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SYNTHESIS OF 4*H*-BENZO[hi]PYRROLO[2,1,5-cd]INDOLIZIN-4-ONE. A NOVEL TYPE OF PHENALENONE ANALOG

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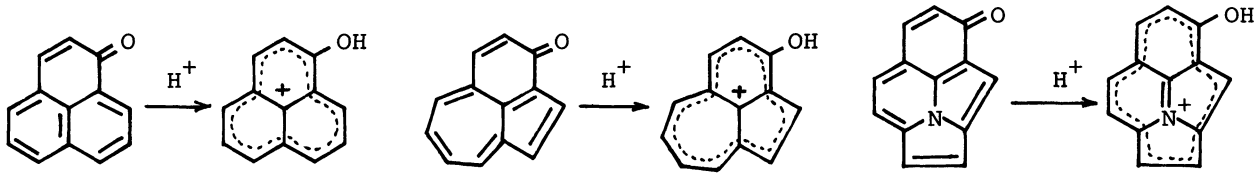
4*H*-Benzo[hi]pyrrolo[2,1,5-cd]indolizin-4-one, an analog of phenalenone, is obtained by a one-pot oxidation of 5,6-dihydro-4*H*-benzo[hi]pyrrolo[2,1,5-cd]indolizine with DDQ in aqueous dioxane. Its characteristic electronic feature is also described, which is different inherently from that of phenalenone or 3*H*-benz[cd]azulen-3-one.

During these two decades much attention has been paid for phenalenone (A)[1] and its iso-π-electronic isomers, i.e., 3*H*-benz[cd]azulen-3-one (B),[2] from the synthetic and physicochemical points of view. Among them, phenalenones and those isomers have been regarded as the model compounds providing the peripherally conjugated 12π systems linked by an internal sp^2-hybridized carbon atom.[3]

Now, the synthesis of 4*H*-benzo[hi]pyrrolo[2,1,5-cd]indolizin-4-one (C) is much interested, because C is a novel analog of phenalenone (A), in which the naphthalene nuclei is replaced by the peripherally iso-π-electronic cycl[3.2.2]azine system. Therefore, the [12]annulene system perturbed by the internal azomethinium ion ($\rangle C{=}N^{+}\langle$) would be furnished by the protonation of C, which is expected to have the more polarized structure than A or B as predicted from MO calculations.[4]



(A) (B) (C)

We wish to communicate here the synthesis of some 4*H*-benzo[hi]pyrrolo[2,1,5-cd]indolizin-4-one derivatives by a one-pot oxidation of 5,6-dihydro-4*H*-benzo[hi]-pyrrolo[2,1,5-cd]indolizines with DDQ in aqueous dioxane. Also, some of those physical properties are discussed.

When DDQ (1.36 g, 6.0 mM) was added to a solution of 5,6-dihydro-1,2-bis(methoxycarbonyl)-3-phenyl-4*H*-benzo[hi]pyrrolo[2,1,5-cd]indolizine (1a)[5] (562 mg, 1.5 mM) in 10% aqueous dioxane (30 ml) at room temperature, the solution became dark green initially and turned red gradually. After being refluxed for 6 h, the solution was filtered to remove the resultant hydroquinone and the filtrate was evaporated. The residue was treated with column chromatography (neutral alumina, chloroform) to give a reddish crystalline 2a in 68% yield as a sole product.

The mass spectrum and elemental analysis of 2a indicate that an allylic meth-

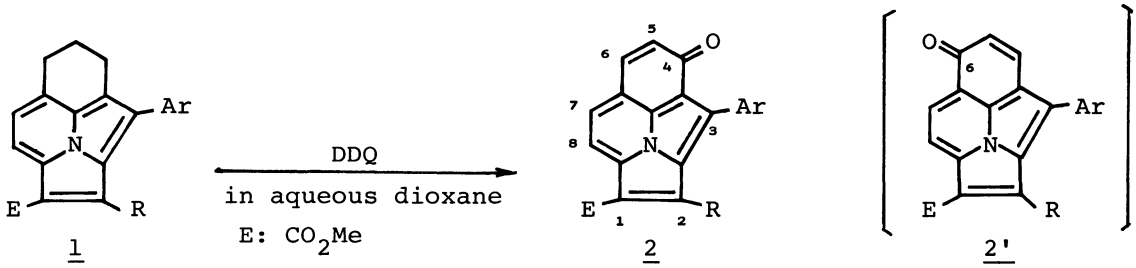
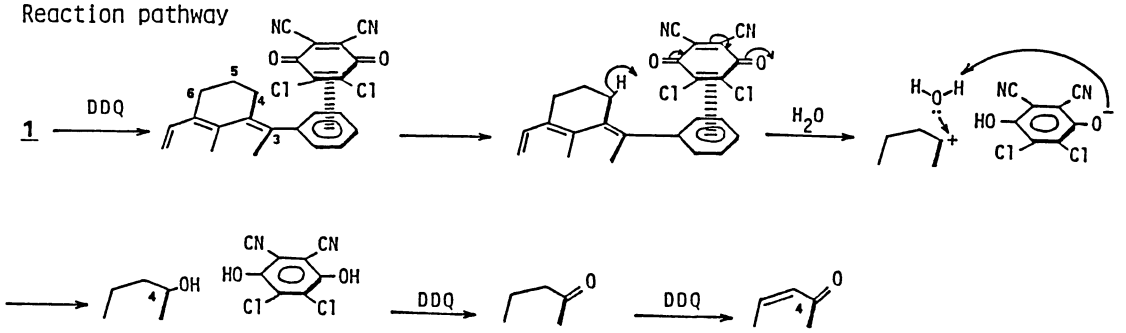


Table 1. Synthesis of 4*H*-Benzo[hi]pyrrolo[2,1,5-cd]indolizin-4-ones 2

Comp.	R	Ar	Molar ratio (DDQ/1)	Time h	Yield %	Mp °C	IR ν_{CO} a)	^{1}H NMR b) δ H-5	H-6	M^+ m/e
2a	E	Ph	4	6	68	189-190	1618	6.42	7.42	385
2b	E	C_6H_4-OCH_3(*p*)	4	6	96	225-226	1600	6.50	7.42	415
2c	E	C_6H_4-Br(*p*)	4	45	trace c)	227-229	1624	6.50	7.44	463,465
			6	54	34					
2d	E	4-biphenyl	4	24	47	256-258	1603	6.51	7.42	461
2e	E	2-naphthyl	6	42	55	219-220	1592	6.53	7.46	438
2f	H	Ph	4	6	69	274-275	1600	6.52	7.42	327

a) At 4-position. b) Measured in $CDCl_3$. c) 1c was recovered almost quantitatively.



Scheme 1.

ylene group of alkyl cyclic chain in 1a is oxidized to carbonyl one and the remaining ethylene moiety is dehydrogenated. The structure of 2a was deduced to 1,2-bis(methoxycarbonyl)-3-phenyl-4*H*-benzo[hi]pyrrolo[2,1,5-cd]indolizin-4-one from the spectral data, especially ^{1}H NMR spectral data.[6] The 3-(*p*-methoxyphenyl) (2b), 3-(*p*-bromophenyl) (2c), 3-(4-biphenyl) (2d), and 3-(2-naphthyl) derivatives (2e) were also obtained by the similar oxidation of the corresponding 5,6-dihydro-4*H*-benzo[hi]pyrrolo[2,1,5-cd]indolizines (1b-1e). Furthermore, 5,6-dihydro-1-methoxycarbonyl-3-phenyl-4*H*-benzo[hi]pyrrolo[2,1,5-cd]indolizine (1f) was oxidized to 1-methoxycarbonyl-3-phenyl-4*H*-benzo[hi]pyrrolo[2,1,5-cd]indolizin-4-one (2f). These results are summarized in Table 1.

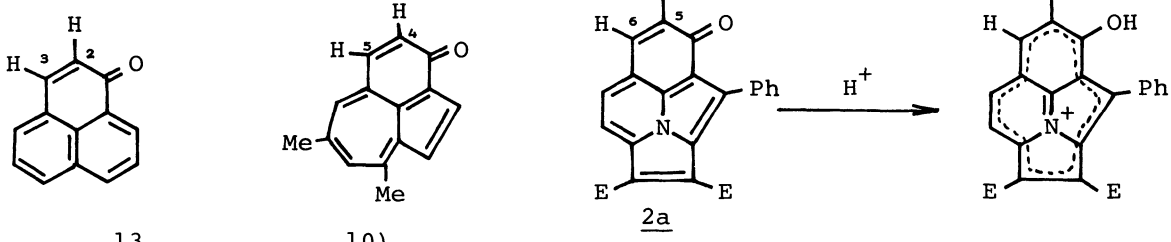
To explain this regioselective oxidation of 1, we suggested the following reaction pathway; i) the formation of CT-complex between DDQ and phenyl ring,[7] ii) the hydride abstraction with DDQ from the allylic methylene at 4-position situated

in a close vicinity to DDQ, iii) the formation of secondary alcohol followed by the oxidation to ketone, iv) the final dehydrogenation to α,β-unsaturated ketone (Scheme 1). It is reasonable that the rate-determining step is the earlier stage in this pathway, e.g., i) or ii). This is supported by the absence of other intermediary products in the oxidation and the results of the reactions of 3-*p*-substituted phenyl derivatives (Table 1). The reactions of 3-(*p*-methoxyphenyl) (1b) and 3-(4-biphenyl) derivatives (1d) were carried smoothly and, on the other hand, 3-(*p*-bromophenyl) one (1c) reacted with DDQ only in the severer conditions.

Now, the physical properties of 2 were also investigated. In the IR spectra of 2 the carbonyl absorption bands at 4-position were observed at somewhat lower wave number regions (1592-1624 cm^{-1}) in comparison with those of phenalenones[1] and 3*H*-benz[cd]azulen-3-ones.[2] Therefore, it is suggested that the carbonyl group in 2 is equally to or more highly polarized than those of the latter two systems.

However, the features of the ^{1}H and ^{13}C NMR spectra as well as electronic spectra of 2 were considerably different from those of phenalenones and their analogs. First, the electronic spectra of 2a in chloroform, methanol, and methanol-sulfuric acid (*ca.* 100:1) are found to be no apparent solvent effect:[8] λmax($CHCl_3$): nm (log ε) 245(4.43), 277(4.26), 283^{sh}(4.25), 299^{sh}(4.30), 311(4.40), 324(4.43), 370^{sh} (3.95), 392(4.09), 424^{sh}(4.20), 441(4.22), 505(4.01), 540^{sh}(3.82).

In the ^{1}H NMR spectrum of 2a in trifluoroacetic acid the chemical shifts moved downfield only to an extent of 0.3-0.6 ppm compared with those in deuteriochloroform. The downfield shifts of the protons at 5 and 6-positions in 2a [Δδ= δ(CF_3COOH)-δ($CDCl_3$): 0.48 and 0.59 ppm, respectively] seem to be fairly small in consideration of the solvent dependency of the chemical shifts of those at 2 and 3-positions in phenalenone (Δδ: above 1.1 ppm)[9] or at 4 and 5-positions in 3*H*-benz-[cd]azulen-3-one system (Δδ: *ca.* 0.8 ppm).[2] As an explanation, the less downfield shifts in 2a could be ascribed to the effect of the paramagnetic ring current arising from the peripheral 12π electron system. Such extensive delocalization of positive charge has been speculated in the protonation of A or B, but is not always supported by the spectral data.[2,9]



2a

In the ^{13}C NMR spectra[10] of 2a the carbonyl carbon signals at 4-position were observed at 180.7 and 177.5 ppm in deuteriochloroform and trifluoroacetic acid, respectively, and less sensitive to kind of solvent.[11]

These findings indicate the interesting electronic feature of 4*H*-benzo[hi]-pyrrolo[2,1,5-cd]indolizin-4-one (C), a highly polarized structure in ground state, little change of π-electron system by protonation, and a contribution of the peripheral 12π conjugated system in acidic media, which are different from those of phenalenone (A) and 3*H*-benz[cd]azulen-3-one (B).

Further investigations on these points are now under progress.

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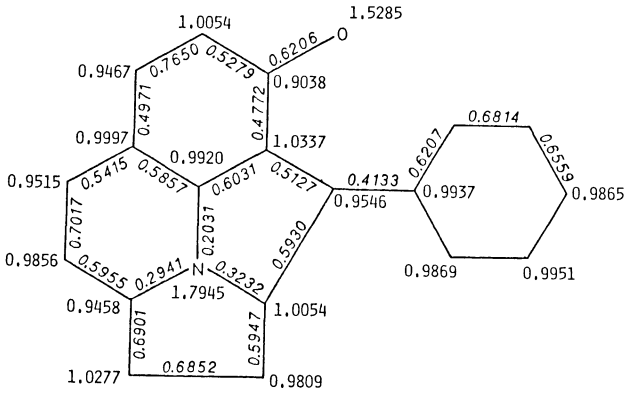
2) R. Neidlein and W. Kramer, Helv. Chim. Acta, 65, 280 (1982) and references cited therein.
3) R. Pettit, J. Am. Chem. Soc., 82, 1972 (1960); V. Boekelheide and C. D. Smith, ibid., 88, 3950 (1966).
4) π-Electron density and bond order of 3-phenyl-4*H*-benzo-[hi]pyrrolo[2,1,5-cd]indol-izin-4-one by ω-method are shown.



5) M. Noguchi, N. Tanigawa, and S. Kajigaeshi, J. Heterocycl. Chem., in press.
6) 2a: ^{1}H NMR($CDCl_3$): δ 3.93, 3.99(each 3H, 3, CH_3), 6.42(1H, d, H-5, J=9.8 Hz), 7.33(1H, d, H-6, J=9.8 Hz), 7.5-7.65(3H, m, phenyl), 7.73(1H, d, H-7, J=8.3 Hz), 7.94(1H, d, H-8, J=8.3 Hz), 8.2-8.3 ppm(2H, m, phenyl).
In the ^{1}H NMR spectra of 1a and 2a, the ring protons at 7-position were observed within a constant value for chemical shift in both case. The signals of the phenyl protons at 3-position of 1a were centered at 7.3-7.6 ppm(5H) and, on the other hand, those of 2a were split at 7.6(3H) and 8.3 ppm(2H), which stemmed from the anisotropic effect of the carbonyl moiety at 4-position.
7) P. P. Fu and R. G. Harney, Chem. Rev., 78, 334 (1978) and references therein.
8) The remarkable difference of electronic spectra of 3*H*-benz[cd]azulen-3-one systems between in neutral and acidic media was reported.[2)]
9) H. Prinzbach, V. Freudenberger, and H. Scheidegger, Helv. Chim. Acta, 50, 1087 (1967).
10) 2a: ^{13}C NMR($CDCl_3$): δ 52.2, 53.1. 116.5, 117.1, 118.0, 119.4, 123.9, 125.8, 130.0, 131.1, 131.5, 132.7, 133.6, 141.6, 162.8, 165.2, 180.7 ppm.
11) The carbonyl carbon signal of 7,9-dimethyl-3*H*-benz[cd]azulen-3-one in trifluoroacetic acid was observed at about 10 ppm higher field than that in deuteriochloroform.[12)]
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