A NEW SYNTHESIS OF 3*H*-CYCL[3.2.2]AZINO[1,2-*e*]CYCL[3.3.2]-AZIN-3-ONE DERIVATIVE

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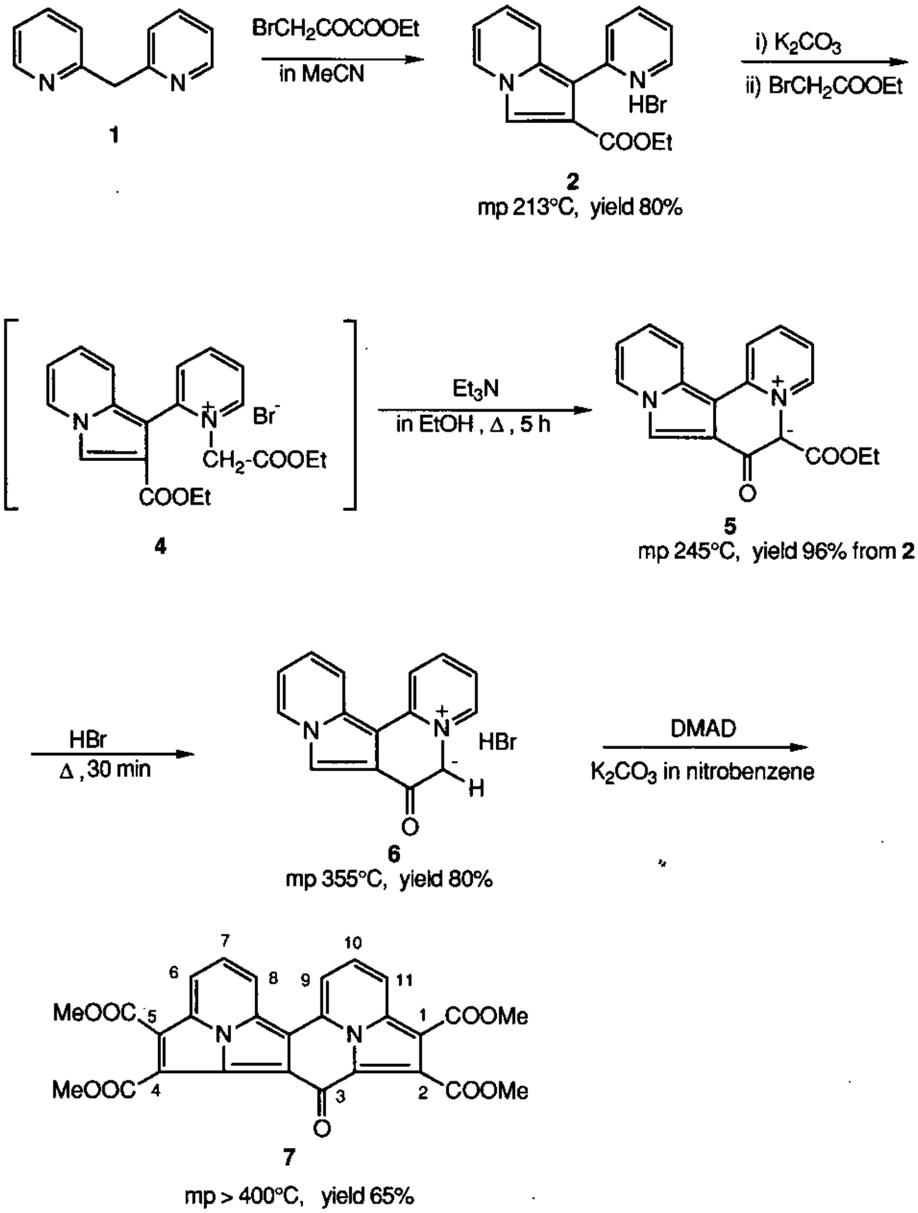
Abstract - Treatment of indolizinoquinolizinium salt (**6**) with dimethyl acetylenedicarboxylate in the presence of K_2CO_3 in refluxing nitrobenzene gave a nitrogen-bridged annulenoannulenone, 3*H*-cycl[3.2.2]azino[1,2-*e*]cycl[3.3.2]azinone derivative (**7**).

In view of the interest in heterocyclic annulenes[1-5] we have previously reported a new nitrogen-bridged annulene heterocyclic system, cyclazine (cycl[3.2.2]azines,[6] cycl[3.2.2]azinophanes,[7] cycl[3.3.2]azinones,[8] cycl[3.3.3]azines[5]). In this communication we wish to report a novel synthesis of 3*H*-cycl[3.2.2]azinocycl[3.3.2]azin-3-one derivative (**7**) by the cyclization of the key intermediate, indolizinoquinolizinium salt (**6**) with dimethyl acetylenedicarboxylate (DMAD).

The starting bispyridylmethane (**1**) used in the present work was prepared according to Newkome's method.[9] The reaction of **1** with ethyl bromopyruvate at room temperature for a week gave pyridylindolizine hydrobromide (**2**) in good yield. Treatment of the hydrobromide (**2**) with K_2CO_3 afforded the free base, pyridylindolizine (**3**) and then the crude free base (**3**) was allowed to react with ethyl

Scheme 1


1
BrCH$_2$COCOOEt
in MeCN
HBr
COOEt
2
mp 213°C, yield 80%
i) K$_2$CO$_3$
ii) BrCH$_2$COOEt
Br$^-$
CH$_2$-COOEt
COOEt
4
Et$_3$N
in EtOH, Δ, 5 h
COOEt
5
mp 245°C, yield 96% from 2
HBr
Δ, 30 min
HBr
H
6
mp 355°C, yield 80%
DMAD
K$_2$CO$_3$ in nitrobenzene
MeOOC
MeOOC
COOMe
COOMe
1
2
3
4
5
6
7
8
9
10
11
7
mp > 400°C, yield 65%

bromoacetate in acetonitrile at room temperature for a week. The crude salt (**4**) resulted above was refluxed with triethylamine in EtOH to produce the cyclic ylide (**5**) in 96% yield from **2**. Heating of **5** in refluxing 47% hydrobromic acid for 30 min gave the salt (**6**) through decarboxylation. After many attempts to obtain cyclazinocyclazinone (**7**), the synthesis of the desired compound (**7**) was achieved on employing the procedure of Farquhar.[10] Reaction of **6** with DMAD in the presence of K_2CO_3 in refluxing nitrobenzene for 1 h gave 1,2,4,5-tetrakiscarbomethoxy-3*H*-cycl[3.2.2]azino[1,2-*e*]cycl[3.3.2]azin-3-one (**7**)[11] in moderate yield. The structure of **7** was supported by a satisfactory elemental analysis, the presence of carbonyl absorptions in the ir spectrum, and the signals of four doublets ($C_{6,8,9,11}$-H) in the ^{1}H-nmr spectrum. Of particular interest is that the six-membered ring proton signals of **7** in trifluoroacetic acid are shifted *ca.* 1 ppm to lower field than those of **7** in DMSO-d_6. Such lower field shift is characteristic of cyclazinone system.[8] Further discussion of the spectra will be presented in a future publication.

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11. For **7**, mp> 400°C (65%); ir(KBr) ν_{max} 1740(CO), 1710(CO), 1630(CO) cm^{-1}; uv(EtOH) λ_{max} 215, 243, 318, 468, 503 nm; ^{1}H-nmr(DMSO-d_6) δ 3.89(3H, s, OCH_3), 3.95(3H, s, OCH_3), 3.96(3H, s, OCH_3), 4.04(3H, s, OCH_3), 6.77-7.59(2H, m), 7.83-9.12(4H, m); ^{1}H-nmr(CF_3COOD) δ 4.33(3H, s, OCH_3), 4.35(3H, s, OCH_3), 4.39(3H, s, OCH_3), 4.43(3H, s, OCH_3), 8.70(1H, t, *J*=8 Hz), 8.98(1H, t, *J*=8 Hz), 9.13(1H, d, *J*=8 Hz), 9.42(1H, d, *J*=8 Hz), 9.48(1H, d, *J*=8 Hz), 9.75(1H, d, *J*=8 Hz). *Anal.* Calcd for $C_{27}H_{18}N_2O_9$: C, 63.04; H, 3.53; N, 5.45. Found: C, 62.99; H, 3.76; N, 5.60.

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