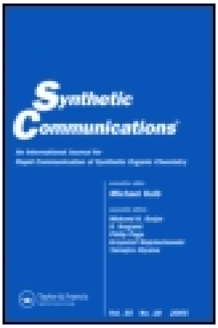

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CARBON-CARBON DOUBLE BOND FORMATION BETWEEN α-HALOKETONES AND ALDEHYDES MEDIATED BY $SnCl_2/Na_2SO_3$: SYNTHESIS OF (E)-α, β-UNSATURATED KETONES

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ABSTRACT: One-pot reactions of α-haloketones with aldehydes in the presence of excess $SnCl_2/Na_2SO_3$ or $SnCl_2$ alone in THF at reflux were found to afford (E)-α, β-unsaturated ketones in fair to good yields.

Several dehalogenating reagents of α-haloketones have been found which could promote carbon-carbon single or double bond formation between α-haloketones and aldehydes efficiently, such as CeI_3 or $CeCl_3/NaI$,[1] $AlCl_3/KI$ or $TiCl_4/KI$,[2] SmI_2[3] and SmI_3.[4] Some tin compounds, such as SnF_2,[5] $Sn(OTf)_2$[6,7] as well as tin metal[8] have also been used as reagents for the reactions of α-halocarbonyl compounds with aldehydes or ketones via tetravalent or divalent tin enolates. Sometimes, $SnCl_2$ in combination with $CeCl_3$[1] or Et_2AlCl[9] has been employed in aldol or Reformatsky-type reactions of α-halocarbonyl compounds with carbonyl compounds, but $SnCl_2$ alone at room temperature has not been

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applied in the aldol reactions between α-haloketones and aldehydes[1]. Previously, the combined reagent $SnCl_2/Na_2SO_3$, as well as $SnCl_2$ alone was found to be an effective dehalogenating reagent of α-haloketones[10]. Now both the combined reagent $SnCl_2/Na_2SO_3$ and $SnCl_2$ alone are reported to be also efficient reagents for carbon-carbon double bond formation between α-haloketones and aldehydes in anhydrous THF solvent under reflux to afford (E)-α, β-unsaturated ketones selectively.

$$ArCOCH_2Br + RCHO \xrightarrow[\text{or } SnCl_2]{SnCl_2/Na_2SO_3} ArCOCH{=}CHR$$

Treatment of equimolar mixture of α-bromoketones and aldehydes with excess anhydrous $SnCl_2$ and Na_2SO_3 in the ratio of 1:1:4:1 in dry THF under reflux for 4-6h gave the corresponding (E)-α, β-unsaturated ketones in fair to good yields. With α, β-unsatured aldehydes, such as cinnamaldehyde and acrolein, the reactions also gave buta-1, 3-dienyl ketones in moderate yields. However, the reactions of α-bromophenyl ketones with p-and m-nitrobenzaldehydes did not give the desired α, β-unsaturated ketones, unknown deep red mixtures being formed instead, probably because of reduction of nitro group with $SnCl_2$. Moreover, with ketones, the desired cabon-carbon bond formation did not occur, even with prolonged reaction time.

Treatment of ethyl bromoacetate and p-chlorobenzaldehyde with an excess of the combined reagent $SnCl_2/Na_2SO_3$ gave no Reformatsky-type product.

In the carbon-carbon double bond formation reactions, excess $SnCl_2$ was used to obtain satisfactory yields of the products. When the molar ratio of α-haloketone: aldehyde : $SnCl_2$: Na_2SO_3 was changed from 1:1:4:1 to 1:1:2:1, the reactions gave only traces of the product. In the absence of $SnCl_2$, no reaction was occurred. In contrast, in the absence of Na_2SO_3, the reactions still gave satisfactory yields of the α, β-unsaturated ketones, though the yields of the products were reduced when compared with those in the presence of excess $SnCl_2/Na_2SO_3$. These results suggest that the reducing reagent $SnCl_2$ plays an key role in the reactions. As

Table 1. Carbon-Carbon Double Bond Formation between α-Haloketones and Aldehydes Promoted by $SnCl_2/Na_2SO_3$ or $SnCl_2^a$

№	α-Haloketone	Aldehyde	Product	Yield (%)[b]
1	$C_6H_5COCH_2Br$	C_6H_5CHO	$C_6H_5CH{=}CHCOC_6H_5$	73
2	$C_6H_5COCH_2Br$	$3\text{-}ClC_6H_4CHO$	$3\text{-}ClC_6H_4CH{=}CHCOC_6H_5$	83 (78)
3	$C_6H_5COCH_2Br$	$4\text{-}BrC_6H_4CHO$	$4\text{-}BrC_6H_4CH{=}CHCOC_6H_5$	84 (81)
4	$C_6H_5COCH_2Br$	$4\text{-}CH_3OC_6H_4CHO$	$4\text{-}CH_3OC_6H_4CH{=}CHCOC_6H_5$	71
5	$C_6H_5COCH_2Br$	$4\text{-}HOC_6H_4CHO$	$4\text{-}HOC_6H_4CH{=}CHCOC_6H_5$	52
6	$C_6H_5COCH_2Br$	$4\text{-}Me_2NC_6H_4CHO$	$4\text{-}Me_2NC_6H_4{=}CHCOC_6H_5$	62
7	$C_6H_5COCH_2Br$	$C_6H_5CH{=}CHCHO$	$C_6H_5CH{=}CHCH{=}CHCOC_6H_5$	72
8	$C_6H_5COCH_2Br$	$CH_2{=}CHCHO$	$CH_2{=}CHCH{=}CHCOC_6H_5$	47
9	$4\text{-}BrC_6H_4COCH_2Br$	C_6H_5CHO	$C_6H_5CH{=}CHCOC_6H_4Br\text{-}4$	76
10	$4\text{-}BrC_6H_4COCH_2Br$	$4\text{-}ClC_6H_4CHO$	$4\text{-}ClC_6H_4CH{=}CHCOC_6H_4Br\text{-}4$	85 (83)
11	$4\text{-}BrC_6H_4COCH_2Br$	$4\text{-}HOC_6H_4CHO$	$4\text{-}HOC_6H_4CH{=}CHCOC_6H_4Br\text{-}4$	55
12	$4\text{-}BrC_6H_4COCH_2Br$	$4\text{-}CH_3OC_6H_4CHO$	$4\text{-}CH_3OC_6H_4CH{=}CHCOC_6H_4Br\text{-}4$	79
13	$4\text{-}BrC_6H_4COCH_2Br$	$4\text{-}Me_2NC_6H_4CHO$	$4\text{-}Me_2NC_6H_4CH{=}CHCOC_6H_4Br\text{-}4$	65

a. A mixture of α-haloketone (2mmol), aldehyde (2mmol), $SnCl_2$ (8mmol), Na_2SO_4 (2mmol), was stirred at r. t. for 2h, then at reflux for 4h.

b. Isolated yields. The data in parentheses were the yields of reactions in the absence of Na_2SO_3.

described previously, it was reported that at room temperature, the use of $SnCl_2$ alone gave no carbon-carbon bond formation product. Nevertheless, we found that the reactions took place with either excess $SnCl_2/Na_2SO_3$ or excess $SnCl_2$ alone with a longer reaction time and a higher reaction temperature. The results were listed in Table 1. The physical constants and spectral data of the products are shown in Table 2.

Table 2. phsical constants and spectral data of products

№	M.P. (℃) (Lit)[2]	^{1}H NMR 8 (ppm)	IR v max (cm^{-1})
1	56-57 (57-58)	7.24-8.0 (10H, m) 8.08 (2H, m)	1670 (s) 1615 (s)
2	75.5 (76)	7.25-7.28 (1H, m) 7.44-7.93 (7H, m) 7.98 (1H, m) 8.00-8.10 (2H, m)	1670 (s) 1615 (s) 680 (s)
3	123 (123.5)	7.13-7.24 (2H, m) 7.27-7.69 (7H, m) 8.01-8.08 (2H, m)	1670 (s) 1610 (s)
4	76-77.5 (77-78)	3.85 (3H, s) 6.75 (2H, m) 7.15-7.78 (7H, m) 7.80-8.10 (2H, m)	1670 (s) 1610 (s) 1270 (s)
5	103-104	6.80-7.03 (2H, m) 7.15-7.79 (7H, m) 7.81-8.07 (2H, m) 9.92 (1H, S)	1665 (s) 1605 (s) 1595 (s)
6	112-114 (114)	3.00 (8H, s) 6.60 (2H, m) 7.10-7.78 (7H, m) 7.90-8.10 (2H, m)	3450 (m) 2920 (m) 1660 (s) 1610 (s)
7	100-102 (101-102)	6.75-7.05 (2H, m) 7.12-7.55 (10h, m) 7.80-8.10 (2H, m)	3040 (m) 1665 (s) 1585 (s)
8	47-48 (48)	1.85 (3H, d, J=5HZ) 6.05-6.75 (3H, m) 7.15-7.45 (4H, m) 7.70-8.00 (2H, m)	1680 (s) 1620 (s)
9	112-113 (113)	7.50-8.20 (11H, m)	1665 (s) 1670 (s) 685 (s)
10	166-167	7.48-8.17 (10H, m)	1670 (s) 1615 (s) 1255 (s)
11	184.5-186	6.79-6.89 (2H, m) 6.67-8.10 (8H, m) 10.19 (1H, s)	1675 (s) 1620 (s) 1610 (s)
12	144-145	3.87 (3H, s) 6.80 (2H, m) 7.25-7.80 (6H, m) 7.90-8.15 (2H, m)	1660 (s) 1615 (s)
13	142-144	3.03 (6H, s) 6.74-6.85 (2H, m)	1665 (s) 2620 (s)

By analogy with the mechanism of cabon-carbon bond formation between α, α'-dibromophenylketones and aldehydes using stannous fluoride (SnF_2)[5], the reactions of α-bromoketones and aldehydes in the presence of excess $SnCl_2$/Na_2SO_3 or $SnCl_2$ alone seem to proceed via tetravalent tin enolates, generated *in situ* by the reductive insertion of $SnCl_2$ into the α-bromoketones, reaction with the aldehydes, and subsequent dehydration to afford the α, β-unsaturated ketones. probably, Na_2SO_3 promotes the debromination of α-bromoketones by $SnCl_2$ to form tin enolates.

EXPERIMENTAL

Reactions of α-Haloketones with Aldehydes in the Presence of Excess $SnCl_2$/Na_2SO_3—General Procedure:

Under anhydrous conditions, a mixture of α-bromophenyl ketone (2mmol), aldehyde (2mmol), $SnCl_2$ (8mmol, 1.53g) and Na_2SO_3 (2mmol, 0.25g) in anhydrous THF (20ml) was stirred at room temperature for 2h, then at reflux for 4h. The reaction mixture was filtered to remove inorganic salts. The solid was washed with ether. To the filterate, brine (5ml) was added, and the mixture was then extracted with ether. The combined extracts were washed with brine, dried with anhydrous $MgSO_4$, filtered and evaporated under reduced pressure. The crude product was purified by recrystallization. All products had physical data and spetral characteristics (IR and ^{1}H-NMR) in agreement with literature data and new compounds also gave satisfactory elemental analyses.

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