Supporting Information File

Chloral hydrate as a ‘water carrier’ for the efficient deprotection of acetals, dithioacetals and tetrahydropyranyl ethers in organic solvents

Sosale Chandrasekhar* and Annadka Shrinidhi

Address: Department of Organic Chemistry, Indian Institute of Science, Bangalore 560 012, India

Email: Sosale Chandrasekhar - sosale@orgchem.iisc.ernet.in

Characterization data

Instruments employed: Perkin-Elmer 410 (FTIR); Bruker AV-400 (NMR); Micromass Q-TOF AMPS MAX 10/6A (HRESIMS); Stuart SMP10 (melting point); Büchi Rotavapor R-200 (rotary evaporator).

IR values are for neat samples and are quoted in cm^{-1} . NMR spectra were recorded in CDCl_3 solution with tetramethylsilane as internal standard at either 400 MHz (δ_{H} , ppm) or 100 MHz (δ_{C} , ppm); the coupling constants (J) are in Hz. Abbreviations: mp (melting point), s (singlet); d (doublet); t (triplet); q (quartet); br (broad); dd (doublet of doublet), etc. The nomenclatures of all the compounds were derived by ChemDraw (CambridgeSoft).

Previously reported literature procedures were utilized for the synthesis of acetals,¹ cyclic ketals,² cyclic thioketals³ and THP ethers.⁴

Optimization studies.

Table. Effect of solvent, temperature and concentration of **1** on the hydrolysis of **2a**

Effect of solvent			Other conditions: 2a (0.7 mmol), 1 (2.1 mmol), time (1 h), r.t.
Entry	Solvent (1 ml)	Isolated yield (%)	
1	no solvent	<15	
2	H_2O	0	
3	$\text{H}_2\text{O}-\text{CHCl}_3$ (1:1)	<5	
4	H_2O -hexane (1:1)	<10	
5	DMF	18	
6	EtOH	20	
7	CH_2Cl_2	40	
8	CHCl_3	38	
9	Et_2O	49	
10	hexane	78	

Effect of temperature			Other conditions: 2a (0.7 mmol), 1 (2.1 mmol), hexane (1 ml), time (1 h), r.t.
Entry	Temperature (° C)	Isolated yield (%)	
1	-10	49	
2	r.t.	78	
3	40	43	
4	70	37	

Effect of amount of CH added			Other conditions: 2a (0.7 mmol), hexane (1 ml), time (1 h), r.t.
Entry	CH (equiv)	Isolated yield (%)	
1	0.1	7	
2	0.5	39	
3	1	53	
4	2	74	
5	3	78	
6	4	82	
7	5	83	

Spectral data for hydrolysed products.

Cyclopentanone (3a). Liquid; $\nu_{\max}$ 2964, 2925, 1747, 1455, 1407, 1277, 1152, 959, 913, 833, 747; δ_{H} 2.18-2.14 (4H, m), 1.99-1.95 (4H, m); δ_{C} 220.1, 37.9, 22.8.

Cyclohexanone (3b/d/r). Liquid; $\nu_{\max}$ 2939, 2863, 2671, 1716, 1449, 1429, 1338, 1311, 1222, 1119, 908, 750, 653; δ_{H} 2.36-2.32 (4H, t, J 6.6), 1.90-1.84 (4H, m), 1.76-1.71 (2H, m); δ_{C} 212.1, 41.8, 26.8, 24.8.

Cycloheptanone (3c). Liquid; $\nu_{\max}$ 2929, 2857, 1698, 1455, 1445, 1409, 1319, 1254, 1161, 1100, 941, 914, 855, 734, 647; δ_{H} 2.51-2.49 (4H, t, J 4.8), 1.73-1.66 (8H, m); δ_{C} 215.3, 43.6, 30.2, 24.1; HRESIMS: 135.0788 (calcd. for $\text{C}_7\text{H}_{12}\text{O} + \text{Na}$ 135.0786).

Acetophenone (3i/j/s). Liquid; $\nu_{\max}$ 3063, 3005, 2924, 1682, 1599, 1583, 1449, 1430, 1360, 1265, 1180, 1024, 955, 927, 760, 690; δ_{H} 7.96-7.94 (2H, m), 7.57-7.43 (3H, m), 2.28 (3H, s); δ_{C} 198.0, 137.0, 133.0, 128.4, 128.2, 26.5; HRESIMS: 143.0472 (calcd. for $\text{C}_8\text{H}_8\text{O} + \text{Na}$ 143.0473).

Benzophenone (3k/l/u). Mp 48 °C (lit.⁵ 48-48.8 °C); $\nu_{\max}$ 3063, 3030, 2896, 1715, 1602, 1584, 1496, 1454, 1409, 1332, 1187, 1091, 1056, 1030, 753, 732, 698; δ_{H} 7.81-7.79 (4H, m), 7.59-7.55 (2H, m), 7.49-7.45 (4H, m); δ_{C} 196.7, 137.5, 132.3, 129.9, 128.2; HRESIMS: 183.0811 (calcd. for $\text{C}_{13}\text{H}_9\text{O} + \text{H}$ 183.0810).

1,3-Diphenylpropan-2-one (3e). Mp 31 °C (lit.⁶ 31-32 °C); $\nu_{\max}$ 3060, 3035, 2929, 1659, 1599, 1447, 1309, 1280, 1176, 1150, 1074, 941, 920, 810, 764, 699; δ_{H} 7.33-7.25 (6H, m), 7.15-7.13 (4H, m), 3.71 (4H, s); δ_{C} 205.6, 133.9, 129.5, 128.7, 127.0, 49.0; HRESIMS: 233.0941 (calcd. for $\text{C}_{15}\text{H}_{14}\text{O}$ + Na 233.0942).

4-Phenylbutan-2-one (3f). Mp 76-78 °C (lit.⁷ 78 °C); $\nu_{\max}$ 3063, 3029, 2925, 1717, 1603, 1479, 1454, 1358, 1162, 1030, 750, 700; δ_{H} 7.29-7.17 (5H, m), 2.91-2.87 (2H, t, J 7.6), 2.77-2.73 (2H, t, J 7.6), 2.13 (s, 3H); δ_{C} 207.9, 140.9, 128.4, 128.2, 126.1, 45.1, 30.0, 29.7; HRESIMS: 171.0788 (calcd. for $\text{C}_{10}\text{H}_{12}\text{O}$ + Na 171.0786).

4-Methylpentan-2-one (3g). Liquid; $\nu_{\max}$ 2966, 2883, 1731, 1367, 1219, 1170, 951, 771; δ_{H} 2.31-2.30 (2H, d, J 6.8), 2.13 (3H, s), 1.72 (1H, s), 0.93-0.92 (3H, d, J 6.8); δ_{C} 208.9, 52.7, 30.3, 24.5, 22.4.

Octan-2-one (3h). Liquid; $\nu_{\max}$ 2972, 2876, 1726, 1389, 1223, 1165, 956, 774; δ_{H} 2.42-2.34 (2H, t, J 7.6), 2.11 (3H, s), 1.60-1.52 (2H, m), 1.33-1.25 (6H, m), 0.897-0.863 (3H, t, J 7.2); δ_{C} 209.0, 43.6, 31.4, 29.6, 28.7, 23.7, 22.3, 13.8; HRESIMS: 151.1099 (calcd. for $\text{C}_8\text{H}_{16}\text{O}$ + Na 151.1099).

Benzaldehyde (3m/p/t). Liquid; $\nu_{\max}$ 3064, 3033, 2820, 1702, 1598, 1455, 1312, 1204, 1167, 1071, 1024, 828, 746, 688; δ_{H} 10.02 (1H, s), 7.89-7.87 (2H, m), 7.63-7.61 (1H, m), 7.55-7.51 (2H, m); δ_{C} 192.4, 134.4, 130.1, 129.7, 128.9; HRESIMS: 129.0315 (calcd. for $\text{C}_7\text{H}_6\text{O}$ + Na 129.0316).

Cyclohexanecarbaldehyde (3n/o). Liquid; $\nu_{\max}$ 2933, 2857, 1705, 1452, 1418, 1313, 1260, 1213, 1021, 946, 895; δ_{H} 9.62 (1H, s), 2.26-2.22 (1H, m), 1.91-1.73 (5H, m), 1.42-1.29 (5H, m); δ_{C} 205.0, 49.9, 25.9, 25.9, 24.9; HRESIMS: 135.0789 (calcd. for $\text{C}_7\text{H}_{12}\text{O}$ + Na 135.0786).

3-Methylbutanal (3q). Liquid; $\nu_{\max}$ 2952, 2937, 2866, 1710, 1468, 1435, 1268, 1158, 1133, 1010, 954, 712; δ_{H} 9.756 (1H, s), 2.31-2.30 (2H, m), 2.248-2.170 (1H, m), 0.996-0.979 (6H, d, J 6.7); δ_{C} 202.962, 52.547, 23.442, 22.541.

Octan-1-ol (5a). Liquid; $\nu_{\max}$ 3340, 2956, 2928, 2858, 1466, 1459, 1379, 1120, 1057, 990, 956, 890, 722; δ_{H} 3.63-3.60 (2H, t, J 6.4), 2.20 (1H, br s), 1.59-1.52 (2H, m), 1.36-1.28 (10H, m), 0.89-0.87 (3H, t, J 6.4); δ_{C} 62.8, 32.7, 31.8, 29.4, 29.2, 25.7, 22.6, 14.0; HRESIMS: 153.1258 (calcd. for $\text{C}_8\text{H}_{18}\text{O}$ + Na 153.1255).

Dodecan-1-ol (5b). Liquid; $\nu_{\max}$ 3426, 3050, 2954, 2921, 2853, 1438, 1421, 1265, 1114, 937, 741, 670; δ_{H} 3.65-3.62 (2H, t, J 5.8), 1.65-1.53 (3H, m), 1.31-1.26 (18H, m), 0.89-0.86 (3H, t, J 6.4); δ_{C} 63.1, 32.8, 31.9, 29.6, 29.5, 29.4, 29.3, 25.8, 22.7, 14.1; HRESIMS: 209.1885 (calcd. for $\text{C}_{12}\text{H}_{26}\text{O} + \text{Na}$ 209.1881).

Phenylmethanol (5c). Liquid; $\nu_{\max}$ 3340, 3031, 2929, 2873, 1607, 1496, 1453, 1208, 1019, 735, 698; δ_{H} 7.33-7.20 (5H, m), 4.55 (2H, s), 2.81 (1H, br s); δ_{C} 140.7, 128.4, 127.4, 126.9, 64.9; HRESIMS: 131.0470 (calcd. for $\text{C}_7\text{H}_8\text{O} + \text{Na}$ 131.0473).

Furan-2-ylmethanol (5d). Liquid; $\nu_{\max}$ 3416, 3121, 2924, 2873, 1597, 1563, 1505, 1357, 1219, 1013, 794, 743, 630; δ_{H} 7.39 (1H, m), 6.34-6.28 (2H, m), 4.59 (2H, s), 2.17 (1H, br s); δ_{C} 153.9, 142.5, 110.3, 107.7, 57.3; HRESIMS: 121.0263 (calcd. for $\text{C}_5\text{H}_6\text{O}_2 + \text{Na}$ 121.0265).

Octan-2-ol (5e). Liquid; $\nu_{\max}$ 33340, 2928, 2852, 1463, 1368, 1158, 1022, 920, 698; δ_{H} 3.81-3.77 (m, 1H), 1.71 (br s, 1H), 1.46-1.26 (m, 10H), 1.19-1.18 (3H, d, J 6.4), 0.90-0.87 (t, 3H); δ_{C} 68.1, 39.3, 31.8, 29.3, 25.7, 23.4, 22.6, 14.0; HRESIMS: 153.1259 (calcd. for $\text{C}_8\text{H}_{18}\text{O} + \text{Na}$ 153.1255).

Cyclohexanol (5f). Liquid; $\nu_{\max}$ 3340, 2928, 2956, 2856, 1466, 1379, 1120, 1054, 956, 722; δ_{H} 3.63-3.57 (1H, m), 2.05-1.87 (3H, m), 1.74-1.68 (2H, m), 1.55-1.52 (1H, m), 1.33-1.14 (5H, m); δ_{C} 70.2, 35.4, 25.4, 24.1.

2-Isopropyl-5-methylcyclohexanol (5g). Mp 43-45 °C (lit.⁸ 44-46.5 °C); $\nu_{\max}$ 3309, 2954, 2923, 2871, 1455, 1369, 1177, 1045, 1026, 994, 919, 846, 668; δ_{H} 3.44-3.38 (1H, m), 2.21-2.13 (1H, m), 1.98-1.95 (1H, m), 1.68-1.59 (2H, m), 1.46-1.33 (2H, m), 1.15-0.80 (12H, m); δ_{C} 71.5, 50.1, 45.0, 34.5, 31.6, 25.8, 23.1, 22.2, 21.0, 16.1; HRESIMS: 179.1413 (calcd. for $\text{C}_{10}\text{H}_{20}\text{O} + \text{Na}$ 179.1412).

1-Phenylethanol (5h). Liquid; $\nu_{\max}$ 3345, 3088, 2929, 2873, 1607, 1486, 1210, 1085, 1015, 745; δ_{H} 7.38-7.27 (5H, m), 4.92-4.87 (1H, q, J 6.8), 1.93 (1H, s), 1.50-1.49 (3H, d, J 6.4); δ_{C} 146.0, 129.1, 126.8, 125.3, 70.1, 22.0; HRESIMS: 145.0627 (calcd. for $\text{C}_8\text{H}_{10}\text{O} + \text{Na}$ 145.0629).

4-Phenylbutan-2-ol (5i). Mp 60-61 °C (lit.⁹ 61 °C); $\nu_{\max}$ 3365, 3102, 2968, 2873, 1602, 1432, 1268, 1058, 1019, 925, 735; δ_{H} 7.30-7.16 (5H, m), 3.86-3.80 (1H, m), 2.79-2.63 (2H, m), 1.80-1.73 (2H, m), 1.23-1.21 (3H, d, J 6.0); δ_{C} 142.0, 128.4, 128.3, 125.8, 67.4, 40.8, 32.1, 23.6; HRESIMS: 173.0945 (calcd. for $\text{C}_{10}\text{H}_{14}\text{O} + \text{Na}$ 173.0942).

1-(Naphthalen-2-yl)ethanol (5j). Mp 75 °C (lit.¹⁰ 76-77 °C); $\nu_{\max}$ 3421, 3112, 2898, 1604, 1425, 1356, 1208, 1077, 1032, 965, 756, 698; δ_{H} 7.80-7.76 (4H, m), 7.47-7.22 (3H, m), 5.03-4.98 (2H, q, J 6.4), 2.20 (1H, br s), 1.55-1.53 (3H, d, J 6.4); δ_{C} 143.1, 133.3, 132.9, 128.2, 127.9, 127.6, 126.1, 125.7, 123.8, 123.7, 70.4, 25.1; HRESIMS: 195.0789 (calcd. for $\text{C}_{12}\text{H}_{12}\text{O} + \text{Na}$ 195.0786).

2-Nitro-1-phenylethanol (5k). Liquid; $\nu_{\max}$ 3544, 3065, 3034, 2921, 1598, 1557, 1495, 1455, 1418, 1379, 1194, 1066, 766, 700; δ_{H} 7.40-7.34 (5H, m), 5.46-5.43 (1H, d, J 9.2), 4.63-4.48 (2H, m), 2.96 (1H, br s); δ_{C} 138.1, 128.9, 128.9, 125.9, 81.2, 70.9; HRESIMS: 190.0478 (calcd. for $\text{C}_8\text{H}_9\text{NO}_3 + \text{Na}$ 190.0480).

Synthesis and characterization of methyl 4-(2-phenyl-1,3-dioxolan-2-yl)benzoate (6a).²

A 100 ml round-bottomed flask was charged with methyl 4-benzoylbenzoate (1 g, 4.2 mmol), 1,2-ethanediol (0.78 g, 12.5 mmol), 50 ml of reagent grade benzene and *p*-toluenesulfonic acid monohydrate (16 mg, 0.04 mmol). The flask was attached to a Dean-Stark apparatus to remove water and the contents refluxed for 6 h. The reaction mixture was cooled to room temperature, extracted with dichloromethane, the extracts washed with saturated sodium bicarbonate solution and dried (Na_2SO_4) to yield methyl 4-(2-phenyl-1,3-dioxolan-2-yl)benzoate (3.76 mmol, 90%). Mp 102-103 °C; $\nu_{\max}$ 3084, 3061, 3030, 2934, 2887, 1732, 1602, 1453; δ_{H} 8.01-7.99 (2H, d, J 8.4), 7.62-7.59 (2H, d, J 8.4), 7.52-7.46 (2H, dd, J 8.4, 1.8), 7.37-7.29 (3H, m), 4.08-4.07 (4H, d, J 3.3), 3.90 (3H, s); δ_{C} 165.9, 142.6, 140.2, 130.8, 129.4, 128.4, 127.8, 126.3, 126.1, 119.1, 64.9, 51.8; HRESIMS: 307.0942 (calcd. for $\text{C}_{17}\text{H}_{16}\text{O}_4 + \text{Na}$ 307.0946).

Synthesis and characterization of methyl 4-(phenyl((tetrahydro-2H-pyran-2-yl)oxy)methyl)benzoate (6b).⁴

Methyl 4-benzoylbenzoate (1 g, 4.2 mmol) and *p*-toluenesulfonic acid (0.08 g, 0.42 mmol) in DCM (5 ml) was treated with dropwise 3,4-dihydro-2H-pyran (0.39 g, 4.6 mmol) with ice cooling. The resulting mixture was stirred at r.t. for 2 h, and then washed with a saturated aqueous sodium hydrogen carbonate solution. The organic layer was washed with a saturated aqueous sodium chloride solution and dried with anhydrous sodium sulfate. The solvent was distilled off to obtain methyl 4-(phenyl((tetrahydro-2H-pyran-2-yl)oxy)methyl)benzoate (3.95 mmol, 95%). Mp 57-59 °C;

$\nu_{\max}$ 3022, 2951, 2916, 2879, 1457, 1323, 1199, 1027, 954, 876, 741; δ_{H} 8.03-7.19 (9H, m), 5.82 (1H, s), 4.73-4.64 (1H, m), 3.89-3.46 (2H, m), 2.06-1.63 (2H, m), 1.63-1.52 (4H, m); δ_{C} 165.9, 148.2, 143.1, 129.4, 129.1, 128.7, 127.5, 126.4, 125.6, 89.4, 78.1, 62.2, 31.3, 26.9, 20.4; HRESIMS: 349.1413 (calcd. for $\text{C}_{20}\text{H}_{22}\text{O}_4 + \text{Na}$ 349.1416).

Methyl 4-benzoylbenzoate (7a). Mp 110 °C (lit.¹¹ 109.5-110.5 °C); $\nu_{\max}$ 2997, 2950, 2888, 1712, 1648, 1596, 1450, 1407, 1279, 1106, 942, 774, 711, 697, 657; δ_{H} 8.16-8.14 (2H, m), 7.85-7.48 (7H, m), 3.96 (3H, s); δ_{C} 141.2, 136.9, 133.1, 132.9, 130.0, 129.7, 129.4, 128.4, 52.4; HRESIMS: 263.0688 (calcd. for $\text{C}_{15}\text{H}_{12}\text{O}_3 + \text{Na}$ 263.0684).

Methyl 4-(hydroxy(phenyl)methyl)benzoate (7b). Mp 64 °C (lit.¹² 62-63 °C); $\nu_{\max}$ 3370, 2959, 1725, 1605, 1487, 1423, 1292, 1180, 1040, 1016, 959, 872, 748, 700; δ_{H} 8.02-7.99 (2H, d, J 8.0), 7.61-7.59 (2H, d, J 8.4), 7.51-7.25 (5H, m), 5.81 (1H, s), 3.89 (3H, s), 3.22 (1H, s); δ_{C} 166.2, 146.9, 141.5, 130.1, 129.4, 128.2, 128.1, 126.0, 125.9, 75.2, 51.7; HRESIMS: 265.0843 (calcd. for $\text{C}_{15}\text{H}_{14}\text{O}_3 + \text{Na}$ 265.0841).

References

- (1) Roy, A.; Rahman, M.; Das, S.; Kundu, D.; Kundu, S. K.; Majee, A.; Hajra, A. *Synth. Commun.* **2009**, *39*, 590-595.
- (2) Daignault, R. A.; Eliel, E. L. *Org. Synth.* **1967**, *47*, 37-39.
- (3) Samajdar, S.; Basu, M. K.; Becker, F. F.; Banik, B. K. *Tetrahedron Lett.* **2001**, *42*, 4425-4427.
- (4) Kameyama, M.; Kamigata, N.; Kobayashi, M. *J. Org. Chem.* **1987**, *52*, 3312-3316.
- (5) McGrath, T. F.; Levine, R. *J. Am. Chem. Soc.* **1955**, *77*, 3634-3636.
- (6) Shapiro, E. L.; Becker, E. I. *J. Am. Chem. Soc.* **1953**, *75*, 4769-4775.
- (7) Wichterle, O.; Hudlicky, M. *Collect. Czech. Chem. Commun.* **1947**, *12*, 101-128.
- (8) Winstein, S.; Morse, B. K.; Grunwald, E.; Jones, H. W.; Corse, J.; Trifan, D.; Marshall, H. *J. Am. Chem. Soc.* **1952**, *74*, 1127-1132.
- (9) Kenyon, J.; Partridge, S. M.; Phillips, H. *J. Chem. Soc.* **1936**, 85-88.
- (10) Okamoto, Y.; Brown, H. C. *J. Am. Chem. Soc.* **1957**, *79*, 1903-1905.

- (11) Corson, B. B.; Dorsky, J.; Nickels, J. E.; Kutz, W. M.; Thayer, H. I. *J. Org. Chem.* **1954**, *19*, 17-26.
- (12) Oi, S.; Moro, M.; Fukuhara, H.; Kawanishi, T.; Inoue, Y. *Tetrahedron* **2003**, *59*, 4351-4361.