CHEMISTRY LETTERS, pp. 1353-1356, 1982.

NOVEL REACTION OF 2-METHYLENEBENZOTHIAZOLINES WITH 3-(2,3-DIPHENYL-2-CYCLOPROPENYLIDENE)PENTANE-2,4-DIONE: FORMATION OF 3a,9-DIHYDROCYCLOPENTA[b][1,4]BENZOTHIAZINES

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Reactions of 3-substituted 2-methylenebenzothiazolines, generated in situ from the corresponding 2-methylbenzothiazolium salts and triethylamine, with 3-(2,3-diphenyl-2-cyclopropenylidene)pentane-2,4-dione give 3a,9-dihydrocyclopenta[b]-[1,4]benzothiazine derivatives.

Dehydrohalogenation of 3-phenacylthiazolium halides leads to generation of thiazolium ylides whose synthetic utility as a 1,3-dipole has been established to a certain extent.[1] In the case of 2-methyl-3-phenacylbenzothiazolium bromide, however, a proton at the methyl group is eliminated to generate 2-methylene-3-phenacylbenzothiazoline which was able to be captured as the Michael adducts to electron-deficient olefins and acetylenes.[2] The 2-methylenebenzothiazoline has an electron-rich exocyclic double bond and is classified as a cyclic ketene acetal.

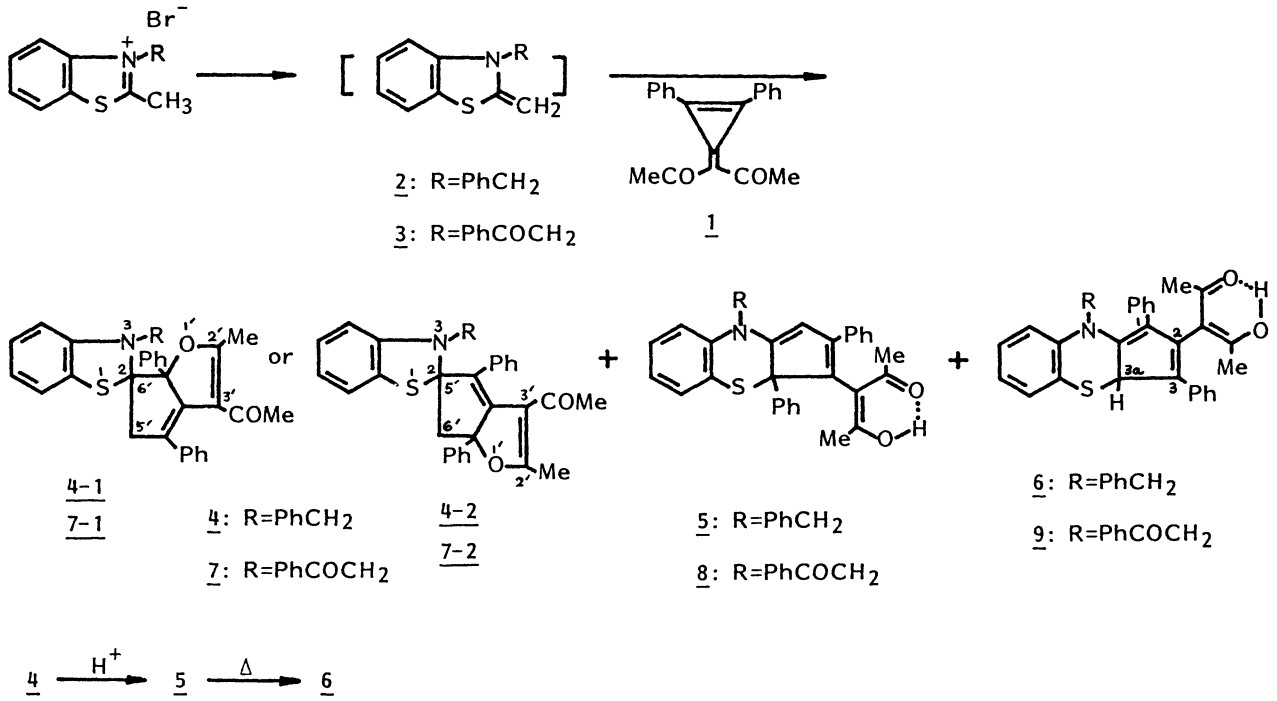
Although ketene acetals are expected to show a pattern of reaction similar to enamines, few examples for the reaction between ketene acetal and methylenecyclopropene have been reported so far.[3] Recent reports have shown that the reactions of enamines with methylenecyclopropenes give different types of products depending upon the nature of substituents of methylenecyclopropenes.[3,4] Similar results are being obtained from the reactions of 2-methylenebenzothiazoline, as a cyclic ketene N,S-acetal, with a variety of methylenecyclopropenes.[5]

In the present communication, we would like to report the reactions of 2-methylenebenzothiazolines with 3-(2,3-diphenyl-2-cyclopropenylidene)pentane-2,4-dione 1 leading to 3a,9-dihydrocyclopenta[b]-[1,4]benzothiazine derivatives. 3-Benzyl- 2 and 3-phenacyl-2-methylenebenzothiazoline 3 were generated in situ by treating the corresponding benzothiazolium salts with triethylamine.

A mixture of equimolar amounts of 1 and 3-benzyl-2-methylbenzothiazolium bromide in dry tetrahydrofuran was treated, at 0 °C under nitrogen, with triethylamine. After 0.5 h at room temperature, the reaction mixture was passed through a short column packed with a small amount of neutral alumina using benzene as an eluent to give three 1:1 adducts, 4, 5, and 6, in 21, 10, and 57 % yields, respectively. In the same reaction for a long time (15 h), a yield of the major product 6 increased up to 84 % with decreased yields of 4 (10 %) and 5 (trace).[6] Although two products, 4 and 6, were isolated by fractional recrystallization, the minor product 5 was too unstable to be isolated in a pure form.[7] Actually, 5 gradually changes into 6 in solution even at room temperature, meaning that 5 is an intermediate of the major product 6.

The 1:1 adduct 4, mp 184-185 °C (dec.), has a low carbonyl stretching vibration at 1660 cm^{-1} showing that the acetyl group in 4 is conjugating with unsaturated system. The ^{13}C-NMR spectrum in which only one acetyl group is observed at 30.7 (q, Me) and 193.9 ppm (s, CO) indicates that one

of the two acetyl groups has participated in a cyclization. The ^{1}H-NMR spectrum shows a pair of diastereotopic methylene hydrogens at 3.90 and 4.22 ppm (J=18 Hz) as well as the another methylene singlet at 3.20 ppm. On the basis of the above and other spectral data,[8] 4 is assumed to be either the benzothiazoline-2-spiro-6'-cyclopenta[b]furan 4-1 or the benzothiazoline-2-spiro-5'-cyclopenta[b]furan 4-2. The similar cyclopenta[b]furan ring formation has been reported in the reactions of 1 with enamines.[9]



Scheme 1

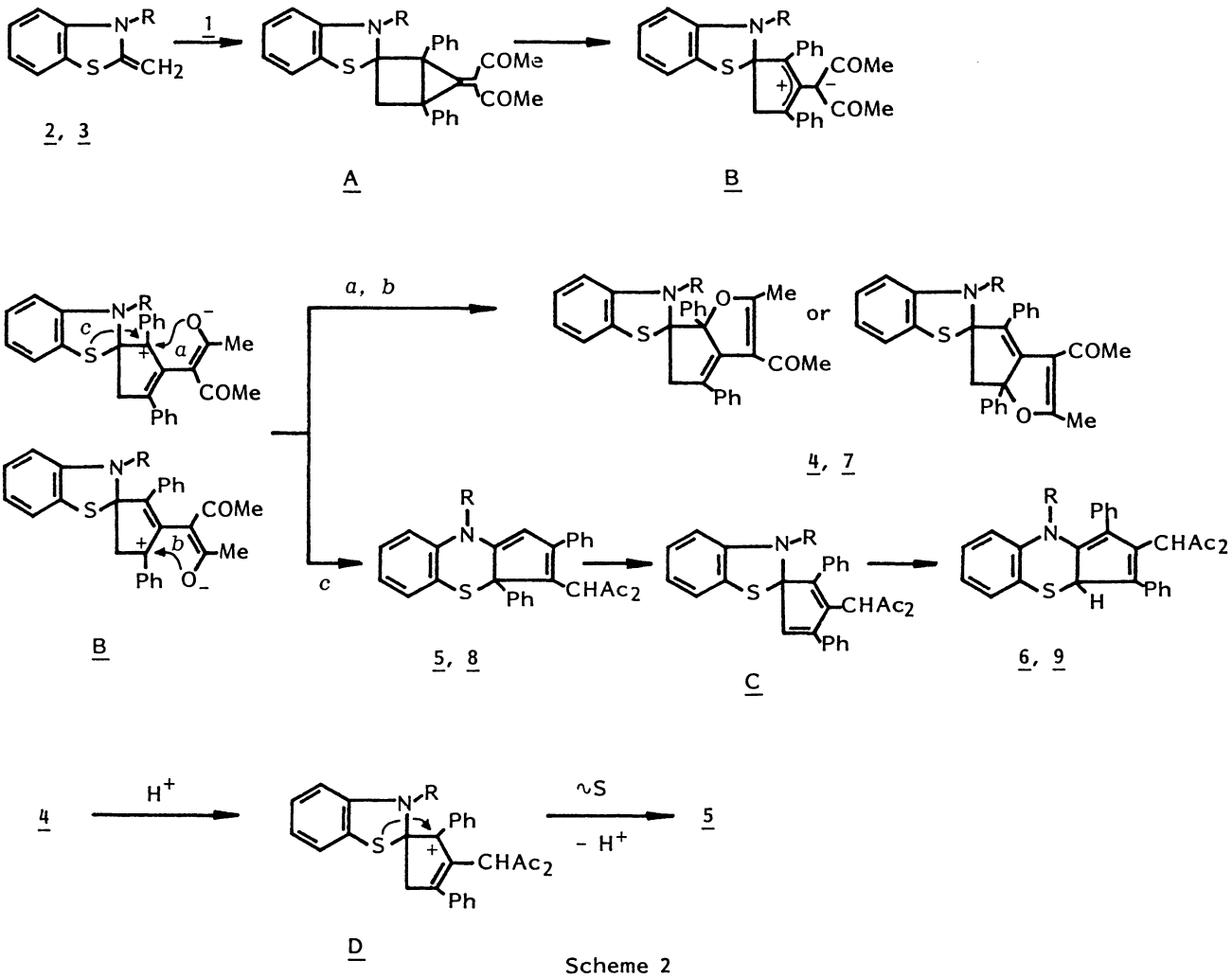
Structural elucidation of the major product 6, 2-(1-acetylacetonyl)-9-benzyl-1,3-diphenyl-3a,9-dihydrocyclopenta[b][1,4]benzothiazine, was accomplished on the basis of the spectral data.[10] The ^{1}H-NMR spectrum shows the signals of a methine and an enolic hydrogen at 4.26 and 16.32 ppm, respectively, indicating that a rearrangement of benzothiazole ring has taken place. The benzylic hydrogens (4.60 and 4.85 ppm) and carbon (52.1 ppm) are observed in considerably lower fields than those of 4 (3.90 and 4.22 ppm for the hydrogens and 48.0 ppm for the carbon). Thus, the benzyl group in 6 should be located on an enamino nitrogen atom.[11]

The precursor 5 for 6 has an enolic hydrogen (16.93 ppm), but an olefinic hydrogen (5.78 ppm) instead of methine hydrogen. The benzyl group (5.02, 5.20, and 53.1 ppm) is under circumstances similar to that of 6. The spectral data are satisfactorily explained for the proposed structure, 3-(1-acetylacetonyl)-9-benzyl-2,3a-diphenyl-3a,9-dihydrocyclopenta[b][1,4]benzothiazine.[12] Both the methyl groups are magnetically quite different since one of the methyl groups is forced to face a phenyl plane at the 3a position.

Similarly, the reaction of 1 with 3 at room temperature for 0.5 h afforded a mixture of three 1:1 adducts, 7, 8, and 9. Isolation of the former two products, 7 and 8, was unsuccessful because of their poor yields. Their formation was confirmed by the inspection of ^{1}H-NMR spectrum of the crude reaction mixture.[13] The major product 9, mp 180-181 °C, isolated in 84 % yield is found to have the same ring structure as 6 on the basis of the spectral data.[14]

When the spiro cyclopenta[b]furan 4 was treated with a catalytic amount of hydrochloric acid in

ethanol, it quantitatively changed into 5 that further thermally isomerized to 6.



Scheme 2

The probable reaction pathways for the formation of the above products are depicted in Scheme 2. The electron-deficient endocyclic double bond of methylenecyclopropene 1 interacts with the electron-rich exocyclic one of 2 and 3 forming a four-membered intermediate A which corresponds to that proposed for the reaction of methylenecyclopropene with enamine.[15] Then it undergoes a ring opening of the fused cyclopropane moiety to yield a zwitterionic intermediate B that is stabilized by the electron-withdrawing acetyl groups. Two possible cyclizations (path *a* and *b*) of B lead to two isomeric cyclopenta[b]furan derivatives, 4 and 7. However, only one of them was actually obtained from the reaction while the regiochemistry was left unresolved.

The rearrangement of sulfur atom in B onto the cationic center followed by deprotonation (path *c*) gives the unstable cyclopenta[b][1,4]benzothiazine, 5 or 8. The lability might be due to steric hindrance between the phenyl group at the 3a position and the acetylacetonyl group. Release from the steric hindrance may cause the 1,5-sigmatropic rearrangement of sulfur atom to give a spiro intermediate C. A further rearrangement gives rise to the less hindered cyclopenta[b][1,4]benzothiazine, 6 or 9.[16]

Protonation onto the oxygen atom of furan ring in 4 easily opens the ring to form an intermediate D which corresponds to a protonated B. The similar rearrangement of sulfur atom with concurrent

deprotonation gives 5.

References

1) a) K. T. Potts, D. R. Choudhury, and T. R. Westby, J. Org. Chem., 41, 187 (1976); b) O. Tsuge, H. Shimoharada, and M. Noguchi, Heterocycles, 15, 807 (1981); c) O. Tsuge, H. Shimoharada, and M. Noguchi, Chem. Lett., 1981, 1199 and 1493; d) O. Tsuge, H. Shimoharada, M. Noguchi, and S. Kanemasa, Chem. Lett., 1982, 711; e) O. Tsuge and H. Shimoharada, Chem. Pharm. Bull., 30, 1903 (1982).

2) O. Tsuge, M. Tanaka, H. Shimoharada, and M. Noguchi, Heterocycles, 16, 1705 (1981).

3) Th. Eicher and J. L. Weber, Topics Current Chem., 57, 1 (1975).

4) O. Tsuge, S. Okita, M. Noguchi, and S. Kanemasa, Chem. Lett., 1982, 847 and 993.

5) O. Tsuge, M. Tanaka, H. Shimoharada, and S. Kanemasa, submitted for publication.

6) The yields of 4 and 5 were determined on the basis of the ^{1}H-NMR spectra of crude product.

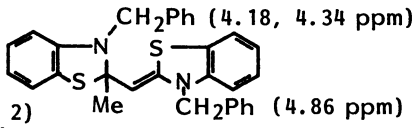
7) The isolated products, 4, 6, and 9, gave the satisfied results of elementary analysis.

8) 4: IR: 1660 (CO), 1550, and 1470 cm^{-1}; ^{1}H-NMR in $CDCl_3$: δ1.80, 2.22 (each 3H, s, Me), 3.20 (2H, s, CH_2), 3.90, 4.22 (each 1H, d, J=18.0 Hz, $PhCH_2$), 5.67 (1H, m, aromatic), and 6.40-7.53 ppm (18H, m, aromatic); ^{13}C-NMR in $CDCl_3$: δ16.3 (q, Me), 30.7 (q, MeCO), 48.0(t, Ph-CH_2), 57.5 (t, CH_2), 93.9, 98.9 (each s, spiro- and 6'a-C), 175.9 (s, 2'-C), and 193.9 ppm (s, CO).

9) Th. Eicher and Th. Born, Tetrahedron Lett., 1970, 985.

10) 6: IR: 1610 (CO), 1540, and 1470 cm^{-1}; ^{1}H-NMR in $CDCl_3$: δ1.70, 1.90 (each 3H, s, Me), 4.26 (1H, s, CH), 4.60, 4.85 (each 1H, d, J=18.0 Hz, $PhCH_2$), 6.70-7.40 (19H, m, aromatic), and 16.32 ppm (1H, s, OH); ^{13}C-NMR in $CDCl_3$: δ23.5, 23.6 (each q, Me), 43.7 (d, CH_2), 52.1 (t, $PhCH_2$), 108.4, 117.0, 120.9 (each s, 1-, 3-, and C(Ac)=C(OH)Me), 190.1, and 191.8 ppm (each s, CO); Mass: m/e 527 (M^+), 436, 394, 350. mp 207-208 °C.

11) It is known that the α-hydrogens of alkyl group on an enamino nitrogen occur in considerably lower fields than those on an ordinary amino nitrogen: (E. M. Kosower and T. S. Sorensen, J. Org. Chem., 27, 3764 (1962), and H. Booth and J. H. Little, Tetrahedron, 23, 291 (1967)). The dimers of 2 and 3 offer another example.[2)]



12) 5: ^{1}H-NMR in $CDCl_3$: δ0.76, 2.28 (each 3H, s, Me), 5.02, 5.20 (each 1H, d, J=18.0 Hz, $PhCH_2$), 5.78 (1H, s, =CH), 6.50-7.60 (19H, m, aromatic), and 16.93 ppm (1H, s, OH); ^{13}C-NMR in $CDCl_3$: δ22.2, 24.4 (each q, Me), 53.1 (t, $PhCH_2$), 191.9, and 195.7 ppm (each s, CO).

13) Two sets of signals were observed besides the set of 9 and were assigned to 7 and 8 in comparison with the spectra of 4 and 5: 7: δ1.86, 2.15 (each 3H, s, Me), 3.30, 3.43 (each 1H, d, J=13.0 Hz, CH_2), and 4.20 ppm (2H, s, $PhCOCH_2$); 8: δ0.73, 2.36 (each s, Me), 5.06, 5.36 (each 1H, d, J=18.0 Hz, $PhCOCH_2$), 5.56 (1H, s, =CH), and 17.10 ppm (1H, s, OH).

14) 9: IR: 1700, 1610 (CO), 1570, 1550 cm^{-1}; ^{1}H-NMR in $CDCl_3$: δ1.76, 1.92 (each 3H, s, Me), 4.41 (1H, s, CH), 4.83, 5.11 (each 1H, d, J=19.0 Hz, $PhCOCH_2$), and 16.35 ppm (1H, s, OH); ^{13}C-NMR in $CDCl_3$: δ23.6 (q, Me), 43.8 (d, CH), 55.1 (t, $PhCOCH_2$), 108.3, 117.4, 120.1 (each s, 1-, 3-, and C(Ac)=C(OH)Me), 190.1, 191.8, and 193.9 ppm (each s, CO); Mass: m/e 555 (M^+), 450, 435, and 105.

15) J. Ciabattoni and E. C. Nathan III, J. Amer. Chem. Soc., 89, 3081 (1967).

16) The reason why only the sulfur atom migrates in the rearrangements would be that the nitrogen migration does not reduce the steric hindrance around the position to which the nitrogen atom migrates.

(Received June 2, 1982)