A novel approach for the direct conversion of alkylsulfonyl derivatives into alkylcarbonyl derivatives *via* tin-free radical carbonylation†‡

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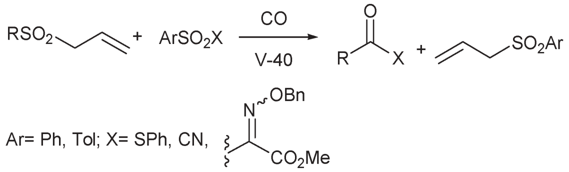
A novel radical approach for the direct conversion of RSO_2X into RCOX in a single step is devised; the present approach is very simple, highly efficient, and minimizes formation of by-product.

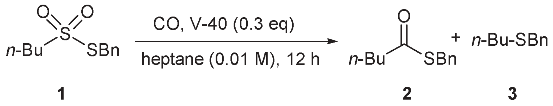
Radical-mediated methodologies allow organic reactions to proceed under very mild conditions with very high synthetic efficiency[1] but they suffer from a major drawback mainly associated with problems of toxicity of organotin compounds.[2,3] An ideal radical methodology that is highly selective, atom economical, and environmentally acceptable remains a challenge.[4] In this regard, we wish to report an unprecedented radical approach for the direct conversion of alkylsulfonyl derivatives into the corresponding alkylcarbonyl derivatives *via* tin-free radical carbonylation,[5] which can not be achieved by conventional methods.

To increase the synthetic efficiency by both maximizing atom utilization and minimizing by-product or waste, we have searched for a new type of a radical reaction in which a substrate could be utilized not only as a radical precursor but also as a radical acceptor. Based on the thermal desulfonylation of alkylsulfonyl radicals to alkyl radicals along with liberation of sulfur dioxide,[6] alkylsulfonyl derivatives seem to be the most attractive for our purpose.[7] Our approach is outlined in Scheme 1 and is based on the preferential formation of an acyl radical rather than the competing reaction of an alkyl radical with an alkylsulfonyl derivative. Thus, the success of the present approach depends critically on avoiding the formation of the RX by-product. Recently, we reported a new tin-free radical carbonylation approach using alkyl allyl sulfone precursors (eqn (1)).[8,9] According to our previous studies, alkylthiosulfonates,[8a] alkylsulfonyl cyanides,[10] and alkylsulfonyl oxime ethers[11] were very promising in their ability to quench the corresponding acyl radicals for the direct conversion into the corresponding carbonyl derivatives under tin-free conditions.

We began our study with *S*-benzyl *n*-butylthiosulfonate (**1**).[12,13] To search for optimum conditions, the effect of CO pressure was examined. When **1** was subjected to pressurized CO (95 atm, autoclave) in heptane (0.01 M) using V-40 (1,1′-azobis(cyclohexane-1-carbonitrile)) as initiator at 100 °C for 12 h, *S*-benzyl thiobutanoate (**2**) was isolated in 82% yield along with some starting material (15%) (eqn (2)).§ It is noteworthy that there was no indication of the formation of benzyl *n*-butyl sulfide (**3**). By increasing the reaction temperature to 120 °C, the starting material was completely consumed. Furthermore, the CO pressure could be lowered to 50 atm. *S*-Benzyl secondary alkylthiosulfonates were less reactive and required a higher pressure of CO (95 atm) to obviate the formation of the corresponding sulfide by-products (Table 1). Thus, remaining reactions were carried out under pressurized CO (50 atm for primary substrates and 95 atm for secondary and tertiary substrates) in heptane (0.01 M in the substrate) using V-40 initiator (0.3 eq) at 120 °C for 24 h.



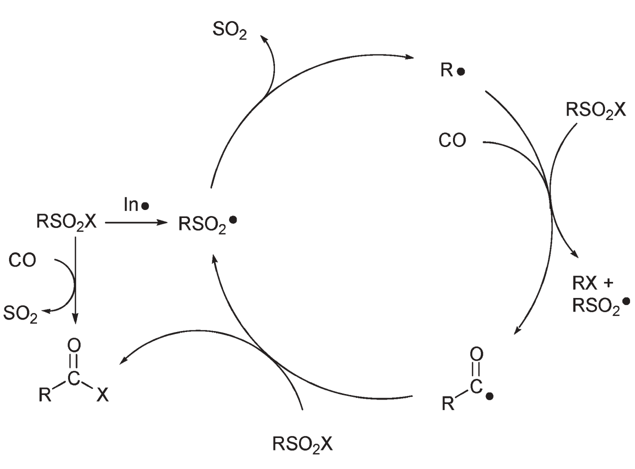
(1)



1		2	3
15%	95 atm /100 °C	82%	
	95 atm /120 °C	91%	
	50 atm /120 °C	97%	
15%	30 atm /120 °C	84%	

(2)

As shown in Table 1, the experimental results obtained here illustrate the efficiency and scope of the present method. Primary *S*-benzyl alkylthiosulfonates underwent clean conversion to the



Scheme 1 The direct conversion of alkylsulfonyl derivatives into alkyl carbonyl derivatives.

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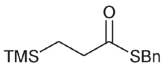
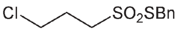
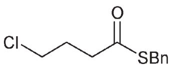
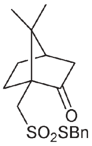
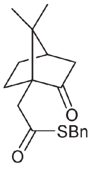
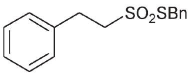
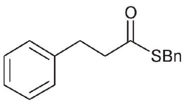
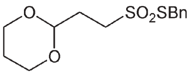
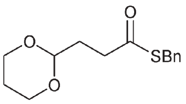
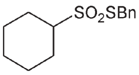
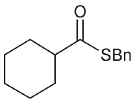
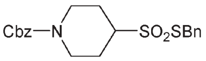
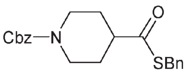
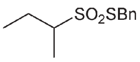
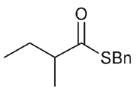
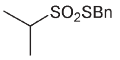
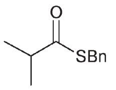
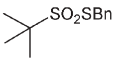
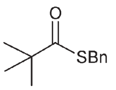
‡ Electronic supplementary information (ESI) available: Experimental section and spectroscopic data. See DOI: 10.1039/b710939c

Table 1 Direct conversion of RSO_2SBn into RCOSBn

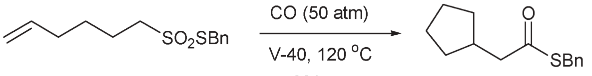
$$RSO_2SBn + CO \xrightarrow[\text{heptane (0.01 M)}]{\text{V-40 (0.3 eq)}} RCOSBn + SO_2$$
$$120\ ^{\circ}C,\ 24\ h$$

Entry	Substrate	CO/ atm	RCOSBn	Yield[a] (%)
1		50		80 (6)
2		50		91
3		50		84 (5)
4		50		94
5		50		78 (7)
6		95		94
7		95		87
8		95		86 (9)
9		95		80 (18)
10		95		19 (67)[b]

[a] Values in parentheses indicate the recovered starting material. [b] Benzyl *tert*-butyl sulfide (9%) was also isolated.

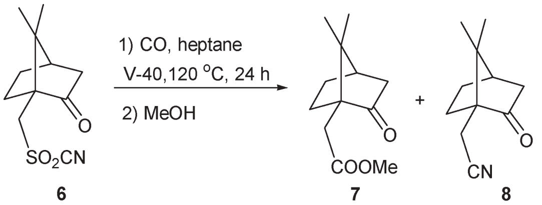
corresponding thiol esters in high yield (entries 1–5). Secondary *S*-benzyl alkylthiosulfonates worked well under 95 atm of CO, yielding the corresponding thiol esters (entries 6 and 7) along with some starting material in two occasions (entries 8 and 9). As we expected, the method reaches a limit with tertiary alkylthiosulfonates (entry 10). Radical reaction of *S*-benzyl *tert*-butylthiosulfonate under the same conditions (95 atm of CO) afforded a small amount of *S*-benzyl 2,2-dimethyl propanethioate (19%) along with 67% recovery of the starting material and some sulfide byproduct (9%). The result would be due to a low reactivity of the *tert*-butyl radical toward *S*-benzyl *tert*-butylthiosulfonate and an unfavorable equilibrium toward the carbonylation process relative to primary and secondary alkyl radicals.

A sequential radical reaction involving cyclization and thioalkoxycarbonylation was briefly studied, although the present approach is not the direct substitution of SO_2 into CO (eqn (3)). When a solution of alkylthiosulfonate **4** and V-40 initiator at pressurized CO (50 atm) was treated in refluxing heptane for 24 h, the desired thiol ester **5** was isolated in 71% yield along with some starting material (15%).



4 **5** (71%) (3)

We next studied the possibility of the direct conversion of alkylsulfonyl cyanides[14] into synthetically more useful acyl cyanides.[15] When the reaction was carried out with **6** under 50 atm of CO using V-40 initiator (0.3 equiv.) in refluxing heptane (0.01 M) at 120 °C for 24 h, methyl ester **7** was isolated in 77% yield along with a small amount of cyanide **8** (7%) after quenching the reaction mixture with methanol. A similar result was also obtained at a higher pressure of CO (95 atm) in refluxing heptane (0.05 M). The best result was obtained under 95 atm of CO at a lower concentration (0.01 M) of **6** using V-40 initiator (0.3 equiv.) in heptane at 120 °C for 24 h (eqn (4)). As shown in eqn (5), several primary alkylsulfonyl cyanides **9** were converted into the corresponding amides **11** *via* acyl cyanides **10**. However, the present approach reaches a limit with secondary alkylsulfonyl cyanides (eqn (6)). When **12** was subjected to similar conditions, nitrile **14** was isolated in 51% yield along with the desired product **13** in 33% yield. At 130 atm of CO, the yield of **13** was increased to 43% along with **14** (42%). Apparently, alkylsulfonyl cyanides are more reactive than alkylthiosulfonates toward alkyl radicals, thereby yielding more alkyl cyanide byproducts.



6 **7** **8** (4)

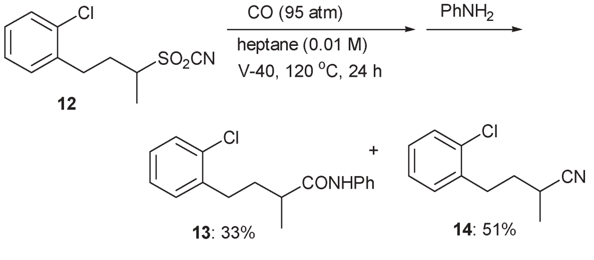
	7	8
50 atm / 0.01 M	77	7
95 atm / 0.05 M	81	12
95 atm / 0.01 M	84	0

$$RSO_2CN \xrightarrow[\text{heptane (0.01 M), 120 °C, 24 h}]{\text{CO (95 atm), V-40 (0.3 eq)}} \underset{\mathbf{10}}{RCOCN} + SO_2$$

9a:R= $EtO_2C(CH_2)_5$
9b:R= $Ph(CH_2)_3$
9c:R= $CH_3(CH_2)_7$

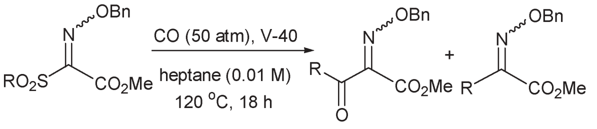
$$\xrightarrow{PhNH_2} RCONHPh \quad (5)$$

11a:70%; **11b**:81%; **11c**:73%



(6)

The present approach could be further applied to the direct conversion of alkylsulfonyl oxime ether **15** into the acylated oxime ether **16** (eqn (7)),[16] which is very useful for the preparation of vicinal tricarbonyl compounds.[17] The reaction could be successfully carried out at pressurized CO (50 atm) at 120 °C for 18 h without the formation of **17** for primary alkylsulfonyl oxime ethers. When the reaction was carried out with secondary alkylsulfonyl oxime ether **15d** under the same condition, **16d** was obtained in 71% yield along with some starting material **15d** (21%). Under 95 atm of CO, **15d** was completely consumed to give **16d** in 92% yield.



(7)

15a:R=Et	**16a**: 96%	**17a**: 0%
15b:R=MeO$_2$C(CH$_2$)$_3$	**16b**: 94%	
15c:R=PhO(CH$_2$)$_4$	**16c**: 93%	
15d:R=cyclohexyl: 21%	**16d**: 71%	

In conclusion, we have discovered the first simple and highly efficient way to convert alkylthiosulfonates, alkylsulfonyl cyanides, and alkylsulfonyl oxime ethers into the corresponding carbonyl compounds in high yields *via* tin-free radical carbonylation. The present strategy would be further applied to other radical-mediated carbon–carbon bond forming reactions.

Notes and references

§ *Typical procedure* for the direct conversion of *S*-benzyl alkylthiosulfonate **1** into *S*-benzyl thiol ester **2**: Dried heptane (20 ml), *S*-benzyl *n*-butylthiosulfonate (**1**) (49 mg, 0.2 mmol), and V-40 (15 mg, 0.06 mmol) were placed in a 50 ml stainless steel autoclave. The autoclave was sealed, purged three times with 10 atm of CO, pressurized with 50 atm of CO, and then heated at 120 °C with stirring for 12 h. After excess CO was discharged at room temperature, the solvent was removed under reduced pressure. The residue was purified by passing through a silica gel column using ethyl acetate and *n*-hexane (1 : 50) as the eluant to give *S*-benzyl thiobutanoate (**2**) (40 mg, 97%).

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