Novel Oxidations on Alumina: Facile Preparation of 3-Nitrofluoren-9-ol and Pure 3-Nitrofluoren-9-one. Derivatives of Fluorene; 36[1]

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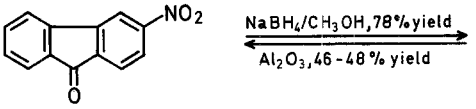
As part of a study, here and in another laboratory, examining the relative potency and sites of activity of the carcinogens – 3-acetamidofluorene, 2-acetamidofluorene, and some of their derivatives – we required substantial quantities of 3-nitrofluoren-9-ol (**1**). The two named fluorenamides, although closely related structurally, have widely disparate patterns of biological and chemical activity.

We found unexpectedly, that good yields of **1** were obtained readily by treating 3-nitrofluoren-9-one (**2**) with sodium borohydride in methanol. This was true even with crude **2** as a starting material; the product was readily purified on silica gel (benzene). We had earlier reacted sodium borohydride with 2-nitrofluoren-9-one and found that a complex mixture resulted; the nitro group was attacked, as expected, as well as the 9-oxo group[2].

As an alternative to purification of **1** on silica gel we tried chromatography on alumina, finding to our surprise, that 46–48% yields of pure **2** were obtained, together with 25 to 30% of 3,3'-azoxyfluoren-9-one, and ~5% of very high-melting unidentified material. Since the purification of crude **2** is tedious and expensive in time and materials – repeated crystallizations from high-boiling solvents and/or sublimation are required – we present this simple, novel oxidation of **1** as a facile alternative.



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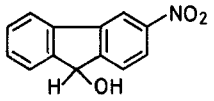

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In a recent communication, Hudlicky[3] reported that certain reactions are greatly facilitated at ordinary temperature if allowed to take place "inside the pores of high surface area materials", e.g., alumina. However, oxidation was not among the reactions he described.

We found that unsubstituted fluoren-9-ol was not affected under the same conditions on alumina, but 2-nitrofluoren-9-ol[2] and 2,4,7-trichlorofluoren-9-ol[4] are both oxidized to the corresponding 9-keto compound in yields of 85% and 100% respectively. The most likely explanation of the latter reaction is simple air oxidation. In the case of 2-nitrofluoren-9-ol there is apparently minor involvment of the nitro group. A very small amount of high-melting, dark material was isolated. But here, also, air oxidation seems to account for most of the reaction.

In the case of the conversion **1**→**2** on alumina the situation is more complex. At least 25 to 30% of the nitro groups are reduced (identified as 3,3'-azoxyfluoren-9-one), and possibly more as represented by 5% of other high-melting material. More than half of the oxidation of **1** to **2**, therefore, is effected by the nitro group rather than by atmospheric oxygen. This leaves an uncertain amount, certainly less than half of the reaction of **1** to **2**, which appears to result from air oxidation. We, therefore, report here a simple oxidation of certain fluorenones, promoted by contact with alumina at ambient temperature, and also the intramolecular oxidation-reduction of an otherwise stable substance (**1**) also promoted by alumina. It is interesting to note a recent report of an intramolecular oxidation-reduction promoted or "catalyzed" by similar contact with alumina[5].

3-Nitrofluoren-9-ol (1):

Sodium borohydride (5 g, 0.13 mol) was added portionwise over a 15 min period to a suspension of **2** (30 g, 0.13 mole) in methanol (1 l) which was stirred in a water bath (maintained at 15–18°). Then the reaction was stirred for 5 min and poured into water (8 l) containing 6 *N* hydrochloric acid (150 ml). The precipitate was collected, washed thoroughly with water, dried, and chromatographed on a silica gel column using benzene as eluent; yield: 23.5 g (78%) of white needles; m.p. 154.5–155.5° (lit.[6], 156°).

$C_{13}H_9NO_3$	calc.	C 68.72	H 3.99	N 6.16
(227.22)	found	68.68	4.06	6.22

I.R. (Nujol): ν_{max} = 3260, 3160, 1030 cm^{-1}.

Oxidation of 1 on Alumina:

A solution of **1** (1 g), dissolved by heating in benzene (30 ml), was placed on a column (2 × 36 cm) packed with aluminum oxide (Merck reagent grade, 100 g) and eluted with benzene. Elution of the yellow band and evaporation of the solvent gave yellow crystals of **2** (0.5 g); m.p. 235–236° (lit.[7], 231–233°). Continued washing of the column gave crude 3,3'-azoxyfluorenone; yield: 0.3 g; m.p. 287–301° (dec.) and a center cut of this fraction provided an analytical sample; m.p. 302–303° (dec.).

$C_{26}H_{14}N_2O_3$	calc.	C 77.60	H 3.51	N 6.96
(402.41)	found	77.62	3.63	6.88

I.R. (KBr): ν_{max} = 1715, 1612, 1462, 1300, 1190, 922, 910, 762, 735, 667 cm^{-1}.

The column was then eluted with methanol/acetic acid (19:1). Evaporation of the solvent gave an unidentified brown solid (0.05 g); m.p. > 360°.

Effect of Contact with Alumina on other Fluoren-9-ols:

Fluoren-9-ol (Aldrich), *2-nitrofluoren-9-ol*[2], and *2,4,7-trichlorofluoren-9-ol*[4] were each dissolved in benzene and passed through an alumina column, as described for **1**, to give respectively: unchanged *fluoren-9-ol; 2-nitro-fluoren-9-one* (yield: 85%), m.p. and mixture m.p. with an authentic sample[8]: 223–224° and yellow needles (yield 1.6%), m.p. 344–345° (dec.); and *2,4,7-trichlorofluoren-9-one* (yield: 100%), m.p. 178–181°, which was identical by I.R. and T.L.C. with an authentic sample[4] (m.p. 183–183.5°).

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