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Chlorination of 3-substituted sydnones using 1,4-dichloro-1,4-diazoniabicyclo[2,2,2]octane bis-chloride

Sadegh Salmanpoor[a], Mahmood Tajbakhsh[b]*, Setareh Habibzadeh[c], Davood Azarifar[d] and Hassan Ghasemnejad-Bosra[e]

[a]*Islamic Azad University-Sari Branch, Mazandaran, Sari, Iran*

[b]*Faculty of Chemistry, Mazandaran University, Babolsar, Iran*

[c]*Industrial Noshiravani University, Babol, Iran*

[d]*Faculty of Chemistry, Bu-ali Sina University, Hamadan, Iran*

[e]*Islamic Azad University-Babol Branch, Medicinal and Basic Science, Mazandaran, Babol, Iran*

1,4-Dichloro-1,4-diazoniabicyclo[2,2,2]octane bis-chloride has been used as effective reagent for the chlorination of 3-arylsydnones to their corresponding 4-chloro derivatives in DMF-H_2O at room temperature. The 1,4-diazabicyclo [2,2,2]octane was regenerated, rechlorinated and reused several times.

Keywords: 1,4-dichloro-1,4-diazoniabicyclo[2,2,2]octane bis-chloride, 3-arylsydnones, 4-chloro-3-arylsydnone, chlorination

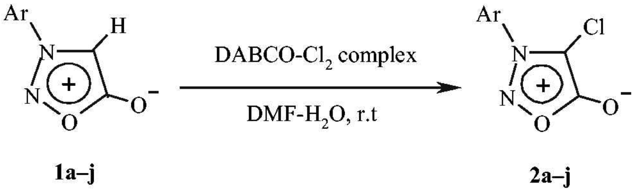
Sydnones are mesoionic heterocyclic compounds[1-4] which were first prepared by Earl and Mackeny in 1935.[5] Sydnones are normally prepared by dehydrative cyclisation of N-nitrosoamino acids[6] and are regarded as dipolar structures. The dipolar nature of sydnones leads to reactions in which they serve as 1,3-dipoles in cycloadditions to form pyrazoles or related species.[7] They have attracted considerable research over the years owing to their biological value.[2] Among various transformations that sydnones undergo, are electrophilic substitution reactions that normally occur at the 4-position if unsubstituted.[1,8]

3-Arylsydnones have been subjected to substitution with the different electrophiles. Substitution at the 4-position of these compounds arises because of the deactivation of the aryl substituent due to the electron-withdrawing effect of the sydnone ring that carries a substantial fractional positive charge at the N-3 position.[9,10]

The chlorination of sydnones (**1a–j**), by various reagents exclusively at 4-position has already been mentioned. A number of methods including chlorine gas,[9] potassium chlorate in moderately concentrated HCl,[11] $PhICl_2/NEt_3$[12-14] and NCS/DMF[15,16] have been reported for the preparation of the 4-chlorosydnones. However, these methods are not successful when strong electron-withdrawing groups are present on the aromatic ring at the 3-position and they suffer from certain disadvantages including the use of expensive reagents, severe reaction conditions, low yields of the products, and problematic removal and recovery of the catalyst.

Results and discussion

In continuation of our interest in the application of N-halo compounds in organic synthesis,[17-24] we found that DABCO–Cl_2 is a new and useful reagent for chlorination of 3-arylsydnones. The results obtained reveal the successful chlorination of 3-arylsydones **1a–j** to their 4-chloro derivatives **2a–j** using DABCO–Cl_2 in DMF-H_2O at room temperature in excellent yields under mild conditions (Scheme 1). In all reactions DABCO was recovered, rechlorinated and reused several times.



Scheme 1

The transformation of **1** → **2** was conducted using 2:1 molar ratio of DABCO-Cl_2 to substrate in DMF-H_2O and the reactions were completed in less than 3h at room temperature. The 4-chloro compounds **2a–j** after removal of DABCO and recrystallisation from ethanol, were obtained in 90–97% yields as shown in Table 1. An interesting feature of the results in the Table 1 is that both electron-releasing and electron-withdrawing groups on the aromatic ring of 3-arylsydnones under these reaction conditions gave an excellent yield of the corresponding 4-chloro derivatives.

The products were characterised on the basis of their physical and spectral analysis (Table 2) and by direct comparison with the literature data.[15,16,25,26]

Table 1 Chlorination of 3-arylsydnones **1a–j** to their 4-chloro derivatives **2a–j**

Entry	Substrate	Product[a]	Ar	Time/h	Yields/%[b]	M.p./°C
1	**1a**	**2a**	C_6H_5	2.6	92	121–123(124–125)[15]
2	**1b**	**2b**	2-$CH_3C_6H_4$	2.3	90	98–100(99–101)[15]
3	**1c**	**2c**	4-$CH_3C_6H_4$	2.1	94	135–137(136–137)[15]
4	**1d**	**2d**	2-$CH_3OC_6H_4$	2.5	97	100–102(101–103)[15]
5	**1e**	**2e**	4-$CH_3OC_6H_4$	2.4	95	99–101(100–103)[16]
6	**1f**	**2f**	2-$NO_2C_6H_4$	2.8	92	113–115(113–114)[24]
7	**1g**	**2 g**	4-$NO_2C_6H_4$	2.7	91	150–152(152–153)[24]
8	**1h**	**2 h**	4-ClC_6H_4	2.6	96	105–107(105–107)[16]
9	**1i**	**2i**	2,4-$Cl_2C_6H_3$	2.9	92	95–97 (95–96)[23]
10	**1j**	**2j**	4-BrC_6H_4	2.5	94	97–99(97–100)[15]

[a]All the isolated products were characterised on the basis of their physical properties and ^1H NMR, ^{13}C NMR, IR spectra and direct comparison with authentic samples. [b]Isolated yields.

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* Correspondent. Email: tajbaksh@umz.ac.ir

Table 2 IR, ^1H NMR and ^{13}C NMR of the 4-chloro sydnones **2a–j**

Product	IR (KBr)/cm^{-1}	^1H NMR ($CDCl_3$) (ppm)	^{13}C NMR (ppm)
2a	3068, 1787, 1466, 1041	7.63–8.28 (m, 5H, Ar)	106.60 (C_4), 126.26–131.86 (Ar) 169.10 (C_5)
2b	3064, 1773, 1226, 1026	2.27 (s, 3H, CH_3), 7.85–8.80 (m, 4H, Ar)	18.29 (Me), 97.58 (C_4), 120.83–133.63 (Ar), 169.27 (C_5)
2c	3069, 1786, 1509, 1044	2.38 (s, 3H, CH_3), 7.48–8.20(m, 4H, Ar)	20.17 (Me), 97.20 (C_4), 119.73–144.44 (Ar), 168.79 (C_5)
2d	3101, 1788, 1501, 1040	4.83 (s, 3H, OCH_3), 8.08–8.62 (m, 4H, Ar)	56.26 (OMe), 97.46(C_4), 113.24–144.53 (Ar), 167.27 (C_5)
2e	3106, 1792, 1489, 1046	3.93 (s, 3H, OCH_3), 7.04–7.88(m, 4H, Ar)	55.75 (OMe), 106.34(C_4), 124.73–134.41 (Ar), 168.11 (C_5)
2f	3094, 1790, 1501, 1055	8.37–9.19 (m, 4H, Ar),	106.17 (C_4), 127.02–146.87 (Ar) 169.95 (C_5)
2g	3104, 1787, 1498, 1048	8.34–9.08(m, 4H, Ar)	106.00 (C_4), 121.56–139.12 (Ar) 168.52 (C_5)
2h	3067, 1793, 1492, 1038	7.86–8.94(m, 4H, Ar)	106.06 (C_4), 118.67–144.50 (Ar) 168.57 (C_5)
2i	3109, 1797, 1498, 1047	8.03–8.69(m, 3H, Ar)	106.24 (C_4), 121.75–137.27 (Ar) 168.77 (C_5)
2j	3097, 1786, 1504, 1046	8.19–8.73(m, 4H, Ar)	99.20 (C_4), 128.92–145.59 (Ar) 167.50 (C_5)

In summary, the present methodology shows that 1,4-dichloro-1,4-diazoniabicyclo[2,2,2]octane bis-chloride is an effective reagent for the chlorination of 3-substituted sydnones. The main advantages of our protocol are the mild, clean, environmentally benign reaction conditions as well as the high yields. Furthermore, this method is also expected to have application in organic synthesis due to the low cost of the reagent. Another feature of this method is that DABCO can be recovered, rechlorinated and reused several times. We believe that this method will be a useful addition to the modern synthetic methodologies.

Experimental

Chemicals were obtained from the 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. All melting points were determined on a Büchi 530 melting point apparatus, and are reported uncorrected.

General procedure for chlorination of 3-arylsydnones

To a stirred solution of 3-arylsydnone **1a–j** (1 mmol) in DMF (5 ml) and H_2O (2 ml) was added 1,4-dichloro-1,4-diazoniabicyclo[2,2,2]octane bis-chloride (0.6 mmol), and the mixture was allowed to stir for 2–3 h at room temperature. After complete conversion of the substrate as indicated by TLC, the mixture was poured into ice water, washed with solution of 1% aqueous HCl (1×10 cm^3) and extracted with CH_2Cl_2 (2×25 ml). The organic layer was dried over $MgSO_4$ and evaporated under vacuum to give an oily residue, which was recrystallised from petroleum ether or ethanol to yield pure crystals of **2a–j** in 90–97% yields.

Regeneration of 1,4-diazabicyclo[2,2,2]octane (DABCO)

The aqueous layer from above procedure was further treated with 10% sodium bicarbonate solution (2×10 cm^3) and 1,4-diazabicyclo[2,2,2]octane (DABCO) was extracted with ether (3×10 cm^3). The ether layer was dried over $MgSO_4$, and evaporated to give pure 1,4-diazabicyclo[2,2,2]octane (0.064 g, 95%), which can be chlorinated and reused several times.

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