Preparations of Furans from α-Bromo Ketones and Enol Ethers Catalyzed by a Rhenium(I) Nitrogen Complex

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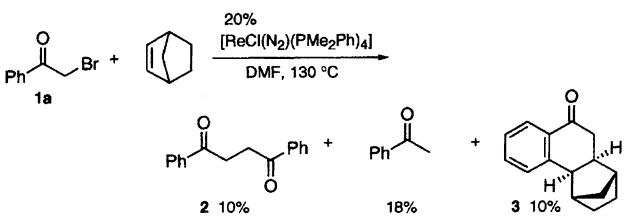
By the catalytic use of a rhenium(I) nitrogen complex, $[ReCl(N_2)(PMe_2Ph)_4]$, α-keto radicals are generated from α-bromo ketones and react with vinyl ethers and silyl enol ethers intermolecularly. Various substituted furans, including tetrasubstituted furans such as furoguaiacin, are prepared by this method.

α-Keto radicals are attractive reaction intermediates in organic synthesis for introduction of functionalized carbon chains. Several methods have been known for the generation of α-keto radicals, such as the hydrogen abstraction of ketones initiated by di-*t*-butyl peroxide,[1] the atom transfer of α-seleno and iodo ketones by using trialkylstannanes as initiators or by photolysis,[2—4] and the oxidation of ketones, silyl enol ethers, and β-keto acids with metallic oxidants.[5—9] To the best of our knowledge, there has been no report on the transition metal-catalyzed generation of α-radicals of ketones and esters from the corresponding α-monohalo ketones and esters,[10] though mono and dichloro(alkoxycarbonyl)-methyl radicals are generated from α-polychloro esters and alkoxy(alkoxycarbonyl)methyl radicals are generated from α-alkoxy-α-chloro esters to react with olefins catalyzed by copper, iron, molybdenum, and ruthenium compounds as catalysts.[11—15]

Recently we have investigated the development of synthetic methods by using low-valent rhenium compounds.[16] As a part of this study, reduction of α-bromo ketones was examined with a low-valent rhenium(I) nitrogen complex, $[ReCl(N_2)(PMe_2Ph)_4]$,[17] and it was found that α-keto radicals were generated by the catalytic use of the rhenium reagent. In this paper, we would like to report the radical generation and their addition reaction to olefinic compounds.

Results and Discussion

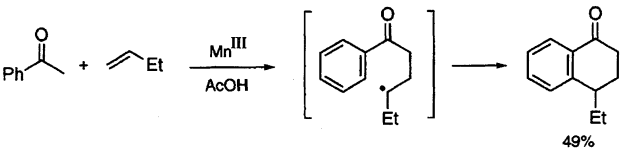
Addition Reaction of α-Keto Radical to Norbornene. When a mixture of 2-bromoacetophenone (**1a**) and 3 molar amounts of norbornene in *N*,*N*-dimethylformamide (DMF) was heated at 130 °C in the presence of 20% molar amount of $[ReCl(N_2)(PMe_2Ph)_4]$, **1a** disappeared and three products: 1,4-diphenyl-1,4-butanedione (**2**), acetophenone, and a cyclic ketone **3** were obtained in 10, 18, and 10% yield, respectively (Eq. 1).



(1)

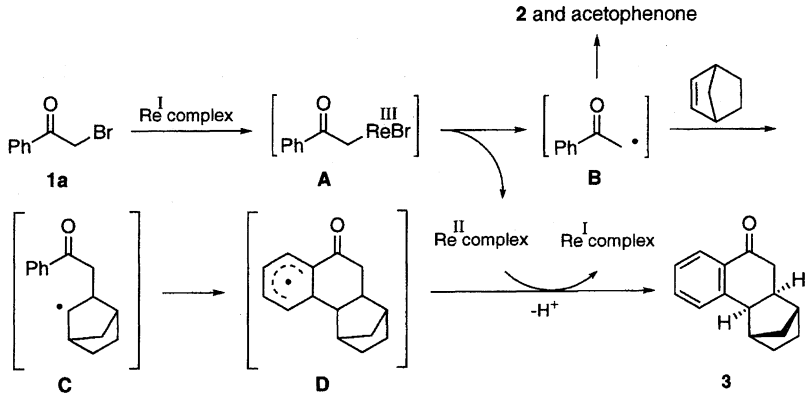
The cyclized product **3** is assumed to be produced as depicted in Scheme 1. That is, a coordinatively unsaturated rhenium(I) complex is generated from $[ReCl(N_2)(PMe_2Ph)_4]$ by thermal dissociation of dinitrogen.[18] The oxidative addition of the α-bromo ketone **1a** to the coordinatively unsaturated rhenium(I) complex proceeds to generate phenacylrhenium(III) complex **A**, which cleaves to generate phenacyl radical **B** and a rhenium(II) complex. The phenacyl radical **B** thus generated adds to norbornene to give a norbornyl radical **C**, which cyclizes intramolecularly with the phenyl group. The resulting cyclohexadienyl radical **D** is oxidized by the rhenium(II) complex to a cyclohexadienyl cation and the successive deprotonation gives the cyclic ketone **3**. This radical process is supported by the fact that the reaction in the presence of galvinoxyl did not afford the cyclized product **3**.

A similar type of the radical addition cyclization reaction was reported by Heiba and Dessau.[6b] That is, an α-keto radical generated from acetophenone by oxidation with manganese(III) acetate adds to an olefin to give a γ-keto radical, which in turn cyclizes intramolecularly to give an α-tetralone derivative (Eq. 2).



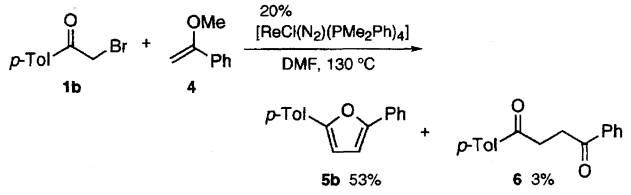
(2)

Addition Reaction of α-Keto Radicals to Vinyl Ethers. The addition reaction of aroylmethyl radicals was examined



Scheme 1.

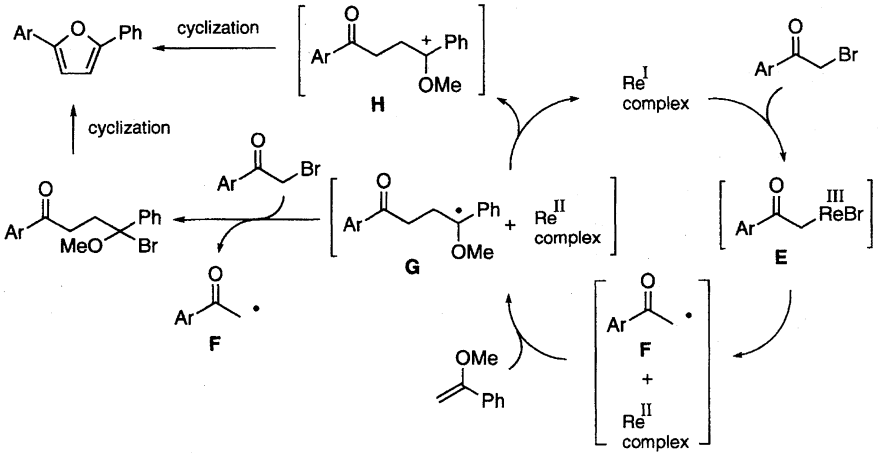
with electron rich olefins instead of norbornene. When a DMF solution of 2-bromo-4′-methylacetophenone (**1b**) and α-methoxystyrene (**4**) was heated in DMF at 130 °C in the presence of 20% molar amount of $[ReCl(N_2)(PMe_2Ph)_4]$, an unsymmetrical furan **5b** and a 1,4-diketone **6** were obtained in 53 and 3% yield, respectively (Eq. 3). Neither symmetrical furan nor symmetrical 1,4-diketone could be detected. Thus, the homocoupling reaction of the α-keto radical did not proceed, but the addition to the olefin **4** occurred exclusively. Since the coupling products **5b** and **6** were obtained in amounts almost 3 times more than the molar amount of the rhenium(I) complex, the reaction obviously proceeded by a catalytic process.



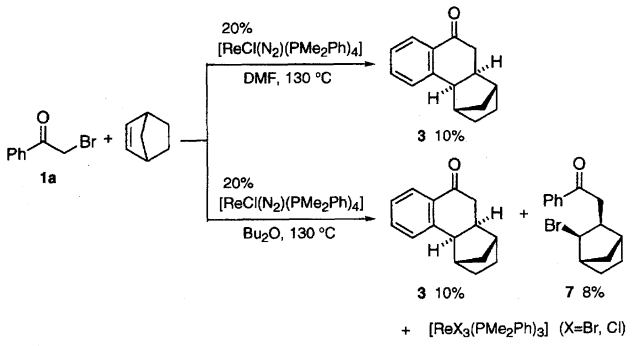
(3)

Two catalytic pathways could be considered, as depicted in Scheme 2. In the first one, the oxidation and reduction with rhenium complexes are concerned in the catalytic process: A radical intermediate **G** generated by the addition of an α-keto radical **F** to α-methoxystyrene is oxidized with the rhenium(II) complex which is formed by the homolytic cleavage of the aroylmethylrhenium(III) complex **E**, regenerating the rhenium(I) complex. There is another catalytic pathway in which the radical intermediate **G** abstracts bromine from the α-bromo ketone to generate another α-keto radical **F**. In this pathway, the rhenium(I) complex plays a role only as a radical initiator.

As mentioned previously, the cyclic ketone **3** was obtained by the reaction of 2-bromoacetophenone (**1a**) and norbornene in DMF, while a norbornyl bromide **7** was isolated along with the cyclic ketone **3** from the reaction in dibutyl ether (Eq. 4). These results indicated that the radical intermediate generated by the addition of α-keto radical to norbornene (**C** in Scheme 1) does not abstract bromine from 2-bromoacetophenone in DMF but partially does in dibutyl ether. In the reaction in dibutyl ether, a trivalent rhenium complex, $[ReX_3(PMe_2Ph)_3]$ (X=Br, Cl), was obtained but was not detected in the reaction in DMF. This trivalent rhenium complex would be formed by the disproportionation of the rhenium(II) complex, $[ReBrCl(PMe_2Ph)_4]$, generated by the homolytic cleavage of the rhenium(III) intermediate (**A** in Scheme 1). As the trivalent rhenium complex and the norbornyl bromide **7** could not be detected from the reaction in DMF, the reaction in DMF is considered to proceed by the oxidation and reduction pathway.



Scheme 2.

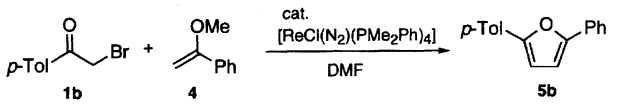


(4)

The reaction of the α-bromo ketone **1b** and the vinyl ether **4** was also tried by the use of 20% molar amounts of some low-valent rhenium(I) complexes, such as $[ReCl(N_2)(PMe_2Ph)_4]$, $[ReCl(CO)(dppe)_2]$, and $[ReBr(CO)_2(PMe_2Ph)_3]$; the furan **5b** was obtained in 53, 20, and 5% yield, respectively. The nitrogen complex exhibited better catalytic activity than the other carbonyl complexes. It is noteworthy that, as shown in Table 1, the yield became better by using a smaller amount of the nitrogen complex (Entries 1—6). The reaction at 153 °C using 2% molar amount of the rhenium(I) complex gave the addition product **5b** in 74% yield (Entry 6). Dimethylphenylphosphine was found to dissociate from the rhenium(I) complex during the reaction and to react with the α-bromo ketone **1b**, giving a phosphonium salt. Accordingly, the use of a smaller amount of the catalyst prevents such a side reaction from consuming the α-bromo ketone. In the presence of galvinoxyl, only a small amount of furan was obtained (Entry 7). This is also consistent with the radical reaction mechanism.

The reaction was examined by employing several 2-bromoacetophenone derivatives having electron-donating and electron-withdrawing groups at the 4′-position. Except the 4′-nitro derivative, the radical addition products to the vinyl ether **4** were obtained in reasonable yield (Table 2, Entries 1—4). The reaction of 2-bromo-4′-nitroacetophenone (**1e**) gave the corresponding furan **5e** in low yield

Table 1. Reactions of 2-Bromoacetophenone with α-Methoxystyrene under Various Conditions[a)]

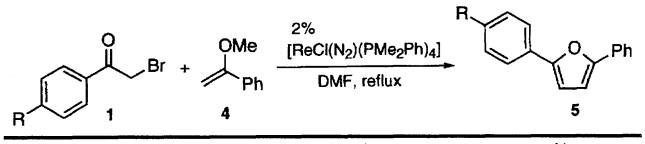


1b 4 5b

Entry	Cat./%	Temp/°C	Yield/%[b)]
1	20	130	53
2	6	130	60
3	20	153	55
4	5	153	67
5	3	153	71
6	2	153	74
7	2	153	5[c,d)]
8	1	153	48[c)]

a) 3 molar amounts of **4** was used. b) A trace amount of 1, 4-diketone **6** was also detected. c) **1b** was recovered. d) An equimolar amount of galvinoxyl was added.

Table 2. Reactions of 2-Bromo-4′-Substituted Acetophenones with α-Methoxystyrene



1 4 5

Entry	α-Bromo ketone[a)]		Yield/%[b)]	
1	**1a**	R = H	**5a**	76
2	**1b**	R = Me	**5b**	74
3	**1c**	R = OMe	**5c**	73
4	**1d**	R = Br	**5d**	69
5	**1e**	R = NO_2	**5e**	32[c)]

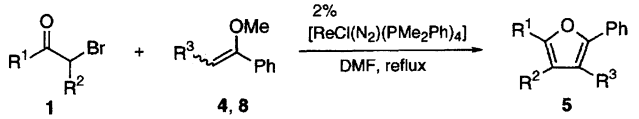
a) 3 molar amounts of **4** were used. b) A trace amount of unsymmetrical 1,4-diketones were also detected. c) 4% molar amount of $[ReCl(N_2)(PMe_2Ph)_4]$ was used. **1e** was recovered.

(Entry 5). Since it has been known that nitrobenzene works as a radical inhibitor,[19)] the nitrophenyl group disturbs the radical process.

In addition to 2-bromoacetophenone derivatives, an aliphatic α-bromo ketone **1f** reacted with α-methoxystyrene to afford 2-phenethyl-5-phenylfuran (**5f**) in 70% yield (Table 3, Entry 1). Trisubstituted furans **5g** and **5h** were prepared in 79 and 68% yield (Entries 2 and 3). As exemplified in the reaction of 2-bromopropiophenone (**1g**) and a vinyl ether **8**, a tetrasubstituted furan **5i** was obtained in 60% yield by using 6% molar amount of the rhenium(I) complex.

Addition Reaction of α-Keto Radicals to Silyl Enol Ethers. Silyl enol ethers were also employed as acceptors of α-keto radicals. When a mixture of 2-bromoacetophenone (**1a**) and 1-(1-*t*-butyldimethylsiloxyethenyl)-4-methylbenzene (**9a**) was heated to reflux in the presence of 2% molar amount of the rhenium(I) complex in DMF, 1-(4-methylphenyl)-4-phenyl-1,4-butanedione (**6**) was obtained in 58% yield after successive desilylation with tetrabutylammonium fluoride (Eq. 5).[20)] A small amount of the homocoupling product **2** of the α-bromo ketone **1a** was produced in this reaction.

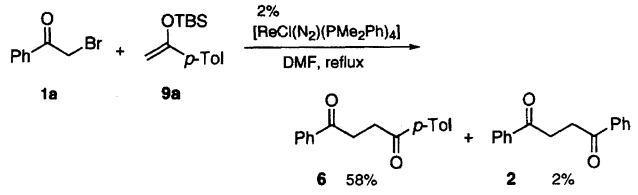
Table 3. Preparations of Substituted Furans



1 4, 8 5

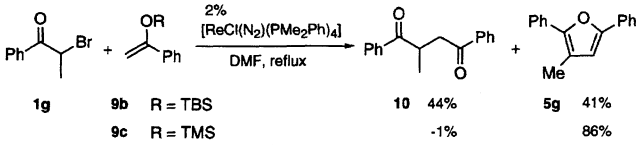
Entry	α-Bromo ketone[a)]			Vinyl ether		Yield/%[b)]
1	**1f**	R^1 = $PhCH_2CH_2$	R^2 = H	**4**	R^3 = H	**5f** 70
2	**1g**	R^1 = Ph	R^2 = Me	**4**	R^3 = H	**5g** 79
3	**1h**	R^1 = Ph	R^2 = Ph	**4**	R^3 = H	**5h** 68
4	**1g**	R^1 = Ph	R^2 = Me	**8**	R^3 = Me	**5i** 60[b)]

a) 3 molar amounts of vinyl ethers were used. b) 6% molar amount of $[ReCl(N_2)(PMe_2Ph)_4]$ was used.



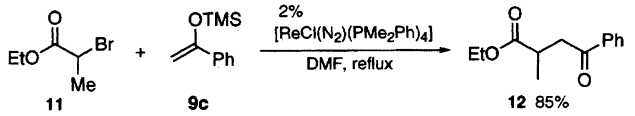
(5)

In the reaction of an α-substituted α-bromo ketone **1g**, the addition products, a 1,4-diketone **10** and a furan **5g**, were obtained in high yield without the formation of the homocoupling product. Though the reaction of the *t*-butyldimethylsilyl enol ether **9b** gave almost equal amounts of the diketone **10** and the furan **5g**, the furan **5g** was obtained almost exclusively from the corresponding trimethylsilyl enol ether **9c** (Eq. 6).



(6)

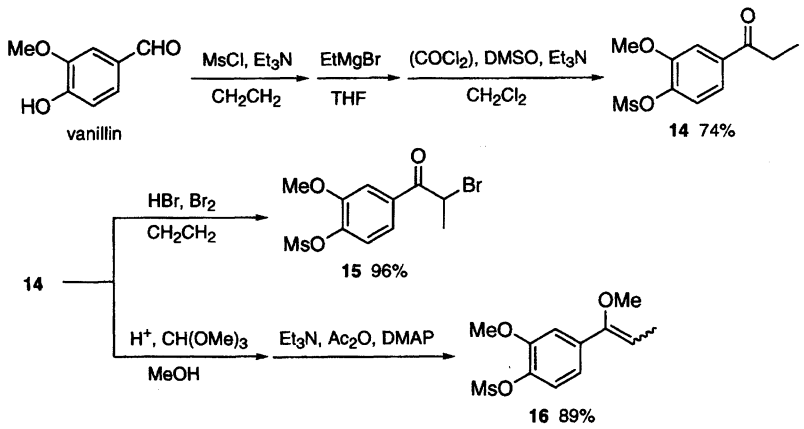
In addition to α-bromo ketones, an α-bromo ester such as ethyl 2-bromopropionate (**11**) was found to generate radical species, and ethyl 3-benzoyl-2-methylpropionate (**12**) was obtained in 85% yield from the reaction with the silyl enol ether **9c** (Eq. 7).



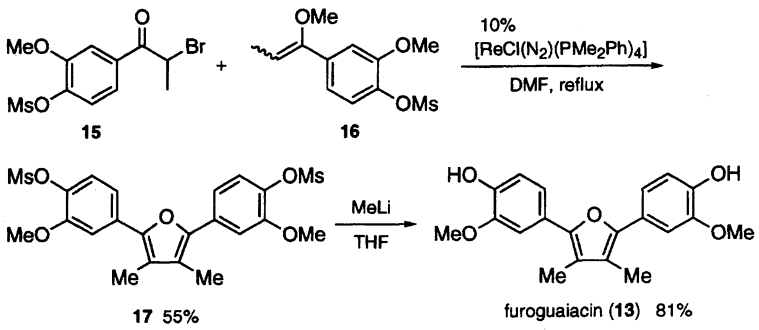
(7)

Preparation of Furoguaiacin. As described above, this rhenium-catalyzed reaction may be utilized to prepare various substituted furans. Furoguaiacin (**13**) is a lignan isolated from the hardwood *Guaiacum officinale* and is known as a 5-lipoxygenase inhibitor.[21,22] This tetrasubstituted furan was expected to be synthesized by the reaction of an α-bromo ketone **15** with a vinyl ether **16**. A hydroxy-protected ketone **14** was derived from vanillin in 74% total yield by methylsulfonylation, alkylation and Swern oxidation (Scheme 3). Treatment of the ketone **14** with bromine in the presence of a catalytic amount of hydrogen bromide (30% acetic acid solution) afforded the α-bromo ketone **15** in 96% yield. After conversion of the ketone **14** to the corresponding acetal, the vinyl ether **16** was prepared by the elimination of methanol by treating the acetal with triethylamine, acetic anhydride, and 4-(dimethylamino)pyridine (DMAP).[23]

When a mixture of the α-bromo ketone **15** and the vinyl ether **16** was heated in DMF in the presence of 10% molar amount of the rhenium(I) complex, the furan **17** was obtained in 55% yield; this was deprotected with methyllithium to give furoguaiacin (**13**) in 81% yield (Scheme 4).



Scheme 3.



Scheme 4.

Experimental

General. ^{1}H NMR (500 MHz) spectra in $CDCl_3$ were recorded on Bruker AM500 and JEOL α-500 spectrometers using $CHCl_3$ as an internal standard (δ=7.24). ^{13}C NMR (125 MHz) spectra in $CDCl_3$ were measured with a Bruker AM 500 spectrometer using $CDCl_3$ as an internal standard (δ=77.0). IR spectra were recorded on a Horiba FT 300-S spectrophotometer. High-resolution mass spectra were obtained with a JEOL JMS-SX102A mass spectrometer. Fast atom bombardment (FAB) mass spectra were obtained with 3-nitrobenzyl alcohol as the matrix. The melting points were uncorrected. Elemental analyses were carried out at The Elemental Analysis Laboratory, Department of Chemistry, Faculty of Science, The University of Tokyo. Dimethylformamide (DMF) was dried over P_2O_5, then distilled from CaH_2, and stored over Molecular Sieves 4A under an argon atmosphere. Dichloromethane was distilled from P_2O_5, then from CaH_2, and dried over Molecular Sieves 4A. Tetrahydrofuran (THF) was freshly distilled from sodium diphenylketyl before use. Silica gel column chromatography was carried out with Merck Art 7734 and Kanto 60N. Preparative TLC was performed on silica gel (Wakogel B-5F). All reactions were carried out under an argon atmosphere.

Chlorotetrakis(dimethylphenylphosphine)(dinitrogen)rhenium was prepared by the literature procedure[17] and its purity was confirmed by an elemental analysis. Found: C, 47.61; H, 5.33; N, 3.70%. Calcd for $C_{32}H_{44}ClN_2P_4Re$: C, 47.91; H, 5.53; N, 3.49%. α-Bromo ketones **1a**,**c**, and **e** were purchased from Tokyo Kasei Kogyo Co., Ltd. or Aldrich Chemical Co., Inc. and purified by distillation or recrystallization. α-Bromo ketones **1b**,**d**,**f**,**g**, and **h** were prepared by the literature procedures.[24] Vinyl ethers **5** and **9** and silyl enol ethers **10** were prepared by the literature procedures.[25,26]

The Reaction of 2-Bromoacetophenone with Norbornene. To chlorotetrakis(dimethylphenylphosphine)(dinitrogen)rhenium (30 mg, 0.037 mmol) was added a DMF (3 ml) solution of 2-bromoacetophenone (37.2 mg, 0.019 mmol) and norbornene (53.2 mg, 0.56 mmol). After the mixture was heated for 4 h at 130 °C, the reaction was quenched with pH 7 phosphate buffer. Organic materials were extracted with ethyl acetate and the combined extracts were washed with water three times and with brine and dried over anhydrous sodium sulfate. The solvent was removed under reduced pressure, and the residue was purified by TLC to afford 1,4-diphenyl-1,4-butanedione (**2**),[27] acetophenone, and (1,2,3,4,4a,10a)-hexahydro-1,4-methano-9(10*H*)-phenanthrone (**3**) in 10, 18, and 10% yield, respectively.

1,2,3,4,4a,10a-Hexahydro-1,4-methano-9(10*H*)-phenanthrone (3). Colorless crystals; mp 73—74 °C (hexane); IR (KBr) 2943, 1684, 1284, 771, 669 cm^{-1}; ^{1}H NMR δ=0.99 (1H, dt, J_d=10.7 Hz, J_t=1.5 Hz), 1.24 (1H, dt, J_d=10.7 Hz, J_t=1.8 Hz), 1.34—1.39 (1H, m), 1.48—1.54 (1H, m), 1.55—1.62 (1H, m), 1.65 —1.71 (1H, m), 2.08 (1H, d, J=2.9), 2.23 (1H, d, J=3.9 Hz), 2.30—2.34 (1H, m), 2.48 (1H, dd, J=4.0, 15.7 Hz), 2.70 (1H, dd, J=9.2, 15.7 Hz), 3.03 (1H, d, J=8.5 Hz), 7.24 (1H, dd, J=7.7, 7.7 Hz), 7.30 (1H, d, J=7.7 Hz), 7.49 (1H, ddd, J=1.4, 7.7, 7.7 Hz), 7.76 (1H, dd, J=1.4, 7.7 Hz); ^{13}C NMR δ=29.6, 30.1, 32.7, 39.5, 42.1, 44.9, 45.7, 47.0, 125.2, 125.9, 129.2, 133.4, 133.9, 145.6, 200.1. Found: C, 84.67; H, 7.60%. Calcd for $C_{15}H_{16}O$: C, 84.87; H, 7.60%. The relative stereochemistry was determined by the NOESY spectrum in which NOEs between H^a and H^b, H^a and H^d, H^b and H^c were observed (Chart 1).

By the reaction in dibutyl ether instead of DMF, after purification by TLC, 1,2,3,4,4a,10a-hexahydro-1,4-methano-9(10*H*)-phenanthrone (**3**) and 2-bromo-3-phenacylbicyclo[2.2.1]heptane (**7**) were obtained in 10 and 8% yield, respectively, and yellow substances were also obtained. R_f value and color of the yellow substances were similar to those of the rhenium(III) complex, trichlorotris(dimethylphenylphosphine)rhenium[28] synthesized by Chatt's procedure. By FAB MS spectra, the parts of the yellow substances were assigned as tribromotris(dimethylphenylphosphine)rhenium and dibromochlorotris(dimethylphenylphosphine)rhenium.

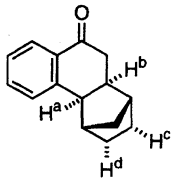


Chart 1.

2-Bromo-3-phenacylbicyclo[2.2.1]heptane (7). Colorless oil; IR (neat) 1685, 1095, 1020, 798 cm^{-1}; ^{1}H NMR δ=1.22 (1H, ddd, J=1.7, 1.7, 10.4 Hz), 1.26—1.35 (2H, m), 1.49—56 (1H, m), 1.63—1.69 (1H, m), 1.88 (1H, ddd, J=1.7, 1.7, 10.4 Hz), 2.05 (1H, dd, J=1.7, 1.7 Hz), 2.51 (1H, ddd, J=6.7, 7.3, 7.8 Hz), 2.57 (1H, d, J=4.9 Hz), 2.96 (1H, dd, J=6.7, 17.8 Hz), 3.43 (1H, dd, J=7.8, 17.8 Hz), 4.38 (1H, dd, J=1.7, 7.3 Hz), 7.44 (2H, dd, J=7.4, 8.2 Hz), 7.54 (1H, tt, J=1.3, 8.2 Hz), 7.97 (2H, d, J=7.4 Hz); ^{13}C NMR δ=27.2, 29.7, 33.7, 42.6, 43.0, 44.9, 48.1, 62.5, 128.0, 128.5, 132.9, 137.1, 199.2. HRMS (EI) Found: m/z 292.0452. Calcd for $C_{15}H_{17}{}^{79}BrO$: M, 292.0463. The relative stereochemistry was determined by the NOESY spectrum in which NOEs between H^a and H^b, H^a and H^d, H^b and H^c were observed (Chart 2).

Tribromotris(dimethylphenylphosphine)rhenium. HRMS (FAB$^+$) Found: m/z 837.8912. Calcd for $C_{24}H_{33}{}^{79}Br_3P_3Re$: M, 837.8903.

Dibromochlorotris(dimethylphenylphosphine)rhenium. HRMS (FAB$^+$) Found: m/z 793.9438. Calcd for $C_{24}H_{33}{}^{79}Br_2ClP_3Re$: M, 793.9408.

General Procedure for the Reaction of α-Bromo Ketones and Vinyl Ethers or Silyl Enol Ethers. To chlorotetrakis(dimethylphenylphosphine)(dinitrogen)rhenium (4.0 mg, 0.0050 mmol) was added a DMF (1 ml) solution of 2-bromoacetophenone (50.2 mg, 0.25 mmol) and α-methoxystyrene (101.1 mg, 0.75 mmol). After the mixture was heated to reflux for 40 min, the reaction was quenched with pH 7 phosphate buffer. Organic materials were extracted with ethyl acetate and the combined extracts were washed with water three times and dried over anhydrous sodium sulfate. The solvent was removed under reduced pressure, and the residue was purified by TLC to afford 2,5-dimethylfuran (42.0 mg, 0.19 mmol; 76%).

The spectral data and the physical properties of the products are as follows.

2,5-Diphenylfuran (5a).[29] Colorless crystals; mp 87 °C (hexane) (lit, 87—88 °C); IR (KBr) 1024, 796, 760, 692, 673 cm^{-1}; ^{1}H NMR δ=6.74 (2H, s), 7.28 (2H, tt, J=1.2, 7.4 Hz), 7.42 (4H, ddd, J=1.2, 7.4, 7.8 Hz), 7.76 (4H, dd, J=1.2, 7.8 Hz); ^{13}C NMR δ=107.2, 123.7, 127.3, 128.7, 130.8, 153.4.

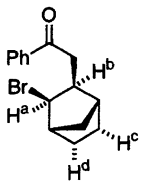


Chart 2.

2-(4-Methylphenyl)-5-phenylfuran (5b).[29] Colorless crystals; mp 101 °C (hexane) (lit, 101—102 °C); IR (KBr) 1498, 1024, 822, 795, 758, 690 cm^{-1}; ^1H NMR δ=2.39 (3H, s), 6.68 (1H, d, J=3.4 Hz), 6.73 (1H, d, J=3.4 Hz), 7.22 (2H, d, J=8.1 Hz), 7.27 (1H, t, J=7.4 Hz), 7.41 (2H, dd, J=7.4, 8.1 Hz), 7.65 (2H, d, J=8.1 Hz), 7.76 (2H, d, J=8.1 Hz); ^{13}C NMR δ=21.3, 106.5, 107.2, 123.6, 123.7, 127.2, 128.1, 128.7, 129.4, 130.8, 137.2, 152.9, 153.6.

2-(4-Methoxyphenyl)-5-phenylfuran (5c).[30] Colorless crystals; mp 119 °C (hexane) (lit, 119.0—119.2 °C); IR (KBr) 1498, 1252, 1028, 835, 791, 764 cm^{-1}; ^1H NMR δ=3.84 (3H, s), 6.60 (1H, d, J=3.4 Hz), 6.72 (1H, d, J=3.4 Hz), 6.95 (2H, d, J=8.7 Hz), 7.26 (1H, t, J=7.4 Hz), 7.41 (2H, dd, J=7.4, 7.8 Hz), 7.69 (2H, d, J=8.7 Hz), 7.75 (2H, d, J=7.8 Hz); ^{13}C NMR δ=55.3, 105.6, 107.2, 114.1, 123.5, 123.9, 125.1, 127.0, 128.6, 130.9, 152.6, 153.4, 159.1.

2-(4-Bromophenyl)-5-phenylfuran (5d).[31] Colorless crystals; mp 129 °C (hexane) (lit, 127 °C); IR (KBr) 1024, 825, 795, 762, 692 cm^{-1}; ^1H NMR δ=6.71 (2H, bs), 7.29 (1H, t, J=7.4 Hz), 7.41 (2H, dd, J=7.4, 7.6 Hz), 7.51 (2H, d, J=8.4 Hz), 7.58 (2H, d, J=8.4 Hz), 7.73 (2H, d, J=7.6 Hz); ^{13}C NMR δ=107.3, 107.8, 121.0, 123.7, 125.1, 127.5, 128.7, 129.6, 130.5, 131.8, 152.2, 153.7.

2-(4-Nitrophenyl)-5-phenylfuran (5e).[31] Orange crystals; mp 132—134 °C (hexane) (lit, 132 °C); IR (KBr) 1603, 1506, 1333, 1107, 756, 752 cm^{-1}; ^1H NMR δ=6.78 (1H, d, J=3.6 Hz), 6.93 (1H, d, J=3.6 Hz), 7.32 (1H, t, J=7.5 Hz), 7.42 (2H, dd, J=7.5, 7.5 Hz), 7.75 (2H, d, J=7.5 Hz), 7.82 (2H, d, J=8.8 Hz), 8.24 (2H, d, J=8.8 Hz); ^{13}C NMR δ=107.8, 111.3, 123.7, 124.1, 124.4, 128.3, 128.9, 130.0, 136.3, 146.3, 151.0, 155.6.

2-Phenethyl-5-phenylfuran (5f) Pale yellow oil; IR (neat) 1549, 1022, 787, 758, 692 cm^{-1}; ^1H NMR δ=3.03—3.10 (4H, m), 6.09 (1H, d, J=3.3 Hz), 6.59 (1H, d, J=3.3 Hz), 7.25—7.29 (4H, m), 7.34 (2H, dd, J=7.5, 7.5 Hz), 7.41 (2H, dd, J=7.8, 7.8 Hz), 7.69 (2H, d, J=7.8 Hz); ^{13}C NMR δ=30.1, 34.4, 105.6, 107.4, 123.3, 126.0, 126.8, 128.3, 128.4, 128.6, 131.1, 141.1, 152.3, 155.1. HRMS (EI) Found: m/z 248.1200. Calcd for $C_{18}H_{16}O$: M, 248.1201.

3-Methyl-2,5-diphenylfuran (5g).[29] Colorless crystals; mp 58 °C (hexane) (lit, 57—58 °C); IR (KBr) 1495, 930, 762, 688, 665 cm^{-1}; ^1H NMR δ=2.34 (3H, s), 6.62 (1H, s), 7.25—7.31 (2H, m), 7.40 (2H, dd, J=7.4, 8.2 Hz), 7.45 (2H, dd, J=7.4, 8.2 Hz), 7.74 (2H, d, J=7.4 Hz), 7.74 (2H, d, J=7.4 Hz); ^{13}C NMR δ=12.1, 110.8, 118.6, 123.7, 125.2, 126.6, 127.2, 128.5, 128.6, 130.8, 131.8, 148.2, 151.7.

2,3,5-Triphenylfuran (5h).[32] Pale yellow crystals; mp 92 °C (hexane) (lit, 91—93 °C); IR (KBr) 1487, 768, 756, 694 cm^{-1}; ^1H NMR δ=6.84 (1H, s), 7.26—7.45 (9H, m), 7.50 (2H, d, J=7.2 Hz), 7.65 (2H, d, J=7.4 Hz), 7.79 (2H, d, J=7.4 Hz); ^{13}C NMR δ=109.4, 123.8, 124.5, 126.1, 127.3, 127.5, 127.5, 128.4, 128.7, 128.7, 128.7, 130.5, 131.1, 134.3, 147.9, 152.5.

3,4-Dimethyl-2,5-diphenylfuran (5i).[33] Colorless crystals; mp 112—114 °C (hexane) (lit, 115 °C); IR (KBr) 1489, 764, 690, 665 cm^{-1}; ^1H NMR δ=2.25 (6H, s), 7.27 (2H, tt, J=1.1, 7.4 Hz), 7.43 (4H, dd, J=7.4, 7.8 Hz), 7.71 (4H, dd, J=1.1, 7.8 Hz); ^{13}C NMR δ=9.9, 119.1, 125.5, 126.6, 128.5, 131.9, 147.3.

1-(4-Methylphenyl)-4-phenyl-1,4-butanedione (6).[34] Colorless crystals; mp 117—118 °C (hexane) (lit, 120—121 °C); IR (KBr) 1678, 1228, 1180, 991 cm^{-1}; ^1H NMR δ=2.40 (3H, s), 3.43 (4H, s), 7.26 (2H, d, J=8.1 Hz), 7.46 (2H, d, J=7.4, 7.8 Hz), 7.55 (1H, t, J=7.4 Hz), 7.92 (2H, d, J=8.1 Hz), 8.02 (2H, d, J=7.8 Hz); ^{13}C NMR δ=21.6, 32.5, 32.6, 128.1, 128.2, 128.6, 129.3, 133.1, 134.3, 136.8, 143.9, 198.3, 198.8.

2-Methyl-1,4-diphenyl-1,4-butanedione (10).[27] Colorless crystals; mp 103—104 °C (hexane) (lit, 102—104 °C); IR (KBr) 1678, 1215, 710, 690 cm^{-1}; ^1H NMR δ=1.27 (3H, d, J=7.1 Hz), 3.10 (1H, dd, J=4.9, 17.9 Hz), 3.71 (1H, dd, J=8.4, 17.9 Hz), 4.13—4.20 (1H, m), 7.43 (2H, t, J=7.7 Hz), 7.47 (2H, t, J=7.8 Hz), 7.52—7.57 (2H, m), 7.97 (2H, d, J=7.5 Hz), 8.04 (2H, d, J=7.5 Hz); ^{13}C NMR δ=17.9, 36.2, 42.3, 128.1, 128.5, 128.5, 128.6, 132.9, 133.1, 136.0, 136.6, 198.4, 203.3.

Ethyl 3-Benzoyl-2-methylpropionate (12).[35] Colorless oil; IR (neat) 1732, 1687, 1215, 1178 cm^{-1}; ^1H NMR δ=1.21 (3H, t, J=7.1 Hz), 1.24 (2H, d, J=7.2 Hz), 2.97 (1H, dd, J=5.5, 17.5 Hz), 3.04—3.11 (1H, m), 3.44 (1H, dd, J=7.9, 17.5 Hz), 4.11 (2H, q, J=7.1 Hz), 7.42 (2H, dd, J=7.4, 7.8 Hz), 7.52 (1H, tt, J=1.2, 7.4 Hz), 7.93 (2H, dd, J=1.2, 7.8 Hz); ^{13}C NMR δ=14.1, 17.2, 34.9, 41.8, 60.5, 127.9, 128.5, 133.0, 136.6, 175.8, 198.0.

3′-Methoxy-4′-methylsulfonyloxypropiophenone (14). To a dichloromethane (170 ml) solution of vanillin (11.6 g, 76.5 mmol) was added triethylamine (14 ml, 100 mmol) and a dichloromethane (10 ml) solution of methanesulfonyl chloride (10.0 g, 87.5 mmol) at −55 °C. After the mixture was stirred overnight with warming gradually to room temperature, the reaction was quenched with water. Organic materials were extracted with dichloromethane. The combined extracts were washed with water twice and with brine and dried over anhydrous sodium sulfate. The solvent was removed under reduced pressure to give the crude methanesulfonate. To a THF (80 ml) suspension of the crude methanesulfonate was added dropwise at −78 °C ethylmagnesium bromide prepared from ethyl bromide (12.1 g, 111 mmol) and magnesium (3.00 g, 123 mmol) in THF (80 ml). After the mixture was stirred for 28 h below −35 °C, the reaction was quenched with saturated ammonium chloride. Organic materials were extracted with ethyl acetate and the combined extracts were washed with water and with brine and dried over anhydrous sodium sulfate. The solvent was removed under reduced pressure to give the crude alcohol. Without purification, the crude alcohol was used to the next reaction. To a dichloromethane (90 ml) solution of oxalyl chloride (15.1 g, 119 mmol) was added dropwise a dichloromethane solution (50 ml) of dimethyl sulfoxide (18.1 g, 232 mmol) at −55 °C. After stirring for 2 min, the crude alcohol was added to the mixture. After stirring for 15 min at the same temperature, triethylamine was added. The mixture was stirred for 5 min at the same temperature and the cooled bath was removed. Water was added to the reaction mixture to quench the reaction. Organic materials were extracted with dichloromethane and the combined extracts were washed with brine and dried over anhydrous sodium sulfate. The solvent was removed under reduced pressure, and the residue was purified by recrystallization. The second crop was obtained from the filtrate by recrystallization. After filtration, the filtrate was purified by column chromatography. The title compound **14** was obtained in 74% (14.7 g, 56.9 mmol) yield. Colorless crystals; mp 91 °C (ethanol); IR (KBr) 1676, 1352, 1155, 1120, 980, 829 cm^{-1}; ^1H NMR δ=1.17 (3H, t, J=7.2 Hz), 2.94 (2H, q, J=7.2 Hz), 3.18 (3H, s), 3.91 (3H, s), 7.32 (1H, d, J=8.3 Hz), 7.52 (1H, dd, J=1.7, 8.3 Hz), 7.59 (1H, d, J=1.7 Hz); ^{13}C NMR δ=8.1, 31.7, 38.6, 56.1, 111.8, 121.3, 124.3, 136.6, 141.5, 151.6, 199.3. Found: C, 51.00; H, 5.42; S, 12.45%. Calcd for $C_{11}H_{14}SO_5$: C, 51.15; H, 5.46; S, 12.41%.

2-Bromo-3′-methoxy-4′-methylsulfonyloxypropiophenone (15). To a dichloromethane (10 ml) solution of 3′-methoxy-4′-methylsulfonyloxypropiophenone (**14**) (984 mg, 3.80 mmol) were added a few drops of hydrogen bromide (30% acetic acid solution). After stirring for 1 min, bromine (0.22 ml, 4.3 mmol) was added dropwise to the mixture. The mixture was stirred for an additional 30 min. The solvent was removed under reduced pressure, and the residue was purified by column chromatography to afford the title

compound **15** (1.23 g, 3.65 mmol; 96%). Colorless crystals; mp 95—96 °C (ethanol); IR (KBr) 1685, 1358, 1165, 1120, 831 cm^{-1}; ^1H NMR δ=1.88 (3H, d, J=6.6 Hz), 3.22 (3H, s), 3.95 (3H, s), 5.23 (1H, q, J=6.6 Hz), 7.39 (1H, d, J=8.4 Hz), 7.62 (1H, dd, J=1.9, 8.4 Hz), 7.68 (1H, d, J=1.9 Hz); ^{13}C NMR δ=20.0, 38.7, 41.1, 56.2, 113.1, 122.1, 124.5, 133.7, 142.1, 151.8, 192.0. Found: C, 39.30; H, 3.84; Br, 24.05; S, 9.78%. Calcd for $C_{11}H_{13}BrO_5S$: C, 39.18; H, 3.89; Br, 23.70; S, 9.51%.

2-Methoxy-4-(1-methoxy-1-propenyl)-1-methylsulfonyloxybenzene (16). To a methanol (4 ml) solution of 3′-methoxy-4′-methylsulfonyloxypropiophenone (**14**) (516 mg, 2.00 mmol) was added trimethyl orthoformate (4 ml) and *p*-toluenesulfonic acid monohydrate (15 mg). After the mixture was heated to reflux for 30 min, the reaction was quenched with saturated sodium hydrogencarbonate. Organic materials were extracted with ethyl acetate and the combined extracts were washed with brine and dried over anhydrous sodium sulfate. The solvent was removed under reduced pressure, and the residue was purified by column chromatography to afford 3′-methoxy-4′-methylsulfonyloxypropiophenone dimethyl acetal. This compound was too viscous to remove the solvent completely. To the crude 3′-methoxy-4′-methylsulfonyloxypropiophenone dimethyl acetal containing a small amount of ethyl acetate was added acetic anhydride (20 ml), triethylamine (20 ml) and 4-(dimethylamino)pyridine (20 mg). After the mixture was heated to reflux for 15 h, the mixture was poured into aqueous sodium hydroxide (25 g of sodium hydroxide in 200 ml of water) at 0 °C. After filtration, organic materials were extracted with ether and the combined extracts were washed with water and brine and dried over potassium carbonate. The solvent was removed under reduced pressure, and the residue was purified by column chromatography to afford the title compound **16** (484 mg, 1.78 mmol; 89%) as a geometrical mixture (E:Z=68:32); Colorless oil; IR (KBr) 1504, 1365, 1159, 1117, 841 cm^{-1}; ^1H NMR δ=1.69 (3H×0.32, d, J=7.0 Hz), 1.78 (3H×0.68, d, J=6.9 Hz), 3.15 (3H×0.32, s), 3.16 (3H×0.68, s), 3.52 (3H×0.68, s), 3.62 (3H×0.32, s), 3.88 (3H×0.32, s), 3.88 (3H×0.68, s), 4.81 (1H×0.32, q, J=7.0 Hz), 5.39 (1H×0.68, q, J=6.9 Hz), 6.98 (1H×0.32, dd, J=1.9, 8.2 Hz), 7.02—7.05 (1H+1H×0.68, m), 7.23 (1H×0.68, d, J=8.6 Hz), 7.26 (1H×0.32, d, J=8.2 Hz); ^{13}C NMR δ=10.9, 12.7, 38.1, 38.2, 55.0, 55.9 (two carbons overlapped), 58.5, 94.8, 110.0, 110.2, 113.2, 118.4, 121.7, 123.8, 124.3, 136.4, 136.5, 137.6, 137.7, 150.9, 151.2, 154.2 (two carbons overlapped). Found: C, 52.93; H, 5.83; S, 11.44%. Calcd for $C_{12}H_{16}O_5S$: C, 52.93; H, 5.92; S, 11.77%.

2,5-Bis(3-methoxy-4-methylsulfonyloxyphenyl)-3,4-dimethylfuran (17). To chlorotetrakis(dimethylphenylphosphine)(dinitrogen)rhenium (18.9 mg, 0.024 mmol) was added a DMF (1 ml) solution of 2-bromo-3′-methoxy-4′-methylsulfonyloxypropiophenone (**15**) (78.9 mg, 0.23 mmol) and 2-methoxy-4-(1-methoxy-1-propenyl)-1-methylsulfonyloxybenzene (**16**) (192.2 mg, 0.71 mmol). After the mixture was heated to reflux for 40 min, the reaction was quenched with pH 7 phosphate buffer. Organic materials were extracted with ethyl acetate and the combined extracts were washed with water three times and dried over anhydrous sodium sulfate. The solvent was removed under reduced pressure, and the residue was purified by TLC and column chromatography to afford the title compound **17** (64.4 mg, 0.13 mmol; 55% yield). Colorless crystals; mp 142—144 °C (hexane–ether); IR (KBr) 1504, 1363, 1358, 1163, 1115, 850 cm^{-1}; ^1H NMR δ=2.22 (6H, s), 3.20 (6H, s), 3.94 (6H, s), 7.23 (2H, dd, J=1.7, 8.4 Hz), 7.27 (2H, d, J=1.7 Hz), 7.34 (2H, d, J=8.4 Hz); ^{13}C NMR δ=9.9, 38.3, 56.1, 110.2, 118.5, 120.2, 124.7, 131.8, 137.1, 146.7, 151.1. Found: C, 53.21; H, 4.86; S, 13.02%. Calcd for $C_{22}H_{24}S_2O_9$: C, 53.22; H, 4.87; S, 12.91%.

Furoguaiacin (13).[22] To a THF (3 ml) solution of 2,5-bis-(3-methoxy-4-methylsulfonyloxyphenyl)-3,4-dimethylfuran (**17**) (7.6 mg, 0.015 mmol) was added methyllithium (1.03 M (1 M=1 mol dm^{-3}) ether solution, 0.30 ml, 0.31 mmol) at 0 °C. After the mixture was stirred for 10 min at 0 °C and kept overnight at room temperature, 0.1 M aqueous citric acid was added to quench the reaction. Organic materials were extracted with ethyl acetate and the combined extracts were washed with brine and dried over anhydrous sodium sulfate. The solvent was removed under reduced pressure, and the residue was purified by TLC and column chromatography to afford the title compound (4.2 mg, 0.013 mmol; 81% yield). Colorless crystals; mp 142—144 °C (dichloromethane–ether)(lit, 148—149 °C); IR (KBr) 3533, 1514, 1259, 1215, 1194 cm^{-1}; ^1H NMR δ=2.18 (6H, s), 3.94 (6H, s), 5.62 (2H, s), 7.14—7.16 (2H, m); ^{13}C NMR δ=9.9, 56.0, 108.6, 114.5, 117.6, 119.3, 124.6, 144.7, 146.6, 147.0.

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References

1) B. Giese, "Radicals in Organic Synthesis: Formation of Carbon-Carbon Bonds," Pergamon, Oxford (1986), p. 73; D. P. Curran, "Comprehensive Organic Synthesis," ed by B. M. Trost and I. Fleming, Pergamon Press, Oxford (1991), Vol. 4, p. 758.

2) D. L. Clive and D. R. Cheshire, *J. Chem. Soc., Chem. Commun.*, **1987**, 1520; D. L. Clive, *Pure Appl. Chem.*, **60**, 1645 (1988).

3) D. P. Curran and C. Chang, *J. Org. Chem.*, **54**, 3140 (1989).

4) J. H. Byers and B. C. Harper, *Tetrahedron Lett.*, **33**, 6953 (1992).

5) D. P. Curran, "Comprehensive Organic Synthesis," ed by B. M. Trost and I. Fleming, Pergamon Press, Oxford (1991), Vol. 4, p. 762, and references cited there in.

6) a) E. I. Heiba and R. M. Dessau, *J. Am. Chem. Soc.*, **93**, 524 (1971); b) E. I. Heiba and R. M. Dessau, *J. Am. Chem. Soc.*, **94**, 2888 (1972); c) R. M. Dessau and E. I. Heiba, *J. Org. Chem.*, **39**, 3457 (1974).

7) B. B. Snider and E. Y. Kiselgof, *Tetrahedron*, **52**, 6073 (1996); B. M. Cole, L. Han, and B. B. Snider, *J. Org. Chem.*, **61**, 7832 (1996).

8) E. Baciocchi, A. Casu, and R. Ruzziconi, *Tetrahedron Lett.*, **30**, 3707 (1989).

9) K. Narasaka, N. Miyoshi, K. Iwakura, and T. Okauchi, *Chem. Lett.*, **1989**, 2169.

10) Intramolecular ene-halogenocyclization of α-iodocarbonyl compounds catalyzed by tetrakis(triphenylphosphine)palladium was already reported, however, the reaction mechanism was not clear. M. Mori, I. Oda, and Y. Ban, *Tetrahedron Lett.*, **23**, 5315 (1982); M. Mori, Y. Kubo, and Y. Ban, *Tetrahedron Lett.*, **26**, 1519 (1985); M. Mori, N. Kanda, I. Oda, and Y. Ban, *Tetrahedron*, **41**, 5465 (1985); M. Mori, N. Kanda, and Y. Ban, *J. Chem. Soc., Chem. Commun.*, **1986**, 1375; M. Mori, N. Kanda, Y. Ban, and K. Aoe, *J. Chem. Soc., Chem. Commun.*, **1988**, 12.

11) S. Murai, N. Sonoda, and S. Tsutsumi, *J. Org. Chem.*, **29**, 2104 (1964); Y. Mori and J. Tsuji, *Tetrahedron*, **28**, 29 (1972); Y. Mori and J. Tsuji, *Tetrahedron*, **29**, 827 (1973).

12) H. Matsumoto, T. Nikaido, and Y. Nagai, *J. Org. Chem.*, **41**,

396 (1976); N. Kamigata and M. Kameyama, *J. Synth. Org. Chem. Jpn.*, **47**, 436 (1989), and references therein.

13) H. Nagashima, H. Wakamatsu, K. Itoh, Y. Tomo, and J. Tsuji, *Tetrahedron Lett.*, **24**, 2395 (1983); H. Nagashima, K. Seki, N. Ozaki, H. Wakamatsu, K. Itoh, Y. Tomo, and J. Tsuji, *J. Org. Chem.*, **55**, 985 (1990).

14) J. H. Udding, K. (C.) J. M. Tuijp, M. N. A. van Zanden, H. Hiemstra, and W. N. Speckamp, *J. Org. Chem.*, **59**, 1993 (1994).

15) Dichloro(alkylaminocarbonyl)methyl radicals are also generated from α-trichloroamide to react olefins. H. Nagashima, N. Ozaki, M. Ishii, K. Seki, M. Washiyama, and K. Itoh, *J. Org. Chem.*, **58**, 464 (1993), and references cited therein.

16) H. Kusama and K. Narasaka, *Bull. Chem. Soc. Jpn.*, **68**, 2379 (1995).

17) J. Chatt, J. R. Dilworth, and G. J. Leigh, *J. Chem. Soc., Dalton Trans.*, **1973**, 612.

18) Thermal dissociation of dinitrogen from $ReCl(N_2)$-$(PMe_2Ph)_4$ was not reported but the photolytic dissociation was already reported: M. G. Bradley and B. R. Hofmann, Jr., *J. Chem. Soc., Chem. Commun.*, **1982**, 1180.

19) S. Stavber, Z. Planinšek, and M. Zupan, *J. Org. Chem.*, **57**, 5334 (1992).

20) Without the desilylative work-up, bis-*t*-butyldimethylsilyl enol ether of the diketone was obtained as a minor product.

21) F. E. King and J. G. Wilson, *J. Chem. Soc.*, **1964**, 4011.

22) J. Watanabe, T. Yanagisawa, Y. Iketani, and H. Mihashi, Japan Kokai Tokkyo Koho JP, 02180846 [90180846]; *Chem. Abstr.*, **114**, 69042e (1991).

23) N. Arai and K. Narasaka, unpublished result. By using this method acetal was disappeared completely without formation of ketone.

24) W. H. Pirkle and K. A. Simmons, *J. Org. Chem.*, **48**, 2520 (1983); L. Blanco, P. Amice, and J. M. Conia, *Synthesis*, **1976**, 194.

25) M. S. Newman and M. C. V. Zwan, *J. Org. Chem.*, **38**, 2910 (1973).

26) T. Mukaiyama and K. Narasaka, *Org. Synth.*, **65**, 6 (1986); E. W. Colvin, "Silicon Reagents in Organic Synthesis," Academic Press, London (1988).

27) H. Stetter, P. H. Schmitz, and M. Schreckenberg, *Chem. Ber.*, **110**, 1971 (1977).

28) J. Chatt, G. J. Leigh, D. M. P. Mingos, and R. J. Paske, *J. Chem. Soc. A*, **1968**, 2636.

29) H. Sheng, S. Lin, and Y. Huang, *Synthesis*, **1987**, 1022.

30) A. Miyamoto, C. Kumaki, H. Irikawa, and Y. Okumura, *Rep. Fac. Sci. Shizuoka Univ.*, **28**, 61 (1994); *Chem. Abstr.*, **121**, 8640w (1994).

31) M. V. Yen, *Ann. Chim.*, **7**, 785 (1962).

32) M. J. Haddadin, B. J. Agha, and R. F. Tabri, *J. Org. Chem.*, **44**, 494 (1979).

33) J. Hambrecht, *Synthesis*, **1977**, 280.

34) A. I. Hashem, M. E. Shaban, and A. F. El-Kafrawy, *Indian J. Chem., Sect. B*, **21B**, 763 (1982).

35) W. M. Best, A. P. F. Cook, J. J. Russell, and D. A. Widdowson, *J. Chem. Soc., Perkin Trans. 1*, **1986**, 1139.