.G., Khalilov, I.N., Abdrakhmanov, I.B., and Tolstikov, G.A., *Khim. Prirodn. Soedin.*, 1989, no. 6, p. 818.
2. Ivanchev, S.S., Tolstikov, G.A., Badaev, V.K., Ivancheva, N.I., Oleinik, I.I., Serushkin, M.I., and Oleinik, L.V., *Vysokomol. Soedin., Ser. A*, 2001, vol. 43, no. 12, p. 2053.
3. Gataullin, R.R., Kazhanova, T.V., Davydova, V.A., Il'yasova, L.T., Karachurina, L.T., Sapozhnikova, E.S., Zarudii, F.S., and Abdrakhmanov, I.B., *Khim.-Farm. Zh.*, 2001, vol. 35, no. 9, p. 28.
4. Gataullin, R.R., Sotnikov, A.M., Spirikhin, L.V., and Abdrakhmanov, I.B., *Russ. J. Org. Chem.*, 2005, vol. 41, no. 5, p. 715.
5. Pikhtovnikov, S.V., Furlei, I.I., Mavrodiev, V.K., Gataullin, R.R., and Abdrakhmanov, I.B., *Izv. Ross. Akad. Nauk, Ser. Khim.*, 2002, no. 12, p. 2135.
6. Love Brian, E. and Nguyen Binh, T., *Synth. Commun.*, 2000, vol. 30, no. 5, p. 963.
7. Skumov, M.Ya., Brailovskii, S.M., and Temkin, O.N., *Izv. Ross. Akad. Nauk, Ser. Khim.*, 2002, no. 4, p. 572.
8. Ruasse, M.-F. and Argle, A., *J. Org. Chem.*, 1983, vol. 48, no. 2, p. 202.
9. Skorobogatova, E.V. and Kartashov, V.R., *Usp. Khim.*, 1998, vol. 67, no. 5, p. 474.
10. Sivasubramanian, S., Aravind, S., and Muthusubramanian, S., *Indian J. Chem., Sect. B*, 1990, vol. 29, no. 1, p. 59.