Reaction of Di-*t*-butyl Thioketone with Aryllithium. Effect of Temperature and Solvent

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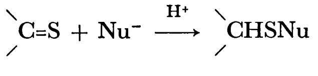
Di-*t*-butyl thioketone reacts with phenyllithium affording both *C*-phenylated and *S*-phenylated products. The product distribution largely depends on the reaction temperature and solvent: the lower the temperature and the more solvated the counter cation, the larger the yield of the *S*-phenylated product. Steric effect is also important: 2,6-dimethylphenyllithium affords only *S*-arylated product. The result has been interpreted in terms of the charge-transfer-intermediate—radical-combination mechanism.

In contrast to carbonyl compounds, thiocarbonyl compounds have abnormal reactivity in the sense that thiocarbonyl-sulfur, in general, reacts with a nucleophile.[1-6]

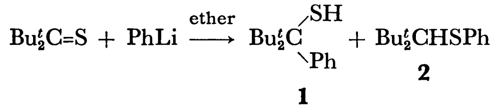


$$\mathrm{{>}C{=}S + Nu^- \xrightarrow{H^+} {>}CHSNu}$$

Although several prausible explanations have been proposed for the thiophilic attack of nucleophiles to thiocarbonyl compounds, none of them are satisfactory to explain the reactivity universally. In a previous paper we reported that the charge-transfer (CT)-intermediate—radical-combination mechanism is most prausible for the reaction of thiocarbonyl compounds with nucleophiles.[6] We now wish to report that the preference of the thiophilic attack over the carbophilic attack in the reaction of phenyllithium with di-*t*-butyl thioketone changes largely with the change of reaction temperature or the solvent and the result is consistent with the previously proposed CT-intermediate—radical-combination mechanism.

Results

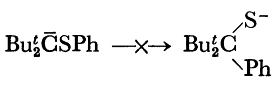
The reaction of di-*t*-butyl thioketone with phenyllithium in ether afforded two products, 2,2,4,4-tetramethyl-3-phenylpentane-3-thiol (**1**) and di-*t*-butylmethyl phenyl sulfide (**2**).



$$\mathrm{Bu^t_2C{=}S + PhLi \xrightarrow{ether} Bu^t_2C(SH)(Ph) + Bu^t_2CHSPh}$$

1   **2**

The yields depended largely on the reaction temperature: for example, **1** was isolated in 80% yield together with trace amount of **2** from the reaction mixture kept at 30 °C, whereas the reaction at −30 °C resulted in the formation of **2** in 80% yield with trace amount of **1**. It was reported that the reaction at 0 °C aforded **1** and **2** in 25 and 35% yields, respectively.[6,7] It has been confirmed that **2** does not rearrange into **1** under the reaction condition. That is, the reaction mixture at −30 °C was warmed to 30 °C before the addition of water and no difference in the yield was observed from that obtained by quenching the reaction mixture at −30 °C.



$$\mathrm{Bu^t_2\bar{C}SPh \not\longrightarrow Bu^t_2C(S^-)(Ph)}$$

Table 1. Reaction of di-*t*-butyl thioketone with phenyllithium in various solvents at 20 °C

Solvent	Yield, %	
	$\mathrm{Bu^t_2CH{-}SPh}$	$\mathrm{Bu^t_2CPh{-}SH}$
Ether	trace	75
Tetrahydrofuran	80	trace
Ether–Hexane (1:1)	trace	70
Ether–THF (1:1)	94	
Ether–THF (9:1)	98	
Ether–THF[a]	43	31

a) Mole-equivalent to phenyllithium.

When the reaction at 20 °C was run in tetrahydrofuran (THF), the sole product isolated was **2**. As shown in Table 1, the effect of THF is striking and the presence of an equivalent-to-phenyllithium amount of THF results in the formation of **2** in 43% yield. On the other hand, the presence of nonpolar hexane in a reaction mixture did not affect the product distribution.

The reaction of di-*t*-butyl thioketone with 2,6-dimethylphenyllithium at 20 °C afforded 1,1-dimethyl-2-*t*-butylcyclopropane and 2,6-dimethylphenyl thiol in 40 and 70% yields, respectively. No product expected from the carbophilic attack of a 2,6-dimethylphenyl anion was detected.

Discussion

Since **1** and **2** are kinetically controlled products of the reaction of di-*t*-butyl thioketone with phenyllithium, the ratio of yields (Y_s/Y_c) may reflect the ratio of rate constants (k_s/k_c) for the formations of products, where

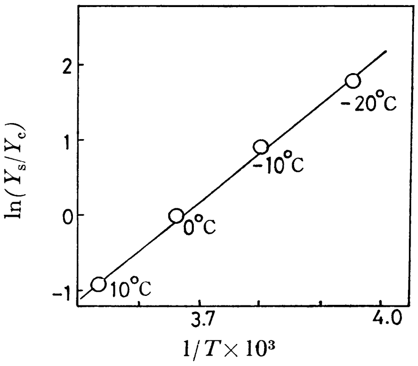


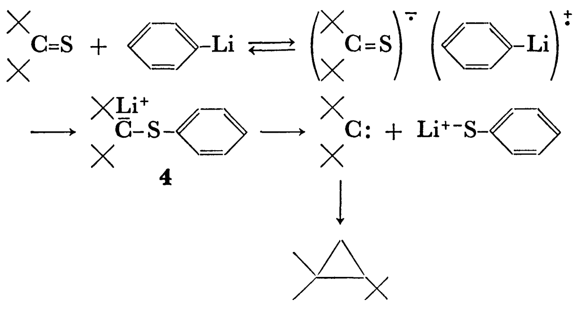
Fig. 1. Temperature-dependency of the ratio of yields of *S*-phenylated and *C*-phehnylated products.

subscripts s and c denote thiophilic and carbophilic attacks, respectively. A plot of $\ln(Y_s/Y_c)$, which is equivalent to $\ln(k_s/k_c)$, against $1/T$ shows a good linear relationship as illustrated in Fig. 1. From the slope and intercept of the line, the differences in apparent parameters of activation were calculated to be −11.2 kcal/mol and −48 e.u. for $\Delta H_s^{\neq}-\Delta H_c^{\neq}$ and $\Delta S_s^{\neq}-\Delta S_c^{\neq}$, respectively. Although the absolute values may not represent the real physical meaning, the values indicate, at least qualitatively, that the thiophilic attack is more favored in enthalpy but much less favored in entropy than the carbophilic attack. Since it is not the sulfur atom but the thiocarbonyl-carbon which has bulky substituents, the result may suggest that the transition state for the carbophilic attack resembles the reactant much more than that for the thiophilic attack. In other words, the electronic structure of the reactant may contribute more for the carbophilic attack than for the thiophilic attack. Together with the fact that a nucleophile which has an β-hydrogen reduces di-*t*-butyl thioketone into the corresponding thiol, the above result leads to the conclusion that **3a** is more important canonical form than **3b** for the anion radical of di-*t*-butyl thioketone as previously proposed.⁶⁾ That is, a phenyl radical is sterically prevented from the carbophilic attack by two *t*-butyl groups and radical combination takes place with the sulfur atom, although the spin density on this atom is smaller than that on the carbon atom.

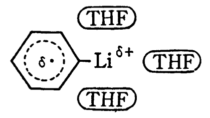
$$\mathrm{Bu}^t_2\dot{\mathrm{C}}\text{–}\bar{\mathrm{S}} \longleftrightarrow \mathrm{Bu}^t_2\bar{\mathrm{C}}\text{–}\dot{\mathrm{S}}$$

3a **3b**

The steric inhibition for the carbophilic attack is also recognized in the reaction with 2,6-dimethylphenyllithium: products from the reaction with this reagent indicate that the reaction proceeds only with the thiophilic attack under the condition where phenyllithium attacks on the thiocarbonyl-carbon. Here, two methyl groups on a phenyl ring interfere further the carbophilic attack. However, since these methyl groups still cause steric crowd in the intermediate carbanion **4**,⁸⁾ it decomposes either to products or to starting materials.



The effect of THF is also understandable with the idea of steric bulk of a nucleophile at the transition state for the carbophilic attack. The cation radical of phenyllithium, which is formed from phenyllithium after the transfer of an electron onto di-*t*-butyl thioketone, still remaines covalent bond character between the lithium and carbon atoms. Since THF has larger ability of solvation than ether, the net bulk of the nucleophile becomes larger in the presence of THF, **5**, than in its



absence and the carbophilic attack is sterically more reduced under the former condition than the latter. The phenomenon is the reverse of that normally observed in nucleophilic attack of anions, where dipolar aprotic solvents make an anion free and reactive by the solvation onto a cation.⁹⁾ We believe that this is another support for the presence of a CT-intermediate in the reaction of di-*t*-butyl thioketone with a nucleophile.

Experimental

Reaction of Di-t-butyl Thioketone with Phenyllithium. The reaction was carried out in a thermostat kept at an appropriate temperature. The general procedure was described in a previous paper.⁶⁾ Products were analyzed on a VPC (Yanagimoto G-1800; Dexil, 1 m; 150 °C; N_2, 0.4 kg/cm^2).

Reaction of Di-t-butyl Thioketone with 2,6-Dimethylphenyllithium. Into 20 ml of ether solution containing 168 mg (1.5 mmol) of 2,6-dimethylphenyllithium, was added 148 mg (1.0 mmol) of di-*t*-butyl thioketone in 20 ml of ether over a period of 24 h under an atmosphere of nitrogen. After the color of the thioketone had disappeared, 30 ml of water was added to the mixture and organic materials were extracted with ether. The extract was subjected to preparative VPC(Varian 920; Dexil, 1 m; 80 °C) and 50 mg (40% yield) of 1,1-dimethyl-2-*t*-butylcyclopropane. NMR $\delta^{\mathrm{TMS}}_{\mathrm{CCl_4}}$ 0.07—0.9 (3H, m), 0.93 (9H, s), 1.00 (3H, s), and 1.44 (3H, s). Mass spectrum M^+: *m/e* 126. Found: C, 85.04; H, 14.43%. Calcd for C_9H_{18}: C, 85.63; H, 14.34%.

The aqueous layer was acidified with dil sulfuric acid and organic materials were extracted with ether. The extract was chromatographed on silica gel with hexane eluent to give 96 mg (70% yield) of 2,6-dimethylphenylthiol. NMR $\delta^{\mathrm{TMS}}_{\mathrm{CCl_4}}$ 2.30 (6H, s), 3.00 (1H, s), and 6.80—6.90 (3H, m).

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