A Novel Synthesis of Indandiones Using the HOF·CH_3CN Complex

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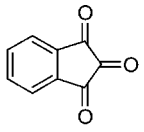
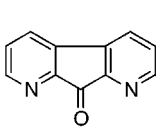
During the past few years, the HOF·CH_3CN complex has proven to be one of the best oxygen-transfer agents organic chemistry has to offer. This feature arises from the nature of the O−F bond where the oxygen is bonded to the most electronegative fluorine, turning it into a very strong electrophile indeed. The complex is easily prepared by bubbling either a commercial or a self-prepared mixture of 10−15% F_2 in nitrogen through aqueous acetonitrile at −15 °C. It is stable for a few hours at 0 °C and reacts quickly with substrates under mild conditions, usually with excellent yields. It has been shown to oxidize sulfur-containing compounds, including electron-depleted ones, to the respective sulfones,[1] aromatic and aliphatic amines to the corresponding nitro derivatives, alcohols and ethers to aldehydes and ketones, and much more, including the ready epoxidation of olefins.[2]

Ninhydrin (**1**),[3] which was discovered in 1910, is an exceptionally useful tool in biochemistry and forensic science. One of its most notable applications is the visualization of latent fingerprints on paper items.[4] There are many studies aimed at enhancing its sensitivity toward amino acids present in palmar sweat.[5] In 1990, Grigg[6] found that 1,8-diazafluoren-9-one (**2**) resembles ninhydrin inasmuch as it gives a strong fluorogenic reaction with amino acids. The compound has since become the main fluorogenic reagent for latent fingerprints in many forensic science laboratories.[7] Still, **2** suffers from some deficiencies, such as high cost and low solubility in nonpolar solvents, so the search for better reagents continues. Very recently, Joullie discovered that 1,2-indandione (**3a**) and some of its derivatives, particularly 5,6-dimethoxy-1,2-indandione (**3b**), can also visualize latent fingerprints by direct fluorogenic reaction at least as efficiently as **2**.[8]



1



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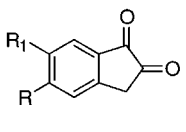
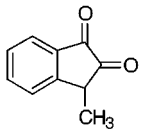
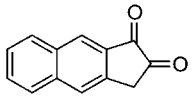


3a R = R$_1$ = H
3b R = R$_1$ = OMe
3c R = OMe; R$_1$ = H



3d



3e

Several methods for preparing 1,2-indandiones are described in the literature involving coupling methods,[9] oxidation of the methylene group in the 2-position using selenium dioxide,[10] and hydrolysis of 2-oximino-1-indanones prepared from 1-indanone derivatives.[11] The last method, although successfully employed for the preparation of several indandiones including **3a**−**c**, fails when the preparation of other potentially interesting derivatives was attempted, including the yet undescribed 3-methyl-1,2-indandione (**3d**) and benzo[*f*]indan-1,2-dione (**3e**). We have recently described a method of α-hydroxylating certain ketones using HOF·CH_3CN[12] and hoped that the combination of the exceptional oxygen transfer ability of this reagent together with the very mild reaction conditions associated with it would help us overcome most difficulties encountered by the previously described methods.

A good way to create an electron-rich region susceptible to electrophilic attack α to ketones is to trap the compound's enol form. We prepared the trimethylsilyl enol ether of 1-indanone (**4a**), dissolved it in chloroform, and added it to a 2-fold excess of a cold (0 °C) solution of HOF·CH_3CN. The reaction was completed in 3−4 min, forming 2-hydroxy-1-indanone (**5a**) in full conversion and good yield. Since the mechanism of oxidizing alcohols with HOF·CH_3CN proceeds through an abstraction of the hydrogen geminal to the hydroxy group, it was of no surprise that the electrophilic oxygen atom of the reagent could not attack the relatively electron-deficient C−H

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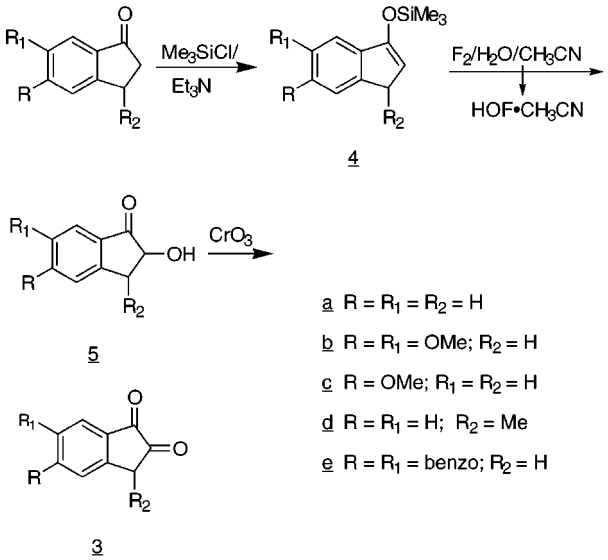
bond α to the carbonyl and that no 1,2-diketo moiety was detected.[13] The hydroxyl group of **5a**, however, could easily be oxidized with chromic acid (Jones reagent), forming the desired **3a** in 65% overall yield from 1-indanone. For comparison, the yield of **3a** formed via the 2-oximino derivative is also 65%, but with only 55% conversion.

This sequence of reactions was similarly efficient with the substituted 5,6-dimethoxy- and 5-methoxy-1-indanones. They were converted to the corresponding trimethylsilyl enol ethers **4b** and **4c** and reacted with $HOF{\cdot}CH_3CN$ to form the 5,6-dimethoxy and 5-methoxy-2-hydroxy-1-indanones (**5b** and **5c**), which after treatment with CrO_3/H_2SO_4 provided the target molecules **3b** and **3c**, respectively, in good overall yields.

The present search for new fluorogenic reagents for latent fingerprints included the synthesis of an indandione substituted on the five-membered ring, 3-methyl-1,2-indandione (**3d**), and also benzo[*f*]indan-1,2-dione (**3e**) with extended conjugation of the aromatic system. Previous attempts to prepare **3e** from benzo[*f*]indan-1-one[14] and **3d** from 3-methyl-1-indanone[15] by conventional methods were unsuccessful. In both cases we had better luck using $HOF{\cdot}CH_3CN$.

Treatment of the above 1-indanones with Me_3SiCl resulted in the corresponding trimethylsilyl enol ethers **4d** and **4e** in very good yields. These enol derivatives



were treated for a short time with $HOF{\cdot}CH_3CN$ solution to produce the unknown 2-hydroxy-3-methyl-1-indanone (**5d**) and 2-hydroxybenzo[*f*]indan-1-one (**5e**) in good yields. It should be noted that **5e** is a quite sensitive compound and the reaction should be stopped after 1 min to avoid formation of a considerable amount of tars. Both hydroxy compounds were eventually oxidized with chromic acid to produce the corresponding target indandiones **3d** and **3e** in better than 60% overall yields.[16]

Experimental Section

^1H NMR and ^{13}C NMR spectra were recorded with a 200 MHz instrument with $CDCl_3$ as solvent and Me_4Si as an internal standard. GC/MS was used to record the mass spectra. FTIR spectra were recorded as neat films or in KBr pellets. Jones reagent (CrO_3/H^+/acetone) was prepared as described in the literature.[17]

General Procedure for Working with Fluorine. Fluorine is a strong oxidizer and a very corrosive material. An appropriate vacuum line made from copper or monel in a well-ventilated area should be constructed for working with this element. For more experimental details, see, for example, ref 18. For the occasional user, however, various premixed mixtures of F_2 in inert gases are commercially available, simplifying the whole process. The reactions themselves can be carried out in glass vessels. If elementary precautions are taken, work with fluorine is relatively simple, and we have had no bad experiences working with it.

General Procedure for Producing the Oxidizing $HOF{\cdot}CH_3CN$. Mixtures of about 10% F_2 with nitrogen were used in this work. The gas mixture was prepared in a secondary container before the reaction was started. This mixture was then passed at a rate of about 400 mL per minute through a cold (−15 °C) mixture of 400 mL of CH_3CN and 40 mL of H_2O. The development of the oxidizing capacity was monitored by reacting aliquots with an acidic aqueous solution of KI. The liberated iodine was titrated with thiosulfate. It is thus possible to achieve concentrations of more than 0.5 mol/L of the oxidizing reagent. NaF (2−3 g) was added in order to reduce the HF content in the oxidation mixture.

General Procedure for Making Trimethylsilyl Enol Ethers.[19] To a stirred mixture of the parent 1-indanones (20 mmol), dissolved in DMF/Et_3N (2:1), was added trimethylsilyl chloride (50 mmol) under nitrogen. The reaction mixture was refluxed for 2−4 h, after which time it was allowed to cool to room temperature. Pentane was then added, the organic layer was washed with bicarbonate and dried, the organic solvent was evaporated, and the desired trimethylsilyl enol ethers of the 1-indanones were isolated and used without further purification.[20]

General Oxidation Procedure Using the $HOF{\cdot}CH_3CN$ Complex. The trimethylsilyl enol ethers (5 mmol) were dissolved in 20 mL of chloroform, cooled to 0 °C, and added in one portion to an excess of 2 mol equiv (10 mmol) of the oxidizing $HOF{\cdot}CH_3CN$ complex in aqueous acetonitrile. After 3−4 min, the reaction mixture was neutralized with saturated sodium bicarbonate and extracted with $CHCl_3$. The combined organic layers were dried over $MgSO_4$ and the solvent evaporated to produce the relevant 2-hydroxy-1-indanone.

Oxidation of the 2-Hydroxy-1-indanones to 1,2-Indanediones. The 2-hydroxy-1-indanones (1−2 g) were dissolved in acetone and cooled to 0 °C. The Jones reagent was added dropwise until the orange color remained unchanged. The mixture was then stirred for an additional 10 min, after which time the excess reagent was destroyed with EtOH. The solids were filtered, and the clear acidic solution was neutralized with alkali and extracted with chloroform. The organic layer was dried over $MgSO_4$ and the solvent evaporated, leaving behind the crude solid 1,2-indandiones.

Trimethylsilyl enol ether of 1-indanone (4a): 88% yield; oil; ^1H NMR δ 7.4−7.2 (4H, m), 5.3 (1H, t, J = 2.3 Hz), 3.2 (2H, d, J = 2.3 Hz), 0.2 (9H, s); MS *m/e* 204 $(M)^+$.

Trimethylsilyl enol ether of 5,6-dimethoxy-1-indanone (4b): 92% yield; oil; ^1H NMR δ 7.0 (1H, s), 6.9 (1H, s), 5.3 (1H, t, J = 2.3 Hz), 3.93 (3H, s), 3.90 (3H, s), 3.2 (2H, d, J = 2.3 Hz), 0.3 (9H, s); MS *m/e* 264 $(M)^+$.

Trimethylsilyl enol ether of 5-methoxy-1-indanone (4c): 93% yield; oil; ^1H NMR δ 7.4 (1H, d, J = 8.3 Hz), 7.1 (1H,

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(20) Although the trimethylsilyl enol ethers were not analytically purified they were obtained in higher than 90% purity. Their physical properties are recorded in the Experimental Section.

bs), 7.0 (1H, dd, $J_1 = 2.3$ Hz, $J_2 = 8.3$ Hz), 5.4 (1H, t, $J = 2.3$ Hz), 3.9 (3H, s), 3.3 (2H, d, $J = 2.3$ Hz), 0.4 (9H, s).

Trimethylsilyl enol ether of 3-methyl-1-indanone (4d): 98% yield; oil; ^{1}H NMR δ 7.8−7.3 (4H, m), 5.4 (1H, d, $J = 1.3$ Hz), 3.4 (1H, dd, $J_1 = 2.5$ Hz, $J_2 = 7.4$ Hz), 1.3 (3H, d, $J = 7.4$ Hz), 0.3 (9H, s).

Trimethylsilyl enol ether of benzo[*f*]indan-1-one (4e): 92% yield; oil; ^{1}H NMR δ 7.9−7.8 (3H, m), 7.77 (1H, d, $J = 8.6$ Hz), 7.45−7.40 (2H, m), 5.6 (1H, t, $J = 2.5$ Hz), 3.4 (2H, d, $J = 2.5$ Hz), 0.4 (9H, s).

2-Hydroxy-1-indanone (5a):[21] obtained from **4a** in 85% yield as a white solid; IR 1712 cm^{-1}; ^{1}H NMR δ 7.7 (1H, d, $J = 7.6$ Hz), 7.6 (1H, t, $J = 7.6$ Hz), 7.4 (1H, d, $J = 7.6$ Hz), 7.4 (1H, t, $J = 7.6$ Hz) 4.6 (1H, dd, $J_1 = 5$ Hz, $J_2 = 8$ Hz), 3.9 (1H, bs), 3.6 (1H, dd, $J_1 = 8$ Hz, $J_2 = 17$ Hz), 3.0 (1H, dd, $J_1 = 5$ Hz, $J_2 = 17$ Hz); MS *m/e* 148 (M)$^+$.

5,6-Dimethoxy-2-hydroxy-1-indanone (5b):[22] obtained from **4b** in 90% yield as a yellow solid; mp 145 °C; IR 1690, 3415 cm^{-1}; ^{1}H NMR δ 7.2 (1H, s), 6.9 (1H, s), 4.5 (1H, dd, $J_1 = 4$ Hz, $J_2 = 7.5$ Hz), 4.0 (3H, s), 3.9 (3H, s), 3.5 (1H, dd, $J_1 = 7.5$ Hz, $J_2 = 17$ Hz), 2.9 (1H, dd, $J_1 = 4$ Hz, $J_2 = 17$ Hz); ^{13}C NMR δ 205.2, 156.4, 149.7, 146.8, 126.5, 107.5, 104.6, 73.9, 56.3, 56.0, 34.9; MS *m/e* 207 (M − 1)$^+$.

2-Hydroxy-5-methoxy-1-indanone (5c):[23] obtained from **4c** in 86% yield as a yellow solid; mp 131 °C; IR 1687 cm^{-1}; ^{1}H NMR δ 7.7 (1H, d, $J = 8.3$ Hz), 6.9 (2H, m), 4.5 (1H, dd, $J_1 = 5$ Hz, $J_2 = 7$ Hz), 4.0 (3H, s),3.5 (1H, dd, $J_1 = 7$ Hz, $J_2 = 16$ Hz), 3.0 (1H, dd, $J_1 = 5$ Hz, $J_2 = 16$ Hz); ^{13}C NMR δ 204.6, 172.4, 166.3, 154.2, 126.4, 116.1, 109.9, 74.1, 55.7, 35.3; MS *m/e* 177 (M − 1)$^+$.

2-Hydroxy-3-methyl-1-indanone (5d): obtained from **4d** as a mixture of stereoisomers in 91% yield; white solid; mp 67−69 °C; IR 1720, 1724, 2800−3100 cm^{-1}; ^{1}H NMR δ 7.8−7.6 (2H, m), 7.5−7.3 (2H, m), 4.6 (1H, d, $J = 7.4$ Hz), 4.1 (1H, d, $J = 5.4$ Hz), 3.7 (1H, m), 3.2 (1H, m), 1.6 (3H, d, $J = 6.9$ Hz), 1.2 (3H, d, $J = 7.2$ Hz); MS *m/e* 162 (M)$^+$. Anal. Calcd for $C_{10}H_{10}O_2$: C, 74.99; H, 5.03. Found: C, 74.69; H, 5.07.

2-Hydroxybenzo[*f*]indan-1-one (5e): obtained from **4e** in 88% yield as a yellow solid; mp 160 °C dec, the reaction was kept at 0 °C for only 1 min in order to avoid formation of tars and undesired products; IR 1720, 3350 cm^{-1}; ^{1}H NMR δ 8.3 (1H, s), 8.0 (1H, d, $J = 8$ Hz), 7.9 (1H, d, $J = 5.4$ Hz), 7.85 (1H, s), 7.7−7.5 (2H, m), 4.7 (1H, dd, $J_1 = 6.2$ Hz, $J_2 = 8.4$ Hz), 3.8 (1H, dd, $J_1 = 8.4$ Hz, $J_2 = 16.4$ Hz), 3.5 (1H, bs), 3.2 (1H, dd, $J_1 = 6.2$ Hz, $J_2 = 16.4$ Hz); ^{13}C NMR 206.6, 143.1, 137.8, 132.6, 131.6, 130.5, 129.0, 127.9, 126.4, 125.5, 125.1, 75.0, 34.6; MS *m/e* 198 (M)$^+$. Anal. Calcd for $C_{13}H_{10}O_2$: C, 78.77; H, 5.08. Found: C, 78.36; H, 4.99.

1,2-Indandione (3a):[24] obtained from **5a** in 85% yield as a white solid; mp 165 °C; IR 1708, 1765 cm^{-1}; ^{1}H NMR δ 7.9 (1H, d, $J = 7.5$ Hz), 7.8 (1H, t, $J = 7.5$ Hz), 7.6 (1H, d, $J = 7.5$ Hz), 7.5 (1H, t, $J = 7.5$ Hz), 3.6 (2H, s); ^{13}C NMR δ 199.7, 187.5, 146.5, 137.6, 136.5, 128.5, 127.4, 125.4, 36.4; MS *m/e* 146 (M)$^+$.

5,6-Dimethoxy-1,2-indandione (3b):[8] obtained from **5b** in 80% yield as a yellow solid; mp 175 °C dec; IR 1704, 1758 cm^{-1}; ^{1}H NMR δ 7.3 (1H, s), 7.0 (1H, s), 4.1 (3H, s), 4.0 (3H, s), 3.6 (2H, s); ^{13}C NMR δ 200, 184.9, 157.8, 149.8, 143.4, 131.1, 107.6, 105.6, 56.5, 56.1, 35.8; MS *m/e* 206 (M)$^+$.

5-Methoxy-1,2-indandione (3c):[25] obtained from **5c** in 83% yield as a yellow solid; mp 162 °C; IR 1708, 1756 cm^{-1}; ^{1}H NMR δ 7.9 (1H, d, $J = 8.5$ Hz), 6.99 (1H, d, $J = 8.5$ Hz), 6.97 (1H, s), 4.0 (3H, s), 3.6 (2H, s); ^{13}C NMR δ 200.46, 184.8, 167.7, 149.9, 142.2, 128.2, 116.6, 110.3, 56.0, 36.7; MS *m/e* 176 (M)$^+$.

3-Methyl-1,2-indandione (3d) was obtained from **5d** in 70% yield as a waxy orange solid. This compound was mentioned only once in the literature,[26] but no physical data were given. Although in our case compound **3d** was obtained in higher than 90% purity we were unable to fully purify it since it decomposed on heating or during chromatography attempts: IR 1722, 1762 cm^{-1}; ^{1}H NMR δ 7.9 (1H, t, $J = 7.4$ Hz), 7.8 (1H, d, $J = 7.4$ Hz), 7.6 (1H, d, $J = 7.4$ Hz), 7.5 (1H, t, $J = 7.4$ Hz), 3.6 (1H, q, $J = 7.4$ Hz), 1.5 (3H, d, $J = 7.4$ Hz); ^{13}C NMR δ 203.4, 187.4, 152.2, 137.9, 135.7, 128.5, 126.3, 125.0, 40.6, 15.8; MS *m/e* 160 (M)$^+$.

Benzo[*f*]indan-1,2-dione (3e): obtained from **5e** in 80% yield as a yellow solid; mp 160 °C dec; IR 1713, 1765 cm^{-1}; ^{1}H NMR δ 8.5 (1H, s), 8.04 (1H, d, $J = 7.5$ Hz), 7.97 (1H, s), 7.9 (1H, s), 7.7 (1H, t, $J = 7.5$ Hz), 7.6 (1H, t, $J = 7.5$ Hz), 3.9 (2H, s); ^{13}C NMR δ 200.9, 187.9, 138.2, 138.4, 133.5, 132.4, 131.1, 130.5, 128.0, 127.7, 127.4, 126.0, 37.2; MS *m/e* 196.052 284 (M)$^+$, calcd for $C_{13}H_8O_2$ 196.052 420.

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