The Meyer-Schuster Rearrangement and Hydrohalide Addition of 3-Alkynyl-3-hydroxy-1*H*-isoindol-1-ones

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Treatment of *N*-methyl and *N*-phenylphthalimide with appropiate lithium acetylides in tetrahydrofuran obtained the acetylenic alcohols **2a** through **2h**. These compounds, when subjected to mildly acidic hydrolysis conditions in aqueous organic solvents, underwent Meyer-Schuster rearrangement to yield the α,β-unsaturated carbonyl compounds **4a** through **4h** which were determined to have the *E* configuration. The phenyl ethynyl analogs of series **4** underwent hydrohalide addition when treated with hydrogen halides in water solution.

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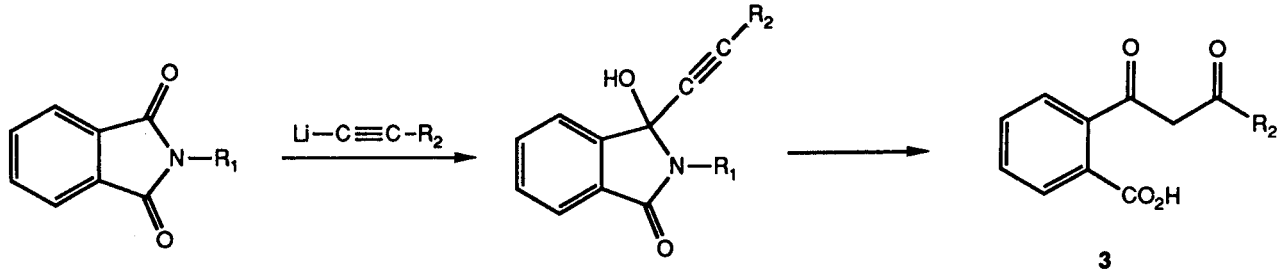
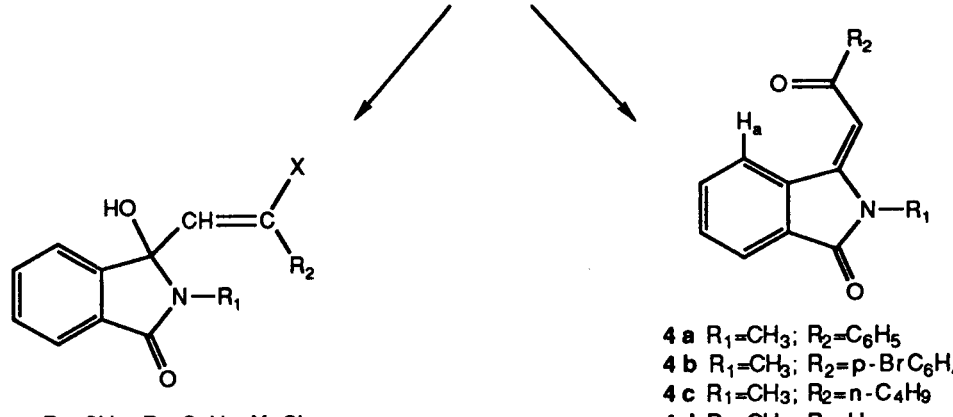
Our initial interest in the acetylenic alcohols **2**, that could be derived from *N*-substituted phthalimides **1**, was based on their potential utility as precursors of 1-(2-carboxyphenyl)propanediones **3**. A series of the latter compounds have been studied for their effect on root geotropism [1]. Previous work indicated that compounds of series **2** could be obtained from metal acetylides and appropiate phthalimides [2-4]. Hydrolysis studies [4] of alcohols derived from *N*-substituted phthalimides and Grignard reagents have indicated that keto acids or *N*-substituted keto amides are readily formed. Thus for series **2**, hydrolysis and hydration in either a sequential or single laboratory operation would yield **3** or the amide derivative.



1a R_1=CH_3
1b R_1=C_6H_5

3

2a R_1=CH_3; R_2=C_6H_5
2b R_1=CH_3; R_2=p-BrC_6H_4
2c R_1=CH_3; R_2=n-C_4H_9
2d R_1=CH_3; R_2=H
2e R_1=C_6H_5; R_2=C_6H_5
2f R_1=C_6H_5; R_2=p-BrC_6H_4
2g R_1=C_6H_5; R_2=n-C_4H_9
2h R_1=C_6H_5; R_2=H



5a R_1=CH_3; R_2=C_6H_5; X=Cl
5b R_1=CH_3; R_2=p-BrC_6H_5; X=Cl
5e1 R_1=C_6H_5; R_2=C_6H_5; X=Cl
5e2 R_1=C_6H_5; R_2=C_6H_5; X=Br

4a R_1=CH_3; R_2=C_6H_5
4b R_1=CH_3; R_2=p-BrC_6H_4
4c R_1=CH_3; R_2=n-C_4H_9
4d R_1=CH_3; R_2=H
4e R_1=C_6H_5; R_2=C_6H_5
4f R_1=C_6H_5; R_2=p-BrC_6H_4
4g R_1=C_6H_5; R_2=n-C_4H_9
4h R_1=C_6H_5; R_2=H

When *N*-methyl and *N*-phenylphthalimides, **1a** and **1b**, were treated with appropiate lithium acetylides in tetrahydrofuran, the acetylenic alcohols **2a** through **2h** were obtained. Compound **2a** was subjected to a number of different hydrolysis conditions. Alkaline hydrolysis reversed the alkynylation to give phenylacetylene and either *N*-methylphthalimide or a phthalic acid salt depending on the rigor of the conditions. None of the expected alkynone product could be isolated. Vigorous acidic hydrolysis in the presence of mercuric ion failed to yield **3** giving instead an intractable mixture of products.

The compounds **2a** through **2h**, when subjected to mildly acidic hydrolysis conditions in aqueous organic solvents, underwent Meyer-Schuster rearrangement [5] to yield the series of α,β-unsaturated carbonyl compounds **4a** through **4h**. A number of phenacylidene phthalimidines (phenacylidene-1*H*-isoindol-1-ones) have been patented [6] for herbicidal activity indicating the possibility of similar biological potential for the compounds of series **4**.

Proton nmr spectra indicate that the ketones in series **4** have the *E* configuration. In each case, an aromatic signal is shifted downfield from the remainder of the aromatic signals which is caused by the deshielding of proton H_a [7] by the carbonyl group fixed in close proximity by the requirements of the *E* configuration. Both configurations of **4d** have been previously prepared by different methods [8-11] and their configurations rigorously characterized. Comparison of mp and spectral data with literature values shows our product has the *E* configuration.

Heating **2a** and **2b** with 5% aqueous hydrochloric acid under reflux for short periods of time (*ca.* 20-60 minutes) resulted in the precipitation of **5a** and **5b** respectively. Longer heating periods or more concentrated acid resulted in the corresponding phthalimidines **4a** and **4b**. Compound **2e**, when heated for 7.5 hours with 10% aqueous hydrochloric acid or 10% aqueous hydrobromic acid, yielded **5e1** and **5e2** respectively. Heating **5a** above its melting point resulted in loss of hydrochloric acid and the formation of the Meyer-Schuster product **4a**. All attempts to achieve the corresponding hydrochloric acid addition products with **2c** failed, yielding only the corresponding phthalimidine **4c**.

Structure designations for series **5** are based on HETCOR and INEPT nmr experiments which were correlated with the model compounds α-chlorostyrene (α-carbon = 139.9 ppm, β-carbon = 112.6 ppm) and β-chlorostyrene (α-carbon = 133.2 ppm, β-carbon = 118.6 ppm). For compound **5a**, the vinylogous hydrogen, which resonates at 6.61 ppm, correlates with the ^{13}C resonance at 125.1 ppm while the halogenated carbon resonates at 137.1 ppm. Allowing for β-alkyl substitution, this is analogous with the α-chlorostyrene model.

In conclusion, 3-alkynyl-3-hydroxy-1*H*-isoindoles undergo Meyer-Schuster rearrangements readily under mildly acidic conditions in organic solvents. The phenyl ethynyl analogs undergo hydrohalide addition, a reaction not reported in other propargylic alcohols, when treated with hydrogen halides in water solution.

EXPERIMENTAL

General Methods.

Melting points were determined in capillary tubes and are uncorrected. Infrared spectra were recorded on a Perkin-Elmer 263B spectrometer. Nuclear magnetic resonance spectra were recorded on a Varian XL300 spectrometer (300 MHz) (Department of Chemistry and Biochemistry, Utah State University, Logan, Utah), a Bruker AC 250 (250 MHz), or a Varian 360L (60 MHz). Chemical shifts are reported in δ (ppm) downfield from internal tetramethylsilane. Elemental analysis were performed by Desert Analytics, Tuscon, Arizona. Dry tetrahydrofuran was obtained by distillation from sodium benzophenone ketyl.

2,3-Dihydro-3-hydroxy-2-methyl-3-phenylethynyl-1*H*-isoindol-1-one (**2a**).

To a solution of phenylacetylene (12.1 g, 0.12 mole) in tetrahydrofuran (200 ml) cooled to $-10°$ and stirred under nitrogen was added 77 ml (0.12 mole) of 1.6 *M* *n*-butyllithium in hexane solution. To the resulting mixture was added dropwise a solution of *N*-methylphthalimide (20.0 g, 0.12 mole) in tetrahydrofuran (200 ml). The mixture was allowed to stir for 1 hour at $-10°$ and then allowed to rise to room temperature overnight. The creamy mixture was poured into 250 ml of 1.0 *M* ammonium chloride and extracted with ether. The ether layer was dried over magnesium sulfate and the solvent removed under reduced pressure leaving a white solid which was recrystallized from benzene/pentane, yield 25.4 g (78%), mp 127-128°; ir (potassium bromide): 3260 (OH), 2230 (C≡C), 1690 (C=O), 690 cm^{-1}; ^1H nmr (60 MHz, deuteriochloroform): δ 2.90 (s, 3H, CH_3), 5.30 (s, 1H, OH), 7.35 (m, 9H, ArH).

Anal. Calcd. for $C_{17}H_{13}NO_2$: C, 77.55; H, 4.98; N, 5.32. Found: C, 77.41; H, 4.91; N, 5.32.

3-(*p*-Bromophenylethynyl)-2,3-dihydro-3-hydroxy-2-methyl-1*H*-isoindol-1-one (**2b**).

In a similar method to the synthesis of **2a**, reaction of *p*-bromophenylacetylene (9.23 g, 51 mmoles) and an equivalent amount of *N*-methylphthalimide yielded 9.44 g (56%) of a light yellow solid, mp 176-178° (recrystallized from benzene/pentane); ir (potassium bromide): 3251 (OH), 2240 (C≡C), 1693 (C=O), 1059, 822, 760 cm^{-1}; ^1H nmr (60 MHz, DMSO-d_6): δ 3.12 (s, 3H, CH_3), 3.38 (s, 1H, OH), 7.00-8.34 (m, 8H, ArH).

Anal. Calcd. for $C_{17}H_{12}BrNO_2$: C, 59.67; H, 3.53; N, 4.09. Found: C, 61.12; H, 3.55; N, 3.94. Repeated C analysis for **2b** consistently showed high percentage values. This compound however, readily yielded pure product **4b**.

3-(1-Hexynyl)-2,3-dihydro-3-hydroxy-2-methyl-1*H*-isoindol-1-one (**2c**).

In a similar method to the synthesis of **2a**, except the reaction temperature was $-78°$ and the mixture was stirred for 20 minutes at $-78°$ before rising to room temperature, reaction of 1-hexyne (61 mmoles) and a equivalent amount of *N*-methylphthalimide yielded 10.8 g (73%) of a white solid, mp 51-53° (re-

crystallized from benzene/petroleum ether); ir (potassium bromide): 3265 (OH), 2234 (C≡C), 1678 (C=O), 756 cm^{-1}; ^1H nmr (250 MHz, deuteriochloroform): δ 0.75 (t, 3H, J = 7.0 Hz), 1.12-1.40 (m, 4H), 2.08 (t, 2H, J = 6.8 Hz), 2.84 (s, 3H), 5.41 (s, 1H, OH), 7.20-7.55 (m, 4H, ArH); ^{13}C nmr: δ 13.5, 18.2, 21.8, 23.9, 30.2, 75.6, 83.5, 86.4, 122.4, 122.9, 129.4, 129.5, 132.5, 146.5, 166.8.

Anal. Calcd. for $C_{15}H_{17}NO_2$: C, 74.05; H, 7.04; N, 5.76. Found: C, 73.94; H, 7.04; N, 5.79.

3-Ethynyl-2,3-dihydro-3-hydroxy-2-methyl-1*H*-isoindol-1-one (**2d**).

In a similar method to the synthesis of **2a**, except the reaction temperature was −78°, reaction of acetylene (3.00 g, 115 mmoles) and an equivalent amount of *N*-methylphthalimide yielded 12.2 g (65%) of a white solid, mp 147-148°; ir (potassium bromide) 3285 (≡C-H), 3164 (OH), 2132 (C≡C), 1692 (C=O), 765 cm^{-1}; ^1H nmr (60 MHz, unisol): δ 2.89 (s, 1H), 3.10 (s, 3H), 7.10 (s, 1H, OH), 7.35-8.00 (m, 4H, ArH).

Anal. Calcd. for $C_{11}H_9NO_2$: C, 70.58; H, 4.85; N, 7.48. Found: C, 70.35; H, 4.83; N, 7.33.

2,3-Dihydro-3-hydroxy-2-phenyl-3-phenylethynyl-1*H*-isoindol-1-one (**2e**).

In a similar method to the synthesis of **2a** reaction of phenylacetylene (8.87 g, 87 mmoles) and an equivalent amount of *N*-phenylphthalimide yielded 21.2 g (75%) of a white solid, mp 160-161° (recrystallized from benzene); ir (potassium bromide): 3324 (OH), 2234 (C≡C), 1689 (C=O), 1073, 756, 691 cm^{-1}; ^1H nmr (250 MHz, acetone-d_6/deuteriochloroform): δ 2.64 (s, 1H, OH), 7.20-7.87 (m, 14H, ArH).

Anal. Calcd. for $C_{22}H_{15}NO_2$: C, 81.21; H, 4.65; N, 4.30. Found: C, 81.34; H, 4.58; N, 4.41.

3-(*p*-Bromophenylethynyl)-2,3-dihydro-3-hydroxy-2-phenyl-1*H*-isoindol-1-one (**2f**).

In a similar method to the synthesis of **2a**, except the reaction temperature was −78° and the mixture was stirred for 4 hours at −78° before rising to room temperature, reaction of *p*-bromophenylacetylene (9.78 g, 54 mmoles) and an equivalent amount of *N*-phenylphthalimide yielded 5.48 g (25%) of a white solid, mp 156-158° (recrystallized from 95% ethanol); ir (potassium bromide): 3300 (OH), 2215 (C≡C), 1780 (C=O) cm^{-1}; ^1H nmr (250 MHz, deuteriochloroform): δ 4.30 (s, 1H, OH), 7.12-7.82 (m, 13H, ArH); ^{13}C nmr: δ 85.0, 85.2, 86.0, 120.0, 122.7, 123.6, 123.9, 127.1, 127.6, 128.9, 129.6, 130.3, 131.6, 133.2, 133.4, 135.1, 145.3, 166.5.

Anal. Calcd. for $C_{22}H_{14}BrNO_2$: C, 65.38; H, 3.49; N, 3.46. Found: C, 65.35; H, 3.40; N, 3.46.

3-(1-Hexynyl)-2,3-dihydro-3-hydroxy-2-phenyl-1*H*-isoindol-1-one (**2g**).

In a similar method to the synthesis of **2a**, except the reaction temperature was −78° and the mixture was stirred for 20 minutes at −78° before rising to room temperature, reaction of 1-hexyne (8.5 g, 100 mmoles) and an equivalent amount of *N*-phenylphthalimide yielded 13.6 g (43%) of a white solid, mp 115-116° (recrystallized from 95% ethanol); ir (potassium bromide): 3385 (OH), 2230 (C≡C), 1685 (C=O) cm^{-1}; ^1H nmr (60 MHz, deuteriochloroform): δ 0.62 (m, 3H), 1.20 (m, 4H), 1.93 (t, 2H), 5.32 (s, 1H, OH), 6.50-8.20 (m, 9H, ArH).

Anal. Calcd. for $C_{20}H_{19}NO_2$: C, 78.66; H, 6.27; N, 4.59. Found: C, 78.88; H, 6.14; N, 4.41.

3-Ethynyl-2,3-dihydro-3-hydroxy-2-phenyl-1*H*-isoindol-1-one (**2h**).

In a similar method to the synthesis of **2a**, except the reaction temperature was −78°, reaction of excess acetylene (6.00 g) and an *N*-phenylphthalimide (16.00 g, 70 mmoles) yielded 9.48 g (54%) of a white solid, mp 171-174° (lit [2] 172°). The ir spectrum was identical to that displayed in the literature [2].

E-2,3-Dihydro-2-methyl-3-(2-oxo-2-phenylethylidene)-1*H*-isoindol-1-one (**4a**).

A 1.00 g (3.8 mmoles) quantity of **2a** was dissolved in 16 ml of 75% aqueous acetone. To this solution was added 0.03 ml of concentrated sulfuric acid and the resulting mixture was heated under reflux for 2 hours. When cooling failed to yield crystals, the solvent was removed and the remaining solid recrystallized from 95% ethanol yielding 0.90 g (90%) of a yellow solid, mp 109-110°; ir (potassium bromide): 1720 (C=O), 1650 (C=C), 1219, 779, 695 cm^{-1}; ^1H nmr (250 MHz, deuteriochloroform): δ 3.31 (s, 3H, CH_3), 6.59 (s, 1H), 7.43-8.03 (m, 8H, ArH), 8.85 (d, 1H, J = 7.5 Hz, ArH_a); ^{13}C nmr: δ 26.3, 100.2, 120.0, 123.1, 127.3, 128.2, 128.6, 131.4, 132.8, 133.2, 133.8, 139.3, 149.2, 167.3, 189.4.

Anal. Calcd. for $C_{17}H_{13}NO_2$: C, 77.55; H, 4.98; N, 5.32. Found: C, 77.41; H, 4.91; N, 5.32.

E-2,3-Dihydro-2-methyl-3-(2-oxo-2-(4-bromophenyl)ethylidene)-1*H*-isoindol-1-one (**4b**).

In a similar method to the synthesis of **4a** reaction of **2b** (1.00 g, 2.9 mmoles) yielded 0.71 g (71%) of a yellow solid, mp 143-145° (recrystallized from 95% ethanol); ir (potassium bromide): 1723 (C=O), 1650 (C=C), 1219, 813, 770 cm^{-1}; ^1H nmr (60 MHz, DMSO-d_6): δ 3.28 (s, 3H, CH_3), 6.69 (s, 1H, =CH), 7.37-8.10 (m, 7H, ArH), 8.84 (m, 1H, ArH_a).

Anal. Calcd. for $C_{17}H_{12}BrNO_2$: C, 59.67; H, 3.53; N, 4.09. Found: C, 59.72; H, 3.40; N, 4.07.

E-2,3-Dihydro-2-methyl-3-(2-oxo-1-hexylidene)-1*H*-isoindol-1-one (**4c**).

In a similar method to the synthesis of **4a** reaction of **2c** (1.00 g, 4.1 mmoles) yielded 0.69 g (69%) of a yellow solid, mp 55-58° (recrystallized from 95% ethanol); ir (potassium bromide): 1700 (C=O), 1669, 1015, 765 cm^{-1}; ^1H nmr (60 MHz, deuteriochloroform): δ 0.89 (t, 3H), 1.27-1.52 (m, 4H), 2.20 (t, 3H), 2.82 (s, 3H), 7.34-7.83 (m, 3H, ArH), 8.92 (m, 1H, ArH_a).

Anal. Calcd. for $C_{15}H_{17}NO_2$: C, 74.05; H, 7.04; N, 5.76. Found: C, 73.67; H, 7.12; N, 5.70.

E-2,3-Dihydro-2-methyl-3-(2-oxoethylidene)-1*H*-isoindol-1-one (**4d**).

A 1.00 g (5.3 mmoles) quantity of **2d** was dissolved in 15 ml of 75% aqueous acetone. To this solution was added 0.04 ml of concentrated sulfuric acid and the resulting mixture was heated under reflux for 1.75 hours. Upon cooling to room temperature, a solid began to form. Methylene chloride was added until the solid dissolved. Solid sodium bicarbonate was added until two liquid layers could be observed. The layers were separated, the aqueous layer extracted with methylene chloride, and the methylene chloride layers combined. After washing the organic phase with water and drying over calcium chloride, the solvent was removed. The remaining solid was recrystallized from 95% ethanol to yield 0.76 g (76%) of light yellow crystals, mp 183-184° (lit [10] 182-183°); ir (potassium bromide): 1730 (C=O), 1665, 1135, 1042, 766 cm^{-1}; ^1H nmr (250 MHz, deuteriochloroform): δ 3.30 (s, 3H), 5.97 (d, 1H, J = 7.7 Hz), 7.59-8.13 (m, 3H, ArH), 8.12 (d, 1H, J = 6.9 Hz, ArH_a), 10.56 (d, 1H, J = 7.7 Hz); ^{13}C nmr: δ 26.3, 105.2, 109.1,

120.9, 124.1, 125.6, 131.7, 133.1, 151.7, 166.8, 187.5.

Anal. Calcd. for $C_{11}H_9NO_2$: C, 70.58; H, 4.85; N, 7.48. Found: C, 70.60; H, 4.84; N, 7.40.

E-2,3-Dihydro-3-(2-oxo-2-phenylethylidene)-2-phenyl-1*H*-isoindol-1-one (**4e**).

A 0.70 g (2.2 mmoles) quantity of **2e** was dissolved in 25 ml of 75% aqueous acetone. To this solution was added 0.20 ml of concentrated sulfuric acid and the resulting mixture was heated under reflux for 7 hours. Upon cooling to room temperature, a solid began to form. Methylene chloride was added until the solid dissolved. Solid sodium bicarbonate was added until two liquid layers could be observed. The layers were separated, the aqueous layer extracted with methylene chloride, and the methylene chloride layers combined. After washing with 5% sodium bicarbonate and water, the organic phase was dried over calcium chloride and the solvent removed. The remaining solid was recrystallized from 95% ethanol to yield 0.61 g (87%) of light yellow crystals, mp 149-151°; ir (potassium bromide): 1736 (C=O), 1724, 1181, 766, 694 cm^{-1}; ^1H nmr (60 MHz, DMSO-d_6): δ 6.56 (s, 1H), 7.10-8.80 (m, 13H, ArH), 9.05 (m, 1H, ArH_a).

Anal. Calcd. for $C_{22}H_{15}NO_2$: C, 81.21; H, 4.65; N, 4.31. Found: C, 81.29; H, 4.54; N, 4.33.

E-2,3-Dihydro-3-(2-oxo-2-(4-bromophenyl)ethylidene)-2-phenyl-1*H*-isoindol-1-one (**4f**).

To a mixture of 10 ml of 70% aqueous acetone and 0.3 ml of concentrated sulfuric acid was added dropwise a solution of **2f** (2.00 g, 6.5 mmoles) in 20 ml of 70% aqueous acetone. The solution was stirred and heated under reflux for 4 hours. Upon cooling to room temperature, the mixture was filtered and the residue recrystallized from 95% ethanol to yield 1.80 g (90%) of **4f**, mp 208-209°; ir (potassium bromide): 1730, 1715, 1178, 1005, 810, 690 cm^{-1}; ^1H nmr (60 MHz, deuteriochloroform): δ 6.51 (s, 1H), 7.30-8.15 (m, 12H, ArH), 8.86 (m, 1H, ArH_a).

Anal. Calcd. for $C_{22}H_{14}BrNO_2$: C, 65.38; H, 3.46; N, 3.46. Found: C, 65.37; H, 3.33; N, 3.41.

E-2,3-Dihydro-3-(2-oxo-1-hexylidene)-2-phenyl-1*H*-isoindol-1-one (**4g**).

In a similar method to the synthesis of **4f**, reaction of **2g** (2.00 g, 5.0 mmoles) obtained 0.80 g (40%) of **4g**, mp 143-145°; ir (potassium bromide): 1729 (C=O), 1715, 1125, 1050, 692 cm^{-1}; ^1H nmr (250 MHz, deuteriochloroform): δ 0.90 (t, 3H, J = 7.3 Hz), 1.28-1.63 (m, 4H), 2.50 (t, 2H, J = 7.4 Hz), 5.88 (s, 1H), 7.31-7.96 (m, 8H, ArH), 9.10 (d, 1H, J = 7.7 Hz, ArH_a); ^{13}C nmr: δ 13.9, 22.2, 26.4, 44.7, 107.8, 123.4, 127.6, 128.8, 128.9, 129.6, 129.7, 131.7, 131.8, 133.7, 133.9, 148.1, 167.3, 199.6.

Anal. Calcd. for $C_{20}H_{19}NO_2$: C, 78.66; H, 6.27; N, 4.59. Found: C, 78.68; H, 6.23; N, 4.53.

E-2,3-Dihydro-3-(2-oxoethylidene)-2-phenyl-1*H*-isoindol-1-one (**4h**).

A 302 mg (1.2 mmoles) quantity of **2h** was dissolved in 12 ml of 95% ethanol with the aid of heat. To the solution was added 1.0 ml of water allowing the mixture to cool to room temperature. A 1.8 ml quantity of concentrated sulfuric acid was added dropwise with stirring. The mixture was stirred for an additional 1 hour, then allowed to stand at room temperature for 2 days resulting in a yellow precipitate. The mixture was placed in a freezer overnight and filtered. The residue was washed with cold 95% ethanol then water. Recrystallization from 40% aqueous ethanol yielded 72 mg (24%) of **4h**, mp 150-152.5° (lit [8] 150-153°); ir (potassium bromide): 1739 (C=O), 1655, 1622, 998, 701 cm^{-1}; ^1H nmr (60 MHz, deuteriochloroform): δ 5.80 (d, 1H, J = 7.0 Hz), 7.10-8.00 (m, 8H, ArH), 8.15 (m, 1H, ArH_a), 10.50 (d, 1H, J = 7.0 Hz).

Anal. Calcd. for $C_{16}H_{11}NO_2$: C, 77.10; H, 4.45; N, 5.62. Found: C, 76.80; H, 4.35; N, 5.53.

3-(2-Chloro-2-phenylethylidene)-2,3-dihydro-3-hydroxy-2-methyl-1*H*-isoindol-1-one (**5a**).

To 6.0 g (23 mmoles) of **2a** was added 130 ml of 5% aqueous hydrochloric acid and the mixture heated under reflux for 1 hour. The mixture was cooled to room temperature and enough methylene chloride was added to dissolve all of the suspended solid. The two layers were separated and the aqueous phase extracted with methylene chloride. The combined organic phase was dried over calcium chloride and the solvent removed. The resulting oil was crystallized from benzene yielding 2.59 g (38%) of a white solid, mp 147-149°; ir (potassium bromide): 3298 (OH), 1685 (C=O), 1105, 769 cm^{-1}; ^1H nmr (300 MHz, deuteriochloroform): δ 2.79 (s, 3H, CH_3), 4.00 (s, 1H, OH), 6.61 (s, 1H), 7.35-7.60 (m, 9H, ArH); ^{13}C nmr: δ 24.0, 89.4, 122.3, 122.6, 125.1, 126.4, 128.3, 129.1, 129.3, 131.0, 132.4, 135.8, 137.1, 146.8, 168.2.

Anal. Calcd. for $C_{17}H_{14}ClNO_2$: C, 68.12; H, 4.71; N, 4.67. Found: C, 68.14; H, 4.71; N, 4.67.

3-(2-Chloro-2-(4-bromophenyl)ethylidene)-2,3-dihydro-3-hydroxy-2-methyl-1*H*-isoindol-1-one (**5b**).

To a 1.40 g (4.1 mmoles) quantity of **2b** was added 30 ml of 5% aqueous hydrochloric acid and the mixture heated under reflux for 20 minutes. The mixture was cooled and extracted with methylene chloride and the organic phase washed with 10% sodium bicarbonate then water. The organic phase was dried over calcium chloride and the solvent removed. The resulting oil was crystallized from benzene yielding 0.82 g (53%) of a white solid, mp 165-167° dec; ir (potassium bromide): 3270 (OH), 1683 (C=O), 830 cm^{-1}; ^1H nmr (250 MHz, DMSO-d_6): δ 2.89 (s, 3H, CH_3), 3.39 (s, 1H, OH), 6.84 (s, 1H), 7.34-7.95 (m, 8H, ArH).

Anal. Calcd. for $C_{17}H_{13}BrClNO_2$: C, 53.92; H, 3.46; N, 3.70. Found: C, 55.07; H, 3.45; N, 3.60.

3-(2-Chloro-2-phenylethylidene)-2,3-dihydro-3-hydroxy-2-phenyl-1*H*-isoindol-1-one (**5e1**).

To a 0.88 g (2.7 mmoles) quantity of **2e** was added 35 ml of 10% aqueous hydrochloric acid and the mixture heated under reflux for 7.5 hours. During this time period a solid began to adhere to the sides of the flask and frequent, vigorous shaking was required to break the solid loose in order that it remain dispersed in the boiling solution. On cooling, the solid was collected by filtration and washed with 10% sodium bicarbonate and water. After recrystallization from benzene there was obtained 0.81 g (83%) of a white solid, mp 179-180° dec; ir (potassium bromide): 3265 (OH), 1693 (C=O), 1060, 755, 704 cm^{-1}; ^1H nmr (60 MHz, DMSO-d_6): δ 3.34 (s, 1H, OH), 6.65 (s, 1H), 7.00-8.80 (m, 14H, ArH).

Anal. Calcd. for $C_{22}H_{16}ClNO_2$: C, 73.03; H, 4.46; N, 3.87. Found: C, 73.01; H, 4.38; N, 3.92.

3-(2-Bromo-2-phenylethylidene)-2,3-dihydro-3-hydroxy-2-phenyl-1*H*-isoindol-1-one (**5e2**).

This compound was prepared in the same manner as **5e1**. From 1.0 g (3 mmoles) of **2e** and 35 ml of 10% aqueous hydro-

bromic acid was obtained 0.81 g (67%) of a white solid, mp 155-156° dec; ir (potassium bromide): 3265 (OH), 1685 (C=O), 1057, 755, 705 cm^{-1}; ^1H nmr (60 MHz, DMSO-d_6): δ 3.34 (s, 1H, OH), 6.85 (s, 1H), 7.00-8.80 (m, 14H, ArH); ^{13}C nmr: δ 90.9, 122.7, 122.8, 124.7, 124.8, 125.9, 127.3, 128.5, 128.6, 129.4, 129.6, 131.7, 132.2, 133.1, 136.8, 138.8, 147.0, 166.7.

Anal. Calcd. for $C_{22}H_{16}BrNO_2$: C, 65.04; H, 3.97; N, 3.45; Br, 19.67. Found: C, 64.96; H, 3.85; N, 3.44; Br, 19.56.

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