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SYNTHESIS OF BENZANNELATED CYCL[3.2.2]AZINE: BENZO[a]CYCL[3.2.2]AZINE

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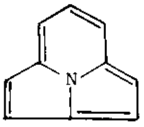
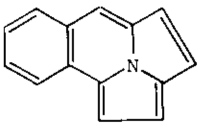
Abstract —— Benzo[a]cycl[3.2.2]azine (3) was synthesized from 6-cyanobenzo[a]indolizine (4) and dimethyl acetylenedicarboxylate.

Recently, we prepared some benzannelated cycl[3.2.2]azines in order to study the effects of benzo-fusion on cycl[3.2.2]azines.[1-3] There are two possible isomers of benzannelated cycl[3.2.2]azine derivatives, benzo[g]cycl[3.2.2]azine (2)[2] and benzo[a]cycl[3.2.2]azine (3). The former compound 2 has already been reported in the literature.[2] However, isomer 3 is a new compound. As a continuation of the work currently in progress in this laboratory, we now report the facile synthesis of 3 according to a modification of Matsumoto's method for the synthesis of cycl[3.2.2]azine. The Matsumoto procedure has also been found to be applicable to the preparation of other cyclazine derivatives.[4-6]



1



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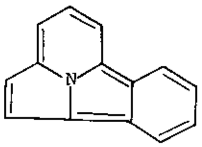

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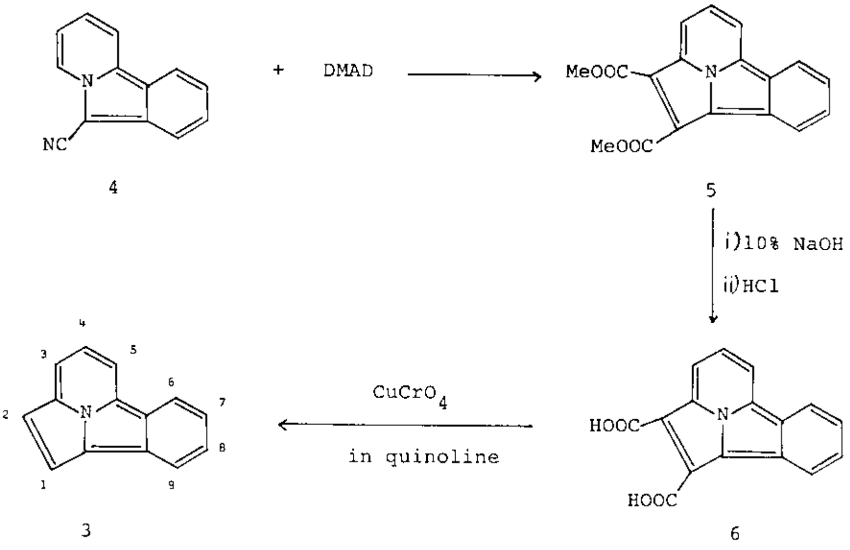

DMAD= dimethyl acetylenedicarboxylate

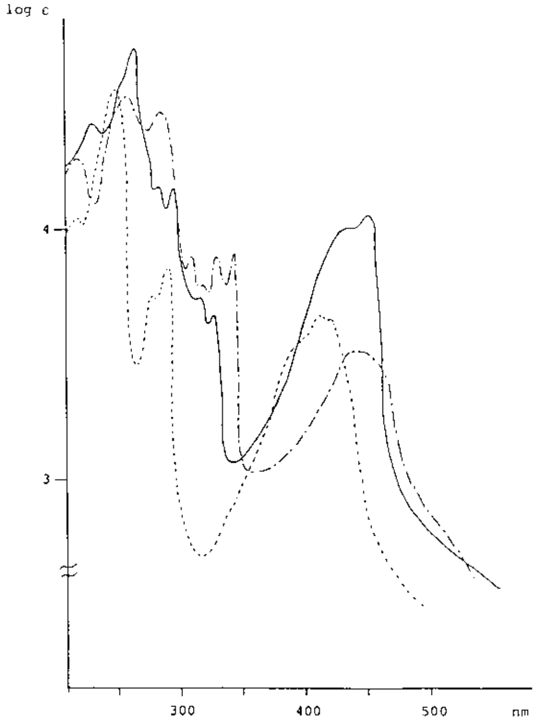

Fig. 1. UV spectra of 1, 2, and 3 in ethanol
1; ------- 2; —·—· 3; ———

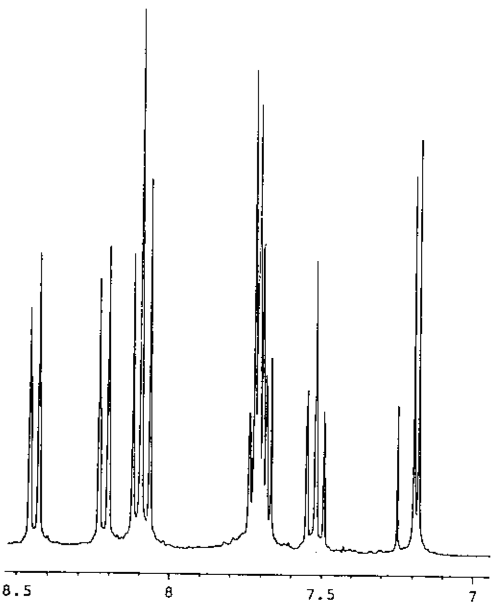

Fig. 1 . ^{1}H-NMR spectrum(270 MHz) of benzo[a]cycl[3.2.2]azine in CDCl$_3$

The [12+2]cycloaddition reaction of 4 with dimethyl acetylenedicarboxylate (DMAD) under refluxing for 20 h in toluene gave the expected product, dimethyl benzo[*a*]cycl[3.2.2]azine-1,2-dicarboxylate (5)[7], in 54% yield. Hydrolysis of the diester 5 with 10% sodium hydroxide proceeded essentially quantitatively to give the diacid 6. Finally, decarboxylation of the diacid using copper chromite in quinoline occurred smoothly to produce the desired benzo[*a*]cycl[3.2.2]azine (3)[8] in 49% yield.

The benzocyclazine 3 has a sweet smell like 2 and is a stable crystalline solid, and recrystallized from methanol, yielding bright yellow leaflets, mp 75°C. The complex of this compound with 2,4,7-trinitro-9-fluorenone gave dark brown needles, mp 218°C. The UV spectrum of 3 is shown in Fig. 2 along with cycl-[3.2.2]azine (1)[9], benzo[*g*]cycl[3.2.2]azine (2)[2], and dibenzo[*a*,*d*]cycl[3.2.2]-azine[5]. The major bands of 3 at 260, 315, and 430 nm are bathochromocally shifted from those of the parent 1 at 255, 308, and 390 nm, respectively, consistent with the longer conjugated aromatic system in the former. ^{1}H-NMR spectrum of 3 is shown in Fig. 1. A proton absorbs at 7.20 ppm (J=3.84 Hz) which is more upfield than that foud in the parent compound 1 (7.40 ppm)[10]. The copling constant of this proton with 1-position is recongnized typical aromatic character, and is smaller than that of benzo[*g*]cycl[3.2.2]azine (2).

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7. 5, yellow needles, mp 176°C. MS m/z: 307(M$^+$, 100). UV λmax(EtOH)nm(log ε):223 (4.69), 241(4.53), 256(4.46), 271(4.58), 304(4.14), 314(4.17), 428(4.06), 454 (4.04). IR νmax(KBr)cm^{-1}: 1735, 1700(CO). ^{1}H-NMR δ (CDCl$_3$)(90MHz)ppm: 4.04(3H, s, OCH$_3$), 4.16(3H, s, OCH$_3$), 7.58-8.10(4H, m, aromatic-H), 8.28-8.49(3H, m,

armatic-H).

8. **3**, bright yellow leaflets, mp 75°C. MS m/z: 191(M^+, 100). UVλmax(EtOH)nm(log): 231(4.40), 260(4.70), 279(4.16), 291(4.16), 314(3.73), 326(3.66), 424 (4.02), 450(4.06). ^{1}H-NMR δ ($CDCl_3$)(270MHz)ppm: 7.16(1H, d, J=3.8 Hz, 2-H), 7.50(1H, m, 7-H), 7.65-7.72(3H, m, 1, 4, 8-H), 8.06(1H, d, J=8.2 Hz, 3-H). 8.09(1H, d, J=6.6 Hz, 5-H), 8.19(1H, d, J=8.2 Hz, 9-H), 8.42(1H, d, J=8.2 Hz, 6-H).

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