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CHEMISTRY OF HETEROCYCLIC COMPOUNDS. 11 ISOMERIZATION OF ACETYLENIC DIOLS 1,4-DIPHENYL-1,4-DI(2'-PYRIDYL)-2-BUTYNE-1,4-DIOL

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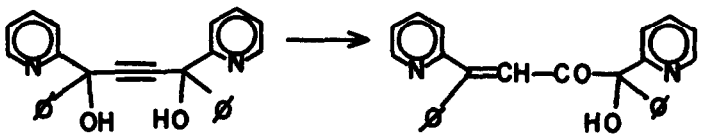
Recently, Sisenwine and Day[1] described the acid-catalyzed isomerization of 1,4-diphenyl-1,4-di(2'-pyridyl)-2-butyne-1,4-diol (1). The major product from this rearrangement was assigned 1,4-diphenyl-1,4-di(2'-pyridyl)-1-buten-3-on-4-ol (2), solely on the basis of its infrared spectrum and elemental analysis. Isomerization of 1 was accomplished simply by heating in ethanol



1 2

and was proposed to involve an allylic-type rearrangement followed by a tautomeric shift to the keto-structure 2. We herein report that the proposed structure 2 is not the major isolated product from this reaction.

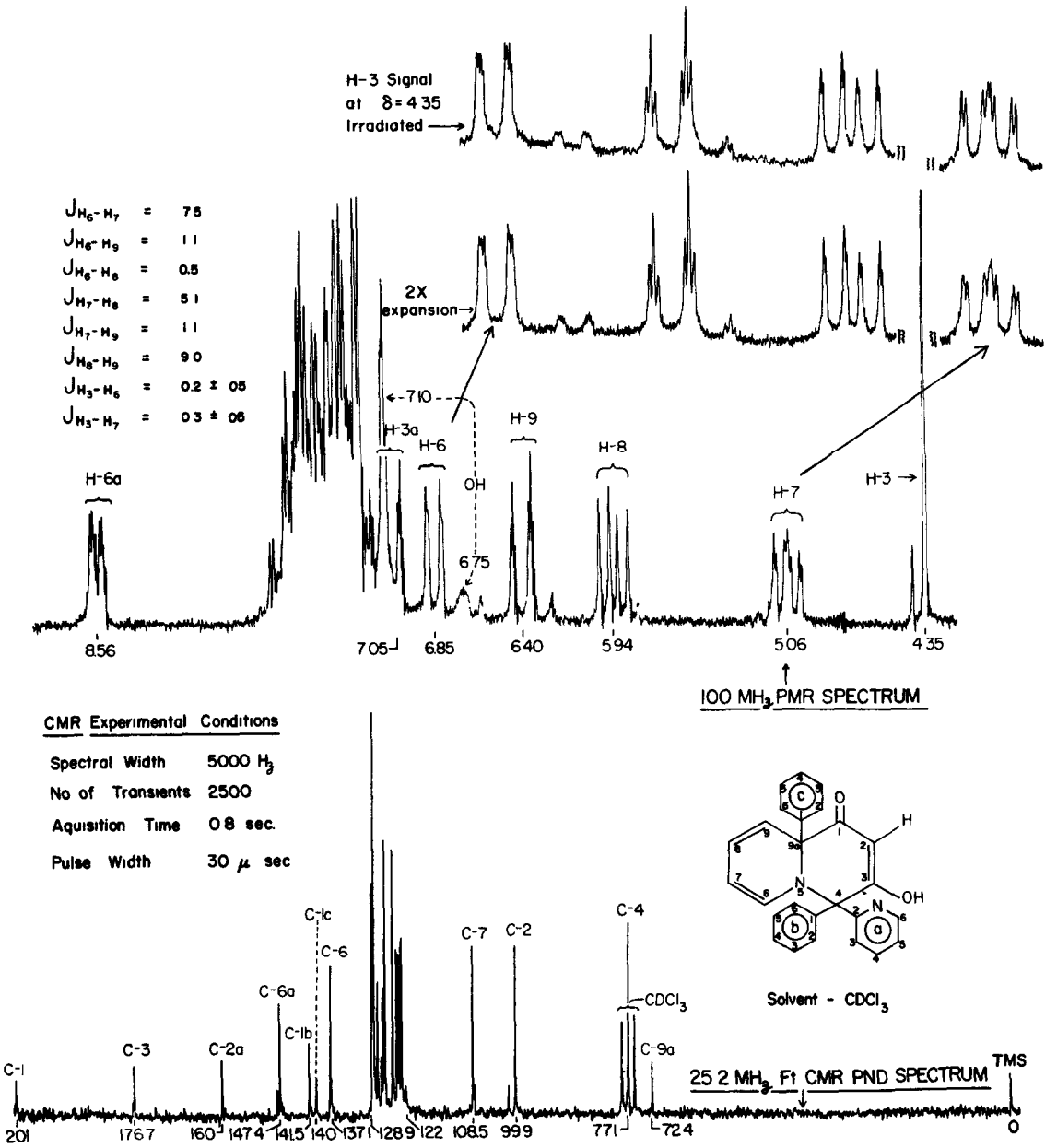
By utilization of their published[1] procedures, we isolated (90%) the crystalline diol 1 m.p. 180-180.5° (lit[1] m.p. 179°), i.r.(Nujol)λ_{max} 3420 (OH), 1590, 1574, 1490, 1450, 1434, 1010, 795, and 695 cm^{-1}, mass spectrum (m/e) 392 (M^+). Isomerization of diol 1 by any one of the following procedures (a) refluxing in ethanol for two hours,[1] (b) heating (neat) at 185° under nitrogen or *in vacuo*, or (c) stirring in absolute methanol with a trace of H_2SO_4 for two hours at ambient temperature afforded in each case (> 80%) the reported yellow crystals m.p. 180-181° (recrystallization from benzene, lit.[1] m.p. 181°).

Although two structural isomers exist for 2, the expected p.m.r spectrum should possess both a singlet for an isolated vinyl hydrogen and a characteristic pattern for the two C-6 pyridyl hydrogens (ca. 8.5 ppm). The observed p m.r. spectrum of the reaction product exhibits an absorption for one C-6 pyridyl hydrogen and a readily discernible vinyl region, which integrates for five hydrogens (see Fig. 1). Based upon the analytical ($C_{26}H_{20}N_2O_2$) and spectral data, the product has been reassigned to structure 3, i.e., 3-hydroxy-4,9a-diphenyl-4-r-(2-pyridyl)-4H-quinolizin-1(9aH)-one.

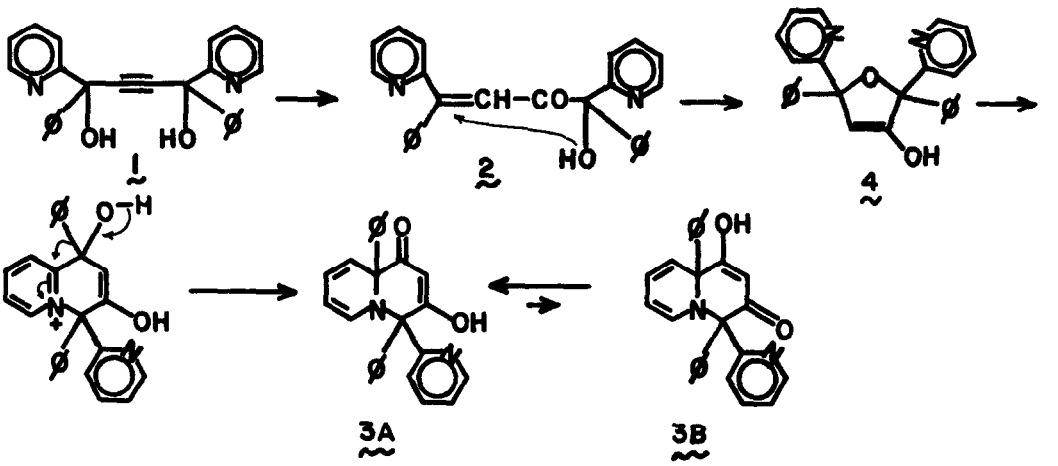
Structural Assignment of 3 follows from the ir [(KBr) 3300 (broad-OH), 1683 (>C=O), 1628, 1592, 1526, 1436, 1388, 1018 cm^{-1}], uv[λ_{max}(MeOH) 408, 274, 264 mμ], ^{13}C(cmr), and ^{1}H(pmr) spectral data. Cmr spectra obtained during proton noise decoupled and single frequency off-center resonance decoupled experimental conditions reveal that the compound possesses 26 different carbon atoms, of which one is attributed to a carbonyl function, two to quaternary carbon atoms bonded directly to a nitrogen atom and 23 olefinic carbon atoms of which 19 bear a single proton. In the pmr spectrum, the chemical shift and spin-spin coupling considerations of resonances at δ = 5 06, 5.94, 6.40 and 6.85 are indicative of a cyclic dieneamine moiety and are assigned to H-7, H-8, H-9, and H-6, respectively. Occurrence of signals at δ = 8.56 and 7.05 (assigned to H-6a and H-3a, resp) establishes the presence of a single 2-pyridyl function, the upfield position of H-3a is indicative of the anisotropy caused by the gem-phenyl group.

The highest pmr signal (δ = 4.35) is assigned to H-2. Further conformation of the HO-C=C-H-C=O moiety was obtained during single frequency selectively decoupled cmr experiments when signals at δ = 99.9, 201, and 176.7 (C-2, C-1, and C-3, resp.) showed an appropriate NOE signal enhancement upon strong irradiation of the H-2 proton (δ = 4.35). The easily exchanged (D_2O) signal at δ = 7.10 is assigned to the C-3 hydroxyl proton, lack of hydrogen-bonding is indicated by both its temperature and concentration dependence.

The presence of smaller signals (variable of solvent) along with the dominant resonances in both the cmr and pmr traces clearly indicates that 3 exists in two tautomeric forms (3A and 3B). In the minor tautomer (3B), the H-9 proton experiences a slight downfield shift due to removal of the peri effect caused by the C-1 carbonyl function present in the major isomer 3A. From the spectral data, the absolute configuration of 3 can not be ascertained, but the relative configuration at positions 4 and 9a can be deduced. In light of (a) no detectable hydrogen-bonding and (b) the unfavorable 1,3 interaction associated with the 4 and 9a diaryl groups, the


H-3 Signal at δ = 4.35 Irradiated
2X expansion
$J_{H_6-H_7}$ = 7.5
$J_{H_6-H_9}$ = 1.1
$J_{H_6-H_8}$ = 0.5
$J_{H_7-H_8}$ = 5.1
$J_{H_7-H_9}$ = 1.1
$J_{H_8-H_9}$ = 9.0
$J_{H_3-H_6}$ = 0.2 ± 0.5
$J_{H_3-H_7}$ = 0.3 ± 0.6
H-6a
H-3a
H-6
OH
H-9
H-8
H-7
H-3
7.10
6.75
8.56
7.05
6.85
6.40
5.94
5.06
4.35
100 MH$_z$ PMR SPECTRUM
CMR Experimental Conditions
Spectral Width 5000 H$_z$
No of Transients 2500
Aquisition Time 0.8 sec.
Pulse Width 30 μ sec
C-1c
C-6
C-7
C-2
C-4
C-6a
C-1b
CDCl$_3$
C-3
C-2a
C-9a
C-1
TMS
Solvent - CDCl$_3$
25.2 MH$_z$ Ft CMR PND SPECTRUM
201
176.7
160
147.4
141.5
140
137.1
128.9
122
108.5
99.9
77.1
72.4
0

SCHEME I



major product is 3-hydroxy-4,cis-9a-phenyl-4-r-(2-pyridyl)-4H-quinolizin-1(9aH)-one. An x-ray analysis of 3 is in progress.

Mechanism of this isomerization is depicted in Scheme 1, in which 1 undergoes a prototropic propargylic rearrangement[2] initially affording 2. Intramolecular Michael cyclization of 2 generates the furan 4[3], which undergoes a ring-opening with subsequent cyclization and pinaco rearrangement (phenyl migration) affording the product 3.

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(2) G. R Lappin, ibid., 16, 419 (1951), also see A W Nineham and R. A Raphael, J. Chem Soc., 1949, 118

(3) For related examples J Salkind and A Kruglow, Chem Ber , 59, 1936 (1926), ibid , 61, 2306 (1928), J Wolinski, Roczniki Chemii, 29, 23 (1955), P P Montijn, L Brandsma, and J F Arens, Rec Trav. Chim , 86, 129 (1967) and L. I Vereshchagin, E I Titova, N V Sushkova, and L D Gavrilov, J Org Chem USSR, 7, 928 (1971)