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BENZOYLATION OF THE SODIUM SALT OF 6(5H)-PHENANTHRIDINONE AND AN O-to-N BENZOYL MIGRATION*

David Y. Curtin and John H. Engelmann

Department of Chemistry

University of Illinois, Urbana, Ill. 61801

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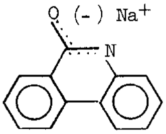
In our study of 1,3 acyl migrations (1,2) heterocycles are of particular interest because of their freedom from complications due to syn-anti isomerism. We were struck by the scarcity of pairs of isomeric N- and O-acyl derivatives in simple aromatic heterocyclic systems such as the α-pyridones and the pyrimidones (3). Preliminary work was carried out on the acylation of the sodium salt of 2-pyridone in benzene. Spectral evidence (4) that mixtures of N- and O-acyl products were being formed led us to shift to a study of the reaction of benzoyl chloride at -20° with the sodium salt (1) of 6-phenanthridinone, prepared from reaction of 6-phenanthridinone in tetrahydrofuran with sodium hydride. Removal of the solvent without heating gave the O-benzoyl product 2, not significantly contaminated with the N-benzoyl isomer 3, to be described. Purification was accomplished by crystallization from toluene-pentane at -20°. When solid 2 was heated rapidly it began to melt at 119°, quickly resolidified and remelted at 190°.** Benzoylation of the sodium salt of the phenanthridinone as before but at ambient temperature followed by treatment with boiling toluene gave N-benzoylphenanthridinone, m.p. 189-192.5°,



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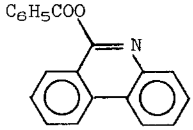
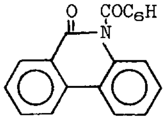


2, m.p. 119°
(with rearrangement)



3, m.p. 190°

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**Differential thermal analysis (10.6°/min) by Mr. S. Byrn showed Δ H (kcal/mole) of 4.7, -6.9, and 12 for the initial endotherm due to melting, the heat of reaction, and the final melting endotherm. The value for the heat of melting of purified N-benzoyl rearrangement product 3 was 9.3 kcal/mole. These results will be described in more detail in a later publication.

which was purified by crystallization from toluene-petroleum ether. Both isomeric benzoylphenanthridinones gave correct analyses for carbon, hydrogen, and nitrogen.

Structures were assigned to 2 and 3 on the basis of the IR and UV spectra. The IR spectrum of the O-benzoyl compound 2 showed a single intense absorption at 1743 cm^{-1} (and no other strong absorption in the carbonyl region above 1600 cm^{-1}). The N-benzoylphenanthridinone 3 showed two strong bands in the carbonyl region, one at 1733 and one at 1656 cm^{-1}. (The absorption at 1656 cm^{-1} may be compared with the carbonyl absorption at 1650 cm^{-1} shown by N-methylphanthridinone (5).) The UV spectrum of 2 (dissolved in a small amount of tetrahydrofuran and diluted with spectral grade hexane) was similar in its maxima and shoulders to that reported (6) for 9-methoxy-phenanthridine and the two largest peaks had λ_{max} 240 and 249 (ϵ 47,200 for each). The N-benzoyl compound 3 showed a similar correspondence with the spectrum of N-methylphenthridinone (6) with λ_{max} of the highest absorption at 237 mμ, ϵ 48,200. The two isomers differed greatly in their reactivity toward piperidine. The O-benzoyl compound 3 reacted with an approximately equimolar amount of piperidine in pentane to give after 12 hr at -20° a 65% yield of N-benzoylpiperidine, m.p. 47-49°, and 84% of phenanthridinone whereas the N-benzoyl compound 3 in the same medium after 12 hr at ambient temperature and 4 hr under reflux gave only a 23% yield of benzoylpiperidine and 75% of the starting N-benzoylphenanthridinone 3 was recovered.

It is clear that acylation of the phenanthridinone anion under the conditions employed here leads at low temperatures predominately to the kinetically controlled product, the O-benzoyl derivative. That the N-isomer is favored at equilibrium is most convincingly shown by an experiment in which the O-isomer 2 was heated in methylene chloride for 6 hr after which the IR spectrum was identical with that of an analytical sample of the N-isomer 3.

2 3

The thermochemistry of the equilibrium between O- and N-methylpyridone has been analyzed with great care by Beak, Bonham and Lee (7) and the N-methyl compound found to be the more stable by some 14 kcal/mole. On the other hand the observation that acylation of 2-pyridone has led only to the O-acyl product, the N-acyl-2-pyridones not yet having been observed (3), and also our preliminary work (4) on the acylation of the sodium salt of 2-pyridone suggest that the equilibrium in the acylpyridone system favors the O-acyl compound. The possibility that the O-acylpyridone is the more stable pyridone derivative but that the N-acylphenanthridine is the more stable isomer in that system is not totally unexpected in view of the observation (8) that N-protonated phenanthridinone is favored over the O-isomer by a significantly greater margin than is the N-protonated pyridone over its O-isomer.

Our work suggests that N-acyl isomers of simple heterocyclic systems may be rather more accessible than is implied by their almost complete absence from the chemical literature. In addition the ease of the O-N benzoyl migration in the phenanthridinone system indicates that such rearrangements may be of general importance in the chemistry of other heterocyclic compounds.

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