

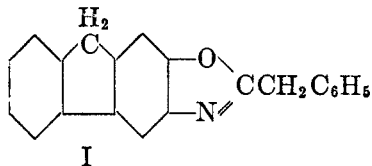
## FLUORENE OXAZOLES

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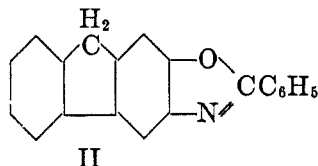
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Derivatives of benzoxazole were reported by Bywater and co-workers (1) to possess anticonvulsant properties. In the hope that fluorene derivatives might have similar properties and less toxicity we undertook the present work.

Two new oxazoles, (I and II), were obtained by condensing 3-amino-2-hydroxyfluorene with phenylacetonitrile and with benzonitrile.



2-benzyl-9H-fluoreno [3,2] oxazole



2-phenyl-9H-fluoreno [3,2] oxazole

The low-boiling compounds, acetonitrile and acrylonitrile failed to react under the conditions employed. Dicyandiamide gave only intractable tars when heated with 3-amino-2-hydroxyfluorene.

The yield of the intermediate, 2-hydroxyfluorene, was considerably improved by hydrolyzing the diazonium chloride in a very dilute solution of sulfuric acid. Nitration of 2-hydroxyfluorene could give either the 1-nitro- or the 3-nitro-2-hydroxyfluorene. Other positions are eliminated by the subsequent formation of the oxazole ring. Previous workers (2) have shown that the nitration of 2-acetylaminofluorene gives, after hydrolysis, 2-amino-3-nitrofluorene. This was proved by the removal of the original 2-amino group and the conversion of the resulting nitro compound to the known 3-hydroxyfluorenone.

Ruiz (3) nitrated 2-methoxyfluorene and by heating the resulting compound in a sealed tube with ammonia obtained the identical 2-amino-3-nitrofluorene of Eckert and Langecker and of Bardout (2).

We have, therefore, assigned the 3-position to the nitro group in the compound obtained by the nitration of 2-hydroxyfluorene.

In an earlier paper Ruiz (4) reported the isolation of 3-acetyl-amino-2-hydroxyfluorene which he described as melting at 215° and which on analysis gave 5.48% nitrogen.

In the present work we heated 3-amino-2-hydroxyfluorene with acetic anhydride and also obtained a compound melting at 214–215°. This compound, however, contained 5.05% nitrogen and gave no reaction for a free phenolic group. A recalculation of the theoretical percentage of nitrogen for the *diacetyl* derivative gives 4.98%, not as Ruiz reports it 5.12%. This compound, m.p. 215°, is, therefore, 3-acetyl-amino-2-acetoxyfluorene.

On pouring the supernatant acetic anhydride solution into water we obtained a compound melting at 163° which gave 5.90% nitrogen and proved to be the 3-acetyl-amino-2-hydroxyfluorene (Calc'd: N, 5.86.) not previously isolated.

## EXPERIMENTAL

*2-Nitrofluorene* and *2-aminofluorene* were prepared by the method given in Organic Syntheses (5) as modified by Reid and Sampey (6).

*2-Hydroxyfluorene*. The method of Ruiz (4) modified as follows was employed. 2-Aminofluorene (25 g., 0.14 mole) was boiled in 900 cc. of water containing 33 cc. of concentrated hydrochloric acid until solution resulted. This was cooled quickly to 40° and a solution of 11 g. of sodium nitrite in 60 cc. of water was added with stirring. The resulting diazonium solution was slowly added (1 hour) to 2500 cc. of boiling water containing 41 cc. of concentrated sulfuric acid. On cooling, a mixture of white and dark-colored crystals separated. This was dissolved in 1250 cc. of warm 10% potassium hydroxide, filtered and acidified; yield 90%; a light cream-colored solid, m.p. 166–168°. Recrystallization from 80% alcohol gave white platelets, m.p. 169–171°. Diels (7) reports 171°.

*3-Nitro-3-hydroxyfluorene*. 2-Hydroxyfluorene (12 g., 0.07 mole) in 300 cc. of glacial acetic acid was slowly nitrated with 4.2 cc. of concentrated nitric acid mixed with an equal volume of water. The mixture was heated on the water-bath for 0.5 hours to complete the reaction and then was poured into 1200 cc. of ice water. A yellow solid melting at 141–146° was obtained in 95% yield. Ruiz (4) reports m.p. 145.6°. The chief contaminant was a dinitro compound. By treating 10 g. with 1000 cc. of boiling 94% ethanol the dinitro compound remained undissolved and was removed by filtration.

*3-Amino-2-hydroxyfluorene*. The filtrate obtained above was treated with 50 g. of sodium hydrosulfite in 200 cc. of water and boiled for 4 hours. About half the alcohol was distilled off and 7 g. of tan material melting with decomposition at 244° was obtained. Ruiz (4) reports 246° dec.

*3-Acetylamino-2-acetoxyfluorene*. To 2 g. of 3-amino-2-hydroxyfluorene in 10 cc. of glacial acetic acid was added 1.6 cc. of acetic anhydride. After refluxing for 2 hours it was allowed to cool and the precipitate was recrystallized twice from absolute alcohol with Darco. Four-tenths gram of fine white needles was obtained, m.p. 214–215°. This is the value given by Ruiz (4) but he mistakenly describes this substance as the monoacetylated compound, *q.v.*

*Anal.* Calc'd for  $C_{17}H_{15}NO_3$ : N, 4.98. Found N, 5.04.

*3-Acetylamino-2-hydroxyfluorene*. As the yield in the preceding experiment was unusually small the filtrate from the reaction was poured into water. There was obtained 0.7 g. of thicker flat needles which, when recrystallized from alcohol, melted at 163°.

*Anal.* Calc'd for  $C_{15}H_{13}NO_2$ : N, 5.86. Found: N, 5.90.

*2-Benzyl-9H-fluoreno[3,2]oxazole*. 3-Amino-2-hydroxyfluorene, 2 g. or 0.01 mole, was refluxed with 20 cc. of phenylacetone nitrile at 229° for 5.5 hours. The mixture first turned black but eventually became red-brown as ammonia was evolved. On standing overnight light yellow needles formed; yield 1 g. (33%), m.p. 176–180°. The yellow material was washed with alkali and with water, dried and recrystallized twice from absolute alcohol with Darco. Colorless needles, m.p. 187°, were obtained. They were insoluble in hot and in cold water, slightly soluble in cold and very soluble in hot absolute alcohol; slightly soluble in cold ligroin (b.p. 90–120°) and somewhat soluble in hot; soluble in cold benzene, acetone, and ether and insoluble in alkali and acid.

*Anal.* Calc'd for  $C_{21}H_{15}NO$ : N, 4.71. Found: N, 4.68, 4.85.

*2-Phenyl-9H-fluoreno[3,2]oxazole*. 3-Amino-2-hydroxyfluorene, 2 g. or 0.01 mole, was boiled with 40 cc. of benzonitrile for 15 hours. This mixture also turned black and then gradually became red-brown. On cooling, 2.2 g. of light tan needles were obtained. After recrystallization from absolute alcohol with Darco, fine light yellow needles were obtained, melting at 184–185°.

The compound was insoluble in hot and in cold water, somewhat soluble in cold ethanol and very soluble in hot ethanol, more soluble in isoamyl alcohol. It was also soluble in cold methanol, benzene, acetone, and glacial acetic acid.

*Anal.* Calc'd for  $C_{20}H_{13}NO$ : N, 4.95. Found: N, 4.87, 4.85.

## SUMMARY

Two new oxazoles derived from fluorene, 2-phenyl-9*H*-fluoreno[3,2]oxazole and 2-benzyl-9*H*-fluoreno[3,2]oxazole, have been prepared and characterized.

3-Acetylamino-2-hydroxyfluorene has been prepared and found to melt at 163° instead of 215° as previously reported. The compound melting at 215° has been shown to be 3-acetylamino-2-acetoxyfluorene.

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