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THE EFFECT OF BENZANNELATION TOWARD CYCL[3.2.2]AZINE. SYNTHESIS AND PHYSICAL PROPERTIES OF DIBENZO[a,h]CYCL[3.2.2]AZINE

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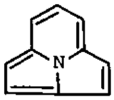
Abstract——Dibenzo[a,h]cycl[3.2.2]azine (**2**) was synthesized by the [2 + 8] cyclization reaction of 1-cyanoisoindolo[2,1-a]isoquinoline (**6**) with dimethyl acetylenedicarboxylate as a key step and the effect of dibenzo-annelation on the six- and five-membered ring parts of the cycl[3.2.2]azine has been investigated.

In the previous papers,[1-3] we have described the synthesis and some physical properties of the monobenzo-annelated cycl[3.2.2]azines (**2** and **3**) on the [a]- and [g]-ring, and some of their related compounds. Recently Mitchell and co-workers showed that the the bond localization was caused by the fusion of benzene or other aromatic rings in the studies of benzannelated dihydrpyrenes.[4-6] In these studies, they have also reported that the transoid fusion of the benzene rings perturbs slightly the diatropicity in the annulenes, whereas the cisoid fusion brings about strongly the bond localization on the annulene macrocyclic ring of dibenzo-annelated pyrene. Matsumoto and his co-workers have already reported the synthesis of a dibenzo-annelated cycl[3.2.2]azine, **5**, having a symmetrical structure among them, and showed that **5** is viewed as the 18π peripheral conjugate system in spite of expected large resonance stabilization owing to the benzene nucleus.[7,8] In an extension of our studies on cycl[3.2.2]azines, we now wish to report the synthesis of the dibenzo-annelated cycl[3.2.2]azine (**4**) which displays the largest bathochromic shift, comparing with other mono- and dibenzo-cyclazine (**2**, **3**, and **5**) and the parent cycl[3.2.2]azine (**1**)[9,10].



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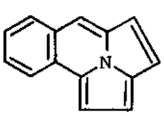

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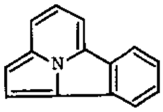

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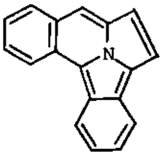

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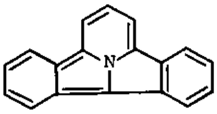

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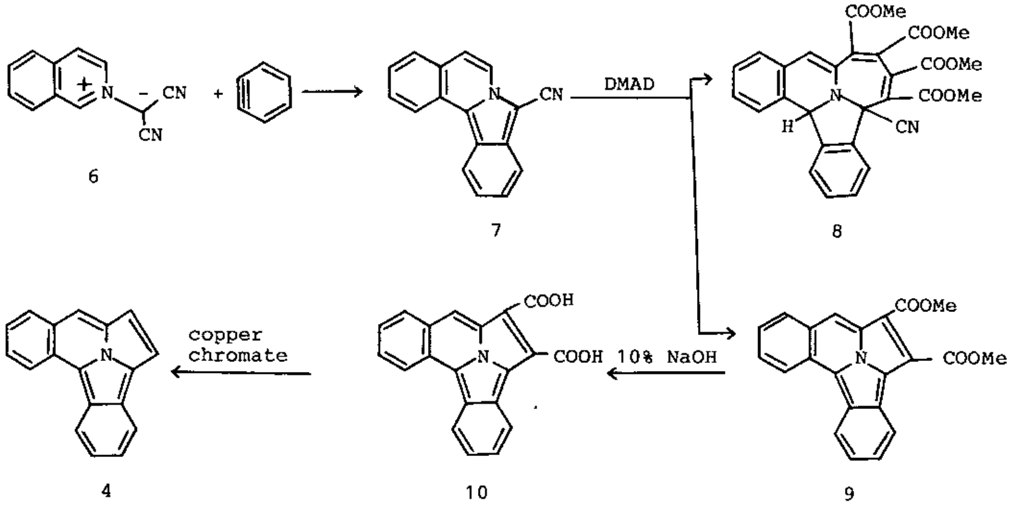
Reaction of isoquinolinium dicyanomethylide (**6**), readily prepared from isoquinoline and tetracyanoethylene oxide, with benzyne generated from anthranilic acid and isoamylnitrite gave 1-cyanoisoindolo[2,1-a]isoquinoline (**7**)[11], mp 168°C, in 74% yield. Compound **7** was allowed to react with dimethyl acetylenedicarboxylate (DMAD) in the presence of a small amount of acetic acid under refluxing for 20 h in toluene to give the desired product, dimethyl dibenzo[a,h]cycl[3.2.2]azine-1,2-dicarboxylate (**9**)[12], mp 185°C, in 26% yield, along with dibenzo[f,i]cycl[4.3.2]azine derivative (**8**)[13], mp 182°C, in 6% yield. The addition of a small amount of acetic acid was important for the improvement of the yield of **9**, though the yield was only 1% without acetic acid. Hydrolysis of the diester (**9**) with 10% sodium hydroxide proceeded essentially quantitatively to give the diacid **10**. Finally, decarboxylation of the diacid using copper chromate in quinoline occurred smoothly to afford the desired dibenzo[a,h]cycl[3.2.2]azine (**4**), mp 139°C, in 32% yield.



Dibenzo[a,h]cycl[3.2.2]azine (**4**) is orange red needles. Its structure was confirmed by elemental analysis and by various spectroscopic data. The complex of this compound with 2,4,7-trinitro-9-fluorenone gave dark brown needles, mp 205°C. In its mass spectrum, prominent peaks are found at m/z 241(M^+, 100), 242(M+1, 20), 240(M-1, 8), 239(M-2, 14), 120(25), and 119(13). In its uv spectrum shown in Fig. 1, **4** shows much more bathochromic shift than absorption maxima of monobenzo-annelated cycl[3.2.2]azines (2 and 3) and the remarkable red shift in comparison with the parent cycl[3.2.2]azine (1), respectively, consistent with the enlargement of the conjugation in polyaromatic system in the former. The behaviors in the aromatic proton chemical shift (7.43-9.07 ppm) of **4** are similar to those of **5** (7.47-8.68 ppm). The vicinal coupling costant for C1-H and C2-H(7.44, 8.06 ppm, $J_{1,2}$=4.57 Hz) is similar to the corresponding value of cycl[3.2.2]azine (1) ($J_{1,2}$=4.4 Hz). However this coupling constant is smaller than that of the corresponding C1-H and C2-H in 2 ($J_{1,2}$=5.0 Hz) and larger than that of C1-H and C2-H in 3 ($J_{1,2}$=3.9 Hz).

In conclusion, dibenzo-annelation in the pentacyclic [10]annulene (**4**) does not cause the expected decrease of diatropicity as is illustrated by the chemical shift of the peripheral protons in the ^1H nmr spectrum. Although the reduction of diatropicity in the dibenzo-fused cycl[3.2.2]azine is not obvious, compound **4** exhibits significant 14 or 18π peripheral conjugation.

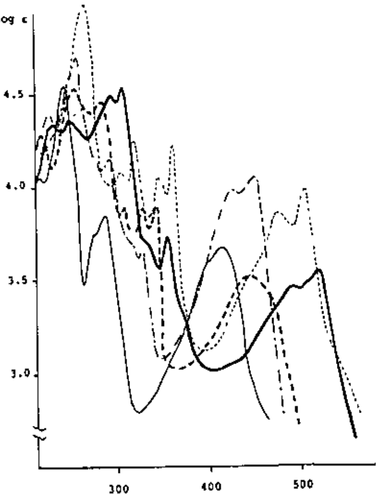


Fig 1. Uvspectra of 1, 2, 3, 4, and 5 in ethanol.
1: ———, 2: – – – – –, 3: —·—·—, 4: ━━━, 5: ·········,

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11) **7**, yellow needles, ms (m/z): 242(M^+, 100), ir(max, KBr)cm^{-1}: 2190(CN), ^1H-nmr($CDCl_3$): δ 7.32-7.93(7H, m), 7.77(1H, d, J=7.7 Hz, 7 or 8-H), 8.33(1H, d, J=7.7 Hz, 7 or 8-H).

12) **9**, red needles, ms (m/z): 357 (M^+, 100), ^1H-nmr ($CDCl_3$): δ 4.10 (3H, s, OMe), 4.22 (3H, s, OMe), 7.59-7.90 (4H, m), 8.25-8.49 (2H, m), 8.68-8.82 (2H, m), 8.98(1H, s, 3-H).

13) **8**, colorless needles, ms (m/z): 526 (M^+, 20), 467 (M^+-41, 100), ^1H-nmr(DMSO-d_6): δ 3.37 (3H, s, OMe), 3.71 (6H, s, 2 x OMe), 3.87 (3H, s, OMe), 7.07-7.17 (2H, m), 7.45-7.77 (5H, m), 7.64 (1H, s, 9b-H), 8.12-8.19 (1H, m), 8.62 (1H, s, 5-H).

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