1,3-Dibromo-5,5-dimethylhydantoin (DBH) as an Efficient Promoter for Acetylation of 3-Arylsydnones in the presence of Acetic Anhydride under Neutral Conditions

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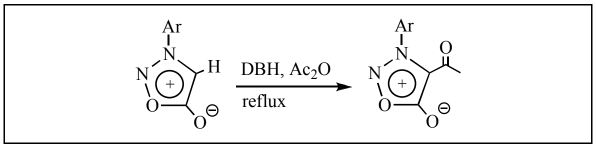

1,3-Dibromo-5,5-dimethylhydantoin (DBH) has been found to efficiently promote the conversion of various 3-arylsydnones to their 4-acetyl congeners in the presence of acetic anhydride under neutral conditions in satisfactory yields.

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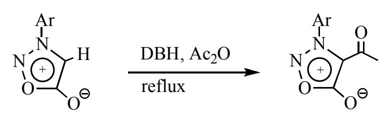
Sydnones such as **1** belong to a class of heterocyclic compounds known as mesoionic [1-2], were first prepared by Earl and Mackney in 1935 [3]. Sydnones are normally prepared by dehydrative cyclization of *N*-nitrosamino acids [4] regarded as dipolar structures. Sydnones have attracted an inordinately large research effort over the years owing to their biological value as antibacterial [5], antitumour [6], antimalarial [7], anti-inflammatory [8], and antihypertensive [9] agents. Among various transformations that sydnones undergo, are electrophilic substitution reactions that normally occur at the 4-position (if unsubstituted) [1,10]. Also, the dipolar nature of sydnones leads to reactions in which they serve as 1,3-dipoles in cycloadditions to form pyrazoles or related species [11].

3-Arylsydnones have been subjected to substitution with the vast majority of electrophiles. This can be accounted for by the deactivation of the aryl substituent due to the electron-withdrawing effect of the sydnone ring N-3 position that bears a substantial fractional positive charge [12,13]. Acylation of sydnones, among other aromatic substitution reactions, is of considerable interest in organic synthesis that has been implemented by various reagents exclusively at the sydnone 4-positions as already mentioned [14-16]. It has been reported that the Lewis acid-catalyzed acylation of 3-arylsydnones with either acetic anhydride or benzyl chloride under Friedel-Crafts conditions fails to produce 4-acylsydnones [17], presumably due to coordination of a Lewis acid catalyst with the negatively charged exocyclic oxygen atom bonded to the sydnone ring [18]. However, successful acylations of sydnones by alkyl anhydrides using different acids have been reported [19-21]. More recently, Montmorillonite K-10 has been reported as an efficient catalyst for acylation of 3-substituted sydnones in the presence of acetic anhydride [22].

In connection with our ongoing research on 1,3-dibromo-5,5-dimethylhydantoin (DBH) as a versatile and convenient reagent used in various transformations [23-27], and also in order to avoid the drawbacks related to the previously reported methods such as the use of acidic media, low reaction yields and troublesome extraction and purification of the products from reaction mixtures, we wish, herein, to report on the reagent DBH as a more robust and efficient promoter for the acetylation of sydnones to their corresponding 4-acetyl derivatives. A similar protocol for the acetylation of alcohols by using acetic anhydride and 1,3-dibromo-5,5-dimethylhydantoin has recently been reported by Zolfigol and his co-workers [28]. In this work, we have observed that 1,3-dibromo-5,5-dimethylhydantoin can efficiently enhance the conversion of the 3-arylsydnones **1a-j** to their 4-acetyl congeners **2a-j** in the presence of acetic anhydride under reflux (Scheme **I**, Table **1**). According to the results shown in the table **1**, the reactions proceed within few hours at 100 °C in satisfactory yields. Numerous repetitions of the reactions under different molar conditions indicated that, the most effective conversions

Scheme I



1a-j **2a-j**

Ar:
(**a**) C_6H_5, (**b**) 2-MeC_6H_4, (**c**) 4-MeC_6H_4, (**d**) 2-MeOC_6H_4, (**e**) 4-MeOC_6H_4, (**f**) 2-$O_2NC_6H_4$, (**g**) 4-$O_2NC_6H_4$, (**h**) 4-ClC_6H_4, (**i**) 2,4-$Cl_2C_6H_3$, (**j**) 4-BrC_6H_4

occur when equimolar amounts of 3-arylsydnones and DBH are used in the reactions. Longer reaction times are required when lesser amounts of DBH are employed. It is also important to note that, no acetylated products were afforded when the reactions were carried out in the absence of DBH. This substantiates the vitality of DBH in promoting the reactions probably by converting acetic anhydride into a more reactive acetylating reagent.

Table 1

Acetylation of the 3-aryl sydnones **1a-j** to the corresponding 4-acetyl sydnones **2a-j** by DBH in Ac_2O under reflux

Entry	Product	Yield (%) [a]	Mp (°C)
1	**2a**	92	143-145
2	**2b**	83	105-107
3	**2c**	87	119-120
4	**2d**	81	104-105
5	**2e**	85	97-98
6	**2f**	80	151-152
7	**2g**	82	208-210
8	**2h**	90	129-131
9	**2i**	80	98-99
10	**2j**	89	169-170

[a] Purified Yields.

EXPERIMENTAL

Chemicals were obtained from Merck and Fluka chemical companies. IR spectra were recorded using a Shimadzu 435-U-04 spectrophotometer (KBr pellets) and NMR spectra were obtained in $CDCl_3$ using a 90 MHz JEOl FT NMR spectrometer. Mass spectra were recorded on a GCMS-QP1100EX spectrometer. All melting points were determined on a Büchi 530 melting point apparatus, and are reported uncorrected.

General Procedure for Acetylation of 3-Arylsydnones 1a-j to the corresponding 4-Acetyl Derivatives 2a-j. To a stirred solution of 3-arylsydnone **1a-j** (1 mmol) in acetic anhydride (2 mmol) was added DBH (0.29 g, 1 mmol), and the mixture was refluxed at 100 °C for 7 h. After complete conversion of the substrates as indicated by TLC using ethylacetate/hexane mixture (1:1), the resulting reaction mixture was poured into ice water to destroy the excess acetic anhydride and neutralized with sodium carbonate. The resulting mixture was filtered, the filtrate was extracted with CH_2Cl_2 (2x25 mL), and then dried with anhydrous $MgSO_4$. After filtration, the solvent was evaporated under reduced pressure to leave a solid brown residue, which was recrystallized from warm ethanol (95%) to yield pure crystals of the products **2a-j** in 80-92% yield (Table **1**). The products were characterized on the basis of their physical and spectral analysis (Table **2**) and by direct comparison with literature data [20,22,29].

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Table 2

IR, ^{1}H-NMR, ^{13}C-NMR and MS (ET) spectral data of the 4-acetyl sydnones **2a-j**

Product	IR (KBr) (cm^{-1})	^{1}H-NMR ($CDCl_3$) (ppm)	^{13}C-NMR ($CDCl_3$) (ppm)	MS (m/z)
2a	3060, 1763, 1665, 1426, 1053, 770	2.36 (s, 3H, COMe), 8.01-8.39 (m, 5H, Ar)	28.14 (CO*Me*), 108.3 (C4), 126.21, 131.25, 136.72, 144.63 (Ar), 166.7 (C5), 183.80 (CO)	204, 161, 149, 147, 145, 105, 104, 77, 76, 63, 51, 50, 43
2b	3053, 1780, 1660, 1425, 1250, 795	2.39 (s, 3H, COMe), 2.69 (s, 3H, Me), 7.93 - 8.30 (m, 3H, Ar), 8.73 - 9.00 (m, 1H, Ar)	16.30 (Me), 28.32 (CO*Me*), 108.40 (C4), 115.19, 132.46, 134.57, 138.30, 138.60, 143.30 (Ar), 165.40 (C5), 184.30 (CO)	218, 175, 161, 160, 138, 118, 90, 89, 77, 64, 50, 43
2c	3058, 2933, 1783, 1678, 1509, 1316, 1050, 827	2.38 (s, 3H, COMe), 2.61 (s, 3H, Me), 7.47 - 7.93 (m, 4H, Ar)	21.30 (Me), 28.32 (CO*Me*), 107.40 (C4), 124.97, 128.59, 140.27 (Ar), 165.80 (C5), 184.10 (CO)	218, 175, 160, 159, 138, 118, 90, 89, 77, 64, 63, 51, 50, 43
2d	3080, 1780, 1680, 1489, 1431, 1038, 770	2.58 (s, 3H, COMe), 3.84 (s, 3H, OMe), 7.80 - 8.45 (dd, 4H, Ar)	28.23 (CO*Me*), 56.50 (OMe), 108.74 (C4), 118.07, 124.78, 132.11, 132.32, 149.10 (Ar), 166.70 (C5), 184.42 (CO)	234, 218, 191, 178, 176, 134, 107, 92, 90, 64, 53, 43
2e	3085, 1786, 1675, 1491, 1442, 1055, 485	2.63 (s, 3H, COMe), 3.94 (s, 3H, OMe), 7.22 -7.822 (m, 4H, Ar)	28.41 (CO*Me*), 55.72 (OMe), 107.30 (C4), 126.57, 129.50, 139.69, 158.32 (Ar), 166.20 (C5), 184.20 (CO)	234, 219, 191, 176, 134, 107, 89, 92, 64, 52, 43
2f	3098, 1788, 1672, 1537, 1359, 1052, 848, 788	2.47 (s, 3H, COMe), 7.56 - 8.44 (m, 4H, Ar)	27.50 (CO*Me*), 106.90 (C4), 126.10, 128.20, 128.80, 133.40, 133.90, 143.30 (Ar), 165.10 (C5), 184.80 (CO)	249, 206, 191, 149, 103, 92, 77, 75, 64, 63, 52, 50, 45, 43
2g	3100, 1795, 1670, 1530, 1350, 1055, 850, 792	2.58 (s, 3H, COMe), 8.26 - 8.80 (m, 4H, Ar)	28.20 (CO*Me*), 106.70 (C4), 126.87, 130.80, 139.29, 148.26 (Ar), 165.80 (C5), 184.30 (CO)	249, 206, 191, 149, 122, 103, 92, 77, 75, 64, 63, 52, 50, 45, 43
2h	3100, 1786, 1663, 1438, 1090, 838	2.60 (s, 3H, COMe), 7.92 - 8.56 (m, 4H, Ar)	27.90 (CO*Me*), 106.60 (C4), 127.01, 137.80, 140.27, 148.86 (Ar), 165.80 (C5), 184.10 (CO)	240, 238, 182, 180, 149, 140, 138, 133, 110, 77, 64, 52, 43
2i	3110, 1790, 1660, 1440, 1100, 840	2.40 (s, 3H, COMe), 7.86 - 8.98 (m, 3H, Ar)	27.20 (CO*Me*), 107.50 (C4), 123.98, 127.43, 132.96, 141.56, 142.42, 145.33 (Ar), 165.60 (C5), 184.80 (CO)	276, 274, 272, 229, 214, 172, 145, 125, 110, 78, 75, 63, 49, 43
2j	3095, 1770, 1675, 1428, 1035, 1039, 770	2.58 (s, 3H, COMe), 7.81- 8.61 (m, 4H, Ar)	27.50 (CO*Me*), 106.80 (C4), 126.90, 128.50, 133.20, 134.80 (Ar), 165.90 (C5), 184.00 (CO)	284, 282, 241, 239, 226, 224, 184, 182, 158, 156, 146, 77, 76, 66, 52, 43

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