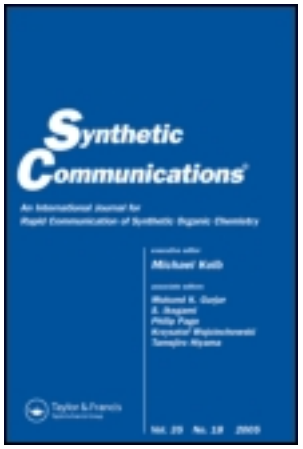

Synthetic Communications: An International Journal for Rapid Communication of Synthetic Organic Chemistry

Publication details, including instructions for authors and subscription information:
http://www.tandfonline.com/loi/lsyc20

Superacid-Promoted Hydroxyalkylation of 1,2-Indandiones

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Accepted author version posted online: 05 Mar 2013.Published online: 03 Jun 2013.

To cite this article: Adam F. Tracy, Matthew P. Abbott & Douglas A. Klumpp (2013): Superacid-Promoted Hydroxyalkylation of 1,2-Indandiones, Synthetic Communications: An International Journal for Rapid Communication of Synthetic Organic Chemistry, 43:16, 2171-2177

To link to this article: http://dx.doi.org/10.1080/00397911.2012.693239

Synthetic Communications®, 43: 2171–2177, 2013

ISSN: 0039-7911 print/1532-2432 online
DOI: 10.1080/00397911.2012.693239

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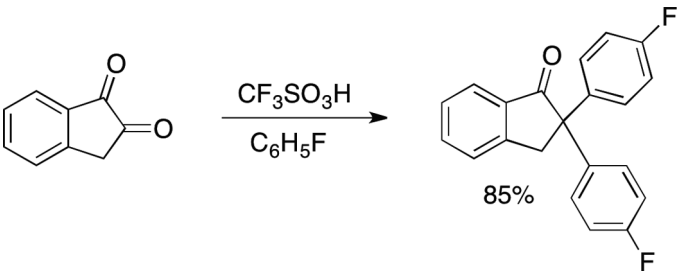
GRAPHICAL ABSTRACT



Abstract *1,2-Indandione reacts efficiently with arenes to give 2,2-diaryl-1-indanones by the hydroxyalkylation reaction. The Brønsted superacid CF_3SO_3H (triflic acid) is an effective catalyst for these condensation reactions. The requisite 1,2-indandiones were prepared from the 1-indanones.*

Keywords Condensation; Friedel–Crafts; indanone; superacid

INTRODUCTION

The hydroxyalkylation reaction is an acid-catalyzed condensation of aldehydes and ketones with arenes.[1] It is a common industrial reaction, as it is used to prepare feedstock chemicals, aromatic monomers, and condensation polymers. In 1995, Yamazaki and coworkers described a superacid-promoted hydroxyalkylation reaction of 2,3-butanedione (**1**) to give the condensation product **3** in excellent yield [Eq. (1)].[2] The diprotonated superelectrophile (**2**) was proposed as an intermediate in the reaction.[3] Several other recent articles have described superacid-promoted hydroxyalkylation reactions with 1,2-dicarbonyl compounds.[4] For example, products **5–7** are prepared from the respective condensation reactions of acenaphthenequinone, isatin, and parabanic acid, with benzene and triflic acid.

Received May 3, 2012.
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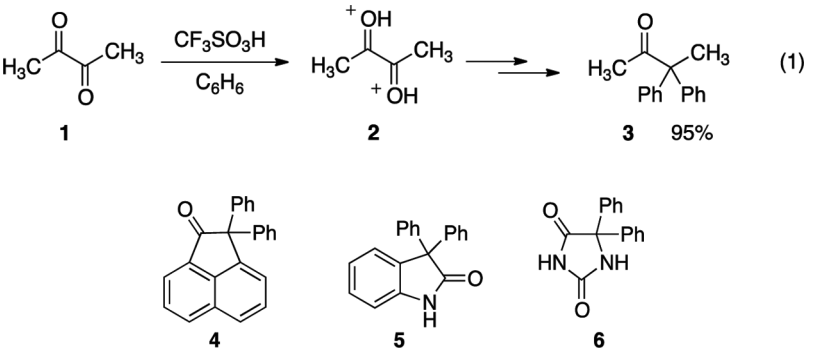
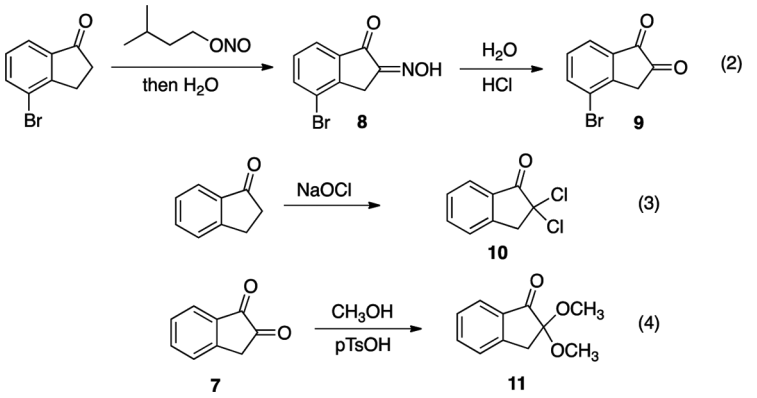


These types of superacid-promoted reactions have also recently been shown to be useful in polymerization chemistry.[5] In the following article, we describe superacid-promoted hydroxyalkylation reactions of 1,2-indandione and substituted derivatives. The conversions lead to 2,2-diaryl-1-indanone products and a mechanism is proposed involving a deprotonated superelectrophilic intermediate.

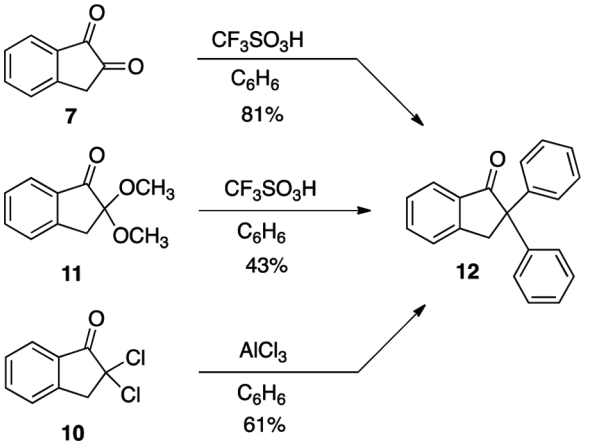
RESULTS AND DISCUSSION

Although 1,2-indandione (**7**) is available from commercial suppliers, substituted derivatives may be prepared from the 1-indanones.[6] Thus, 4-bromoindanone was converted to the oxime **8** by reaction with isoamylnitrite, and hydrolysis liberates the substituted 1,2-indandione **9** [Eq. (2)]. Similar reactions were done with 5-methoxyindanone and 4-methoxyindanone to prepare the respective 1,2-diketones. We also sought to compare the reactions of 2,2-dichloro-1-indanones (**10**) and 2,2-dimethoxy-1-indanones (**11**) as possible substrates in the synthesis.



The desired compounds were prepared by chlorination of the 1-indanone [Eq. (3)] and by acetalization of 1,2-indandione [Eq. (4)].[6,7]

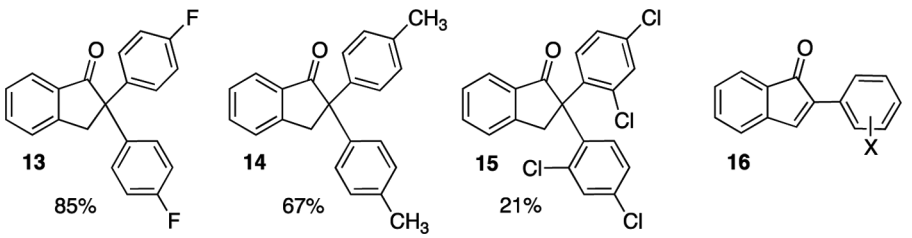
With 1,2-indandione, the condensation product (**12**) is formed in 81% yield by reaction at the 2-position (Scheme 1). The identity of **12** was verified by comparison with an authentic sample of **12** (prepared from a different approach[8]), and it was



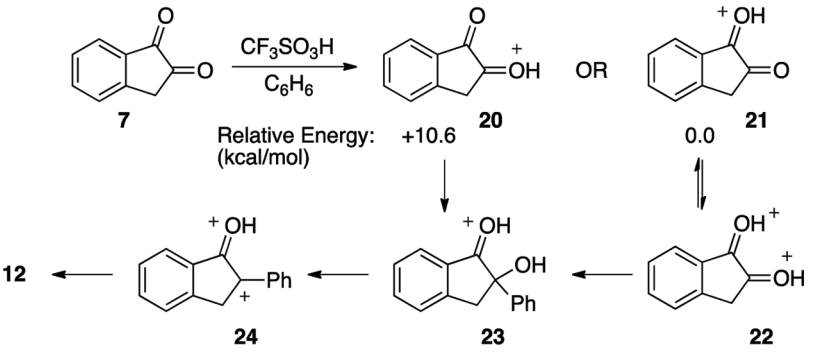
Scheme 1. Synthetic approaches to 2,2-diphenyl-1-indanone **(12)**.

clear that condensation occurs exclusively at the 2-carbonyl group. The regiochemistry of condensation was also confirmed by x-ray crystallographic analysis. During the course of our studies, we found that some 1,2-indandiones were prone to decompose during storage. This prompted us to explore the possibility of protecting the diketone as the dimethoxyacetal. Although the acetal substrates were easily prepared and indefinitely stable, the condensation reaction from **11** provided compound **12** in a disappointing 43% yield. As an alternative strategy from the dichloride, compound **10** gave product **12** in a fair yield of 61%.

Using substituted arenes, the condensation reactions provide the products in good yields. Thus, reaction of **7** with triflic acid and fluorobenzene or toluene gives the respective products (**13** and **14**) in 85% and 67% yields (Scheme 2). The electrophilic aromatic substitution occurs with excellent regioselectivity, as gas chromatography (GC) and NMR analysis shows at least a 20:1 *para*/*ortho* ratio. This is a trend previously observed with other 1,2-dicarbonyl systems—very good regioselectivity is seen in the condensation reactions with alkylbenzenes and monohalogenated benzenes.[4] We also obtained the condensation product from 1,3-dichlorobenzene (**15**), although the yield is considerably lower. In some cases, minor amounts of the intermediate product inden-1-ones (i.e., **16**) could also be detected by GCMS analysis. Finally, substituted 1,2-indandiones were also prepared and reacted with

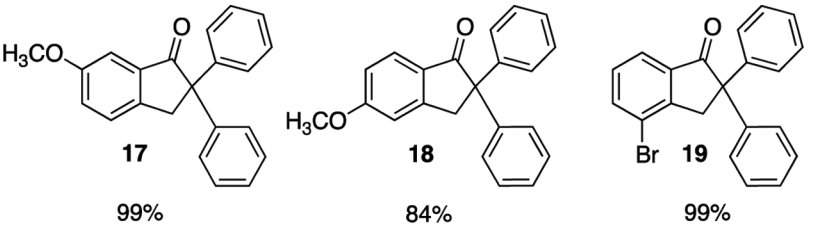


Scheme 2. Products **(13–15)** from the reaction of 1,2-indandione.



Scheme 3. Proposed reaction mechanism with DFT calculated relative energies of monocations **20** and **21**.

CF_3SO_3H and benzene. 6-Methoxy and 5-methoxy-substituted1,2-indandiones provide condensation products **17** and **18**, respectively. Similarly, 4-bromo-1,2-indandione gives the condensation product **19** in excellent yield from CF_3SO_3H.



Hydroxyalkylation reactions generally occur via carboxonium intermediates by protonation of aldehyde or ketone carbonyl groups.[1] In the case of 1,2-indandione (**7**), initial protonation could occur at either the 1- or 2-carbonyl group (Scheme 3). Density functional theory (DFT) calculations [B3LYP 6-311 G (d,p) level] indicate that protonation at the 1-carbonyl group is significantly favored.[9] However, condensation occurs at the 2-carbonyl. Benzene (and other arenes) are weak nucleophiles, and consequently, direct attack of benzene at the 2-carbonyl group of **21** is not considered a likely reaction step. Two plausible mechanisms can be suggested. A second protonation of **21** leads to superelectrophile **22** and reaction with benzene then occurs to provide adduct **23**. This mechanistic path could also involve only a partially diprotonated species where the 2-carbonyl group is forming a strong hydrogen bond to the superacid. Alternatively, reaction through the monoprotonated species (**20**) could directly give **23** and further reaction steps then lead to product **12**.

CONCLUSION

Using the Brønsted superacid CF_3SO_3H, 1,2-indandiones form condensation products with benzene and substituted arenes. The chemistry provides easy access

Table 1. Analytical data for condensation products **13–15** and **17–19**

No.	Mp (°C)	^{1}H NMR	^{13}C NMR	Mass spectrum (low res.; EI)	Mass spectrum (high res.; EI)
13	143–145	$CDCl_3$, δ: 3.91 (s, 2H), 6.98 (m, 4H), 7.25–7.31 (m, 4H), 7.44–7.47 (m, 1H), 7.56 (d, 1H, $J = 7.3$ Hz), 7.68–7.71 (m, 1H), 7.84 (d, 1H, $J = 7.6$ Hz)	$CDCl_3$, δ: 44.8, 61.5, 115.3 (d, $J_{C\text{-}F} =$ 21.2 Hz), 125.3, 125.9, 128.2, 129.7 (d, $J_{C\text{-}F} =$ 7.9 Hz), 135.4, 135.6, 139.1, 151.6, 161.7 (d, $J_{C\text{-}F} = 245$ Hz), 204.9	320 (M+), 270, 225, 196, 190	Calcd. for $C_{21}H_{14}OF_2$, 320.10128; found 320.10207
14	108–111	$CDCl_3$, δ: 2.34 (s, 6H), 3.92 (s, 2H), 7.11 (d, 4H, $J = 8.2$ Hz), 7.20 (d, 4H, $J = 8.2$ Hz), 7.41–7.44 (m, 1H), 7.53 (d, 1H, $J = 7.6$ Hz), 7.65–7.68 (m, 1H), 7.83 (d, 1H, $J = 7.6$ Hz)	$CDCl_3$, δ: 20.9, 44.9, 62.2, 125.2, 125.8, 127.8, 128.0, 129.1, 135.2, 135.8, 136.3, 140.6, 152.1, 205.6	312 (M+), 269, 253, 220, 178	Calcd. for $C_{23}H_{20}O$, 312.15142; found 312.15193
15	194–196	$CDCl_3$, δ: 4.21 (s, 2H), 7.08 (d, 2H, $J = 8.4$ Hz), 7.18 (dd, 2H, $J = 8.6$, 2.2 Hz), 7.45–7.48 (m, 6H), 7.66–7.69 (m, 1H), 7.92 (d, 1H, $J = 7.4$ Hz)	$CDCl_3$, δ: 43.8, 62.9, 124.5, 126.2, 127.1, 128.0, 131.4, 131.8, 134.1, 134.9, 135.8, 136.3, 137.1, 152.0, 204.8	424/422/420 (M+), 387/385, 286, 252/250, 143, 125	Calcd. for $C_{21}H_{12}OCl_4$, 419.96422; found 419.96345
17	151–154	$CDCl_3$, 300 MHz, δ: 3.86 (s, 3H), 3.87 (s, 2H), 7.25–7.33 (m, 12H), 7.44 (d, 1H, $J = 9.3$).	$CDCl_3$, 300 MHz, δ: 44.3, 55.6, 63.6, 106.2, 124.8, 126.6, 126.7, 128.2, 129.4, 136.9, 143.6, 144.9, 159.8, 205.3	314 (M+), 253, 237, 223, 165.	Calcd. for $C_{22}H_{18}O_2$, 314.13068; found 314.13160
18	135–137	$CDCl_3$, 300 MHz, δ: 3.86 (s, 3H), 3.87 (s, 2H), 7.25–7.33 (m, 12H), 7.439 (d, 1H, $J = 9.3$ Hz)	$CDCl_3$, 300 MHz, δ: 44.9, 55.7, 62.9, 109.11, 115.9, 126.7, 126.9, 128.2, 128.4, 128.9, 143.9, 155.0, 165.9, 203.5	314 (M+), 285, 237, 223, 165	Calcd. for $C_{22}H_{18}O_2$, 314.13068; found 314.13000
19	114–117	$CDCl_3$, 300 MHz, δ: 3.90 (s, 1H), 7.24–7.38 (m, 11H), 7.79 (d, 1H, $J = 7.5$ Hz), 7.84 (dd, 1H, $J = 7.8$, 8.7 Hz).	$CDCl_3$, 300 MHz, δ: 45.6, 62.9, 121.4, 124.0, 127.0, 128.6, 129.8, 137.6, 138.0, 142.9, 151.7, 204.6	364/362 (M+), 284, 265, 252, 178	Calcd. for $C_{21}H_{15}OBr$, 362.03063; found 362.03151

to aryl-functionalized 1-indanones. Moreover, the condensation occurs with good positional selectivity in reactions with substituted benzenes.

EXPERIMENTAL

Solvents and reagents were purchased from commercial suppliers and used as received. The triflic acid was distilled from an Ar atmosphere prior to its use.

Compounds were purified using standard flash chromatography–grade silica gel. Low-resolution mass spectra (LRMS) were obtained from a commercial GC instrument equipped with a mass selective detector. High-resolution mass spectra (HRMS) were obtained by an external analytical laboratory. All NMR spectra were obtained from a Bruker Avance DRX-500 instrument.

Preparation of Condensation Products 12–15 and 17–19

The 1,2-Indandione (1 mmol) is dissolved in CH_2Cl_2 (5 mL), and the aromatic compound (1 mL) is added. The vessel is purged with Ar and then triflic acid (1 mL, 11 mmol) is slowly added to the solution with stirring. After 3 h, the mixture is poured over ice. The resulting mixture is extracted twice with chloroform, and the organic extracts are combined. The organic solution is washed with water ($2\times$) and then brine ($2\times$) and dried over anhydrous sodium sulfate. Filtration and removal of the solvent provides the crude condensation product. In some cases, the resulting product is greater than 95% pure (GC analysis) and requires no further purification. However, mixtures were purified by flash chromatography (hexanes–ether).

Alternative Condensation Procedure for 12

2,2-Dichloro-1-indanone (0.15 g, 1 mmol) is dissolved in benzene (5 mL), and anhydrous aluminum chloride (0.67 g, 5 mmol) is added. The solution is refluxed under Ar for 4 h and then poured over ice. The resulting mixture is extracted twice with chloroform, and the organic extracts are combined. The organic solution is washed with water ($2\times$) and then brine ($2\times$), and dried over anhydrous sodium sulfate. Filtration and removal of the solvent provides the crude condensation product. Compound **12** is then isolated by flash chromatography (hexanes–ether).

ACKNOWLEDGMENT

Financial support from the NIH National Institute of General Medical Sciences (GM085736-01A1) is gratefully acknowledged.

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