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Short Report

Tribromoisocyanuric Acid/Triphenylphosphine: a New System for Conversion of Alcohols into Alkyl Bromides

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Foi desenvolvido um método fácil e eficiente para a conversão de alcoóis em brometos de alquila em meio neutro, utilizando ácido tribromoisocianúrico e trifenilfosfina (razão molar 1,0:0,7:2,0, álcool/ácido tribromoisocianúrico/trifenilfosfina) em diclorometano à temperatura ambiente. Esse método pode ser aplicado para a conversão de alcoóis primários, secundários, benzílicos e alílicos, sendo os brometos correspondentes obtidos em 67-82% de rendimento. Alcoóis terciários não são reativos sob estas condições.

An efficient and facile method has been developed for the conversion of alcohols into alkyl bromides under neutral conditions using tribromoisocyanuric acid and triphenylphosphine (molar ratio 1.0:0.7:2.0, alcohol/tribromoisocyanuric acid/triphenylphosphine) in dichloromethane at room temperature. This method can be applied for the conversion of primary, secondary, benzylic and allylic alcohols, and their corresponding bromides are obtained in 67-82 % yield. Tertiary alcohols do not react under these conditions.

Keywords: alcohols, alkyl bromides, tribromoisocyanuric acid, triphenylphosphine

Introduction

Alkyl bromides are versatile compounds from both academic and industrial points of view that can be easily converted into a variety number of other functional groups through well-known methodologies.[1] Furthermore, several marine organic bromides with interesting biological activity have also been described.[2] Among the diverse methodologies described in the literature for the preparation of such compounds, the conversion of alcohols into the corresponding bromides is the most convenient.[3] Several reagents can accomplish this transformation, including the harmful and corrosive HBr/H_2SO_4,[4] phosphorous (oxy)bromides[5,6] or $SOBr_2$.[6] However, a very attractive mild methodology is based on the Appel reaction that uses a combined system of triphenylphosphine (TPP) with an electrophilic source or bromine, such as CBr_4,[7] 2,4,4,6,-tetrabromo-1,5-cyclohexadienone,[8] (poly) bromocarbonyls,[9] and various *N*-bromo compounds.[3,10,11]

Tribromoisocyanuric acid (TBCA, Figure 1) is a safe and stable electrophilic brominating reagent.[12] We have studied its utilization for bromination of alkenes,[13] arenes,[14] β-dicarbonyl compounds,[15] as well as for the bromodecarboxylation of cinnamic acids.[16] Furthermore, TBCA possesses some advantages compared to other *N*-bromo reagents, as it can easily be prepared from inexpensive materials (cyanuric acid, KBr and oxone)[17] and also presents high atom economy (i.e., maximizing the atomic mass from the reagents that can be incorporated into the product).[18]

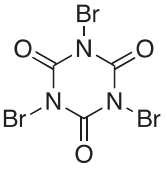

Figure 1. Tribromoisocyanuric acid (TBCA).

Continuing our interest on the chemistry of trihaloisocyanuric acids,[19] we present here our initial results on the utilization of the system TBCA/triphenylphosphine for conversion of alcohols into alkyl bromides.

Results and Discussion

In initial experiments, it was chosen 2-octanol as model substrate to test the methodology. Using an equimolar

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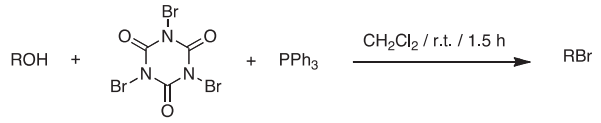
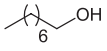
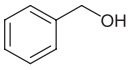
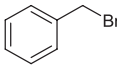
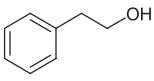
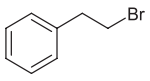
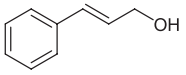
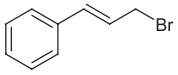
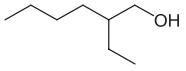
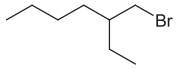
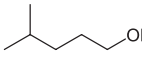
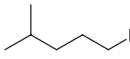
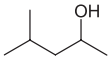
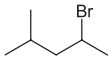
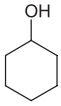
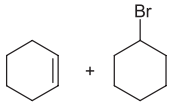
amount of the reagents (1.0:0.34:1.0, alcohol/TBCA/TPP), the reaction was slow. However, the reaction proceeded with complete substrate conversion using a molar ratio of 1.0:0.7:2.0 (alcohol/TBCA/TPP) within 1.5 h in CH_2Cl_2 at room temperature. Therefore, the results of the reaction of alcohols with TBCA/TPP to produce the corresponding alkyl bromides (along with triphenylphosphine oxide and cyanuric acid) are shown in Table 1. In general, the reactions proceeded smoothly for the conversion of primary, secondary, benzylic and allylic alcohols to their corresponding alkyl bromides (67-82%). On the other hand, tertiary alcohols do not react, even in acetonitrile under reflux. Analysis of the crude reactions by gas chromatography (GC) indicated that the alkyl bromides were obtained pure, with exception of cyclohexyl bromide, which was formed as a mixture with cyclohexene (ca. 2:3 by gas chromatography-mass spectrometry (GC-MS)). In addition, although TBCA is a useful reagent for the alcohol oxidation[20] and bromination of alkenes[13] and arenes,[14] none of these products were detected by the analytical techniques employed, showing that the method is quite general and suitable for the conversion of benzylic and allylic alcohols into their corresponding bromides.

Table 1. Conversion of alcohols into alkyl bromides



Alcohol	Product	Yield / %[a]
		73
		82
		78
		70
		75
		67
		76
		70
		61+39[b]
	no reaction	-

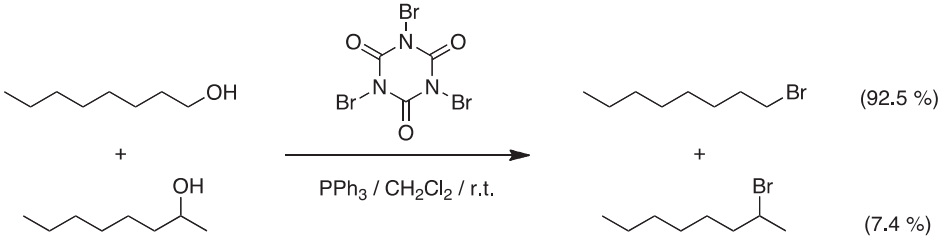
[a]Isolated yield, based on alcohol. [b]Determined by GC-MS.

A competitive reaction was designed for showing the chemoselectivity of the TBCA/TPP system toward alcohols (Scheme 1). Therefore, a mixture of equimolar amounts of 1-octanol and 2-octanol was subjected to the conditions described in Table 1 and it was observed that the primary alcohol is 12.5 more reactive than the secondary alcohol (determined by GC-MS).

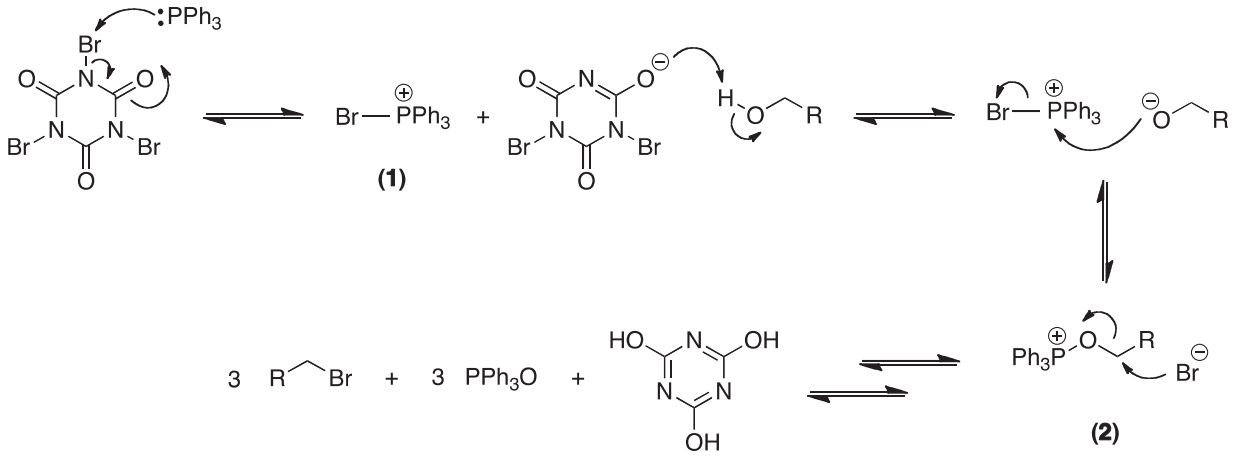
Based on the above results, a S_N2 process could be involved in the reaction of alcohols with TBCA/TPP to produce alkyl bromides, as also observed in similar reactions with different *N*-bromo compounds.[3,11] A plausible scheme for this transformation (Scheme 2) proceeds by TBCA bromination of TPP to produce a bromophosphonium salt (**1**) that is further converted into the oxyphosphonium intermediate (**2**). Bromide anion attack on the intermediate **2** gives the alkyl bromide and triphenylphosphine oxide. After two repetitions of the whole process, cyanuric acid is also formed and precipitates at the end of the reaction.

Conclusions

In summary, we have developed a very convenient route for the preparation of primary and secondary alkyl bromides from alcohols under neutral conditions. The reaction is easily reproducible, the conditions are mild and the reagents are easily available. Although the yields using our



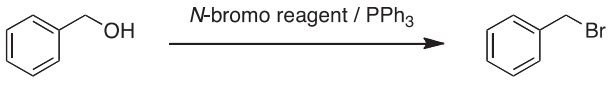
Scheme 1.

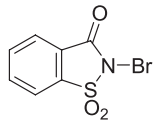
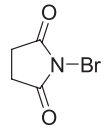
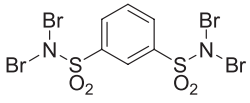
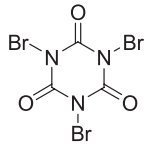


Scheme 2.

methodology is lower than similar reactions (Table 2), the advantages of TBCA compared to other *N*-bromo reagents, such as easily preparation and high atom economy, turn our methodology very convenient.

Table 2. Preparation of benzyl bromide using diverse *N*-bromo reagents



N-bromo reagent	Atom economy / %[a]	Yield / %	Reference
	30.5	90	3
	44.9	81	21
	57.9	90	11
	65.5	78	this work

[a]Mass % of the reagent transferred to the product.

Experimental

General information

All chemicals and solvents were used as received. Tribromoisocyanuric acid was prepared as described.[17] The spectra were recorded on a Bruker AC-200 spectrometer at 200 MHz (^{1}H) and 50 MHz (^{13}C) in $CDCl_3$ solutions with tetramethylsilane (TMS) as internal standard. High-resolution gas chromatography was performed on a HP-5890-II gas chromatograph with flame ionization detector (FID) using a 30 m (length), 0.25 mm internal diameter (ID), and 25 μm (phase thickness) RTX-5 capillary column and H_2 (flow rate 50 cm s^{-1}) as carrier gas (split: 1:10). Infrared (IR) spectra were recorded on a Nicolet 740 FT-IR spectrometers (KBr film). GC-MS analyses were performed on a Shimadzu GCMS-QP2010S gas chromatograph with electron impact (70 eV) by using a 30 m DB-5 silica capillary column.

General procedure for the preparation of alkyl bromides

TBCA (1.4 mmol) was added to a stirred solution of TPP (4 mmol) in CH_2Cl_2 (50 cm^3). After 5 min, the alcohol (2 mmol) was added and the suspension was stirred at room temperature. After 1.5 h, cyanuric acid was filtered off, the liquid was washed with water (2 × 25 cm^3) and the organic phase was dried (Na_2SO_4) and evaporated on a rotatory evaporator under reduced pressure. The residue was treated with pentane and filtered through a silica gel (70-230 mesh) pad. The pure alkyl bromide was obtained after evaporation of pentane.

2-bromooctane: boiling point (bp) 190 °C (lit: 188.5 °C);[22] IR (KBr) ν/cm^{-1} 2958, 2927, 2858, 1457, 1378, 1259, 1218, 1146, 1007, 725, 618, 541; ^{1}H NMR (CDCl3, 200 MHz) δ 0.90 (t, 3H, C$\underline{H}_3$-$(CH_2)_5$), 1.43-1.49 (m, 8H, CH_3-$(C\underline{H}_2)_4$), 1.72 (d, 3H, C$\underline{H}_3$-CHBr), 1.76-1.97 (m, 2H, C$\underline{H}_2$-CHBr), 4.14 (m, 1H, C$\underline{H}$Br); ^{13}C NMR (CDCl3, 50 MHz) δ 14.3 (C8), 22.8 (C7), 26.7 (C1), 27.9 (C6), 28.9 (C5), 31.9 (C4), 41.4 (C3), 52.1 (C2); MS (70 eV) *m/z* 123 (M^+ + 2 - C_5H_{11}), 121 (M^+ - C_5H_{11}), 113, 71, 57 (100%), 43, 41.

1-bromooctane: bp 198 °C (lit: 201 °C);[23] IR (KBr) ν/cm^{-1} 2958, 2927, 2855, 1466, 1439, 1378, 1256, 1099, 911, 723, 647, 564; ^{1}H NMR (CDCl3, 200 MHz) δ 0.89 (t, 3H, C$\underline{H}_3$), 1.28-1.45(m, 10 H, CH_3-(C$\underline{H}_2$)$_5$), 1.81-1.91 (m, 2H, C$\underline{H}_2$-CH_2Br), 3.41 (t, 2H, C$\underline{H}_2$Br); ^{13}C NMR ($CDCl_3$, 50 MHz) δ 14.0 (C8), 22.6 (C7), 28.2 (C6), 28.7 (C5), 29.1 (C4), 31.7 (C3), 32.8 (C2), 33.9 (C1); MS (70 eV) *m/z* 194 (M^+ + 2), 192 (M^+), 151, 149, 137, 135, 123, 121, 109, 107, 95, 93, 71, 57, 43 (100%).

1-bromo-2-phenylethane: bp 218 °C (lit: 220-225 °C);[24] IR (KBr) ν/cm^{-1} 3085, 3062, 3027, 2964, 2944, 2862, 1602, 1584, 1496, 1454, 1431, 1314, 1262, 1215, 1196, 1030, 919, 750, 699, 648, 542, 487; ^{1}H NMR ($CDCl_3$, 200 MHz) δ 3.18 (t, 2H, *J* 7.9, PhC$\underline{H}_2$), 3.59 (t, 2H, *J* 7.9, C$\underline{H}_2$Br), 7.20-7.39 (m, 5H, C$\underline{H}_{arom}$); ^{13}C NMR ($CDCl_3$, 50 MHz) δ 33.0 (C$\underline{H}_2$Br), 39.6 (Ph$\underline{C}H_2$), 127.1 (C_{arom}), 128.7 (C_{arom}), 128.9 (C_{arom}), 139.1 (C_{arom}); MS (70 eV) *m/z* 186 (M^+ + 2), 184 (M^+), 140, 105, 91 (100%), 77, 65, 51.

benzyl bromide: IR (KBr) ν/cm^{-1} 3086, 3063, 3030, 2967, 2931, 2857, 1601, 1586, 1495, 1453, 1378, 1226, 1201, 1098, 1068, 1028, 917, 812, 757, 694, 604, 547, 454. ^{1}H NMR ($CDCl_3$, 200 MHz) δ 4.51 (s, 2H, C$\underline{H}_2$Br), 7.27 – 7.44 (m, 5H, C$\underline{H}_{arom}$); ^{13}C NMR ($CDCl_3$, 50 MHz) δ 33.7 (C$\underline{H}_2$Br), 128.5 (C_{arom}), 128.9 (C_{arom}), 129.2 (C_{arom}), 137.9 (C_{arom}); MS (70 eV) *m/z* 172 (M^+ + 2), 170 (M^+), 91 (100%), 74, 65, 51.

cinnamyl bromide: IR (KBr) ν/cm^{-1} 3083, 3058, 3027, 2959, 2924, 2852, 1644, 1596, 1576, 1495, 1449, 1430, 1302, 1203, 1075, 970, 841, 748, 691, 622, 572, 493; ^{1}H NMR ($CDCl_3$, 200 MHz) δ 4.18 (d, 2H, *J* 7.8, C$\underline{H}_2$), 6.41 (dt, 1H, *J* 15.6, 7.8, C$\underline{H}$-CH_2Br), 6.67 (d, 1H, *J* 15.6, PhC$\underline{H}$), 7.27-7.43 (m, 5H, C$\underline{H}_{arom}$); ^{13}C NMR ($CDCl_3$, 50 MHz) δ 33.6 (C$\underline{H}$-Br), 125.4 (C$\underline{H}$-CH_2Br), 126.9 (C_{arom}), 128.5 (C_{arom}), 128.8 (C_{arom}), 134.7 (Ph$\underline{C}$H), 136.0 (C_{arom}); MS (70 eV) *m/z* 117 (M^+ - Br, 100%), 102, 91, 77, 63, 58, 51.

1-bromo-2-ethylhexane: IR (KBr) ν/cm^{-1} 2961, 2929, 2873, 2859, 1458, 1436, 1379, 1267, 1253, 1226, 1099, 779, 765, 727, 650, 619. ^{1}H NMR ($CDCl_3$, 200 MHz) δ 0.85-0.92 (m, 6H, 2 CH_3), 1.20-1.53 (m, 9H, C$\underline{H}_2$-C$\underline{H}$-(C$\underline{H}_2$)$_3$), 3.45 (m, 2H, C$\underline{H}_2$Br); ^{13}C NMR ($CDCl_3$, 50 MHz) δ 11.1 (C$\underline{H}_3$), 14.2 (C$\underline{H}_3$), 23.1 (C5), 25.4 (C4), 29.1 (CH_3-C$\underline{H}_2$-CH), 32.1 (C3), 39.3 (C1), 41.3 (C2); MS (70 eV) *m/z* 165 (M^+ + 2 - Et), 163 (M^+ - Et), 137, 135, 83, 71, 57 (100%), 41.

1-bromo-4-methylpentane: IR (KBr) ν/cm^{-1} 2958, 2935, 2871, 2852, 1468, 1438, 1386, 1368, 1299, 1254, 1208, 1169, 1099, 1052, 924, 751, 736, 640, 564, 539; ^{1}H NMR ($CDCl_3$, 200 MHz) δ 0.91 (d, 6H, C$\underline{H}_3$), 1.26-1.37 (m, 2H, C$\underline{H}_2$-CH(CH_3)$_2$), 1.49-1.69 (m, 1H, C$\underline{H}$), 1.80-1.97 (m, 2H, C$\underline{H}_2$-CH_2Br), 3.41 (t, 2H, C$\underline{H}_2$Br); ^{13}C NMR ($CDCl_3$, 50 MHz) δ 22.6 (C5), 27.6 (C4), 31.0 (C3), 34.3 (C2), 37.6 (C1); MS (70 eV) *m/z* 166 (M^+ + 2), 164 (M^+), 151, 149, 123, 121, 109, 107, 95, 93, 85, 69, 56, 43 (100%).

2-bromo-4-methylpentane: IR (KBr) ν/cm^{-1} 2983, 2960, 2924, 2872, 2827, 1467, 1452, 1379, 1259, 1199, 1149, 1051, 1001, 989, 921, 858, 813, 617, 540; ^{1}H NMR ($CDCl_3$, 200 MHz) δ 0.90 (d, 3H, C$\underline{H}_3$CH), 0.92 (d, 3H, C$\underline{H}_3$CH|), 1.44-1.54 (m, 1H, C$\underline{H}$(CH_3)$_2$), 1.71 (d, 3H, C$\underline{H}_3$-CHBr), 1.77-1.96 (m, 2H, C$\underline{H}_2$), 4.13-4.24 (m, 1H C$\underline{H}$Br); ^{13}C NMR ($CDCl_3$, 50 MHz) δ 21.6 (C5), 22.9 (C5'), 26.9 (C4), 27.0 (C1), 50.2 (C2), 50.5 (C3); MS (70 eV) *m/z* 121 (M^+ - *i*Pr), 109, 107, 85, 69, 57, 55, 43 (100%).

cyclohexyl bromide: MS (70 eV) *m/z* 164 (M^++2), 162 (M^+), 83 (100%), 67, 55, 41.

Supplementary Information

^{1}H and ^{13}C NMR, IR and MS spectra of synthesized compounds are available free of charge at http://jbcs.sbq.org.br as PDF file.

Acknowledgment

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