Synthesis of 1,2-Diacylbenzenes from *o*-Hydroxyaryl Ketone Acylhydrazones Using [(Diacetoxy)iodo]benzene

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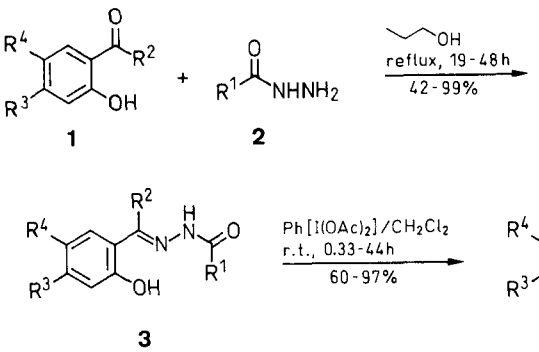
2'-Hydroxyacetophenone and 2'-hydroxypropiophenone acylhydrazones **3** are oxidized to 1,2-diacylbenzenes **4** using [(diacetoxy)-iodo]benzene in dichloromethane at room temperature in a synthetically useful and high yield reaction.

[(Diacetoxy)iodo]benzene,[1] has been a useful reagent in organic synthesis.[2] In our laboratories, it has been employed to prepare β-acetoxy ketones,[3] α-hydroxy dimethylacetals,[4] azoxy compounds,[5] diimide,[6] 1,2-bis(ethoxycarbonyl)hydrazine,[7] and 1,2,4-triazoline-3,5-diones.[7] The reagent has had limited use in the oxidation of hydrazones. In the presence of [(diacetoxy)iodo]benzene, benzophenone hydrazone was reacted with carboxylic acids to make diphenylmethyl esters[8] and *tert*-butoxycarbonylhydrazones of aromatic aldehydes were oxidized to 1,3,4-oxadiazolin-2-ones.[9] We have now successfully synthesized 1,2-diacylbenzenes from *o*-hydroxyaryl ketone acylhydrazones using [(diacetoxy)iodo]benzene.

1,2-Diacylbenzenes have been of interest primarily as fluorescence reagents for both qualitative and quantitative high-sensitivity analyses for amines and amino acids.[10] Diacetylbenzene, in particular, was used in a fluorometric assay for biotinase using biocytin because of it's ability to react selectively with lysine.[11] 1,2-Diacylbenzenes have also proven to be useful precursors to anthraquinone derivatives,[12] isoquinolines,[13] isoindoles,[14] imidazo[2,1-*a*]isoindoles,[15] *N*-arylphthalimidines,[16] 3-phenylphthalides,[17] hydroxyphenylindanones,[17] and 1,3-diphenyl-2-nitroindene.[18] The synthesis of 1,2-diacylbenzenes is commonly accomplished through oxidation of benzhydrols with selenium dioxide[15] or 3-alkyl phthalides with potassium permanganate, air or ceric ammonium nitrate.[19] In isolated cases, they have been prepared by oxidation of *o*-ethylacetophenone,[20] indanes,[21] benzofurans,[22] 1,4-dialkylnaphthalenes,[23] *o*-alkoxyacetophenones,[24] and indene derivatives[25] or by acylating benzene with *o*-acetylbenzoyl chloride.[26] Recently, a more generalized and simple route to 1,2-diacylbenzenes employing lead tetraacetate oxidation of *o*-hydroxyaryl ketone acylhydrazones was reported.[27] This methodology was extended to the preparation of 1,2,3-triacylbenzenes[28] and *o*-acylaryl esters[29] from acyl hydrazones of 2,6-diacylcresols and (ethoxycarbonyl)hydrazones of *o*-hydroxyaryl ketones, respectively. Since [(diacetoxy)iodo]benzene



1 **2** **3** **4**

1–4	R^1	R^2	R^3	R^4
a	Ph	Me	H	H
b	Ph	Me	OMe	H
c	Ph	Me	H	Me
d	Me	Me	H	H
e	C_6H_4OMe-4	Me	H	H
f	C_6H_4Me-4	Me	H	H
g	$C_6H_4NO_2$-4	Me	H	H
h	2-furyl	Me	H	H
i	2-thienyl	Me	H	H
j	Ph	Et	H	H
k	Me	H	H	H

Scheme 1

Table. 1,2-Diacylbenzenes **4a—k** Prepared

Product	Yield[a] (%)	Time (h)	mp (°C)[b]	Molecular Formula[c] or Lit. mp (°C)	IR[d] υ(cm^{-1})	^{1}H NMR[e] (400 MHz) δ, J (Hz)	^{13}C NMR[e] (100 MHz) δ	MS[f] m/z
4a	90	3	95–97	96–97[33]	1676	2,53 (s, 3 H, CH_3), 7.41–7.45 (m, 3 H, 7.53–7.64 (m, 4 H), 7.74–7.76 (m, 1 H), 7.88–7.90 (m, 1 H)	27.32, 128.20, 128.34, 129.12 129.18, 129.63, 132.00, 132.81, 137.17, 137.66, 140.80, 197.54, 198.34	224 (M+,CI+), 209, 147, 77
4b	94	7	106–108	oil[27]	1665	2.37 (s, 3 H, CH_3), 3.78 (s, 3 H, OCH_3), 6.76 (d, 1 H, J = 2.6), 6.94 (dd, 1 H, J = 2.6, J = 8.7), 7.27–7.43 (m, 3 H), 7.62–7.67 (m, 2 H), 7.80 (d, 1 H, J = 8.7)	27.00, 56.17, 114.11, 114.61, 128.81, 129.39, 129,79, 132.49, 133.21, 137.56, 144.23, 163.39, 196.54, 197.75	225 (M+,CI+), 239, 77
4c	71	3	oil	118–120[27]	1682	2.37 (s, 6 H), 7.17–7.32 (m, 4 H), 7.37–7.41 (m, 1 H), 7.53 (s, 1 H), 7.60–7.65 (m, 1 H)	21.61, 27.95, 128.66, 128.82, 129.56, 130.00, 132.70, 133.07, 137.73, 138.01, 138.71, 140.53, 197.96, 199.38	239 (M+,CI$^+$), 223, 161, 105
4d	70	44	38–39	39–40[27]	1682	2.51 (s, 6 H), 7.53 (s, 4 H)	28.72, 128.01, 131.35, 139.65, 200.67,	162 (M,EI), 147, 91
4e	60	3	108–109	$C_{16}H_{14}O_3$ (254.3)	1686 1651	21.51 (s, 3 H, CH_3), 3.84 (s, 3 H, OCH_3), 6.86–6.93 (m, 2 H), 7.35–7.40 (m, 1 H), 7.52–7.64 (m, 2 H), 7.68–7.76 (m, 2 H), 7.84–7.89 (m, 1 H)	27.86, 55.71, 113.99, 128.40, 129.46, 129.79, 130.49, 131.88, 132.20, 137.92, 141.23, 163.76, 196.64, 198.90	255 (M+,CI+), 239, 147
4f	97	2	72–73	$C_{16}H_{14}O_2$ (238.3)	1684	2.39 (s, 3 H, CH_3), 2.50 (s, 1 H, CH_3), 7.20 (d, 1 H, J = 0.5), 7.22 (d, 1 H, J = 0.6), 7.57–7.65 (m, 4 H), 7.85–7.88 (m, 1 H)	21.91, 27.76, 128.48, 129.42, 129.44, 129.69, 129.85, 132.28, 134.98, 137.92, 141.25, 144.01, 197.64, 198.79	239 (M+,CI+), 223, 147, 119
4g	83	27	150–152	151–153[27]	1680	2.48 (s, 3 H, CH_3), 7.34–7.36 (m, 1 H, 7.58–7.67 (m, 2 H), 7.78 (d, 1 H, J = 2.0), 7.79 (d, 1 H, J = 2.0), 7.89–7.91 (m, 1 H), 8.17–8.19 (m, 2 H)	27.02, 123.88, 128.23, 129.91, 130.05, 130.57, 133.24, 137.00, 140.31, 142.27, 150.28, 196.15, 198.14	269 (M,EI), 254, 208, 180, 104, 76
4h	80	1/3	110–111	$C_{13}H_{10}O_3$ (214.2)	1678 1647	2.55 (s, 3 H, CH_3), 6.52–6.53 (m, 1 H), 7.01–7.02 (m, 1 H), 7.52–7.54 (m, 1 H), 7.58–7.64 (m, 3 H), 7.82–7.84 (m, 1 H)	27.73, 112.56, 119.10, 128.80, 129.05, 130.57, 132.06, 138.76, 139.28, 147.02, 152.95, 184.97, 199.29	215 (M+,CI+), 199, 197, 186, 185, 147
4i	77	1	92–94	93–94[34]	1686	2.54 (s, 3 H, CH_3), 7.06–7.08 (m, 1 H), 7.30–7.32 (m, 1 H), 7.50–7.52 (m, 1 H), 7.59–7.62 (m, 2 H), 7.67–7.69 (m, 1 H), 7.84–7.86 (m, 1 H)	28.03, 128.84, 128.50, 129.42, 130.34, 132.10, 134.32, 134.47, 138.12, 140.27, 144.69, 189.93, 198.96	231 (M+,CI+), 215, 147, 111
4j[g]	95	3	67–69		1673	1.01 (t, 3 H, J = 7.23), 2.83 (q, 2 H, J = 7.22), 7.32–7.36 (m, 3 H), 7.44–7.53 (m, 3 H), 7.66–7.68 (m, 2 H), 7.76–7.78	7.88, 32.93, 128.24, 128.31, 128.54, 129.22, 129.65, 131.50, 132.71, 137.11, 137.99, 140.48, 197.48, 200.23	239 (M+,CI+), 209, 161, 105
4k	71	1/2	39–41	41–42[19]	1626	2.65 (s, 3 H, CH_3), 6.97–7.01 (m, 1 H), 7.11–7.13 (m, 1 H), 7.41–7.45 (m, 1 H), 7.71–7.74 (m, 1 H), 10.12 (s, 1 H)	11.16, 108.41, 117.77, 120.05, 126.63, 133.71, 157.73, 162.63, 164.80	(EI), 147, 121, 105

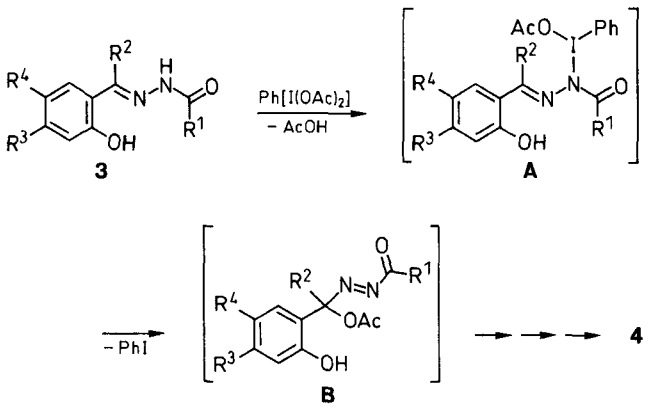
[a] Yield of isolated products.
[b] Melting points were determined on a Thomas-Hoover capillary melting point apparatus and are uncorrected.
[c] Satisfactory microanalysis for **4f** (C ± 0.48, H ± 0.03) and **4e, 4h** were obtained: C ± 0.22, H ± 0.03.
[d] All spectra were measured using an IBM FTIR/32 spectrophotometer (System 9000).
[e] All spectra were measured in $CDCl_3$ (TMS as internal standard) (WP-Bruker).
[f] All spectra were measured using a Finnigan MAT 90 spectrometer.
[g] Physical and spectral properties were not reported.[17]

reactivity is known to bear close analogy of that of lead tetraacetate[30] and is less hazardous, toxic, and costly than lead(IV) compounds, a new synthetic approach would be desirable. We now report a new, high yield route (Scheme 1), to 1,2-diacylbenzenes **4** using [(diacetoxy)iodo]benzene under mild conditions.

Commercially available *o*-acylphenols **1** were reacted with benzo-, aceto- or heterocyclic carbohydrazides **2**, obtained either commercially or from their corresponding acids,[31] to prepare the hydrazones **3**.[32] Reaction of hydrazones **3a–k** with [(diacetoxy)iodo]benzene in dichloromethane at room temperature yielded the corresponding 1,2-diacylbenzenes **4a–k** in 60–97% yield. The physical characteristics and spectroscopic data for the 1,2-diacylbenzenes **4a–k** are listed in the Table. ^{1}H NMR spectra of compounds **4a–i** and **4k** show a singlet at δ = 2.37–2.65 for the acetyl group. The triplet at δ = 1.01 and quartet at δ = 2.83 with J = 7.23 ± 0.01 Hz in the ^{1}H NMR spectrum of 2-propanoylbenzophenone (**4j**) result from the propanoyl group. ^{13}C NMR spectra of 1,2-diacylbenzenes **4a–c, 4e–g**, and **4j** show two characteristic signals at δ = 196.15–200.23 for two carbonyl groups.

The spectrum for diacetylbenzene **4d** contains a single carbonyl peak at δ = 200.67. The heterocyclic 1,2-diacylbenzene derivatives **4h** and **4i** have characteristic carbonyl resonances at δ = 184.97 and 189.93 respectively, due to the electron donating heteroaromatic groups as well as peaks at δ = 199.29 and 198.96 for their respective acetyl groups. The carbonyl signals for 2-acetylbenzaldehyde (**4k**) were at δ = 162.63 and 164.80.

A reasonable pathway for the reaction could begin with a ligand exchange by the *o*-hydroxy ketone acylhydrazone **3** with an acetate group on [(diacetoxy)iodo]benzene to produce intermediate **A** (Scheme 2). After reductive elimination of iodobenzene accompanied by addition of the acetate group to the hydrazone carbon yielding intermediate **B**, the reaction could follow the same route as that proposed by Katritzky[32] for the oxidation with lead tetraacetate.



Scheme 2

Compounds with electron-donating substituents at R^1 (**4f, 4h, 4i**) react faster in comparison with compounds with either less electron-donating or electron-withdrawing substituents at R^1 (**4d, 4g**). The reaction also shows a large rate dependence on substituents at R^2. With R^2 = H (**4k**) the reaction proceeded to completion in 30 minutes whereas with R^2 = Me (**4d**) the reaction took 44 hours. The methyl group at R^2 may sterically hinder the approach of the acetate anion at the hydrazone carbon. This effect could be balanced by the electron-donating ability of substituents at R^1, R^2, and R^3 to determine the overall rate of the reaction. In the case of **4b**, an electron-withdrawing substituent at R^3 decelerated the reaction (7 hours) with respect to **4a** (3 hours).

This new method for the synthesis of 1,2-diacylbenzenes from *o*-hydroxyaryl ketone acylhydrazones is significant because a wide variety of functionalized 1,2-diacylbenzenes can be obtained from inexpensive and easily prepared starting materials in high yields under mild reaction conditions. The reagent for the transformation, [(diacetoxy)iodo]benzene, is not hazardous, nontoxic, inexpensive and readily available. The reactions interesting mechanistically[32] and 1,2-diacylbenzenes are useful compounds for the synthesis of new fluorogenic reagents and heterocycles.

In conclusion, we have presented a simple method of wide scope for the ready preparation of 1,2-diacylbenzenes in high yields.

2′-Hydroxyacetophenone and 2′-Hydroxypropiophenone Acylhydrazones 3a–k; General Procedure:

The *o*-acylphenol **1** (17.0 mmol) was added to a stirred solution of hydrazide **2** (17.0 mmol) in 1-propanol (125 mL) and the solution was heated to reflux for 19–48 h. The solution was filtered to afford the *o*-hydroxyaryl ketone acylhydrazone **3** which was used without further purification.

1,2-Diacylbenzenes 4a–k; General Procedure:

[(Diacetoxy)iodo]benzene (0.64 g, 2.0 mmol) was added to a stirred solution of the *o*-hydroxy aryl ketone acylhydrazone **3** (1.0 mmol) in CH_2Cl_2 (10 mL). The reaction was allowed to proceed at r.t. until the [(diacetoxy)iodo]benzene had completely dissolved to form a clear solution. It was also monitored by TLC. The mixture was then partitioned between H_2O (10 mL) and CH_2Cl_2 (20 mL). The aqueous layer was extracted with CH_2Cl_2 (3 × 5 mL). The combined extracts were washed with sat. aq $NaHCO_3$ (3 × 5 mL), dried ($MgSO_4$), filtered, and concentrated in vacuo to give the crude 1,2-diacylbenzene **4**. The pure product **4** was isolated by column chromatography on silica gel using EtOAc/hexanes (40:60) as eluent. All compounds were fully characterized on the basis of IR, ^{1}H NMR, ^{13}C NMR, and MS spectroscopy and by elemental analysis or comparison of physical data with literature values.

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