BULLETIN OF THE CHEMICAL SOCIETY OF JAPAN, VOL. 52 (10), 3123—3124 (1979)

Reactive Troponoids and *o*-Aminophenol. IV. The Synthesis of 8-Arylazocyclohepta[*b*][1,4]benzoxazine by the Reaction of Arylazotropolone with *o*-Aminophenol[1)]

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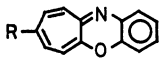
(Received February 17, 1979)

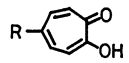
Synopsis. 8-Phenylazocyclohepta[*b*][1,4]benzoxazine was obtained by the dehydration of 5a-hydroxy-8-phenylhydrazonocyclohepta[*b*][1,4]benzoxazine, which had itself been obtained by the reaction of 5-phenylazotropolone with *o*-aminophenol.

In previous papers, we have reported the formation of cyclohepta[*b*][1,4]benzoxazine (**1a**) and its derivatives by the reactions with *o*-aminophenol of troponoids which have one or two leaving groups.[2–4)] Many years ago, Nozoe and his coworkers found that 5-nitrosotropolone (**2a**) and 5-arylazotropolone (**2b**) reacted with *o*-phenylenediamine to give quinoxalotropone derivatives,[5)] while 5-nitrosotropolone gave the condensation products (**3a**) by a reaction with *o*-aminophenol; the latter reaction has not, however, been examined in detail.[6)]

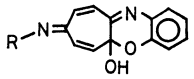
In this paper, the present author wishes to describe the results of the reactions of 5-phenylazo- and 5-(*p*-tolylazo)tropolone with *o*-aminophenol.



1a R=H
1b R=N=N-Ph
1c R=N=N-C$_6$H$_4$-CH$_3$
1d R=N=O



2a R=N=O
2b R=N=N-Ph
2c R=N=N-C$_6$H$_4$-CH$_3$



3a R=OH
3b R=NH-Ph
3c R=NH-C$_6$H$_4$-CH$_3$

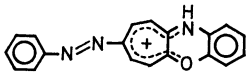
Results and Discussion

The heating of 5-phenylazotropolone (**2b**) with *o*-aminophenol (**4**) in ethanol under reflux resulted in the repid, quantitative precipitation of sparingly soluble crystals (**3b**). From elemental analysis ($C_{19}H_{15}N_3O_2$), the mass-spectral determination of mol wt (*m/e* 317 (M^+)), and other spectral data, **3b** seems to be 5a-hydroxy-8-phenylhydrazonocyclohepta[*b*][1,4]benzoxazine. Similarly, 5a-hydroxy-8-(*p*-tolylhydrazono)cyclohepta[*b*][1,4]benzoxazine (**3c**) was obtained from 5-(*p*-tolylazo)tropolone (**2c**) and **4**. It is because of the contribution of the arylazo or nitroso group that **3b**,**c** and **3a** do not undergo dehydration to form **1b**,**c** and **1d** respectively under these reaction conditions.

When **3b** and **3c** were left in acetic acid in the presence of sulfuric acid, they underwent dehydration to form 8-phenylazo- (**1b**) and 8-(*p*-tolylazo)cyclohepta[*b*][1,4]benzoxazine (**1c**) respectively. These structures were determined by mass and elemental analyses and by means of the spectral data. When **1b**,**c** were allowed to stand in ethanol, upon the addition of 1 M NaOH or 1 M HCl at room temp. for 3 h, **1b**,**c** reverted to **3b**,**c**, which were then decomposed into **2b**,**c** and **4** when heated with an excess of alkali for 2 h.

The dehydration of **3a** failed to produce 8-nitrosocyclohepta[*b*][1,4]benzoxazine (**1d**) under the same reaction conditions as were used in the case of **3b**,**c** to **1b**, **c**.

The NMR data of **1b** measured in trifluoroacetic acid and chloroform-*d* show a sflift of the seven-membered ring protons by 0.86—1.07 ppm and that of the benzene ring protons by only 0.10—0.22 ppm towards a lower magnetic field. This indicates that the positive charge of the cation (**5**) derived from **1b** is delocalized over both the seven-membered ring and the heterocyclic part, as in the case of cyclohepta[*b*][1,4]-benzoxazine (**1a**).[2)]



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Experimental

If not otherwise stated, the instruments and methods were as previously described.[2)]

5a-Hydroxy-8-phenylhydrazonocyclohepta[b][*1,4*]*benzoxazine(3b)*: A mixture of 5-phenylazotropolone (**2b**) (2.0 g, 8.7 mmol), *o*-aminophenol (**4**) (2.0 g, 18.3 mmol), and ethanol (16 ml) was refluxed for 3 h. After cooling, the resulting red crystals (3.2 g) were filtered and recrystallized from ethanol to give 2.7 g (96%) of **3b**; red needles; mp 198 °C; λ_{max}^{MeOH} nm (log ε): 205 (4.73), 234 (4.36), 278 (4.06), and 440 (4.32); $\lambda_{max}^{MeOH+NaOH}$ nm (log ε): 277 (4.05), 410 (4.00)^{sh}, and 472 (4.20); IR (KBr): 3300 (NH) and 3200 cm^{-1} (OH); NMR (60 MHz in DMSO-d_6): δ 9.72 (br. s, 1H, OH), 9.09 (s, 1H, NH), and 6.2—8.0 ppm (m, 13H). Found: C, 71.88; H, 4.86; N, 13.50%; M^+, 317. Calcd for $C_{19}H_{15}N_3O_2$: C, 71.91; H, 4.76; N, 13.24%; M, 317.

*5a-Hydroxy-8-(*p*-tolylhydrazono)cyclohepta*[b][*1,4*]*benzoxazine (3c)*. A mixture of 5-(*p*-tolylazo)tropolone (**2c**) (2.0 g, 8.2 mmol), **4** (1.8 g, 16.4 mmol), and ethanol (4.5 ml) was refluxed for 9 h. After cooling, the resulting crystals were filtrated. Recrystallization from ethyl acetate gave 2.3 g (87 %) of **3c** as orange red needles; mp 231 °C; λ_{max}^{MeOH} nm (log ε): 205 (4.72), 250 (4.35), 300 (4.04), and 442 (4.33); $\lambda_{max}^{MeOH+NaOH}$

nm (log ε): 293 (4.05), 405 (4.09), and 480 (4.26); IR (KBr): 3400 (NH) and 3250 cm^{-1} (OH); NMR (60 MHz in DMSO-d_6): δ 9.40 (s, 1H, NH), 6.9—8.2 (m, 12H), and 2.40 ppm (s, 3H, CH_3). Found: C, 72.20; H, 5.13; N, 12.33%; M^+, 331. Calcd for $C_{20}H_{17}N_3O_2$: C, 72.49; H, 5.17; N, 12.33%; M, 331.

5a-Hydroxy-8-(hydroxyimino)cyclohepta[b][*1,4*]*benzoxazine (**3a**).* A mixture of 5-nitrosotropolone (**2a**) (400 mg, 2.6 mmol), **4** (290 mg, 2.66 mmol), and MeOH (40 ml) was stirred at room temp. The suspension became clear once, and then yellow crystals were precipitated. After filtration, recrystallization from ethyl acetate gave 540 mg (86%) of **3a**; pale yellow needles; mp 198 °C.

8-Phenylazocyclohepta[b][*1,4*]*benzoxazine (**1b**).* A mixture of **3b** (800 mg, 2.5 mmol), acetic acid (15 ml), and concd sulfuric acid (1.4 ml) was allowed to stand at room temp for 1 day. The solution was then neutralized with aq $NaHCO_3$ and extracted with ether. The extract was concentrated, and the residue was chromatographed on a silica-gel column. From the benzene fraction, 600 mg (80%) of **1b** was obtained as brown, triangular structures; mp 210 °C (from benzene); λ_{max}^{MeOH} nm (log ε): 205 (4.45), 231 (4.32), 263 (4.44), 322 (4.30), 450 (4.43)^{sh}, 471 (4.48), 500 (4.40)^{sh}, and 570 (3.76)^{sh}; $\lambda_{max}^{MeOH+HCl}$ nm (log ε): 205 (4.38), 235 (4.37), 265 (4.38), 274 (4.41), 333 (4.26), and 535 (4.39); $\lambda_{max}^{MeOH+NaOH}$ nm (log ε): 258 (4.32), 321 (4.14), 448 (4.52), 505 (4.28)^{sh}, and 570 (4.16)^{sh}; NMR (100 MHz in $CDCl_3$): δ 7.76 (2H, m, $C_{2',6'}$–H), 7.43 (3H, m, $C_{3',4',5'}$–H), 7.14 (1H, dd, J=13.0, 2.0 Hz, C_9–H), 6.89 (1H, dd, J=10.5, 2.0 Hz, C_7–H), 6.86 (3H, m, $C_{1,2,3}$–H), 6.51 (1H, m, C_4–H), 6.29 (1H, d, J=13.0 Hz, C_{10}–H), and 5.72 ppm (1H, d, J=10.5 Hz, C_6–H); NMR (100 MHz in $CDCl_3$+CF_3COOD): δ 8.06 (C_9–H, $\Delta\delta$=0.92 ppm), 7.90 ($C_{2',6'}$–H, $\Delta\delta$=0.14 ppm), 7.88 (C_7–H, $\Delta\delta$=0.99 ppm), 7.53 ($C_{3',4',5'}$–H, $\Delta\delta$=0.10 ppm), 7.15 (C_{10}–H, $\Delta\delta$=0.86 ppm), 6.96 ($C_{1,2,3}$–H, $\Delta\delta$=0.10 ppm), 6.79 (C_6–H, $\Delta\delta$=1.07 ppm), and 6.73 ppm (C_4–H, $\Delta\delta$=0.22 ppm). Found: C, 76.23; H, 4.19; N 13.77%; M^+, 299. Calcd for $C_{19}H_{13}N_3O$: C, 76.24; H, 4.38; N, 14.04%; M, 299.

8-(p-Tolylazo)cyclohepta[b][*1,4*]*benzoxazine (**1c**).* A mixture of **3c** (400 mg, 1.2 mmol), acetic acid (10 ml), and concd sulfuric acid (0.5 ml) was heated at 75—80 °C for 2 h After standing over night, water (50 ml) was added to the solution, and it was neutralized with $NaHCO_3$ and extracted with benzene. The extract was chromatographed on a silica-gel column. From the benzene–ethyl acetate (20: 1) fraction, 250 mg (64%) of **1c** was obtained as brown needles; mp 219 °C (from benzene); λ_{max}^{MeOH} nm (log ε): 206 (4.39), 230 (4.25), 264 (4.41), 328 (4.28), 455 (4.45)^{sh}, 474 (4.49), 500 (4.41)^{sh}, and 560 (4.37)^{sh}; $\lambda_{max}^{MeOH+HCl}$ nm (log ε): 206 (4.31), 233 (4.28), 265 (4.36), 275 (4.39), 341 (4.17), and 540 (4.37); $\lambda_{max}^{MeOH+NaOH}$ nm (log ε): 268 (4.35), 333 (4.21), 475 (4.50), 510 (4.37)^{sh}, and 570 (4.02)^{sh}; NMR (60 MHz in $CDCl_3$): δ 7.70 (2H, m, $C_{2',6'}$–H), 7.30 (2H, m, $C_{3',5'}$–H), 7.10 (1H, m, C_9–H) 6.87 (1H, m, C_7–H), 6.80 (3H, m, $C_{1,2,3}$–H), 6.45 (1H, m, C_4–H), 6.27 (1H, d, J=13 Hz C_{10}–H), 5.70 (1H, d, J=10 Hz C_6–H), and 2.38 ppm (3H, s, CH_3). Found: C, 76.67; H, 4.63; N, 13.06%; M^+, 313. Calcd for $C_{20}H_{15}N_3O$: C, 76.66; H, 4.83; N, 13.41%, M, 313

*Conversion of **1b,c** into **3b,c**.* A solution of **1b,c** (5 mg) in ethanol (1 ml) and three drops of 1 M HCl or 1 M NaOH was allowed to stand at room temp for 3 h. The neutralized solution was found to be **3b,c** by means of the TLC and UV absorptions

A solution of **1b,c** or **3b,c** (5 mg) in ethanol (1 ml) and 1 M NaOH (1 ml) was refluxed or 2 h. The neutralized solution was found to be a mixture of **2b,c** and **4** by means of the TLC and UV absorptions.

The author wishes to express his deep gratitude to Professor Emeritus Tetsuo Nozoe and Professor Kahei Takase (Tohoku University) for their encouragement and advice, and also to Dr. Haruki Tsuruta (Takasago Perfumery Co., Ltd.) for his valuable discussion.

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