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Article

Solvent-Free Oxidation of Secondary Alcohols to Carbonyl Compounds by 1, 3-Dibromo-5, 5-Dimethylhydantoin (DBDMH) and 1, 3-Dichloro-5, 5-Dimethylhydantoin (DCDMH)

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Aldeídos e cetonas são intermediários importantes principalmente na construção de esqueletos carbônicos. A oxidação de álcoois é tão importante que um grande número de métodos e reagentes foi relatado com essa proposta. Reagentes *N*-halo são amplamente utilizados em síntese inorgânica e como continuação do nosso interesse na aplicação de compostos *N*-halo em síntese inorgânica, dibromo dimetilidantoína (DBDMH) e dicloro dimetilidantoína (DCDMH) foram usados na oxidação de álcoois e nosso trabalho em andamento está baseado no desenvolvimento de protocolos de oxidação altamente eficientes. Observamos a oxidação de álcoois secundários com quantidades estequiométricas de DBDMH e DCDMH em condições livre de solventes, na faixa de temperatura de 70-80 ºC.

Aldehydes and ketones are important intermediates, especially for the construction of carbon-skeletons. The oxidation of alcohols is so important that a large number of methods and reagents have been reported for this purpose. *N*-halo reagents are widely used in organic synthesis and as a continuation of our interest in the application of *N*-halo compounds in organic synthesis, dibromo dimethylhydantoin (DBDMH) and dichloro dimethylhydantoin (DCDMH) were used for the oxidation of alcohols and our ongoing work on development of highly efficient oxidation protocols. We observed the oxidation of secondary alcohols with stoichiometric amounts of DBDMH and DCDMH under solvent-free conditions in the range of temperature 70-80 ºC.

Keywords: oxidation, carbonyl compound, dibromo dimethylhydantoin, dichloro dimethylhydantoin, solvent free

Introduction

Because of the wide-ranging utility of aldehydes and ketones as an important synthetic intermediates, especially for the construction of carbon-skeletons[1,2] and preparation of many drugs, vitamins and fragrances,[3] many methods are reported for the preparation of these type of compounds. The oxidation of alcohols, as a method of the preparation of aldehydes and ketones, is so important that a large number of methods and reagents have been reported for this purpose.[4-8] Nevertheless, the development of newer methods and methodologies is currently gaining much attention due to the importance of these oxidation reactions.[9]

A large group of substances generically called *N*-halo reagents is widely used in organic synthesis and in the chemistry of natural compounds.[10] 1,3-dichloro-5,5-dimethylhydantoin (DCDMH) (Scheme 1) is an *N*-halo reagent which is a stable, low cost and commercially available heterocyclic which has rarely been used as a source of chlorine ion or radical in chlorination[11,12] or oxidation reactions.[13,14] 1,3-dibromo-5,5-dimethylhydantoin (DBDMH) (Scheme 1) is an inexpensive and commercially available reagent used for organic synthesis. Recently, DBDMH has found widespread applications as an useful

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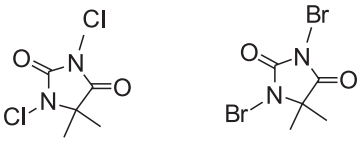
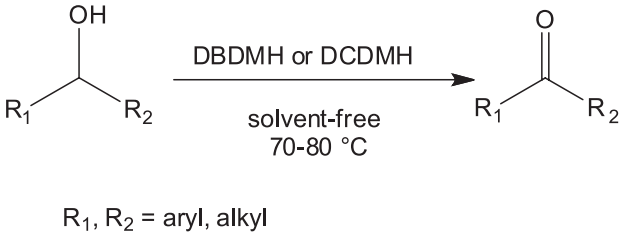
catalyst in various chemical reactions such as the oxidation of pyrazolines[15] and thiols.[16]



Scheme 1. 1,3-dichloro-5,5-dimethylhydantoin (DCDMH) and 1,3-dichloro-5,5-dimethylhydantoin (DBDMH).

As our knowledge, there are no reports on application of DBDMH and DCDMH in the synthesis of carbonyl compounds until now and also in continuation of our interest in the application of *N*-halo compounds in organic synthesis, we have examined the activity of DBDMH and DCDMH in the oxidation of alcohols. Herein, in this research, the oxidation of secondary alcohols with stoichiometric amounts of DBDMH and DCDMH under solvent-free conditions in the range of temperature 70-80 ºC, can be carried out (Scheme 2).



Scheme 2. The synthesis of carbonyl compound.

Experimental

All chemicals were purchased from Merck or Fluka Chemical Companies. The known products were identified by comparison of their melting points and spectral data with those reported in the literatures.[17,18] The purity determination of the substrates and reaction monitoring were accompanied by thin layer chromatography (TLC) on silica gel polygram SILG/ UV 254 plates.

General Procedure

A mixture of alcohols (1 mmol) and DBDMH or DCDMH (1-1.5 mmol) in a 10 mL round-bottomed flask sealed with a stopper, was stirred in an oil-bath for the appropriate time and temperature (Table 1) under solvent-free condition. Then, as monitored by TLC (eluent *n*-hexane/acetone 10:2), hot water (10 mL) was added to mixture and stirred magnetically for 10 min. Then, the solution was extracted with (CH_2Cl_2/water (2 × 10 mL)) and organic phase dried over anhydrous Na_2SO_4 (1g). Evaporation of the solvent gave the corresponding carbonyl compounds. Melting points and spectral data of all products are fully consistent with those previously reported. The structures of the products were confirmed from physical and spectroscopic data such as melting points, ^{1}H NMR and ^{13}C NMR spectra, fully consistent with those previously reported.[17,18]

In these reactions, *N*-halo reagents were converted to dimethylhydantoin. Duo to high solubility of dimethylhydantoin in hot water,[19] *N*-halo reagents should not be remained in the reaction mixture. If any reagent remains in the mixture we can also neutralize it by using 0.5 g H_2SO_4 supported on 0.5 g SiO_2 (m/m 50%).

Results and discussion

To assess the efficiency and the scope of the *N*-halo reagent in the synthesis of ketones, the oxidation of

Table 1. Oxidation of alcohols with DBDMH and DCDMH in the absence of solvent

entry	R_1	R_2	time / min	Yield[a,c,d] / %	time / min	Yield[b,c,d] / %	Melting point / °C (lit.)
1	C_6H_5	Ph	30	94	45	92	46-47(48-49)[20,21]
2	2-ClC_6H_5	Ph	30	92[e]	60	90[e]	48-49(45-47)[22]
3	4-ClC_6H_5	Ph	15	95	20	90	73-75(73-75)[22,23]
4	4-$MeOC_6H_5$	Ph	30	91[e]	45	82[e]	60-62(59-62)[22,24]
5	4-$NO_2C_6H_5$	Ph	25	89[e]	100	88[e,f]	139-140(136-137)[21,24]
6	C_6H_5	Me	60	90	90	93	–[20,21,24]
7	4-$CH_3C_6H_5$	Me	80	80	90	82	–[21]
8	4-ClC_6H_5	Me	–	–	–	–	–
9	3-$NO_2C_6H_5$	Me	100	87[g]	120	85[g]	75-77(76-79)[h,22,25]
10	4-$NO_2C_6H_5$	Me	–	–	–	–	–

[a]DBDMH; [b]DCDMH; [c]Reagent:substrate ratio is 1:1 unless otherwise noted; [d]Temperature was 70 ºC unless otherwise noted; [e]At 80 ºC; [f]Reagent:substrate ratio 1.5:1; [g]At 75 ºC; [h]3-nitroacetophenone-2, 4-dinitrophenylhydrazone.

secondary alcohols was examined in the presence of DBDMH and DCDMH in the range of temperature 70-80 ºC under solvent-free condition. The corresponding results are displayed in Table 1. As it can be seen in Table 1, the reactions were carried out efficiently within 15-100 min, and the desired products were produced in high to excellent yields (82-95%). Thus, DBDMH and DCDMH are highly efficient and mild reagents for the oxidation of alcohols. For the comparison of DBDMH with DCDMH, it should be mentioned that N-Br and N-Cl groups which are bonded to carbonyl group in the presented reagents as oxidant, could be released as Br^+ and Cl^+ easily. Table 1 indicates that bromine ion is more selective than chlorine ion; therefore DBDMH in comparison with DCDMH has higher efficiency in this reaction condition (shorter times and higher yields).

Since DBDMH and DCDMH contain Br and Cl atoms, respectively, which bonded to nitrogen atoms in heterocyclic rings, by *in situ* generation of Br^+ and Cl^+ from the reagents, the alcohol is converted to a hypobromite or hypochlorite which readily loses hydrogen bromide or hydrogen chloride to form the carbonyl product.[26]

To show the advantage, applicability and efficiency of DBDMH and DCDMH over the reported reagents for the synthesis of ketones, we have compared the results of our reagents with other reported reagents. As shown in Table 2, DBDMH and DCDMH can act as effective reagents with respect to reaction times and yields of the obtained products.

In another investigation, to confirm that these reagents could produce aliphatic and cyclic ketones or aliphatic and aromatic aldehydes from secondary aliphatic and cyclic or primary aliphatic and aromatic alcohols, we have performed these reactions with our reagents. As shown in Table 3, the yield of these reactions were very low and most of the starting material was remained in the mixture.

Conclusions

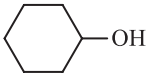
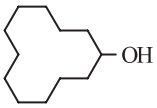
In conclusion, we have introduced a new method for the synthesis of secondary aromatic ketones via the oxidation of secondary alcohols such as benzhydrol and its derivatives and 1-phenyl ethanol and its derivatives

Table 2. Comparison result of DBDMH and DCDMH with other reported catalysts in the synthesis of benzophenone

entry	Reagent	Condition	time / min	Yield / %	Reference
1	DBDMH	Solvent free, 70 ºC	30	94	This work
2	DCDMH	Solvent free, 70 ºC	45	92	This work
3	PhIO	Ru catalysis, CH_3CN, 25 ºC	480	63	5
4	TBBDA[b]	MW	6	75	26
5	PBBS[c]	MW	6	60	27
6	BNBBS[a]	CH_2Cl_2, r.t.	320	95	27

[a]*N*,*N*,*N'*,*N'*-tetra-bromobenzene-1,3-disulphonamide; [b]poly(*N*-bromobenzene-1,3-disulfonamide); [c]*N*,*N'*-dibromo-*N*,*N'*-1,2-ethanediylbis (benzenesulfonamide); MW: microwave; r.t.: room temperature.

Table 3. Oxidation of primary and secondary aliphatic, primary aromatic and cyclic alcohols with DBDMH and DCDMH in the absence of solvent

entry	Reactant	Substrate:Reagent	time[a,b] / h	Yield / %	time[a,c] / h	Yield / %
1	$C_6H_5CH_2OH$	1:1	0.75	40	1	30
2	4-$OMeC_6H_5CH_2OH$	1:1.5	1	30	1.5	28
3	4-$ClC_6H_5CH_2OH$	1:1.5	2	25	2.3	25
4	4-$NO_2C_6H_5CH_2OH$	1:2	2.5	30	3	25
5		1:1	2	35	2.5	30
6		1:1.5	2.5	30	3	25
7	$CH_3CH_2CH_2CH_2CH_2OH$	1:1	3	27	3.2	22
8	$CH_3CH_2CH(OH)CH_3$	1:1.5	1.5	38	2	30

[a]Longer time did not increase the yields; [b]DBDMH; [c]DCDMH.

using 1,3-dibromo-5,5-dimethylhydantoin (DBDMH) and 1,3-dichloro-5,5-dimethylhydantoin (DCDMH) as homogenous *N*-halo reagents in the range of temperature 70-80 ºC under solvent-free condition. The advantages of the presented method are efficiency, high yield, short reaction time, cleaner reaction profile, simplicity, not requiring highly specialized equipment and expensive reagents. It is necessary to mention that previous related reactions require long times, toxic solvent and, etc. to complete reactions.

As it shown, because of low yield and remaining of unreacted starting materials, these reagents were not suitable for oxidation of benzyl and primary and secondary aliphatic alcohols to corresponding carbonyl compounds.

Supplementary Information

Supplementary information (Table S1) is available free of charge at http://jbcs.sbq.org.br as PDF file.

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