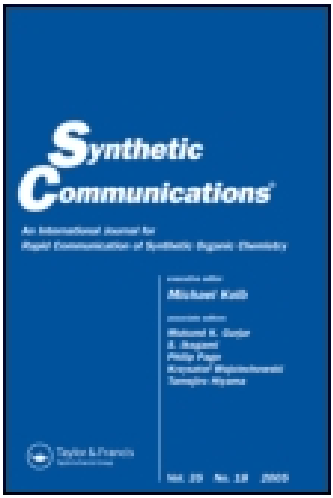

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Polystyrene-Supported Iodobenzene Diacetate (PSIBD)-Mediated Synthesis of 1,2-Diacylbenzenes from 2-Hydroxyaryl Aldehyde/Ketone Acylhydrazones

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Polystyrene-Supported Iodobenzene Diacetate (PSIBD)–Mediated Synthesis of 1,2-Diacylbenzenes from 2-Hydroxyaryl Aldehyde/Ketone Acylhydrazones

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Abstract: Synthesis of some new 1,2-diacylbenzenes is described by the oxidation of 2-hydroxyaryl aldehyde/ketone acylhydrazones using polystyrene-supported iodobenzene diacetate (PSIBD) in good yield.

Keywords: 1,2-Diacylbenzenes, 2-hydroxyaryl aldehyde/ketone acylhydrazones, polystyrene-supported iodobenzene diacetate (PSIBD)

INTRODUCTION

1,2-Diacylbenzenes are important molecules because of their potential to serve as starting materials in organic synthesis.[1] The presence of two carbonyl groups *ortho* to each other at the benzene ring allows the formation of novel heterocycles as well as other nonheterocyclic aromatic compounds. For example, 1,2-diacylbenzenes have proven to be useful precursors to isoquinolines,[2] isoindoles,[3] imidazo[2,1-*a*]isoindoles,[4] N-arylphthalimidines,[5,6] and 1,3-diphenyl-2-nitroindene.[7] 1,2-Diacylbenzenes have been of interest as fluorescence reagents for high-sensitivity detection and quantitative measurements of biological compounds bearing a primary amino group, such as amino acids and peptides.[8] They have

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also been used for a highly specific thin-layer chromatography (TLC)-fluorescent detection of oxazepam and lorazepam.[9] Diacetylbenzene, in particular, was used in a fluorometric assay for biotinase because of its ability to react selectively with lysine.[10]

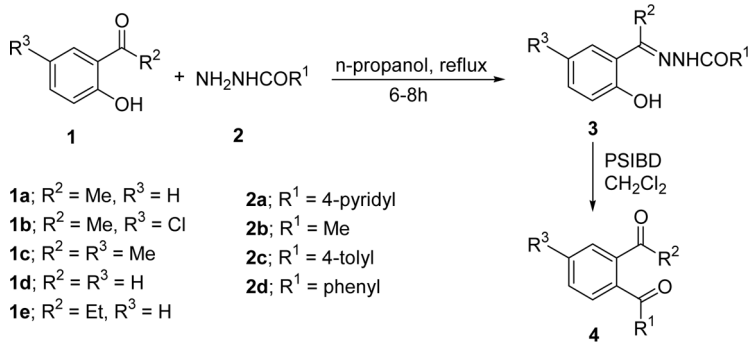
There are several methods for the preparation of 1,2-diacylbenzenes such as oxidation of benzhydrols with selenium dioxide[4] and *o*-hydroxyaryl ketone acylhydrazones with lead tetraacetate[11] or hypervalent iodine reagents.[12,13] Synthesis of 1,2-diacylbenzenes from 2-hydroxyaryl aldehyde/ketone acylhydrazones is significant, because a wide variety of functionalized 1,2-diacylbenzenes can be obtained from inexpensive and easily prepared starting materials in high yield under mild reaction conditions. The polystyrene-supported reagent to be utilized for the transformation of 2-hydroxyaryl aldehyde/ketone acylhydrazones to 1,2-diacylbenzenes is nontoxic, inexpensive, and readily available. Moreover, the by-product iodopolystyrene, generated in situ, can be easily recycled.

Recently hydrazone derivatives have been demonstrated to possess various types of biological activities (antimicrobial, anticonvulsant, antidepressant, analgesic, anti-inflammatory, antimalarial, antiviral, antiplatelet, antitubercular and antitumoral activities).[14] Hydrazones possessing an azomethine proton (–NHN=CH–) constitute an important class of compounds for new drug development.[14]

RESULTS AND DISCUSSION

Commercially available 2-hydroxyaryl aldehyde/ketones (**1**) and isonicotinic acid hydrazide, benzoic acid hydrazide, 4-toluic acid hydrazide, or acetic acid hydrazide (**2**) were refluxed together in n-propanol to prepare the 2-hydroxyaryl aldehyde/ketone acylhydrazones (**3**), which were used without further purification. In a typical oxidation procedure, 2-hydroxyaryl aldehyde/ketone acylhydrazones (**3**) in dichloromethane was stirred with a slight excess of polystyrene-supported iodobenzene diacetate (PSIBD) at 40°C (Scheme 1). A mild effervescence (evolution of N_2) was generally observed upon addition of oxidant. The products were purified by percolation through a column of silicagel using hexane–ethyl acetate as eluent.

Hydrazones can exist as four isomers because of the geometric isomerism with respect to the imino group (*E*, *Z* isomers) and rotational isomerism as a result of hindered rotation about the amide linkage (*anti-syn* conformers). X-ray spectroscopic analysis revealed that in the solid state acyl and aroylhydrazones form only *E*-isomers.[15] It was also demonstrated that in the solid state acylhydrazones of benzaldehyde



3,4	R^1	R^2	R^3	3,4	R^1	R^2	R^3
a	4-pyridyl	Me	H	**f**	Me	Me	Cl
b	4-pyridyl	Me	Me	**g**	Me	Et	H
c	4-pyridyl	H	H	**h**	4-tolyl	H	H
d	4-pyridyl	Et	H	**i**	4-tolyl	Me	Cl
e	4-pyridyl	Me	Cl	**j**	4-tolyl	Et	H
				k	Ph	Me	Cl

Scheme 1. Synthesis of the **3a–k** and **4a–k**.

form *syn*-conformers that aggregate to centrosymmetric dimers because of their intermolecular hydrogen bonding. Only *syn-E* isomers possess C=O and N–N groups in a *trans*-conformation that permits the formation of dimers. It was also shown that aroylhydrazones form only the *anti*-conformer, both in the solid state[15] and in solution.[16]

The hydrazones in the present study were thoroughly analyzed by NMR, which showed that most of the hydrazones (**3a–e** and **3h–k**) form only the *E*-isomer, with the *anti*-conformer in solution (DMSO-d_6). Table 1 revealed that in hydrazones **3a–e** and **3h–k** the OH and NH proton resonated at δ 12.09–13.26 and 10.20–11.40, respectively, indicating thereby the existence of intramolecular hydrogen bonding having the *anti-E* conformation. On the other hand, the hydrazones **3f, g** also form an *E*-isomer, but with both *anti-* and *syn*-conformers (Fig. 1). Analysis of ^{1}H NMR spectrum of **3g** demonstrated that OH is represented by two signals at δ 12.13 and 13.28. The possible reason for such splitting is participation of the part of the 2-hydroxy group proton in an intramolecular hydrogen bond with the nitrogen atom of the imino group. There were also two signals from the NH proton at δ 9.97 and 10.31. The percentage of *anti*-conformer, calculated from the intensities of the corresponding signals, possessing a hydroxy group that form intramolecular hydrogen

Table 1. ^{1}H NMR spectra of 2-hydroxyaryl aldehyde/ketone acylhydrazones (**3**)

Compound	C_3-H	C_4-H	C_6-H	R^1	R^2	R^3	NH	OH
3a	6.96 (d, $J = 8.0$ Hz)	7.27–7.32 (m)	7.52 (dd, $J = 7.2$, 1.2 Hz)	7.81 (d, 2H, $J = 4.7$ Hz, $C_{3'}$-H, $C_{5'}$-H), 8.76 (d, 2H, $J = 4.7$ Hz, $C_{2'}$-H, $C_{6'}$-H)	2.48 (s, 3H, CH_3)	6.87–6.91 (m, 1H)	11.27	13.12
b	6.67 (d, $J = 8.5$ Hz)	6.96 (d, $J = 8.5$ Hz)	7.24 (s)	7.75 (d, 2H, $J = 5.5$ Hz, $C_{3'}$-H, $C_{5'}$-H), 8.76 (d, 2H, $J = 5.5$ Hz, $C_{2'}$-H, $C_{6'}$-H)	2.43 (s, 3H, CH_3)	2.51 (s, 3H, CH_3)	11.24	13.11
c	6.89–6.98 (m)	7.28–7.32 (m)	7.28–7.32 (m)	7.85 (dd, 2H, $J = 4.4$, 1.5 Hz, $C_{3'}$-H, $C_{5'}$-H) 8.78 (dd, 2H, $J = 4.5$, 1.4 Hz, $C_{2'}$-H, $C_{6'}$-H)	8.57 (s, 1H)	6.89–6.98 (m, 1H)	11.39	12.09
d	6.95 (d, $J = 8.2$ Hz)	7.27–7.31 (m)	7.54 (dd, $J = 8.0$, 0.9 Hz)	7.79 (d, 2H, $J = 5.8$ Hz, $C_{3'}$-H, $C_{5'}$-H), 8.77 (d, 2H, $J = 5.8$ Hz, $C_{2'}$-H, $C_{6'}$-H)	1.24 (t, 3H, $J = 7.6$ Hz, CH_3), 3.00 (q, 2H, $J = 7.6$ Hz, CH_2)	6.87–6.91 (m, 1H)	11.39	13.27
e	6.93 (d, $J = 8.7$ Hz)	7.23 (d, $J = 8.7$ Hz)	7.47 (s)	7.81 (d, 2H, $J = 4.7$ Hz, $C_{3'}$-H, $C_{5'}$-H), 8.76 (brs, 2H, $C_{2'}$-H, $C_{6'}$-H)	2.47 (s, 3H, CH_3)	—	11.37	13.14
f (anti)	6.89–6.91 (m)	7.17–7.23 (m)	7.42 (d, $J = 2.4$ H-Hz)	2.16 (s, 3H, CH_3)	2.61 (s, 3H, CH_3)	—	10.45	13.15
f (syn)	6.97 (d, $J = 8.8$ Hz)	7.33 (dd, $J = 8.8$,	7.60 (d, $J = 2.5$ H-	2.33 (s, 3H, CH_3)	2.55 (s, 3H, CH_3)	—	10.15	13.02

		2.4 Hz)	Hz)					
g (anti)	6.96 (dd, $J = 8.0$, 0.7 Hz)	7.22–7.30 (m)	7.42–7.49 (m)	2.17 (s, 3H, CH_3)	1.19–1.24 (m, 3H, CH_3), 2.80–2.87 (m, 2H, CH_2)	6.85–6.87 (m, 1H)	10.31	13.28
g (syn)	6.96 (dd, $J = 8.0$, 0.7 Hz)	7.22–7.30 (m)	7.42–7.49 (m)	2.34 (s, 3H, CH_3)	1.19–1.24 (m, 3H, CH_3), 2.80–2.87 (m, 2H, CH_2)	6.91–6.93 (m, 1H)	9.97	12.13
h	6.99 (d, $J = 8.2$ Hz)	7.22–7.30 (m)	7.22–7.30 (m)	2.42 (s, 3H, $C_{4'}$-CH_3), 7.22–7.30 (m, 2H, $C_{3'}$-H, $C_{5'}$-H), 7.85 (d, 2H, $J = 7.8$ Hz, $C_{2'}$-H, $C_{6'}$-H)	8.53 (s, 1H)	6.87–6.91(m, 1H)	11.4	12.55
i	6.93 (d, $J = 8.6$ Hz)	7.20 (dd, $J = 8.7$, 2.4 Hz)	7.43 (d, $J = 2.5$ Hz)	2.43 (s, 3H, $C_{4'}$-CH_3), 7.28 (d, 2H, $J = 8.0$ Hz $C_{3'}$-H, $C_{5'}$-H), 7.83 (d, 2H, $J = 7.3$ Hz, $C_{2'}$-H, $C_{6'}$-H)	2.43 (s, 3H, CH_3)	—	10.67	13.25
j	6.99 (d, $J = 7.7$ Hz)	7.25–7.28 (m)	7.48 (dd, $J = 8.0$, 1.4 Hz)	2.42 (s, 3H, $C_{4'}$-CH_3), 7.25–7.28 (m, 2H, $C_{3'}$-H, $C_{5'}$-H), 7.77 (d, 2H, $J = 7.2$ Hz, $C_{2'}$-H, $C_{6'}$-H)	1.28 (t, 3H, $J = 7.6$ Hz, CH_3), 2.92 (q, 2H, $J = 7.6$ Hz, CH_2)	6.85–6.89 (m, 1H)	10.2	13.23
k	6.93 (d, $J = 8.7$ Hz)	7.21 (dd, $J = 8.7$, 2.2 Hz)	7.42–7.50 (m)	7.42–7.50 (m, 2H, $C_{3'}$-H, $C_{5'}$-H), 7.54–7.58 (m, 1H, $C_{4'}$-H), 7.91 (d, 2H, $J = 7.3$ Hz, $C_{2'}$-H, $C_{6'}$H)	2.44 (s, 3H, CH_3)	—	10.84	13.26

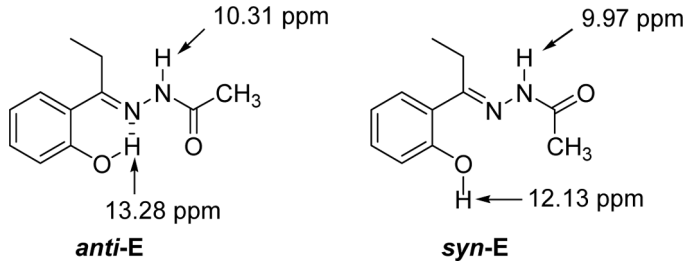


Figure 1. *Anti*- and *syn*-conformers of **3g**.

bond, is slightly larger than the *syn*-conformer, which lacks the possibility of forming such bond.

The *E*-configuration of hydrazones may also be explained on the basis of a signal attributed to methyl/ethyl groups (R^2) in ^{13}C NMR spectra. The methyl signal appeared at δ 13.2–13.7 and ethyl signal at δ 10.5–11.0 (CH_3) and 18.6–19.2 (CH_2) (Fig. 2).

This finding is analogous with the ^{13}C NMR spectra of hydrazones in which one methyl group resonated more at the upper field in one isomer than in the other (17.7 vs 24.0 ppm), probably due to a sterically upfield shift (Fig. 3).[17]

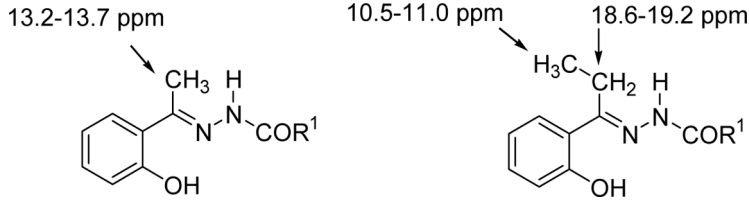


Figure 2. Chemical shifts of methyl/ethyl protons in **3**.

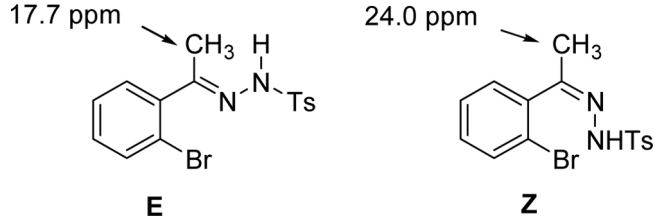


Figure 3. Chemical shifts of methyl carbon in E and Z isomers.

It was also observed that hydrazones with electron-donating substituents at R^1 (**3h–j**) react relatively faster than hydrazones with electron-withdrawing substituents at R^1 (**3a–e**). The reaction also shows a large rate dependence on substituents at R^2. With $R^2 = H$ (**3h**), the reaction proceeded to completion in 1 h, whereas with $R^2 = Et$ (**3d, 3g**) the reaction took 12 h. The ethyl group at R^2 may sterically hinder the approach of the acetate anion at the hydrazone carbon (see mechanism).

^1H NMR spectra of compounds **4a, b, e, f, i**, and **k** show a singlet at δ 2.49–2.51 for the acetyl group. The triplet at δ 1.08 and quartet at δ 2.80–2.95 with $J = 7.2$ Hz in the ^1H NMR spectra of **4d, g**, and **j** results from the ethyl group. ^{13}C NMR spectra of 1,2-diacylbenzenes show two characteristic signals at δ 196.2–201.7 for two carbonyl groups. The carbonyl signals for 2-acyl benzaldehydes were at δ 161.4–165.0. The ^1H NMR and ^{13}C NMR spectra of 1,2-diacylbenzenes (**4**) are given in the Tables 2 and 3 respectively.

1,2-Diacylbenzenes (**4**) exhibit rotational isomerism and may exist in four forms (Fig. 4). Analysis of NMR data indicates that form I and III do not exist; form II and IV are present in solution. Compounds **4a–b**, **4d–e**, **4g**, and **4i–k** (where $R^1 = 4$-pyridyl, 4-tolyl and phenyl and $R^2 = Me$ and Et) exist as rotational isomer II instead of IV, because H-6 resonated at δ 7.8 in comparison to H-3, which appeared at δ 7.3. Further, compounds **4c** and **4h** (where $R^1 = 4$-pyridyl and 4-tolyl and $R^2 = H$) also exist as rotational isomer II because H-6 resonated at δ 7.8 in comparison to H-3, which appeared at δ 7.1, probably shielded as a result of the anisotropy of R^1 groups. Additionally, this shielding may also be due to the different orientation achieved by R^2 groups, where $R^2 = H$ instead of Me or Et. However, compound **4f** (where $R^1 = R^2 = Me$) exists as rotational isomer IV as indicated by ^1H NMR signals for H-6 and H-3, which appeared at δ 7.46 and δ 7.63, respectively. This is probably because the two groups are identical; therefore **4f** can adopt either conformation II or IV.

The possible mechanism of this reaction may follow a route similar to that proposed by Katritzky[18] with lead tetraacetate. The reaction begins with ligand exchange of the 2-hydroxyaryl aldehyde/ketone acylhydrazones (**3**) with an acetate group on polystyrene-supported iodobenzene diacetate (PSIBD) to produce intermediate **5**. The reductive elimination of iodopolystyrene is accompanied by the intramolecular migration of the acetate group to the hydrazone carbon, giving the azoacetate (**6**), which then give 1,3,4-oxadiazoline (**7**), followed by cyclization and loss of acetic acid to give 1,3-dioxane intermediate (**8**). Elimination of nitrogen with formation of epoxide then gives intermediate **9**, which undergoes electrocyclic rearrangement to form the 1,2-diacylbenzenes (**4**) (Scheme 2).

Table 2. ^{1}H NMR spectra of 1,2-diacylbenzenes (**4**)

Compound	C_3-H	C_4-H	C_6-H	R^1	R^2	R^3
4a	7.41 (dd, $J = 7.4$, 1.3 Hz)	7.64–7.72 (m)	7.96 (dd, $J = 7.4$, 0.8 Hz)	7.50 (dd, 2H, $J = 4.4$, 1.6 Hz, $C_{3'}$-H, $C_{5'}$-H), 8.73 (dd, 2H, $J = 4.4$, 1.5 Hz, $C_{2'}$-H, $C_{6'}$-H)	2.54 (s, 3H, CH_3)	7.64–7.72 (m)
b	7.31 (d, $J = 7.6$ Hz)	7.48–7.49 (m)	7.70 (s)	7.48–7.49 (m, 2H, $C_{3'}$-H, $C_{5'}$-H), 8.71 (dd, 2H, $J = 4.5$, 1.4 Hz, $C_{2'}$-H, $C_{6'}$-H)	2.51 (s, 3H, CH_3)	2.51 (s, 3H, CH_3)
c	7.15 (d, $J = 8.7$ Hz)	7.46–7.51 (m)	7.86 (dd, $J = 7.8$, 1.4 Hz)	7.99 (dd, 2H, $J = 4.5$, 1.4 Hz, $C_{3'}$-H, $C_{5'}$-H), 8.87 (dd, 2H, $J = 4.5$, 1.4 Hz, $C_{2'}$-H, $C_{6'}$-H)	10.04 (s, 1H, CHO)	7.04–7.7 (m, 1H)
d	7.39–7.41 (m)	7.62–7.70 (m)	7.93–7.95 (m)	7.50 (dd, 2H, $J = 4.3$, 1.6 Hz, $C_{3'}$-H, $C_{5'}$-H), 8.73 (dd, 2H, $J = 4.4$, 1.6 Hz, $C_{2'}$-H, $C_{6'}$-H)	1.08 (t, 3H, $J = 7.2$ Hz, CH_3), 2.95 (q, 2H, $J = 7.2$ Hz, CH_2)	7.62–7.70 (m, 1H)
e	7.36 (d, $J = 8.4$ Hz)	7.66 (dd, $J = 8.0$, 1.9 Hz)	7.88 (d, $J = 1.9$ Hz)	7.48 (dd, 2H, $J = 4.4$, 1.6 Hz, $C_{3'}$-H, $C_{5'}$-H), 8.75 (dd, 2H, $J = 4.4$, 1.5 Hz, $C_{2'}$-H, $C_{6'}$-H)	2.51 (s, 3H, CH_3)	—
f	7.63 (d, $J = 8.2$ Hz)	7.53 (dd, $J = 1.8$, 8.2 Hz)	7.46 (d, $J = 1.8$ Hz)	2.54 (s, 3H, CH_3)	2.50 (s, 3H, CH_3)	—
g	7.46–7.48 (m)	7.51–7.57 (m)	7.63–7.65 (m)	2.55 (s, 3H, CH_3)	1.23 (t, 3H, $J = 7.2$ Hz, CH_3), 2.80 (q, 2H, $J = 7.2$ Hz, CH_2)	7.51–7.57 (m)

h	7.13 (dd, $J = 8.4$, 0.8 Hz)	7.41–7.46 (m)	7.83 (dd, $J = 8.2$, 1.60 Hz)	2.43 (s, 3H, $C_{4'}$-CH_3), 7.33 (d, 2H, $J = 8.0$ Hz, $C_{3'}$-H, $C_{5'}$-H), 8.00 (d, 2H, $J = 8.0$ Hz, $C_{2'}$-H, $C_{6'}$-H)	10.20 (s, 1H, CHO)	7.00–7.04 (m, 1H)
I	7.35 (d, $J = 8.0$ Hz)	7.57 (dd, $J = 8.1$, 1.6 Hz)	7.80 (d, $J = 2.0$ Hz)	2.40 (s, 3H, $C_{4'}$-CH_3), 7.21–7.23 (m, 2H, $C_{3'}$-H, $C_{5'}$-H) 7.63 (dd, 2H, $J = 6.5$, 1.72 Hz, $C_{2'}$-H, $C_{6'}$-H)	2.49 (s, 3H, CH_3)	—
j	7.37–7.39 (m)	7.53–7.60 (m)	7.83–7.85 (m)	2.39 (s, 3H, $C_{4'}$-CH_3), 7.21 (d, 2H, $J = 7.9$ Hz, $C_{3'}$-H, $C_{5'}$-H), 7.60–7.66 (m, 2H, $C_{2'}$-H, $C_{6'}$-H)	1.08 (t, 3H, $J = 7.2$ Hz, CH_3), 2.90 (q, 2H, $J = 7.2$ Hz, CH_2)	7.53–7.60 (m)
k	7.36 (d, $J = 8.1$ Hz)	7.59 (dd, $J = 8.0$, 2.0 Hz)	7.81 (d, $J = 1.5$ Hz)	7.41–7.45 (m, 2H, $C_{3'}$-H, $C_{5'}$-H) 7.53–7.57 (m, 1H, $C_{4'}$-H) 7.71–7.73 (m, 2H, $C_{2'}$-H, $C_{6'}$-H)	2.50 (s, 3H, CH_3)	—

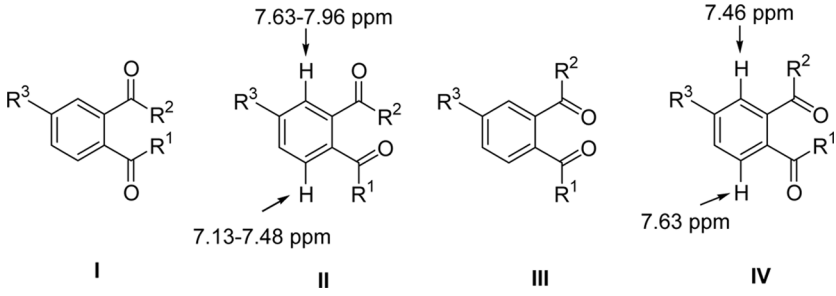
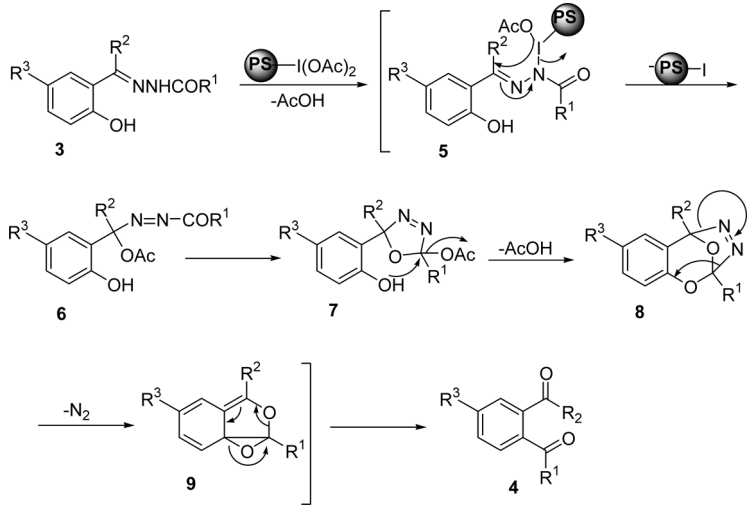


Figure 4. Rotational isomers of **4**.

EXPERIMENTAL

Melting points were determined in open capillaries and are uncorrected. FTIR spectra were obtained in KBr on Shimadzu FTIR 8210 PC and Perkin-Elmer Spectrum RX1 instruments and are reported in centimeters^{-1}. ^{1}H and ^{13}C NMR spectra were determined on a Bruker Avance II NMR spectrometer operating at 400 MHz and 100 MHz, respectively, in $CDCl_3$/DMSO-d_6 and are expressed as parts per million (ppm) with respect to TMS. 2-D NMR (correlation spectroscopy [COSY] and heteronuclear single-quantum coherence [HSQC]) spectra were also recorded for a few samples. Elemental analysis was carried out on a Perkin-Elmer 2400 instrument. 2-Hydroxyaryl aldehydes and ketones and acid hydrazides were purchased from Aldrich.



Scheme 2. Mechanism for the synthesis of **4a–k**.

Table 3. ^{13}C NMR spectra of 1,2-diacyl benzenes (**4**)

Compound	C_1	C_2	C_3	C_4	C_5	C_6	R^1	R^2	R^3	COR^1	COR^2
4a	139.7	136.8	129.7	133	130.3	128	121.7 ($C_{3'}$, $C_{5'}$), 143.3 ($C_{4'}$), 150.5 ($C_{2'}$, $C_{6'}$)	26.8 (CH_3)	—	196.8	197.9
b	137.5	136.7	130.1	133.2	140.9	128.3	121.8 ($C_{3'}$, $C_{5'}$), 143.6 ($C_{4'}$), 150.5 ($C_{2'}$, $C_{6'}$)	27.0 (CH_3)	21.4 (CH_3)	196.8	198.4
c	157.9	107.5	117.8	134.3	120.1	126.6	120.3 ($C_{3'}$, $C_{53'}$), 130.4 ($C_{43'}$), 151.0 ($C_{23'}$, $C_{63'}$)	—	—	161.4	165
d	139.6	137	128.8	132.6	130.3	128.1	121.8 ($C_{3'}$, $C_{5'}$), 143.3 ($C_{4'}$), 150.5 ($C_{2'}$, $C_{6'}$)	7.8 (CH_3) 32.3 (CH_2),	—	196.8	200.9
e	138.8	136	131.9	133	136.8	129.8	128.6 ($C_{3'}$, $C_{5'}$), 129.3 ($C_{2'}$, $C_{6'}$), 139.6 ($C_{4'}$)	27.6 (CH_3)	—	196.6	197.6
f	141.6	135.6	129.2	130	137.3	126.9	28.6 (CH_3)	27.6 (CH_3)	—	199	200.6
g	138.3	140.5	130.5	127.1	128.3	131.5	28.3 (CH_3)	8.2 (CH_3), 34.9 (CH_2)	—	201	205.8
h	157.6	108.2	117.6	133.6	120.4	126.5	21.7 ($C_{4'}$-CH_3), 127.0 ($C_{3'}$, $C_{5'}$), 129.9 ($C_{2'}$, $C_{6'}$), 120.4 ($C_{1'}$), 142.8 ($C_{4'}$)	—	—	163.4	163.9
i	139.6	135.8	129.8	131.8	138.9	129.2	21.7 ($C_{4'}$-CH_3), 129.1 ($C_{3'}$, $C_{5'}$), 129.5 ($C_{2'}$, $C_{6'}$), 134.3 ($C_{1'}$), 144.2 ($C_{4'}$)	27.8	—	196.2	197.7
j	140.8	137.9	128.5	131.6	129.6	128.3	21.7 ($C_{4'}$-CH_3), 129.1 ($C_{3'}$, $C_{5'}$), 129.5 ($C_{2'}$, $C_{6'}$), 134.6 ($C_{1'}$), 143.8 ($C_{4'}$)	8.06 (CH_3), 33.1 (CH_2)	—	197.5	201.7
K	139.6	136.0	129.8	133.3	136.8	129.2	128.6 ($C_{3'}$-C_5), 129.3 ($C_{2'}$, $C_{6'}$), 131.9 ($C_{4'}$), 138.8 ($C_{1'}$)	27.6 (CH_3)	—	196.6	197.6

Preparation of 2-Hydroxyaryl Aldehyde/Ketone Acylhydrazones (3)

2-Hydroxyaryl aldehyde/ketone (10.0 mmol) was added to a solution of acid hydrazide (10.0 mmol) in n-propanol (50 ml), and the solution was heated to reflux for 6–8 h. The solid obtained was filtered to afford 2-hydroxyaryl aldehyde/ketone acylhydrazones (**3**), which were used without further purification.

Data

Isonicotinic Acid [1-(2-Hydroxyphenyl)-ethylidine]-hydrazide (3a)

Yield 75%; mp 240°C (lit.[11a] mp 240–244°C); IR (cm^{-1}): 3432, 3238, 1679, 1610, 1535, 1492, 1452, 1409, 1282, 1240, 1147, 1064, 831, 763; ^{13}C NMR (DMSO-d_6) δ: 13.6, 117.3, 117.9, 118.6, 121.4, 127.5, 131.0, 139.9, 149.6, 158.9, 159.4, 162.4.

Isonicotinic Acid [1-(2-Hydroxy-5-methylphenyl)-ethylidine]-hydrazide (3b)

Yield 70%; mp 230°C; IR (cm^{-1}): 3440, 3170, 2920, 1674, 1600, 1535, 1480, 1410, 1362, 1320, 1290, 1230, 1150, 1100, 1058. Anal. calcd for $C_{15}H_{15}N_3O_2$: C, 66.90; H, 5.61; N, 15.60%. Found: C, 66.92; H, 5.58; N, 15.63%.

Isonicotinic Acid (2-Hydroxybenzylidine)-hydrazide (3c)

Yield 80%; mp 253–54°C; IR (cm^{-1}): 3428, 3174, 3008, 2842, 1683, 1617, 1566, 1490, 1407, 1390, 1355, 1290, 1274, 1157, 1066, 850, 771; ^{13}C NMR (DMSO-d_6) δ: 116.3, 117.2, 118.7, 121.0, 130.2, 131.1, 139.6, 149.7, 150.7, 157.9, 161.1. Anal. calcd. for $C_{13}H_{11}N_3O_2$: C, 64.72; H, 4.60; N, 17.72%. Found: C, 64.70; H, 4.63; N, 17.65%.

Isonicotinic Acid [1-(2-Hydroxyphenyl)-propylidene]-hydrazide (3d)

Yield 85%; mp 248°C; IR (cm^{-1}): 3410, 3186, 3047, 2981, 1681, 1600, 1525, 1488, 1450, 1406, 1263, 1147, 1058, 827, 775; ^{13}C NMR (DMSO-d_6) δ: 11.0, 19.2, 117.3, 117.5, 118.0, 121.7, 127.3, 130.9, 140.1, 149.5, 159.4, 162.2, 162.9. Anal. calcd. for $C_{15}H_{15}N_3O_2$: C, 66.90; H, 5.61; N, 15.60%. Found: C, 66.93; H, 5.64; N, 15.60%.

Isonicotinic Acid [1-(5-Chloro-2-hydroxyphenyl)-ethylidine]-hydrazide (3e)

Yield 82%; mp 242°C; IR (cm^{-1}): 3448, 3230, 2923, 1670, 1602, 1546, 1479, 1413, 1365, 1325, 1294, 1230, 1155, 1107, 1068, 817, 756; ^{13}C NMR (DMSO-d_6) δ: 13.7, 99.4, 121.5, 122.3, 126.9, 130.6, 149.6, 157.5, 162.7. Anal. calcd. for $C_{14}H_{12}ClN_3O_2$: C, 58.04; H, 4.17; N, 14.50%. Found: C, 58.00; H, 4.10; N, 14.45%.

Acetic Acid [1-(5-Chloro-2-hydroxyphenyl)-ethylidine]-hydrazide (3f)

Yield 88%; mp 228–229°C; IR (cm^{-1}): 3402, 3186, 3101, 2927, 1676, 1596, 1467, 1388, 1342, 1309, 1282, 1232, 1161, 1016, 833, 765. Anal. calcd. for $C_{10}H_{11}ClN_2O_2$: C, 52.99; H, 4.89; N, 12.36%. Found: C, 52.90; H, 4.93; N, 12.30%.

Acetic Acid [1-(2-Hydroxyphenyl)-propylidene]-hydrazide (3g)

Yield 78%; mp 194°C; IR (cm^{-1}): 3390, 3249, 3039, 2970, 1666, 1606, 1525, 1490, 1473, 1452, 1377, 1336, 1305, 1265, 1215, 1062, 1020, 860, 761; ^{13}C NMR (DMSO-d_6) δ: 10.2, 10.6, 18.6, 18.7, 20.6, 20.8, 117.0, 117.41, 117.48, 117.5, 117.7, 118.5, 126.7, 127.0, 130.4, 130.6, 156.4, 157.7, 158.2, 159.2, 166.2, 171.8. Anal. calcd. for $C_{11}H_{14}N_2O_2$: C, 64.06; H, 6.84; N, 13.58%. Found: C, 64.10; H, 6.80; N, 13.50%.

4-Methylbenzoic Acid (2-Hydroxybenzylidine)-hydrazide (3h)

Yield 80%; mp 202–203°C; IR (cm^{-1}): 3413, 3218, 3047, 2916, 1650, 1623, 1610, 1571, 1488, 1367, 1305, 1288, 1195, 1149, 1072, 877, 738. Anal. calcd. for $C_{15}H_{14}N_2O_2$: C, 70.85; H, 5.55; N, 11.02%. Found: C, 70.80; H, 5.60; N, 11.00%.

4-Methylbenzoic Acid [1-(5-Chloro-2-hydroxyphenyl)-ethylidine]-hydrazide (3i)

Yield 76%; mp 240°C; IR (cm^{-1}): 3416, 3265, 1645, 1604, 1562, 1519, 1469, 1379, 1325, 1290, 1230, 1184, 1159, 1118, 1103, 902, 881, 835, 817, 744. Anal. calcd. for $C_{16}H_{15}ClN_2O_2$: C, 63.47; H, 4.99; N, 9.25%. Found: C, 63.40; H, 5.02; N, 9.30%.

4-Methylbenzoic Acid [1-(5-Chloro-2-hydroxyphenyl)-propylidine]-hydrazide (3j)

Yield 65%; mp 176–177°C; IR (cm^{-1}): 3415, 3230, 1631, 1608, 1571, 1527, 1483, 1444, 1276, 1259, 1217, 1178, 1099, 906, 827, 754; ^{13}C NMR (DMSO-d_6) δ: 10.5, 18.7, 21.0, 117.4, 117.6, 117.9, 126.9, 127.4, 128.6, 129.7, 130.6, 142.0, 159.4, 159.9, 163.8. Anal. calcd. for $C_{17}H_{18}N_2O_2$: C, 72.32; H, 6.43; N, 9.92%. Found: C, 72.30; H, 6.40; N, 9.95%.

Benzoic Acid [1-(5-Chloro-2-hydroxyphenyl)-ethylidine]-hydrazide (3k)

Yield 72%; mp 212–214°C; IR (cm^{-1}): 3406, 3222, 1641, 1608, 1577, 1517, 1479, 1460, 1375, 1323, 1288, 1228, 1159, 1107, 1026, 904, 875, 848, 823, 796; ^{13}C NMR (DMSO-d_6) δ: 13.2, 118.7, 120.0, 122.3, 126.7, 127.6, 127.8, 130.3, 131.4, 132.5, 155.6, 157.5, 164.3. Anal. calcd. for $C_{15}H_{13}ClN_2O_2$: C, 62.40; H, 4.54; N, 9.70%. Found: C, 62.35; H, 4.50; N, 9.65%.

Preparation of 1,2-Diacylbenzenes (4)

Polystyrene-supported iodobenzene diacetate (PSIBD) (1.5 mmol) was added to a stirred solution of the 2-hydroxyaryl aldehyde/ketone acylhydrazones (**3**) (1.0 mmol) in dichloromethane (10 ml). After the **3** was consumed (monitored by thin-layer chromatography, TLC), the mixture was filtered to remove the resin and washed with 5 ml of dichloromethane and 6 ml of water. The aqueous layer was extracted with dichloromethane. The combined extract was washed with saturated sodium bicarbonate solution, dried over magnesium sulphate, filtered, and concentrated in vacuo to give crude 1,2-diacylbenzene. The pure product was isolated by column chromatography on silica gel (60–120 mesh) using hexane–ethyl acetate (90:10) as eluent.

Data

1[2-(Pyridine-4-carbonyl)-phenyl]-ethanone (4a)

Yield 85%; mp 114°C (lit.[11a] mp 115–116°C); IR (cm^{-1}): 3034, 1677, 1595, 1567, 1486, 1411, 1364, 1327, 1269, 935.

1[5-Methyl-2-(pyridine-4-carbonyl)-phenyl]-ethanone (4b)

Yield 78%; mp 124°C; IR (cm^{-1}): 3034, 2920, 1676, 1599, 1558, 1490, 1404, 1356, 1302, 1286, 939. Anal. calcd. for $C_{15}H_{13}NO_2$: C, 75.30; H, 5.48; N, 5.85%. Found: C, 75.25; H, 5.50; N, 5.80%.

2-(Pyridine-4-carbonyl)-benzaldehyde (4c)

Yield 90%; mp 115–116°C; IR (cm^{-1}): 3085, 2166, 1726, 1645, 1549, 1451, 1374, 1347, 1251, 993; Anal. Calcd for $C_{13}H_9NO_2$: C, 73.92; H, 4.29; N, 6.63%. Found: C, 73.90; H, 4.25; N, 6.60%.

1[2-(Pyridine-4-carbonyl)-phenyl]-propan-1-one (4d)

Yield 65%; mp 75°C; IR (cm^{-1}): 3077, 2970, 2874, 2908, 1720, 1678, 1593, 1561, 1459, 1405, 1375, 1349, 1275, 1221, 935. Anal. calcd. for $C_{15}H_{13}NO_2$: C, 75.30; H, 5.48; N, 5.85%. Found: C, 75.28; H, 5.50; N, 5.80%.

1[5-Chloro-2-(pyridine-4-carbonyl)-phenyl]-ethanone (4e)

Yield 70%; mp 78°C; IR (cm^{-1}): 1683, 1591, 1556, 1404, 1359, 1325, 1284, 1251, 1101, 964, 941, 839, 756. Anal. calcd. for $C_{14}H_{10}ClNO_2$: C, 64.75; H, 3.88; N, 5.30%. Found: C, 64.70; H, 3.80; N, 5.26%.

1-(2-Acetyl-5-chlorophenyl)-ethanone (4f)

Yield 75%; mp 45°C; IR (cm^{-1}): 1687, 1589, 1556, 1481, 1361, 1286, 1230, 1103, 960, 823, 771. Anal. calcd. for $C_{10}H_9ClO_2$: C, 61.08; H, 4.61%. Found: C, 61.00; H, 4.60%.

1-(2-Acetylphenyl)-propan-1-one (4 g)

Yield 68%; oil; IR (cm^{-1}): 2979, 2939, 1685, 1595, 1569, 1411, 1357, 1263, 1218, 1068, 1016, 948, 763. Anal. calcd. for $C_{11}H_{12}O_2$: C, 74.98; H, 6.86%. Found: C, 74.90; H, 6.85%.

2-(4-Methylbenzoyl)-benzaldehyde (4h)

Yield 85%; mp 164°C; IR (cm^{-1}): 1625, 1614, 1593, 1544, 1498, 1487, 1400, 1257, 1234, 1180, 1066, 1018, 945, 820, 750. Anal. calcd. for $C_{15}H_{12}O_2$: C, 80.34; H, 5.39%. Found: C, 80.30; H, 5.40%.

1-[5-Chloro-2-(4-methylbenzoyl)-phenyl]-ethanone (4i)

Yield 70%; mp 80–81°C; IR (cm^{-1}): 3039, 2912, 1685, 1660, 1587, 1556, 1407, 1359, 1311, 1288, 1251, 1180, 1149, 1101, 968, 929, 842. Anal. calcd. for $C_{16}H_{13}ClO_2$: C, 70.46; H, 4.80%. Found: C, 70.40; H, 4.75%.

1-[2-(4-Methylbenzoyl)-phenyl]-prop-1-one (4j)

Yield 66%; mp 86°C; IR (cm^{-1}): 3058, 2970, 1687, 1662, 1604, 1566, 1442, 1407, 1375, 1350, 1313, 1271, 1220, 1151, 954, 929, 831, 773. Anal. calcd. for $C_{17}H_{16}O_2$: C, 80.93; H, 6.39%. Found: C, 80.90; H, 6.40%.

1-(2-Benzoyl-5-chlorophenyl)-ethanone (4k)

Yield 72%; oil; IR (cm^{-1}): 3010, 2915, 1690, 1665, 1585, 1560, 1405, 1350, 1310, 1280, 1250, 1180, 1150, 1101, 960, 929, 840. Anal. calcd. for $C_{15}H_{11}ClO_2$: C, 69.64; H, 4.29%. Found: C, 69.59; H, 4.30%.

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