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Novel Intermolecular Heterocycle Exchange Reaction of Cyclohepta[b][1,4]benzoxazines and Their S-Analogs with 1,2-Bifunctional Reagents[1)]

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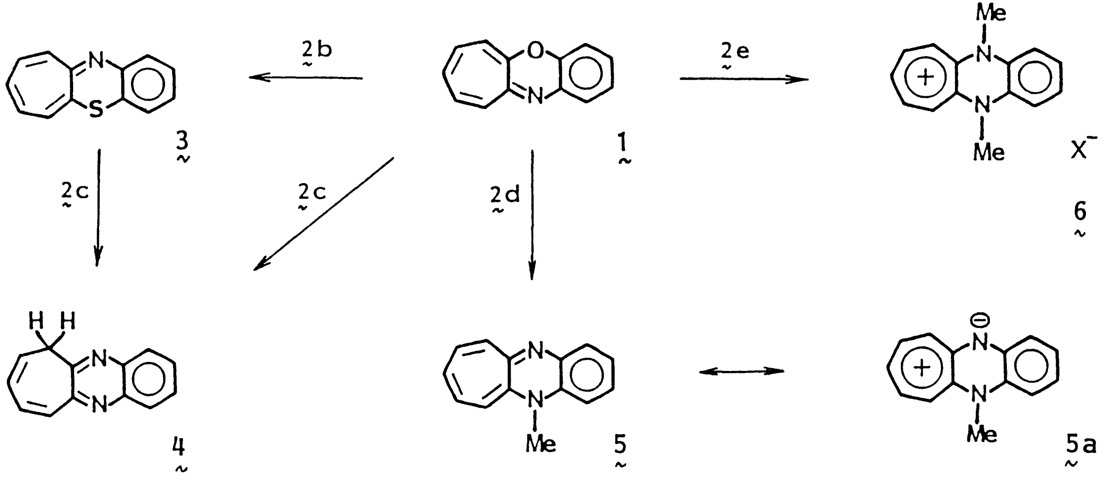
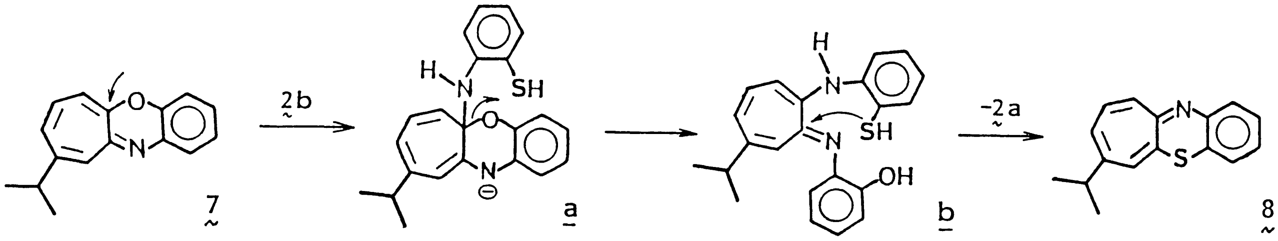
The benzoxazine and the benzothiazine moieties of cyclohepta[b][1,4]benzoxazines and their S-analogs were easily exchanged with o-aminobenzenethiol, o-phenylenediamine and other related 1,2-bifunctional reagents in ethanol. The exchange of the two fused heterocycles of a tropylium compound is also described.

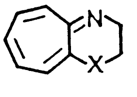
In the preceeding communication we reported novel intermolecular heterocycle exchange reactions of cyclohepta[b][1,4]benzoxazine **1** with o-aminophenol **2a** and its 4-methyl derivative.[2)] In this communication we wish to describe another hetercycle exchange reaction of **1** and its S-analog **3** with o-aminobenzenethiol **2b**, o-phenylenediamine **2c**, its N-methyl and N,N'-dimethyl derivatives (**2d** and **2e**) and aliphatic 1,2-bifunctional reagents.

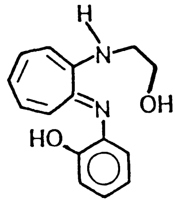


When 1 was treated with an excess of 2b, cyclohepta[b][1,4]benzothiazine 3[3] was formed in a high yield. Similarly, both 1 and 3 were converted into the diazine analog 4 of the quinoxalo form[4,5] by the reaction with 2c. The reverse reaction of 3 or 4 to 1 did not take place apparently because of the less favorable nucleophilicity of 2a. Conversion of 1 to N-methyl derivative 5[6] and N,N'-dimethyl cation 6[7] was also achieved by the heterocycle exchange reaction with 2d and 2e. 9-Isopropylcyclohepta[b][1,4]benzoxazine 7[8] and 2b gave a thiazine analog 8[9] which did not isomerize anymore with 2b.



Compound 1 also reacted with aliphatic amines such as ethylenediamine and 2-aminoethanethiol, giving rise to the 2,3-dihydrocyclohepta[b]diazine and thiazine (9a,b, X=NH, S),[10] respectively. The reaction of 1 with 2-aminoethanol initially afforded 2-aminotroponeimine 10,[11] which, owing to the weak nucleophilicity of the alcoholic hydroxyl group, became 11[12] by dehydrocyclization. On the other hand, 3 with ethylenediamine exclusively gave 2-phenyl-4,5-dihydro-1H-imidazol 12[13] instead of similar heterocycle-exchanged products.


9a,b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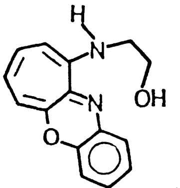
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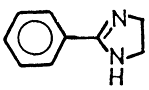
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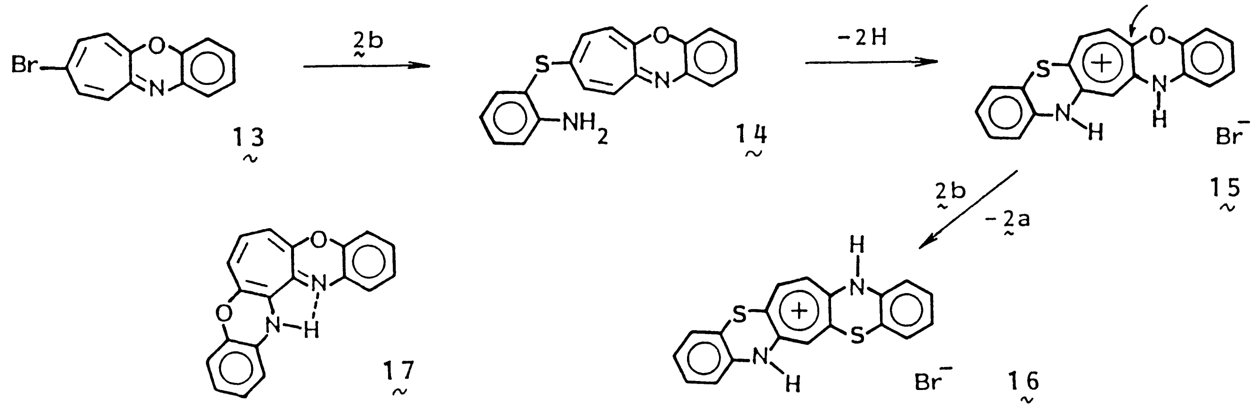

The tropylium compound such as 15[14] having two annelated hetero-rings obtained from 8-bromo compound **13**15)via S-substituted compound **14**14)gave **16**14) also by the exchange of its benzoxazino moiety with excess of **2b**. On the other hand, compound **17**16)having a strong intramolecular H-bonding did not suffer any heterocycle exchange with **2b**.

The experimental evidence descrived so far would prove the validity of our former assumption2) concerning the reaction pathway for this unprecedented intermolecular exchange of the whole heterocycles. It shows a characteristic feature of the complex reactivities of these heterocyclic system (**1**, **3**,and **4**), in which an intramolecular shift of a heterocycle is also observed frequently, as will be reported eleswhere.

References

1) T. Nozoe, K. Shindo, H. Wakabayashi, H. Okai, and S. Ishikawa, presented at the 18th Japanese Symposium on the Chemistry of Nonbenzenoid Aromatic Compounds, Toyama, October 1985, Abstr. p.87.

2) T.Nozoe, H.Okai, H.Wakabayashi, and S.Ishikawa, Chem. Lett., preceeding paper.

3) T. Nozoe, T. Asao, and K. Takahashi, Bull. Chem. Soc. Jpn., 34, 146 (1961); K. Shindo, S. Ishikawa, and T. Nozoe, ibid., 58, 165 (1985).

4) **4**: Pale yellow needles (from $CHCl_3$); mp 68-69 °C; UV (MeOH) 235, 243, and 342 nm (log ε 4.21, 4.21, and 3.94); ^{1}H NMR (270 MHz in CD_3CN) δ =3.59 (2H, d, J=5.8 Hz, CH_2), 6.08 (1H, dt, J=10.3 and 5.8 Hz, H-7), 6.28 (1H, dd, J=10.3 and 5.3 Hz, H-8), 6.80 (1H, dd, J=11.7 and 5.3 Hz, H-9), 7.71 (2H, m, H-2,3), 7.28 (1H, d, J=11.7 Hz, H-10), and 8.05 (2H, m, H-1,4); MS, m/z 194 (M^+). Anal. ($C_{13}H_{10}N_2$) C, H, N.

4a (BF_4^- salt): Dark green needles (from EtOH); mp 227-229 °C; UV (MeOH) 236, 279, 289, 332, 345, 447, 463, 495, 573, 620, 684, and 764 nm (log ε 4.28, 4.43, 4.53, 3.99, 3.97, 3.93, 4.06, 3.95, 3.00, 3.02, 2.89, and 2.42); ^{1}H NMR (270 MHz in CD_3CN) δ =5.68 (2H, d, J=11.2 Hz, H-6,10), 6.04 (1H, t, J=9.5 Hz, H-8), 6.14 (2H, m, H-2,3), 6.62 (2H, dd, J=11.2 and 9.5 Hz, H-7,9), and 7.95 (2H, brs, NH). Anal. ($C_{13}H_{11}N_2BF_4$) C, H, N.

5) T. Fukunaga, presented at the 23rd IUPAC Congress, Boston, 1971, Abstr. p.103 and private communication.

6) **5**: Dark green needles (from EtOH); mp 68 °C ; UV (MeOH) 229, 252, 274, 324, 409 429, 458, 525, 568, 630, and 696 nm (log ε 4.09, 4.08, 4.22, 3.87, 3.84, 3.91, 3.75, 2.83, 2.81, 2.65, and 2.36); ^{1}H NMR (270 MHz, $CDCl_3$) δ =2.36 (3H, s, CH_3), 4.42 (1H, d, J=9.5 Hz, H-6), 5.62 (1H, dd, J=10.2 and 7.5 Hz, H-8), 5.57 (1H, d, J=13 Hz, H-10), 5.84 (2H, m, H-7,9), 6.14 (1H, dd, J=8 and 1.5 Hz, H-4), 6.57 (1H, ddd, J=8, 7.5, and 1.5 Hz, H-2), 6.62 (1H, ddd, J=8, 7.5, and 2.5 Hz, H-3), and 6.63 (1H, dd, J=8, 2.5 Hz, H-1); MS, m/z 208(M^+). Anal. ($C_{14}H_{12}N_2$) C, H, N.

7) **6** (Cl^-salt): Dark green needles (from EtOH); mp 230 °C; UV (MeOH) 239, 278, 283, 325, 441, 578, 620, and 732 nm (log ε 4.18, 4.18, 4.23, 3.89, 3.81, 3.07, 3.05, and 2.56); ^{1}H NMR (270 MHz, CD_3CN) δ =3.10 (6H, s, Me), 6.25 (2H, d, J=11 Hz, H-6,10), 6.57 (1H, t, J=9.5 Hz, H-8), 6.71 (2H, m, H-1,4), 6.95 (2H, m, H-2,3),

7.24 (2H, dd, J=11 and 9.5 Hz, H-7,9).

8) T. Nozoe and T. Someya, Bull. Chem. Soc. Jpn., 51, 3316 (1978).

9) 8: ^1H NMR(270 MHz in $CDCl_3$) δ=1.09 (6H, d, J=6.6 Hz, Me), 2.42 (1H, m, J=6.6 Hz, CH), 6.05 (1H, d, J=8.1 Hz, H-8), 6.08 (1H, s, H-6), 6.14 (1H, d, J=11.7 Hz, H-10), 6.34 (1H, dd, J=11.7 and 8.1 Hz, H-9), 6.85 (1H, dd, J=8.1 and 1.1 Hz, H-4), 6.93 (1H, td, J=8.1 and 1.1 Hz, H-3), 7.04 (1H, td, J=8.1 and 1.1 Hz, H-2), and 7.10 (1H, dd, J=8.1 and 1.5 Hz, H-1).

10) 9a: Pale yellow needles, mp 134 °C; UV (MeOH) 254, 366, and 424 nm (log ε 4.37, 3.88, and 3.80); ^1H NMR (100 MHz in $CDCl_3$) δ=3.53(4H, s, CH_2), 6.08 (1H, t, J=9 Hz, H-7), 6.20 (2H, d, J=10 Hz, H-5,9), and 6.51 (2H, dd, J= 10 and 9 Hz, H-6,8); MS, m/z 146(M^+).

9b: Yellow solid, ; UV (MeOH) 243, 268, and 377 nm (log ε 4.07, 3.99, and 3.75); ^1H NMR (270 MHz in CD_3CN) δ=2.94 (2H, t, J=5 Hz, CH_2), 3.80 (2H, t, J=5 Hz, CH_2), 6.28-6.42 (3H, m, H-7,8,9), and 6.48-6.58 (2H, m, H-5,6); MS, m/z 163(M^+).

11) 10: Yellow oil; UV (MeOH) 254, 269, 344, 361, 412, and 415 nm (log 4.28, 4.19, 3.85, 3.91, 4.00, and 3.85); ^1H NMR (270 MHz in C_6D_6) δ=3.03 (2H, t, J=5.1 Hz, CH_2), 3.34 (2H, t, J=5.1 Hz, CH_2), 5.46 (3H, br, NH and OH), 5.84 (1H, d, J=9.5 Hz, H-3), 6.07 (1H, dd, J=9.5 and 8.5 Hz, H-5), 6.39 (1H, ddd, J=11.7, 8.5, and 5.1 Hz, H-6), 6.61 (1H, t, J=9.5 Hz, H-4), 6.83 (1H, td, J=8 and 1.5 Hz, H-5'), 6.95 (1H, dd, J=8 and 1.5 Hz, H-3'), 6.96 (1H, td, J=8 and 1.5 Hz, H-4'), 7.08 (1H, d, J=11.7 Hz, H-7), and 7.22 (1H, dd, J=8, and 1.5 Hz, H-6'); Found: m/z 256.1201. Calcd for $C_{15}H_{16}N_2O_2$: M, 256.1211.

12) 11: Red solid, mp 100-104 °C; UV (MeOH) 232, 263, and 475 nm; ^1H NMR (270 MHz in C_6D_6) δ=2.70 (2H, t, J=5.1 Hz, CH_2), 3.20 (2H, t, J=5.1 Hz, CH_2), 5.52 (1H, dd, J=9.7 and 1 Hz, H-9), 5.66 (1H, td, J=9.7 and 1 Hz, H-7), 5.92 (1H, dd, J=9.7 and 1 Hz, H-6), 5.97 (1H, td, J=9.7 and 1 Hz, H-8), 6.37 (1H, dd, J= 7.5 and 1.5 Hz, H-4), 6.50 (1H, td, J=7.5 and 1.5 Hz, H-3), 6.55 (1H, td, J=7.5 and 1.5 Hz, H-2'), and 6.96 (1H, dd, J=7.5 and 1.5 Hz, H-1); O-Ac Derivative: Red solid, m/z 296 (M^+).

13) G. Ewin and J. O. Hill, Aust. J. Chem., 28, 909 (1975).

14) 14: Brown needles, mp 126-128 °C; UV (MeOH) 264, 312, and 435 nm; ^1H NMR (100 MHz in $CDCl_3$) δ=4.27 (2H, s, NH_2), 5.25 (1H, d, J=10.3 Hz, H-6), 5.59 (1H, dd, J=10.3 and 1.0 Hz, H-7), 6.00 (1H, d, J=1.0 Hz, H-9), 6.00 (1H, s, H-10), and 6.3-6.8 (8H, m, H-1,2,3,4,3',4',5',6'); MS, m/z 318 (M^+).

15: Blue-violet solid; UV (MeOH) 286, 300, 343, and 542 nm; MS, m/z 316 (M^+-HBr).

16: Yellowish green solid; UV (MeOH) 299, 357, 445, and 566 nm; ^1H NMR (270 MHz in CD_3OD) δ=6.20 (1H, s, H-14), 6.62 (1H, s, H-6), 6.77 (1H, d, J=11.7 Hz, H-13), 6.65-7.12 (8H, m, H-1,2,3,4,8,9,10,11), 7.33 (1H, s, NH), and 7.90 (1H, s, NH); MS, m/z 332 (M^+-HBr).

15) H. Wakabayashi, S. Ishikawa, S. Sugiura, and T. Nozoe, presented at 49th Spring Meeting of the Chemical Society of Japan, Tokyo, April 1984, Abstr. p.752.

16) T. Someya, H. Okai, H. Wakabayashi, and T. Nozoe, Bull. Chem. Soc. Jpn., 56, 2756 (1983).

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