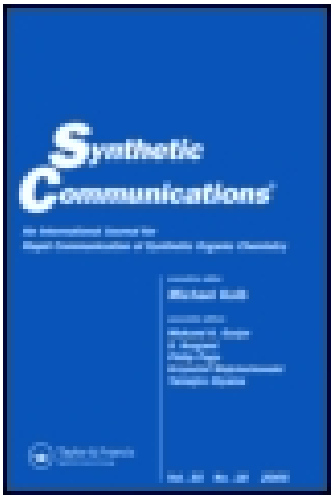

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N-Bromosuccinimide: A Facile Reagent for the Oxidation of Benzylic Alcohols to Aldehydes

Subbarayappa Adimurthy [a] & Paresh U. Patoliya [a]
[a] Analytical Science Division , Central Salt and Marine Chemicals Institute , Bhavnagar, India
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N-Bromosuccinimide: A Facile Reagent for the Oxidation of Benzylic Alcohols to Aldehydes

Subbarayappa Adimurthy and Paresh U. Patoliya
Analytical Science Division, Central Salt and Marine Chemicals Institute, Gijubhai Badheka Marg, Bhavnagar, India

Abstract: The oxidation of benzylic alcohols to aldehydes using *N*-bromosuccinimide (NBS) under ambient conditions without use of a transition-metal catalyst has been described.

Keywords: aldehydes, benzylic alcohols, *N*-bromosuccinimide

INTRODUCTION

Oxidation of alcohols to carbonyl compounds is a pivotal transformation in organic chemistry, and numerous methods using a variety of reagents and conditions have been developed.[1] Carbonyl compounds are an important group of molecules in synthetic chemistry because they are essential constituents of pharmaceuticals, dyes, fragrances, and industrially important chemicals.[2,3] Metal-based reagents are widely used for the oxidation of variety of a compounds under anhydrous conditions, including primary and secondary alcohols. Extensive work has led to development of a good number of chromium complexes such as dipyridine chromium(VI) oxide,[4] chromium trioxide-3,5-dimethylpyrazole complex,[5] pyridinium chlorochromate (PCC),[6] pyridinium dichromate (PDC),[7] 2,2′-bipyridinium chlorochromate (BIPCC),[8] pyridinium flurochromate,[9] quinolinium flurochromate,[10]

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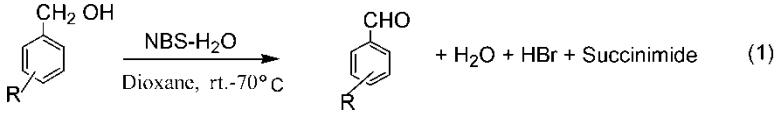
Address correspondence to Subbarayappa Adimurthy, Analytical Science Division, Central Salt and Marine Chemicals Institute, Gijubhai Badheka Marg, Bhavnagar 364 002, India. E-mail: adimurthy@csmcri.org or sadimurthy@yahoo.com

quinolinium chlorochromate,[11] and 2,6-dicarboxypyridinium chlorochromate[12] for the oxidation of alcohols to corresponding aldehydes and ketones. A number of other useful methods have also been reported via H_2O_2-mediated oxidation of alcohols catalyzed by tungsten systems such as tungstic acid,[13] quaternary ammonium tetrakis(diperoxotungsto)phosphates,[14] sodium tungstate–$[(n\text{-}C_4H_9)_4N]Cl$,[15] and sodium tungstate–quaternary ammonium hydrogen sulfate.[16] In the past decade, there has been increasing interest in other metal-catalyzed reagent systems capable of converting alcohols to the corresponding keto compounds.[17] Recently, *o*-iodoxybenzoic acid,[18] [hydroxy(tosyloxy)iodo]benzene,[19] polyaniline–$VO(acac)_2$,[20] oxoperoxo-molybdenum(VI) and tungsten(VI) complexes,[21] *N*-methylbenzylammoniumflurochromate–SiO_2,[22] other catalysts with molecular oxygen,[23] H_2O_2–imidozolium phosphotungstate complex,[24] *N*-hydroxy phthalimide in combination with a ruthenium complex,[25] H_2O_2/HBr with 2,2,6,6-Tetramethylpiperidine-1-oxxyl (TEMPO) as catalyst,[26] and ruthenium-based complex-catalyzed aerobic oxidation of alcohols[27] have been successfully used for this purpose. Unfortunately, most of these methods suffer the drawbacks associated with the hazard of peroxides, costly heavy-metal catalysts, and formation of by-products. The increasing awareness of environmental risks and green and sustainable chemistry has led to a search for cleaner and simpler processes to address many of the traditional industrial problems.

RESULTS AND DISCUSSION

Recently, we have reported the preparation of an atom-efficient and eco-friendly brominating reagent[28] and its utility in a variety of bromination reactions including the batch-scale preparation of *N*-bromosuccinimide (NBS) in high purity.[29] Our interest in exploring the potential applications of NBS prompted us to investigate the oxidation of benzylic alcohols to benzaldehydes by a facile and convenient method without the use of transition metals (Eq. (1). We report our findings in the present communication.



To check the feasibility of the method, the initial reaction was carried out with benzyl alcohol at ambient temperature (25–30°C) with comparatively low conversion (53.7%) but benzaldehyde was selectively obtained in 84.4% isolated yield, whereas at 70°C, the conversion was 100% with isolated yields of 60% benzaldehyde and 34% benzyl bromide. In the cases of 4-nitro-, 4-bromo-, and benzyl alcohols, also 34%, 7.4% and 13%, respectively, corresponding benzyl bromide formation was observed (entries 2 and 8,

Table 1. Oxidation of benzylic alcohols to aldehydes with N-Bromosuccinimide.

			At rt (25–30°C)			At 70°C		
Entry	alcohol	Product	Conversion (%)	Time (h)	Yield (%)[a]	Conversion (%)	Time (h)	Yield (%)
1	$PhCH_2OH$	PhCHO	53.7	1.5	84.4	100	1.0	94[b]
2	$4\text{-}NO_2C_6H_4CH_2OH$	$4\text{-}NO_2C_6H_4CHO$	67	2.0	93.3	78.6	2.0	93[c]
3	$3\text{-}NO_2C_6H_4CH_2OH$	$3\text{-}NO_2C_6H_4CHO$	57	2.0	89	71	1.0	100
4	$2\text{-}NO_2C_6H_4CH_2OH$	$2\text{-}NO_2C_6H_4CHO$	24	2.0	71	47	1.0	90
5	$4\text{-}ClC_6H_4CH_2OH$	$4\text{-}ClC_6H_4CHO$	50	1.5	90.6	71	1.0	86.4
6	$3\text{-}ClC_6H_4CH_2OH$	$3\text{-}ClC_6H_4CHO$	50	1.5	88	63	1.0	99
7	$2\text{-}ClC_6H_4CH_2OH$	$2\text{-}ClC_6H_4CHO$	32	1.5	81	60	1.0	95.2
8	$4\text{-}BrC_6H_4CH_2OH$	$4\text{-}BrC_6H_4CHO$	63	1.0	92	100	1.0	91[d]
9	$4\text{-}MeC_6H_4CH_2OH$	$4\text{-}MeC_6H_4CHO$	59	1.0	93.5	—	1.0	—
10	$4\text{-}MeOC_6H_4CH_2OH$	$4\text{-}MeOC_6H_4CHO/4\text{-}BrC_6H_4OMe$	100	3.0	19/70	57	1.5	72/19
11	$3\text{-}MeOC_6H_4CH_2OH$	$3\text{-}MeO(4\text{-}Br)C_6H_3CH_2OH$	71.6	2.0	97	100	1.5	84
12	$2\text{-}MeOC_6H_4CH_2OH$	$2\text{-}MeOC_6H_4CHO/2\text{-}MeO\text{-}(5\text{-}Br)C_6H_3CH_2OH$	100	1.0	20/79	100	1.0	0/83

[a]Isolated yields based on conversion.
[b]34% Benzyl bromide.
[c]7.4% 4-Nitrobenzylbromide.
[d]13% 4-(Br) benzylbromide.

Table 1). The reaction of 4-methoxy benzyl alcohol with NBS at room temperature yielded 4-methoxy benzaldehyde and 4-bromoanisole in 19% and 70% respectively with 100% conversion (entry 10, Table 1), whereas at 70°C, more aldehyde formation (with 57% conversion) was observed. 3-Methoxy benzyl alcohol does not gave any aldehyde at all; instead, ring bromination was found even at 70°C. A similar strategy was observed with 2-methoxy benzyl alcohol at higher temperature. At 70°C, the conversions were found to be efficient in most cases studied except entry 10, Table 1. Interestingly, the overoxidation has been ruled out in any case by the present method.

In conclusion, we have developed a facile, efficient, and convenient method for the oxidation of benzylic alcohols to aldehydes under ambient to mild conditions employing *N*-bromosuccinimide in an aqueous medium. These transformations can be conveniently adapted to the wide range of benzylic alcohols in the absence of transition-metal catalysts, and the over-oxidations to acids has been ruled out.

EXPERIMENTAL

^{1}H NMR spectra were recorded on a Bruker-200-MHz FT-NMR DPX-200 in $CDCl_3$ with tetramethylsilane (TMS) as an internal standard, and ^{13}C NMR spectra were recorded at 50 MHz. Melting points were recorded on Veego capillary instrument and are uncorrected. Analytical thin-layer chromatography (TLC) was performed on Aluchrosep silica gel $60/UV_{254}$ with ultraviolet (UV) light purchased from Merck. Benzylic alcohols purchased from Aldrich. Purification of the reaction products was carried out by column chromatography using silica gel (100–200) mesh.

Procedure for the Oxidation of Benzylic Alcohols to Aldehydes

Benzaldehyde: 1.0 g (9.26 mmol) of benzylalcohol in 10 mL of dioxane was taken in a 100-mL, round-bottomed flask. *N*-bromosuccinimide (1.65 g, 9.26 mmol) and 3–4 drops of water were added. The mixture was stirred at room temperature for 90 min. The reaction mixture was washed with 2 mL of 5% sodium thiosulfate solution, and it was extracted with diethyl ether (15 mL × 3). The combined organic extract was dried over anhydrous sodium sulfate. Evaporation of solvent left the crude product, which was purified by column chromatography over silica gel (hexane–ethyl acetate 9:1) to get the pure benzaldehyde as colorless liquid (0.445 g, 4.20 mmol) in 84.4% yield based on the recovery of starting material (0.463 g, 4.29 mmol). The same reaction carried out at 70°C yielded 60% benzaldehyde (0.301 g, 2.84 mmol) and 34% benzyl bromide (0.277 g, 1.62 mmol).

5-Bromo-2-methoxy benzyl alcohol (entry 12, Table 1): ^{1}H NMR (200 MHz $CDCl_3$): (δ) 2.34 (1H, s), 3.82 (3H, s), 4.62 (2H, s), 6.71–6.75 (1H, d, $J = 8.6$), 7.32–7.37 (2H, dd, $J = 8.4$ & 2.4). ^{13}C NMR (50 MHz $CDCl_3$): (δ) 56.16, 61.65, 112.52, 113.51, 131.75, 131.86, 140.06. IR: ν_{max} (KBr): 3293, 2917, 2842, 1486, 1406, 1367, 1291, 1245, 1174, 1124, 1032, 976, 878, 799, 705, 621 cm^{-1}.

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