OPTIMIZATION OF CONDITIONS FOR THE FACILE, EFFICIENT & SELECTIVE α-BROMINATION OF METHYL AND METHYLENE KETONES

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ABSTRACT: *The H_2SO_4 was demonstrated as an efficient and regio-selective catalyst for the α-bromination of methylarylketones and cyclic ketones under mild conditions. A detailed comparative study was performed on the α-bromination of α-hydrogen bearing cyclic and acyclic ketones by employing a variety of acidic, basic and neutral reagents under different conditions; among all reagents, H_2SO_4 appeared to afford the best results. Theselectivity of formation of α-bromo and α,α-dibromoketones was found to be dependent on the equivalents of H_2SO_4 used and to a lesser extent on the temperature conditions.*

Key words: α-bromination, selective, methyl ketone, methylene ketone

1. INTRODUCTION

Halogenated organic compounds are important synthetic intermediates due to feasibilityof their transformation into a variety of functional molecules. The α-bromination of carbonyl compounds is an important reaction in organic synthesis since the resulting α-bromo compoundsserve as important precursors in the synthesis of variety of molecules, including biologically active compounds.[1-2]Phenacyl bromides are of particular important molecules because they are widely used as precursors of various pharmaceutically important heteroaromatics such as imidazoles, selenazoles, and oxazoles.[3-4]

Quite a significant amount of literature is available for bromination protocols of methylarylketonesthat involve use of:Br_2 or its complexes in the presence of protic or Lewis acid,[5-11]bases,[12-15]*N*-bromosuccinimide (NBS),[16-22]NBS/NH_4OAc,[23]a combination of *N*-halosuccinimide/TsOH/CH_3CN,[24] hypervalent iodine sulfonate/magnesium halides under microwaves[25]and HBr/O_2/hv.[26]Nevertheless, these brominating reagents have some limitations including their low atom efficiency, the need for reagent residue removal and that molecular bromine is required for their preparation.The regioselectivityand mono-halogenation of ketones are still problems that have not been solved.[27-32]

Although bromine is hazardous with associated risks in handling and transport, it is still being used by industry as well as academia due to its low cost, easy availability, and the lack of a better alternative. We report herein our efforts to find a facile, selective and economical protocol for the bromination of cyclic ketones and methylarylketones bearing a variety of substituents. The bromination was tried by employing different reagents under acidic (Br_2/H_2SO_4 and Br_2/AcOH), neutral (NBS and NBS/AIBN) and basic (Br_2/NaOH, Br_2/DBU, Br_2/Et_3N) conditions.

2. RESULTS & DISCUSSION

The significance of selectivity cannot be ignored when a projected synthetic scheme may result in a number of potential products. The lack of selectivity often leads to formation of a number of products that result in an overall decrease in yield of the desired product.

The phenacyl bromides are important molecules because they are widely used as precursors of a wide range of compounds of commercial and pharmaceutical significance. The bromination of α-hydrogen bearing ketones often leads to non-selective bromination rendering mono-bromo products along with dibromo product as a minor / side product. In order to device a facile, industrially applicable and economical strategy for selective bromination, the acetophenone, used as model substrate, was subjected to α-bromination by using different reagentswhich rendered bromoproducts with different selectivities

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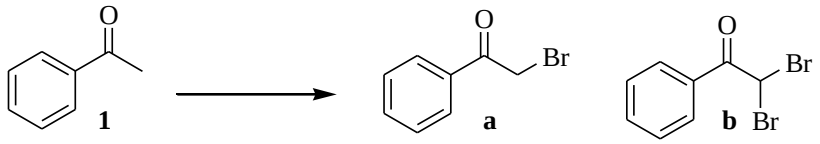


Table 1: Optimization of conditions for the selective bromination of acetophenone

Sr. No	Reagent (eq^)	Eq of Br_2^	Solvent	Temperature (time)	% Yield a	b
1	NaOH (0.5)	0.5	MeOH	Rt (3h)	25	-
2	NaOH (0.75)	0.75	MeOH	Rt (5 h)	34	-
3	DBU	0.5	$CHCl_3$	Rt (5 h)	15	-
4	DBU	1.5	$CHCl_3$	Rt (5 h)	17	-
5	DBU	1.5	$CHCl_3$	Reflux (3 h)	*	
6	Et3N	0.5	$CHCl_3$	Rt (3 h)	32	12
7	Et3N	0.75	$CHCl_3$	Rt (5 h)	42	24
8	NBS (1.5)	-	CCl_4	hv (4 h)	21	15
9	NBS (1.5)	-	CCl_4	hv (8 h)	28	23
10	NBS (2.5)	-	CCl_4	hv (4 h)	45	48
11	NBS (3.0)	-	CCl_4	Reflux (2.5 h)	51	43
12	AcOH (excess)	1.0	-	Reflux (3 h)	-	100
13	H_2SO_4 (0.1)	0.5	$CHCl_3$	Rt (4 h)	-	-
14	H_2SO_4 (0.2)	0.5	$CHCl_3$	Rt (4 h)	67	-
15	H_2SO_4 (0.2)	1.0	$CHCl_3$	Rt (4 h)	100	-
16	H_2SO_4 (0.4)	1.0	CH_2Cl_2	Rt (4h)	62	23
17	H_2SO_4 (0.4)	1.5	CH_2Cl_2	Rt (4h)	70	21
18	H_2SO_4 (0.5)	1.5	CH_2Cl_2	Reflux (6 h)	12	81
19	H_2SO_4 (0.5)	2.5	CH_2Cl_2	rt (4 h)	10	84
20	H_2SO_4 (0.6)	1.5	CH_2Cl_2	rt (4 h)	~5	95
21	H_2SO_4 (0.6)	2.0	CH_2Cl_2	Reflux (6 h)	-	100

^ Equivalents with respect to acetophenone; *a number of products were observed on TLC.

The α-bromination of acetophenone under base catalyzed conditions resulted in quite low transformationsyielding. The NBS afforded mono bromo as well as dibromo product in almost 1:1 both under photochemical and thermolytic conditions. When acetophenone was treated with Br_2 in the presence of AcOH (used as solvent) only dibromo product was isolated as the exclusive product. While with H_2SO_4 catalyzed conditions, both mono and dibromo products were obtained. The relative ratio of the two products was found to be dependent on the equivalents of H_2SO_4 used. The mono-bromo product was isolated exclusively when 0.2 equivalents of H_2SO_4 were employed while with 0.6 equivalents dibromo product was isolated as the only product.

The H_2SO_4mediated bromination appeared to be of greater industrial utility due to the easy availability and economy of reaction involving Br_2 and H_2SO_4. If the concentration of $H_2SO_4$is optimized, we can easily prepare mono and/or dibromo products depending upon the desired product. These results prompted us to explore H_2SO_4 as potential candidate for the selective bromination of various methyketones.

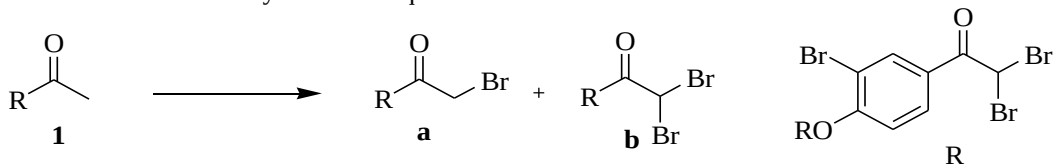


Table 2: H_2SO_4 mediated Bromination of Methylketones

	R	Br_2^	H_2SO_4^	Temperature (time)	%Yeild a	b	c
2	4-ClPh	1.0	0.2	Rt (4 h)	97	-	-
		1.5	0.6	Reflux (6)	-	100	-
3	4-MePh	1.0	0.2	Rt (4 h)	90	10	-
		1.5	0.6	Reflux (6)	100	-	
4	2-thiophenyl	1.0	0.2	Rt (4 h)	76	-	-
		1.5	0.6	Reflux (6)	8	83	-
5	4-HOPh	1.0	0.2	Rt (2.5 h)	93	-	-
		1.5	0.6	Reflux (3.5)	8	82	5
6	3- NO_2Ph	1.0	0.2	Rt (4 h)	94	-	-
		1.5	0.6	Reflux (6)	-	100	-
7	4-MeOPh	1.0	0.2	Rt (1.5 h)	100	-	-
		1.5	0.6	Reflux (4)	-	86	~10
		2.0	0.5	Reflux (5)	-	76	20
8	3,4-$(MeO)_2$Ph	1.0	0.2	Rt (1.5 h)	100	-	-
		1.5	0.6	Reflux (4)	-	100	-

^ Equivalents with respect to methylketones. All reactions were carried out in CH_2Cl_2

The brominated products were characterized by means of mass spectrometry as well as NMR. The appearance of [M] an [M+2] in 1:1 relative abundance indicated formation of mono bromoproducts while the appearance of three molecular ion peaks (i.e, [M], [M+2] and [M+4]) in 1:2:1 indicated dibromination. In case of 4-hydroxyacetophenone and 4-methoxyacetophenone, along with formation of mono and/or dibromo another product was also formed that showed four molecular ions in MS spectrum. The appearance of the four signals in relative abundance of 1:3:3:1 indicated the formation of a tribromoproduct. The ^{1}H NMR provided a futher better picture by the appearance of four aromatic signals for both mono and dibromo products and appearance of singlet of two aliphatic protons in case of mono-bromo product and the appearance of 1H singlet in case of dibromination. The 1H-NMR of the tribrominated product displayed the presence of three aromatic protons and single aliphatic protons. The same was also supported by ^{13}C NMR. The structure of tribrominated product was also confirmed by single crystal XRD (figure 1).

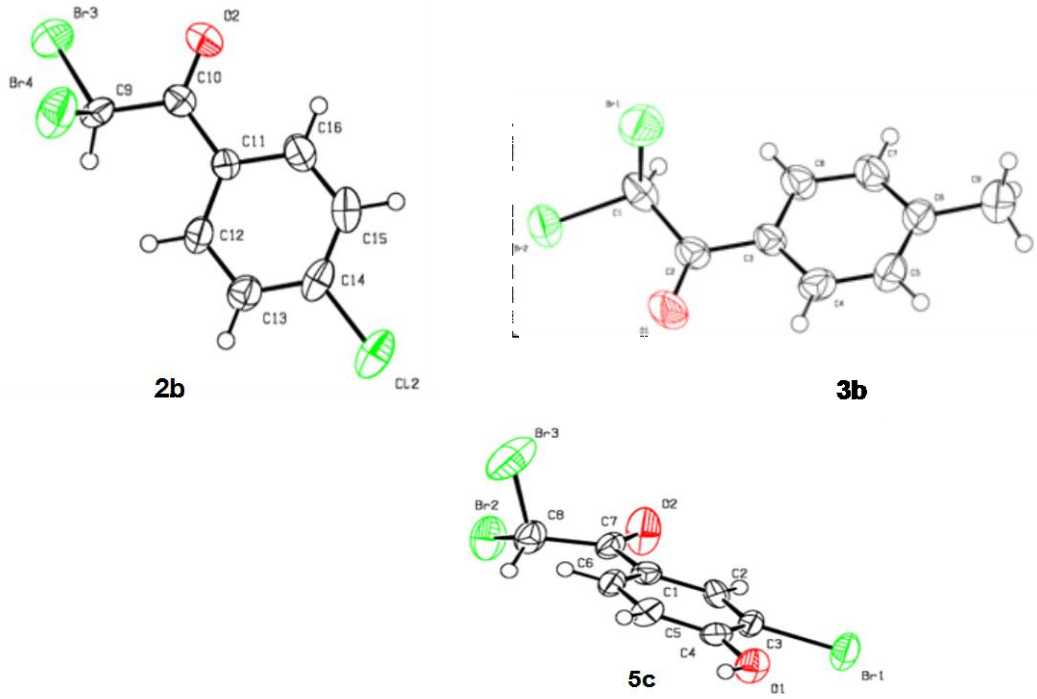


Figure 1: The ORTEP diagram of 2b, 3b and 5c

After the successful optimization of conditions for bromination of methyl ketones, the optimization for selective bromination of cyclic ketones was tried. 1-tetralone **10** and 1-indanone **9** were taken as models for the optimization. The synthesis of α-bromotetralone **11**was tried under different conditions which yielded different results (table **3**). The base catalyzed bromination of 1-tetralone **9** afforded a number of inseparable products irrespective of the nature of base used. It has been extensively reported that acid catalyzed condition result exclusively in the formation of mono-halogenation product. On this basis, the 1-tetralone was treated with Br_2 water using AcOH and/or H_2SO_4 as a catalyst. We observed that there exists a competition between the mono and dibromination depending upon the amount of acid added as a catalyst. When a catalytic amount of acid was employed, the mono bromo product **11** was the major product; however, when stoichiometric amount of acid was added or when acid was used as a solvent, the 2,2-dibromo product **12**was formed exclusively. The α-bromination was also tried under free radical conditions by making use of N-bromosuccinamide (NBS). The reaction was carried out under photolytic (using 100W tungsten bulb) as well as thermal conditions to induce N-Br cleavage. Both of these reactions worked well and yielded same product **11** as a pale yellow oil that was an eye and skin irritant as well as light and temperature sensitive. Best results were obtained by using NBS in portions instead of adding all of the amount at once.

The formation of mono bromo product **11**was confirmed by ^{1}H NMR that displays 5H in the aliphatic region with the most downfield proton (H^2) appearing at 4.76 ppm (dd, J = 4.5, 3.9 Hz). The appearance of 4H in the aromatic region confirms that aromatic ring has not been affected under the reaction conditions. Further confirmation of the formation of 2-bromo-1-tetralone **11** comes from the DEPT 135° which indicates presence of two triplet and a doublet carbons at 26.1, 31.9 and 50.5 ppm respectively.

Table 3: ***Synthesis of α-halo-1-tetralone*****.**

Entry	X_2 (equiv)	*Cat* (eq. to **180**)	Solvent	Reaction duration (temp)	Product
1	Br_2 (1.05)	NaOH (1.0)	H_2O	2 h (rt)	*
2	Br_2 (1.5)	Pyr (1.05)	CCl_4	3 h (reflux)	*
3	Br_2 (1.05)	Et_3N (1.05)	$CHCl_3$	3 h (reflux)	*
4	Br_2 (1.5)	H_2SO_4 (1-2drop)	CH_2Cl_2	4 h (reflux)	**11** (75%), **12**(10%)
5	Br_2 (2.4)	H_2SO_4 (0.5)	$CHCl_3$	4 h (reflux)	**12** (95%)
6	-	NBS (1.5)	$CHCl_3$	reflux (2 h)	**11**(80%)
7	-	NBS (1.5)	$CHCl_3$	6 h (reflux)∫	**11**(72%)
8	Br_2 (2.6)	AcOH		3 h (reflux)	**12**(98%)
9	I_2 (2.0)	H_2SO_4 (4.0)	$CHCl_3$	4 h (reflux)	-
10	I_2 (2.0)	AcOH (10)	$CHCl_3$	28 h (reflux)	**13** (88%)

*A large number of inseparable products were formed; []irradiated with 100 W tungsten bulb.

The formation of 2,2-dibromo-1-tetralone **12** is indicated by appearance of $[M]^{+\cdot}$ in LR EIMS at 302, 304 and 306 amu (1:2:1) thus confirming the presence of two Br atoms. The ^{1}HNMR indicates presence of 4H in aromatic region and two sets of dd (each of 2H integration) in aliphatic region at 3.06 and 3.09 ppm. The structure of the dibromo-product **12**is also supported by single crystal XRD that reveals the presence of two Br atoms (figure 2).

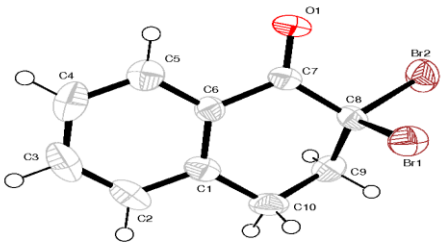


Figure 2: Single Crystal XRD of dibromo-1-tetralone 12.

The effectiveness of H_2SO_4 for the α-iodination was explored by using I_2. The reaction was very slow and required constant refluxing, interruption in the reflux time resulted in poor yield of the product. The yield of the product remained unaffected the amount of H_2SO_4 and/or I_2 used during the reaction. Furthermore, diiodo product was never isolated even if excessive I2 was employed or the higher equivalents of H_2SO_4 were employed.

The mono-iodination is confirmed by LR EIMS by appearance of $[M]^{+\cdot}$ at 272 amu (56%). The appearance of 5H in the aliphatic region in ^{1}H NMR confirm the substitution of a single proton with I atom. The most down field value (i.e, 5.00 ppm) was attributed to the H^2 proton (t, J = 4.5 Hz) which is affected by the –I effect of I as well as the C=O. The appearance of diastereotopy of 4H in the aliphatic region is consistent with the existence of a chiral center. The single crystal XRD also confirms the structure of iodo product **13** and indicates the product to be a *racemate* of *R*&*S* isomers (figure 3).

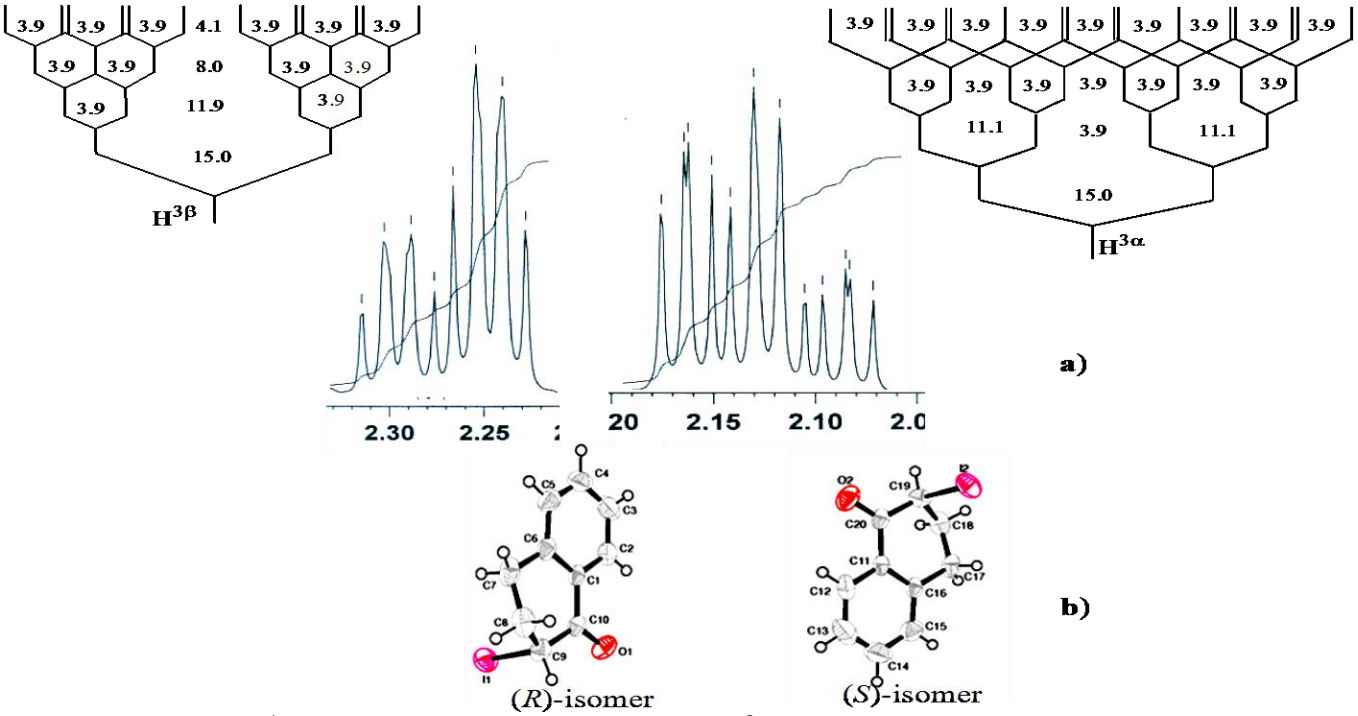
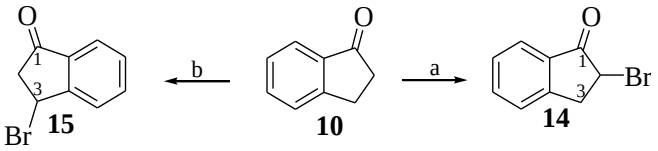


Figure 3: a) A portion of ^{1}H NMR spectrum showing diastereotopy of H^3; b) Single Crystal XRD structure of 2-iodo-1-tetralone 13 showing both enantiomers as mirror images.

The advantage of the **13** is that it is stable and doesn't decompose so readily unless exposed to light or high temperature as do its bromo-counterpart, **11.** Furthermore, the product **13** is not an irritant that makes its use an easy task.

The 2-bromo-1-indanone**14** was synthesized by heating the 1-indanone **10** with NBS under photochemical conditions for 2 hour using 100 W tungsten bulb. The reaction was quite clean which afforded succinimde as the only side product which was filtered off and the organic layer after washing with water and drying over anhydrous Na_2SO_4 afforded the 2-bromoindanone **14** as colorless solid. The appearance of C=O and C-Br stretching vibrations at 1712 and 673 cm^{-1} indicated the formation of bromo ketone. The ^{1}H-NMR indicated the presence of four aromatic and three aliphatic protons which confirmed the substitution of a single aliphatic proton with bromine. The aliphatic protons appeared as three sets of dd at 3.08 (J = 19.8, 2.7 Hz), 3.40 (J = 19.8, 7.2 Hz) and 5.69 (J = 7.2, 2.7 Hz). The most downfield chemical shift was assigned to H^2 which is under influence of –I effect of two highly electron withdrawing groups i.e., bromine and carbonyl carbon.



Reagent & conditions: a) NBS, hv, rt, DCM, 2 h; b) AIBN, NBS, DCM, reflux, 2h

The NBS mediated bromination has been extensively reported to be mediated by Lewis acids or by radical initiators. So in order to check the effectiveness of free radical initiator promoted bromination, the reaction of indanone was carried out with NBS in the presence of AIBN as a catalyst. The product thus formed appeared as a different spot on TLC. The mass spectrum as same as that of 2-bromo-1-indanone thus indicating mono-bromination while the 1H-NMR suggested the product to be 3-bromo-1-indanone**15**. The formation of the 3-bromo-1-indanone **15** was indicated by the presence of four aromatic protons and three protons in the aromatic region. The three aliphatic protons appeared as three sets of dd at 3.44 (J = 18.3, 3.0 Hz), 3.86 (J = 18.3, 7.8 Hz), 4.68 (J = 7.8, 3.0 Hz). The most downfield of these values was assigned to the H^3 which is under the influence of –I effect of bromine. The remaining two chemical shifts were attributed to H^4 protons which appear differently due to presence of a chiral center in their immediate vicinity. The ^{13}C-NMR provided further supportive evidence by confirming the presence of a d and a t carbon in the aliphatic region at 40.6 and 48.1 ppm corresponding to C^2& C^3.

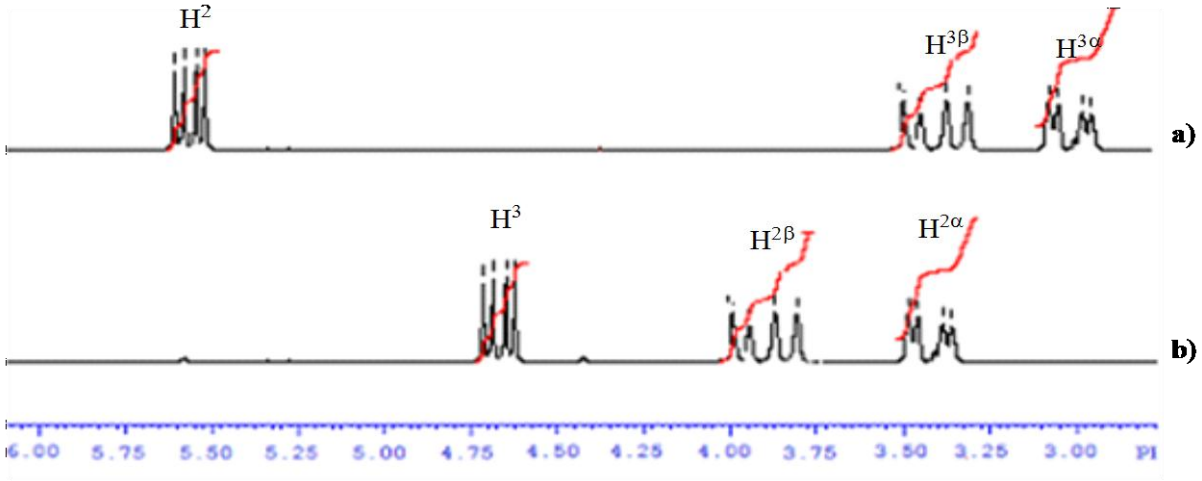


Fig. 4: Portions of ^{1}H NMR showing aliphatic region of a) 2-bromoindan-1-one 14; b) 3-bromoindan-1-one 15.

Table 4: Synthesis of 2,2-dibromoindan-1-one 16.

Entry	Br_2 (^)	Reagent (^)	Solvent	Reflux (h)	Product (% yield)
1	Br_2 (1.0)	H_2SO_4(0.2)	$CHCl_3$	4	**14** (62) &**16** (20)
2	Br_2 (1.5)	H_2SO_4 (0.5)	CH_2Cl_2	4	**16**(84)
3	Br_2 (1.5)	AcOH	AcOH	3	**16**(92)
4	Br_2 (2.0)	Et_3N (1.03)	$CHCl_3$	2	**14** (15), **16** (18)
5	Br_2 (2.0)	KOH (1.05)	MeOH	3	*

^ Equivalents to indanone; * a number of spots were observed on TLC which yielded only **17** upon chromatographic separation.

The dibromination of indanonewas successfully carried out by refluxing indan-1-one with Br_2 in the presence of H_2SO_4 and/or AcOH. The high equivalents of H_2SO_4 or AcOH as solvent yields only dibromo **16** product (table 4).

The IR 2,2-dibromoindan-1-one **16** shows prominent absorption at 1730 and 579 cm^{-1} indicating the presence of C=O and C-Br. The appearance of a singlet of 2H integration at 4.11 ppm in ^{1}H NMR and the appearance of a quaternary C and a CH_2 in BB/DEPT-135° at 55.0 and 57.7 ppm confirms the formation of 2,2-dibromoindan-1-one **16**. The δ of C^2 and C^3 are a big surprise. The –R effect of carbonyl and –I effect of two Br atoms would be making C^3 more downfield;

however, the former effect is not applicable to C^2. The ESI MS confirms the presence of two Br atoms because three peaks in 1:2:1 appears at 311, 313 and 315 amu as [M], [M+2], [M+4] adducts with Na ion. The further confirmation of the structure of **16** was provided by single crystal XRD ensuring the presence of two Br atoms at C^2 (figure 5).

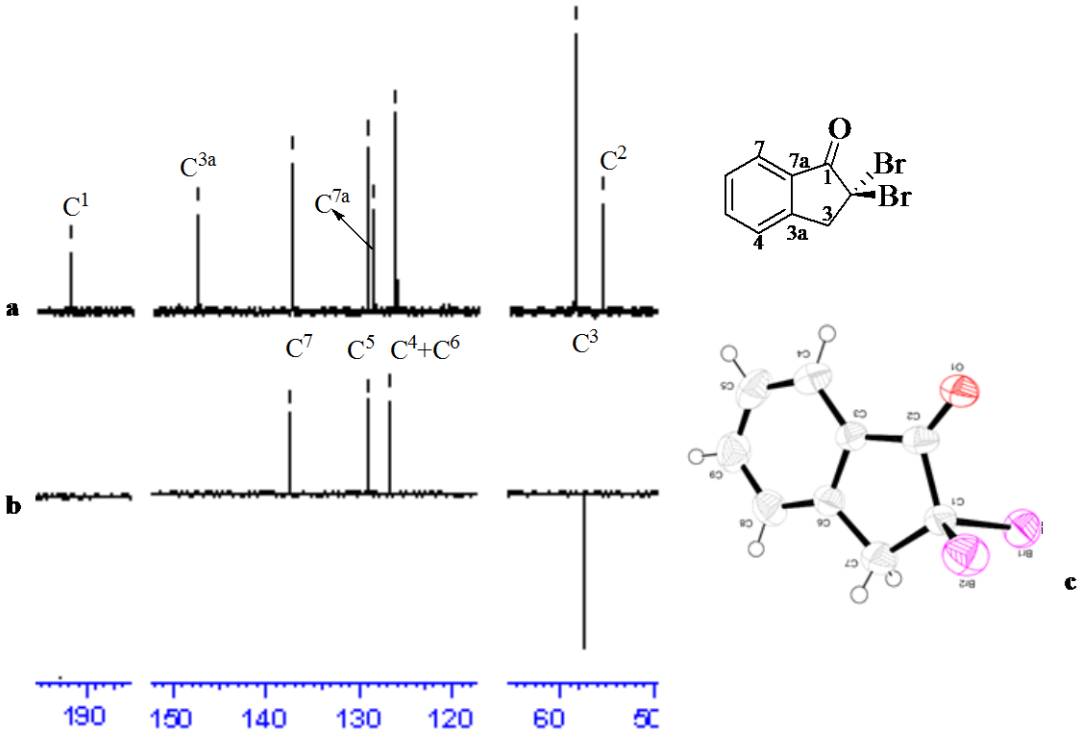


Figure 5: a)The BB; b)DEPT-135° and c) ORTEP diagram of 2,2-dibromoindan-1-one 16.

3 EXPERIMENTAL

The TLC was carried out on pre-coated silica gel (0.25 mm thick layer over Al sheet, Merck, Darmstadt, Germany) with fluorescent indicator. The spots were visualized under UV lamps (λ 365 and 254 nm) of 8 W power or $KMnO_4$ dip and heating. The compounds were purified either on a glass column packed silica gel (0.6–0.2 mm, 60Å mesh size, Merck) or by crystallization. All solutions were concentrated under reduced pressure (25 mm of Hg) on a rotary evaporator (Laborota 4001, Heidolph, Germany) at 35–40 °C. Melting points were determined using a MF-8 (Gallenkamp, Burladingen, Germany) instrument and are reported uncorrected. The IR-spectra are recorded on Prestige 21 spectrophotometer (Shimadzu, Japan) as KBr discs. The LREIMS are carried out on a Fisons Autospec Mass Spectrometer (VG, New Jersey, USA). The ^1H (300, 400 and 500 Hz) and ^{13}C-NMR (75 MHz) are recorded on AM-300, 400 and 500 MHz instruments (Bruker, Massachusetts, USA) in $CDCl_3$ using TMS as internal standard.

3.1 Generalized Procedure for mono bromination:

The Br_2 (0.8 mL, 2.42 g, 15 mmol, 1 eq) was added as drops to the solution of ketone (15.0 mmol, 1 eq) in $CHCl_3$ (20 mL) acidified with H_2SO_4 (4.5 mmol, 0.44 g, 0.2 mL). The resulting reaction mixture was refluxed for 3 h. After the completion of reaction time, the reaction mixture was washed with H_2O (3×20 mL) the resulting organic layer was dried over *anhydrous* Na_2SO_4, filtered and concentrated *in vacuo* to afford mono-bromo product.

3.2 Generalized Procedure for H_2SO_4 mediated dibromination:

A: The Br_2 (1.18 mL, 3.63 g, 22.5 mmol, 1.5 eq) was added as drops to the solution of ketone (15.0 mmol, 1 eq) in CH_2Cl_2 (20 mL) acidified with H_2SO_4 (0.39 mL, 0.73 g, 7.5 mmol, 0.6 eq). The resulting reaction mixture was refluxed for 3 h. After the completion of reaction, the reaction mixture was washed with H_2O (3×20 mL) the resulting organic layer was dried over *anhydrous* Na_2SO_4, filtered and concentrated *in vacuo* to affordproduct(s) as crystalline solids.

2-Bromo-1-phenylethanone: MP: 45-46°C (Lit. 45-46°C); **IR** ($\acute{\upsilon}_{max}$, cm^{-1}) KBr disc: 2951 (=C-H), 1694 (C=O), 685 (C-Br); ^1H NMR (500 MHz, $CDCl_3$, δ in ppm):4.46 (2H, s, CH_2), 7.49 (2H, t, J = 7.4 Hz, $H^{3'}$), 7.61 (1H, dd, J = 7.4,1.5 Hz, $H^{4'}$), 7.98 (2H, dd, J = 7.4, 1.5 Hz, $H^{2'}$); ^{13}C NMR(75 MHz): δ (ppm)30.9 (CH_2), 128.8 (2×, d, $C^{3'}$),, 128.9 (d, $C^{4'}$), 133.9 (2×, d, $C^{2'}$), 134.0 (s, $C^{1'}$), 191.2 (s, C^1); Mass 198, 200 $[M]^{+\cdot}$ (7%), 119 $[M\text{-}Br]^+$ (96%), 105 $[PhCO]^+$ (100%), 77 $[Ph]^+$ (22%).

2-Bromo-4′-chloro-1-phenylethanone: MP: 77-79°C (Lit.); **IR** ($\acute{\upsilon}_{max}$, cm^{-1}) KBr disc: 2954 (=C-H), 1697 (C=O), 721 (C-Cl), 667 (C-Br); ^1H NMR (500 MHz) 4.42 (s, 2H), 7.46 (d, J= 8.5 Hz, 2H), 7.92 (d, J= 8.5 Hz, 2H); 13C NMR 31.1, 129.8, 130.9, 132.8, 141.1, 190.8; Mass

2-Bromo-4'-methyl-1-phenylethanone: MP: 46; **IR** ($\acute{\upsilon}_{max}$, cm^{-1}) KBr disc: 2952, 1692, 1572, 1391, 1284, 1193, 995, 801, 685; ^1H NMR: ($CDCl_3$, 300MHz): 2.42 (s, 3H), 4.42 (s, 2H), 7.28 (d, J= 8.5 Hz, 2H), 7.78 (d, J= 8.5 Hz, 2H) ppm;

13C NMR: 21.9, 31.1, 129.2, 129.7, 131.5, 145.5, 191.1; Mass

2-**Bromo-4'-methoxy-1-phenylethanone**: MP: 76-78°C; **IR** ($\acute{\upsilon}_{max}$, cm^{-1}) KBr disc: 2938, 1688, 1597, 1510, 1326, 1263, 1208, 1167, 1115, 1016, 986, 745, 685 cm−1; ^{1}H NMR: ($CDCl_3$, 500 MHz): 7.97 (d, J= 8.9 Hz, 2H), 6.96 (d, J= 8.9 Hz, 2H), 4.40(s, 2H), 3.89 (s, 3H); 13C NMR; Mass

2-Bromo-4'-hydroxy-1-phenylethanone: MP:; **IR** ($\acute{\upsilon}_{max}$, cm^{-1}) KBr disc: ^{1}H NMR: ($CDCl_3$, 400 MHz): 4.78 (2H, s, CH2), 6.89 (2H, d, J = 8.8), 7.89 (2H, d, 8.8 Hz, H), 10.55 (1H, s, O-H).13C NMR (75MHz): 33.9, 115.9, 125.87, 131.95, 163.1, 190.3.Mass: 215, 217 [M] (24%), 137 (100%), 121 (46%).

2-Bromo-3-nitro-1-phenylethanone: MP:; **IR** ($\acute{\upsilon}_{max}$, cm^{-1}) KBr disc:; ^{1}H NMR: ($CDCl_3$, 300 MHz): 4.49 (2H,s, CH2), 7.74 (1H, t, J = 7.9), 8.34 (1H, dd, J = 7.9, 1.1), 8.48 (1H, dd, 8.2, 1.1 Hz), 8.82 (1H, t, 1.9Hz); 13C NMR: 30.2, 123.58, 127.94, 130.13, 134.35, 134.99, 148.30, 189.3; Mass 242, 244 [M] (29%), 150, 134, 120.

2-Bromo-4'-nitro-1-phenylethanone:MP: ; **IR** ($\acute{\upsilon}_{max}$, cm^{-1}) KBr disc:; ^{1}H NMR: ($CDCl_3$, 300 MHz): 4.47 (2H, s), 8.16 (2H, d, 9.1 Hz), 8.35 (2H, d, 9.1 Hz); 13C NMR: 30.36, 123.88, 129.92, 138.29, 150.51, 189.84; Mass

2-Bromo-1-(3,4-dimethoxyphenyl)ethanone: mp: 80.5–81.6 °C (lit. 80–81 °C)**; IR** ($\acute{\upsilon}_{max}$, cm^{-1}) KBr disc: 2966, 1682, 683, cm**;** ^{1}H NMR: ($CDCl_3$, 500 MHz): δ7.62 (dd, J= 8.4 Hz, J= 1.9 Hz, 1H), 7.55 (d, J= 1.9 Hz, 1H), 6.91 (d, J= 8.4 Hz, 1H), 4.41 (s, 2H), 3.97 (s, 3H), 3.95 (s, 3H).

2-Bromo-1-thiophen-2-ylethanone: MP: 29-30°C; IR ($\acute{\upsilon}_{max}$, cm^{-1}) KBr disc: ^{1}H NMR: ($CDCl_3$, 300 MHz)δ: 7.81 (dd, *J*= 3.9, 1.0 Hz, 1H), 7.72 (dd, *J*= 4.9, 1.0 Hz, 1H), 7.17 (dd, *J*= 4.9, 3.9 Hz, 1H), 4.36 (s, 2H); ^{13}C-NMR; Mass

2-bromoindanone: R_f: 0.62 (CH_2Cl_2/*n*-hexane, 1:1); IR ($\acute{\upsilon}_{max}$, cm^{-1}) KBr disc: 2844 (=C-H), 1712 (C=O), 673 (C-Br); ^{1}H NMR (300 MHz, $CDCl_3$, δ in ppm): 3.08 (1H, dd, *J* = -19.8, 2.7 Hz, $H^{3\alpha}$), 3.40 (1H, dd, *J* = -19.8, 7.2, $H^{3\beta}$), 5.69 (1H, dd, *J* = 7.2, 2.7, H^2), 7.41 (1H, ddd, *J* = 7.3, 7.3, 0.9 Hz, H^6), 7.50-7.55 (1H, m, H^4), 7.62 (1H, ddd, *J* = 7.2, 7.2, 1.2, H^5), 7.62 (1H, bd, *J* = 7.8 Hz, H^7); ^{13}C NMR (75 MHz, $CDCl_3$, δ in ppm): 40.7 (t, C^3), 48.1 (t, C^2), 123.4 (d, C^4), 127.5 (d, C^6), 129.6 (d, C^5), 135.6 (d, C^7), 135.7 (s, C^{3a}), 154.2 (s, C^{7a}), 201.5 (s, C^1).

2-bromotetralone: R_f: 0.58 (EtOAc / *n*-hexane, 1:4); d (g/cm^3): 1.59; UV log Є ($\lambda_{max,}$ nm): 3.57363 (295.5); IR ($\acute{\upsilon}_{max}$, cm^{-1}) KBr: 3078(=C-H), 1712(C=O), 630 (C-Br); ^{1}H NMR (300 MHz, $CDCl_3$, δ in ppm): 2.46-2.63 (1H, m, $H^{4\alpha}$), 2.95 (1H, ddd, *J* = -17.1, 4.5, 4.5 Hz, $H^{3\alpha}$), 3.13 (1H, q, *J* = 3.9 Hz, $H^{4\beta}$), 3.35 (1H, ddd, *J* = -15.9, 10.2, 5.7 Hz, $H^{3\beta}$), 4.76 (1H, dd, *J* = 4.5, 3.9 Hz, H^2), 7.32 (1H, d, *J* = 7.5 Hz, H^5), 7.39 (1H, d, *J* = 7.5 Hz, H^7), 7.56 (1H, ddd, *J* = 7.5, 7.5, 1.5 Hz, H^6), 8.12 (1H, dd, *J* = 7.8, 1.2 Hz, H^8); ^{13}C NMR (75 MHz, $CDCl_3$, δ in ppm): 26.1 (t, C^4), 31.9 (t, C^3), 50.5 (d, C^2), 127.1 (d, C^5), 127.6 (s, C^{4a}), 128.6 & 128.8 (d, C^6 &C^7), 134.1 (d, C^8), 143.0 (s, C^{8a}), 190.5 (s, C^1). Mass 224, 226 (18%), 144 (33%), 118 (100%).

2,2-dibromophenylethanone: MP: 73-75°C; ^{1}H NMR: 6.75 (1H, s), 7.32-7.37 (3H, m), 7.80-7.86 (2H, m);^{13}C NMR: 39.7, 128.9, 129.6, 130.8, 134.4, 185.9; Mass : 278, 149, 105; MS (ESI): 276 $[M+H]^+$, 278 $[M+2+H]^+$, 280.9 $[M+4+H]^+$.

2,2-dibromo-4-chlorophenylethanone: MP: 99°C; 1H NMR: 6.63 (1H, s), 7.42 (2H, d, *J* = 8.0 Hz), 8.10 (2H, d, *J* = 8.0 Hz); ^{13}CNMR:Mass: 312, 232 [M-Br], 139 (100%)

2,2-dibromo-4´-methylphenylethanone: MP: 89°C; ^{1}H NMR: 2.44 (s, 3H), 6.70 (s, 1H), 7.30 (t, *J*= 8.0 Hz, 2H), 7.97 (2H, t, *J*= 8.0 Hz); ^{13}C-NMR: 21.8 (q, CH_3), 39.9 (d, CH), 127.9 (2×, d, C^3), 129.7 (2×, d, C^2), 133.8 (s, C^1), 145.7 (s, C^4), 185.6 (s, C^2)

2,2-Dibromo-1-(4´-nitrophenyl)ethanone: MP 111°C; ^{1}HNMR($CDCl_3$) 6.91 (s, 1H, CH), 8.12–8.10 (d, 2H, Ar), 8.3–8.1 (d, 2H, ArH).

2,2-dibromotetralone: R_f: 0.43 (EtOAc / *n*-hexane 1:3); MP: 48°C; IR ($\acute{\upsilon}_{max}$, cm^{-1}) KBr disk: 2980 (=C-H), 1722 (C=O) and 575 (C-Br); LR EIMS (m/z, amu): 302, 304, 306 $[M]^{+\cdot}$(11, 22, 10%), 223, 225 $[M^{+\cdot}\text{-}Br]^+$ (26%), 118 $[M^{+\cdot}\text{-}C_2H_2Br_2]^{+\cdot}$ (100%, A), 90 $[A\text{-}CO]^{+\cdot}$ (21%); ^{1}H NMR (300 MHz, $CDCl_3$, δ in ppm): 3.06 (2H, dd, *J* = 5.7, 4.5 Hz, H^4), 3.09 (2H, dd, *J* = 3.9, 3.6 Hz, H^3), 7.25 (1H, d, *J* = 6.9 Hz, H^5), 7.37 (1H, ddd, *J* = 7.5, 7.5, 0.6 Hz, H^7), 7.53 (1H, ddd, *J* = 7.5, 7.5, 1.5 Hz, H^6), 8.16 (1H, dd, *J* = 7.8, 1.5 Hz, H^8).

2,2-dibromoindanone: **R_f:** 0.48 (EtOAc/*n*-hexane 1:3), **MP**: 125°C; **UV** log Є (λ_{max}, nm): 4.5890 (233); **IR** ($\acute{\upsilon}_{max}$, cm^{-1}) KBr disc: 2920 (=C-H), 1730 (C=O), 579 (C-Br); **ESI MS**$[M+Na]^{+\cdot}$(amu): 310.8671, 312.8649, 314.8628 (found in 1:2:1), 310.8682, 312.8662, 314.8641 (calc.); **^{1}H NMR:** (300 MHz, $CDCl_3$, δ in ppm): 4.11 (2H, s, H^3), 7.30-7.36 (2H, m, H^4 & H^6), 7.59 (1H, ddd, *J* = 7.5, 7.5, 1.2 Hz, H^5), 7.71 (1H, d, *J* = 7.8 Hz, H^7)*;* **^{13}C NMR**: (75 MHz, $CDCl_3$, δ in ppm): 55.0 (s, C^2), 57.7 (d, C^3), 126.1, 126.2 (d, C^4,C^6), 128.5 (s, C^{3a}), 128.9 (d, C^5), 137.2 (d, C^7), 147.2 (s, C^{7a}), 193.1 (s, C^1).

2,2-Dibromo-1-(2-thienyl)ethanone:^{1}H NMR: 8.03–7.98 (m, 1H), 7.80–7.76 (m, 1H), 7.22–7.18 (m, 1H), 6.48 (s, 1H).

2,2-Dibromo-1-(p-anisyl)ethanone: ^{1}H NMR: 8.08 (d, J= 9.0 Hz, 2H), 6.98 (d, *J*= 9.0 Hz, 2H), 6.66 (s, 1H), 3.90 (s, 3H).

2,2-Dibromo-1-(3,4-dimethoxyphenyl)ethanone: mp: 79.0–81.7 °C; **IR** ($\acute{\upsilon}_{max}$, cm^{-1}) KBr disc: 2967, 1676, 689, 621; ^{1}H-NMR ($CDCl_3$) δ: 7.74 (dd, *J* = 8.4, 2.0 Hz, 1H), 7.62 (d, *J*= 2.0 Hz, 1H), 6.92 (d, *J*= 8.4 Hz, 1H), 6.69 (s, 1H), 3.98 (s, 3H), 3.95 (s, 3H); ^{13}C-NMR (CD_3COCD_3): 186.8 (s, C^1), 156.9, 151.6 (s, $C^{3'}$, $C^{4'}$), 130.2 (s, $C^{1'}$), 113.7, 112.8(d, $C^{2'}$, $C^{5'}$), 57.4, 57.3 (OCH_3), 43.3(CH).

CONCLUSION

The H_2SO_4 mediated α-bromination has been found to be an effective, efficient, economical and industrially useful method. Selectivity can be easily achieved just by varying the equivalents of H2SO4. The detailed monitoring of reaction has proved that the reaction is only effected by amount of H_2SO_4 only and is unaffected by the concentration of halogenating agent used.

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