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SYNTHESIS OF 1,4-DIKETONES BY OXIDATIVE COUPLING OF KITONE ENOLATES AND TRIMETHYLSILYL ENOL ETHERS WITH CUPRIC TRIFLUOROMETHANESULFONATE

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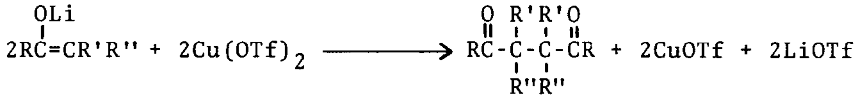
1,4-Diketones are versatile intermediates for the syntheses of some natural products and related compounds having cyclopentanone or furan ring systems. Many synthetic routes to these 1,4-diketones have been reported.¹⁾ One of the new methods for synthesizing 1,4-diketones is $CuCl_2$-promoted dimerization of ketone enolates, reported by Saegusa and his coworkers.¹⁾ According to their procedure, methyl ketones were dimerized to 1,4-diketones in good yields, but the increase in alkyl substitution at the coupling site resulted in a remarkable reduction in the yield of 1,4-diketone. In our present study, 1,4-diketones were found to be effectively prepared by the oxidative dimerization of ketone enolates with $Cu(OTf)_2$, especially even in the cases of ketones possessing alkyl substituent at the coupling site.²⁾



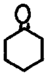
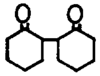
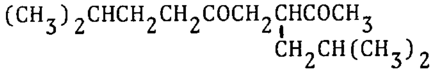
$$2R\overset{\overset{\text{OLi}}{|}}{C}=CR'R'' + 2Cu(OTf)_2 \longrightarrow R\overset{\overset{O}{\|}}{C}-\underset{\underset{R''}{|}}{\overset{\overset{R'}{|}}{C}}-\underset{\underset{R''}{|}}{\overset{\overset{R'}{|}}{C}}-\overset{\overset{O}{\|}}{C}R + 2CuOTf + 2LiOTf$$

A typical procedure is as follows; to a solution of lithium enolate of propiophenone (1 mmol) in THF (5 ml), generated from propiophenone and lithium diisopropylamide at -78°C, was added a solution of $Cu(OTf)_2$ (1.1 mmol) in isobutyronitrile (1.1 ml) followed by the subsequent stirring at -78°C for 30 min and then at room temperature for 30 min. After the reaction mixture poured into water was extracted with ether, the extracts were submitted to preparative TLC (silica gel) to give 0.80 mmol (80% yield) of 1,4-diphenyl-2,3-dimethylbutan-1,4-dione. In a similar way, 1,4-diketones were prepared.

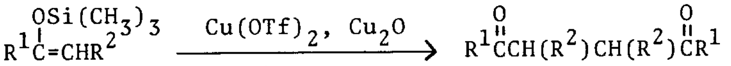
These results show that ketones possessing alkyl substituent at the coupling site are dimerized to afford 1,4-diketones in good yields. It was also noted that the use of isobutyronitrile as a cosolvent was effective in the above dimerization reaction and the similar solvent effect was also found in the coupling reaction of silyl enol ether with $Cu(OTf)_2$ as mentioned below.

Next, the coupling reaction of silyl enol ether to 1,4-diketone was found to proceed by the treatment of silyl enol ether with $Cu(OTf)_2$ in the presence of Cu_2O in isobutyronitrile.³,⁴⁾ Thus, the reaction of 2-trimethylsiloxystyrene (1 mmol) with $Cu(OTf)_2$ (1.1 mmol) in the presence of Cu_2O (4 mmol) in

Table I. Yield of 1,4-Diketones

No	Starting Ketones	1,4-Diketones (%)
1	$CH_3CO-C_6H_5$	$C_6H_5-COCH_2CH_2CO-C_6H_5$ (83)
2	$CH_3CH_2CO-C_6H_5$	$C_6H_5-COCH(CH_3)CH(CH_3)CO-C_6H_5$ (80)
3	$CH_3CH_2COCH_2CH_3$	$CH_3CH_2COCH(CH_3)CH(CH_3)COCH_2CH_3$ (63)
4		 (73)
5	$(CH_3)_2CHCH_2CH_2COCH_3$	$[(CH_3)_2CHCH_2CH_2COCH_2]_2$ (64)  $(CH_3)_2CHCH_2CH_2COCH_2\underset{CH_2CH(CH_3)_2}{CH}COCH_3$ (12)

isobutyronitrile (5 ml) at 0°C for 2 hr afforded the corresponding 1,4-diketone in 55% yeild.



$$R^1\overset{OSi(CH_3)_3}{C}=CHR^2 \xrightarrow[(CH_3)_2CHCN]{Cu(OTf)_2,\ Cu_2O} R^1\overset{O}{\overset{\|}{C}}CH(R^2)CH(R^2)\overset{O}{\overset{\|}{C}}R^1$$

$R^1 = C_6H_5$ $R^2 = H$ 55%
$R^1 = C_6H_5$ $R^2 = CH_3$ 27%

Other Cu(II) salts such as $Cu(O_2CCF_3)_2$, $CuCl_2$ or CuO than $Cu(OTf)_2$ were not effective for the coupling reaction of silyl enol ether. In the absence of Cu_2O the reaction of silyl enol ether with $Cu(OTf)_2$ gave a complex result including the trace amount of 1,4-diketone. Moreover, the use of isobutyronitrile as a solvent was crucial in the above coupling reaction. When acetonitrile was used as a solvent, a small amount of a by-product containing a nitrile group was also obtained and in the case of dimethylformamide (DMF), dimethylsulfoxide (DMSO) or hexamethylphosphorictriamide (HMPA) as a solvent, 1,4-diketone was obtained only in a trace amount.

In conclusion, $Cu(OTf)_2$ is an effective reagent for the oxidative coupling reaction of ketone enolates and trimethylsilyl enol ethers to the corresponding 1,4-diketones and the application of the present method to organic syntheses is now being investigated.

References

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