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PHOTOCHEMISTRY OF N-AROYLANTHRANILIC ACIDS

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Abstract —— Irradiation of the N-aroylanthranilic acids (1b), (7), (11), and (15) in the presence of either sodium borohydride or potassium hydroxide afforded a mixture of the dihydrophenanthridones (3a and b), (6), (8), (12), (14), and (16), the phenanthridones (2), (9), and (13), and the biphenyls (4), (10), and (17).

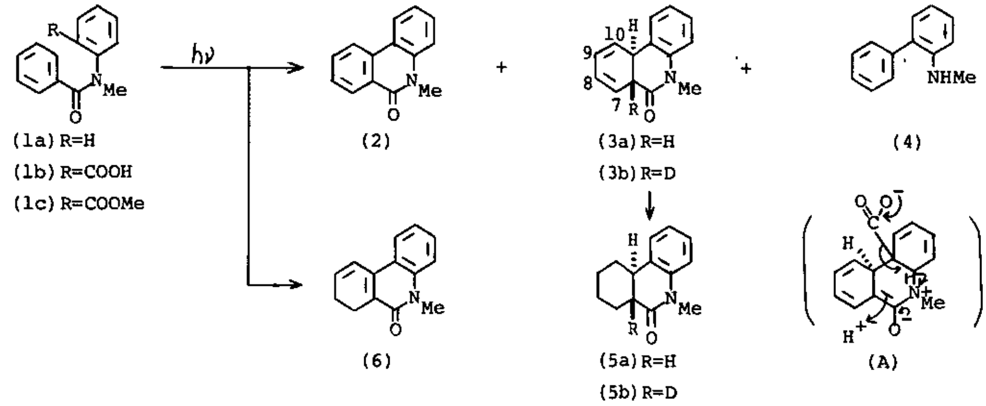
Reductive photocyclization of enamides of the N-benzoylenamine and N-furoylenamine types has proved to be extremely valuable for the construction of heterocyclic compounds including yohimbine and ergot alkaloids[1]. As an extension of the study on the reductive photocyclization of various types of enamides, we investigated reductive photocyclization of enamides of the benzanilide type and found that the o-carboxy-substituted benzanilides undergo photocyclization under a basic condition to give the dihydrophenanthridones.

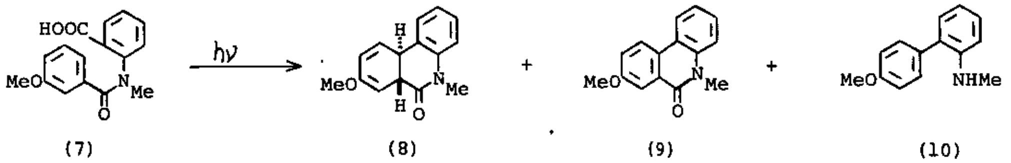
Reductive photocyclization[2] of unsubstituted benzanilide (1a) was unsuccessful under various conditions giving only the starting anilide recovered completely. We then investigated reductive photocyclization of the o-carboxy-substituted benzanilide (N-benzoylanthranilic acid)(1b) which was shown[3] to undergo photocyclization in acetic acid to give the phenanthridone (2). All the starting N-aroylanthranilic acids were prepared simply by acylation of methyl anthranilate with the aroyl chlorides and hydrolysis.
Irradiation of the acid (1b) in ether-methanol (9:1) at 5-10°C with a low pressure mercury lamp in the presence of sodium borohydride for several hours led to the formation of two types of lactams (2) and (3a) along with the biphenyl (4) in 17, 11, and 6 % yields respectively. Since the latter lactam (3a) was readily converted by oxidation to the former lactam (2) and also catalytically reduced over platinum dioxide to give the known[4] trans-hexahydrolactam (5a), it

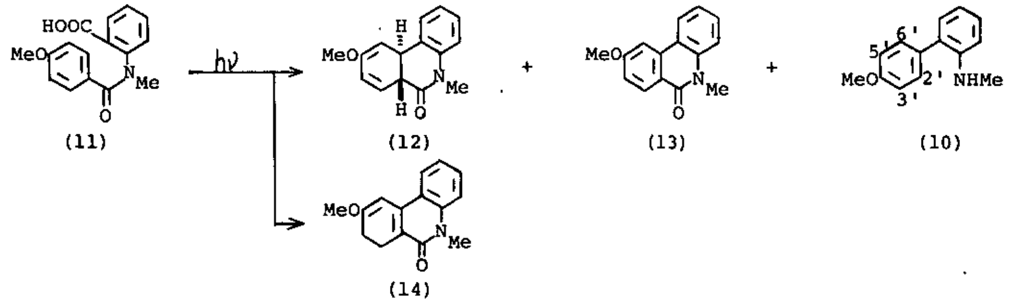
was firmly established that the lactam (3a) has the trans-diene structure which was also assigned from nmr spectra [δ 6.73-5.97 (4H, m, 7-, 8-, 9-, and 10-H), 3.57 (1H, br.d, J=22Hz, 6a-H), and 2.97 (1H, br.d, J=22Hz, 10a-H)]. The structure of the biphenyl (4) was unambiguously established by direct comparison with the authentic sample[5].

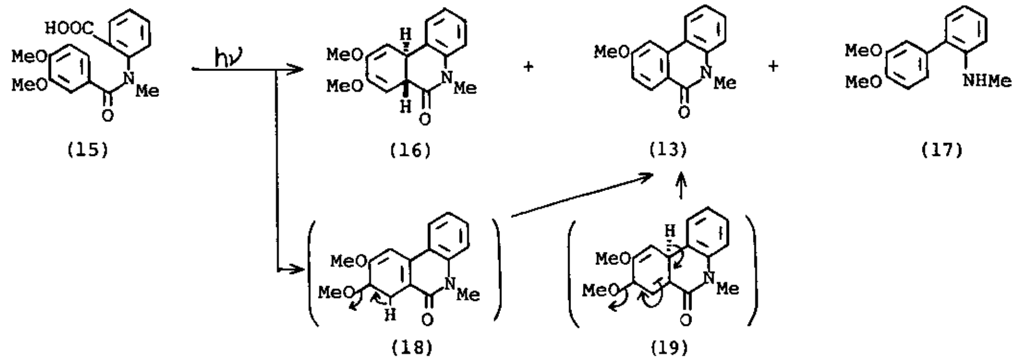
In order to clarify the reaction mechanism on the formation of the dihydrolactam (3a), we used deuterated reagents in the irradiation reaction. Irradiation of the acid (1b) in the presence of sodium borodeuteride in ether-methanol gave a mixture of the dihydrolactam (3a), the aromatized lactam (2), and the biphenyl (4) in 11, 17, and 6 % yields respectively, all of which were not deuterated. However, similar irradiation in the presence of sodium borohydride in ether-deuterium methoxide afforded the same type of three products, (3b)[6] in 10%, (2) in 19%, and (4) in 5% yields respectively, of which the unstable lactam (3b) was found to be deuterated at the 6a-position on the basis of the mass and nmr spectral analyses of the hexahydrophenanthridone (5b)[6], prepared readily from the dihydrolactam (3b). Upon considering the above result and the fact that irradiation of neither the acid (1b) in the absence of sodium borohydride nor the corresponding ester (1c) in the presence of sodium borohydride gave a photocyclized product but the starting anilide recovered, we propose the reaction mechanism as follows; in the presence of sodium borohydride, the starting acid (1b) would first form the sodium carboxylate which then undergoes photocyclization to form an intermediate (A). The enolate moiety in the intermediate (A) would be subjected to protonation by the solvent (methanol) followed by simultaneous decarboxylation to give the dihydrolactam (3a). On an assumption that photocyclization of the acid (1b) could occur under a basic condition enough to form the corresponding acid's salt, we next investigated irradiation of the acid (1b) in the presence of 0.1% potassium hydroxide in ether-methanol. As expected, the photocyclized dihydrolactam (6)[6] and the aromatized lactam (2) were obtained in 13 and 14% yields respectively in addition to small amount of the biphenyl (4).

Similar irradiation of the substituted N-benzoylanthranilic acids (7), (11), and (15) in the presence of either sodium borohydride or potassium hydroxide resulted in the formation of similar type of the photocyclized products. Irradiation of the m-methoxy-substituted acid (7) afforded a mixture of the unstable dihyd-


hν
(1a) R=H
(1b) R=COOH
(1c) R=COOMe
(2)
(3a) R=H
(3b) R=D
(4)
(6)
(5a) R=H
(5b) R=D
(A)
NMe
NHMe
10
9
8
7


HOOC
MeO
hν
(7)
(8)
(9)
(10)
NHMe


HOOC
MeO
hν
(11)
(12)
(13)
(10)
(14)
6'
5'
2'
3'
NHMe


HOOC
MeO
MeO
hν
(15)
(16)
(13)
(17)
(18)
(19)
NHMe

rolactam (8)[6] in 20%, the aromatized lactam (9) in 7%, and the biphenyl (10) in 7% yields respectively, irrespective of the reaction condition using sodium borohydride or potassium hydroxide. On the other hand, irradiation of the p-methoxy-substituted acid (11) afforded three types of products, (12)[6] in 19%, (13) in 15%, and (10)[5] in 5% yields respectively in the presence of sodium borohydride while irradiation in the presence of potassium hydroxide afforded only the dihydrolactam (14)[6], isomeric to (12), in 41% yield. The biphenyl (10), which was unexpectedly obtained by irradiation of the acid (11), exhibited nmr signals at δ 7.36 and 6.99 due to 2'-, 3'-, 5'-, and 6'-protons as A_2B_2 pattern and identical with the biphenyl obtained from the m-methoxy-substituted acid (7).

Finally, under the reaction condition either in the presence of sodium borohydride or potassium hydroxide, irradiation of the dimethoxy-substituted acid (15) afforded a mixture of the dihydrolactam (16)[6] in 10-19%, the biphenyl (17)[6] in 2%, and the monomethoxy-substituted and aromatized lactam (13) in 7% yields respectively, the latter of which was identical with the lactam (13) obtained from the p-methoxy-substituted acid (11) as a result of elimination of methanol from the originally formed unstable dihydrolactam such as (18) or its congener (19). Thus, we established that the N-aroylanthranilic acids undergo photocyclization even under basic condition to give a mixture of unstable dihydrophenanthridones, the aromatized ones, and small amount of the biphenyls.

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REFERENCES

1 I. Ninomiya and T. Naito, The Alkaloids , ed. by A. Brossi, Academic Press, New York, 1983, Vol. XXII, p. 189.

2 T. Naito, Y. Tada, Y. Nishiguchi, and I. Ninomiya, Heterocycles, 1981, 16, 1137.

3 I. Ninomiya, T. Kiguchi, S. Yamauchi, and T. Naito, J. Chem. Soc., Perkin Trans. 1, 1980, 197.

4 I. Ninomiya, S. Yamauchi, T. Kiguchi, A. Shinohara, and T. Naito, J. Chem. Soc., Perkin Trans. 1, 1974, 1747.

5 M. Marky, H. Schmid, and H-J. Hansen, Helv. Chim. Acta, 1979, 62, 2129.

6 Satisfactory nmr and mass spectra were obtained for all new compounds.

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