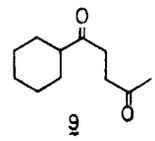
vides a simple, high-yield procedure for reductive succinoylation of the ketone functionality, which has been performed in lower yield through multiple steps.[1] In addition, the reaction conditions are definitely milder than those required in the former procedure. Results are summarized in Table I.[4]

The potential of γ-keto ester for further transformation is notable: 1,4-diketone **9** was prepared in 67% overall yield



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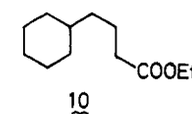

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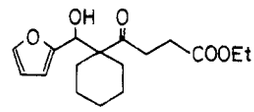
(thiacetalization, OH^-, MeLi, and $CuCl_2/CuO$), and ester **10** was obtained by hydrogenolysis of the ketone function (thioacetalization and W-2 Raney nickel) in 74% yield starting from keto ester **8**.

Carbon electrophiles also react with **3**. Of two possible approaches, one involves specific activation of enol silyl ether to form an enolate species without affecting the neighboring ester group. Quaternary ammonium fluoride allowed such reaction to occur.[5] Treatment of silyl ether **5** and furfural (1 equiv) with tetrabutylammonium fluoride[6] (30 mol %) at low temperature gave pure aldol **11** in 69% yield after chromato-



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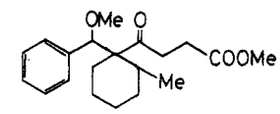

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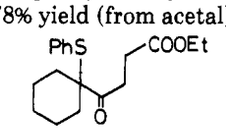
graphic purification. We were unable to detect any regioisomer or lactone which might be formed by intramolecular O-acylation reaction of the enolate species.

Another methodology is to trap the enol silyl ether by a Lewis acid activated carbonyl carbon.[7] On such occasions, further reaction of **3** may be best carried out in situ. Thus, the coupling of three components, 2-methylcyclohexanone, succinate moiety, and benzaldehyde acetal was quickly achieved without isolating any intermediates. The isolated yield of **12** was 70%. Two procedures described here represent new entries to the conversion of C–O bonds of the carbonyl group to two C–C bonds, namely, geminal alkylation.[8]

Regiospecific introduction of a heteroatom to **3** is also possible.[9] Addition of phenylsulfenyl chloride[10] to **5** prepared in situ gave **13** in 78% yield (from acetal).



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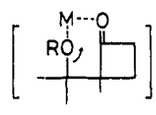
Comparison of **2** and **3** reveals that the ketone group of the ring cleavage product is "masked" in **2**, and thereby selective functionalization with respect to the ester moiety of **3** at the stage of **2** is envisioned. Actually, such a possibility has already been demonstrated.[1] In light of these studies, the present method proved versatile for preparing substituted γ-keto esters, as well as synthetic transformations centered on the parent ketone group.

On the basis of a crossover experiment,[11] we suggest here that a complex **14**, instead of hemiacetal **15** or diketone **1**, di-



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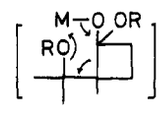

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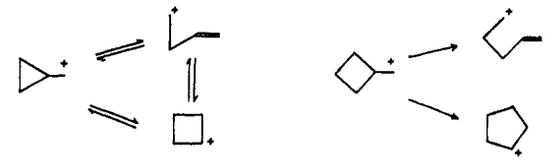
rectly breaks down to silyl ether **3**. The completely different effect of proton[1] and Lewis acid on cyclobutanone **2** is remarkable, and probably indicates that cyclobutanone **2** behaves as a bidentate ligand of the Lewis acid as in **14**.

Cyclopropylcarbinyl cation is known to undergo both a ring enlargement and a ring cleavage reaction.[12] Nonetheless, only a ring enlargement reaction has been recorded in the reactions



of cyclobutylcarbinyl cation.[12] It is interesting to note that the present reaction represents, at least in a formal sense, a ring-opening reaction of cyclobutylcarbinyl cation. We are presently investigating the generality of the ring-cleavage reaction.

References and Notes

(1) E. Nakamura and I. Kuwajima, *J. Am. Chem. Soc.*, **99**, 961 (1977).
(2) Yields are based on spectroscopically pure products. Enol silyl ethers were characterized by IR, NMR, and mass spectra, and hydrolyzed to the corresponding keto esters, which showed correct elemental compositions. Other products in the text were characterized by IR and NMR as well as microanalysis or high-resolution mass spectroscopy.
(3) Bp 110 °C (bath temp) (0.04 mm); IR (neat) 1745 (s), 1677 (m); NMR (CCl_4) 0.12 (s), 1.26 (t, J = 7 Hz), 1.3–2.6 (m), 2.36 (s), 4.10 ppm (q, J = 7 Hz). This compound is sensitive to moisture and should be stored in a sealed ampule.
(4) Reaction rates differ greatly among substrates. The adduct of **4** and acetone dimethyl acetal rearranges slowly even at 0 °C (1 equiv of $SnCl_4$), whereas cyclohexanone acetal forms the expected rearranged product rapidly at −40 °C.
(5) I. Kuwajima and E. Nakamura, *J. Am. Chem. Soc.*, **97**, 3257 (1975); R. Noyori, K. Yokoyama, J. Sakata, I. Kuwajima, E. Nakamura, and M. Shimizu, *ibid.*, **99**, 1265 (1977).
(6) Commerical TBAF hydrate was dried at ~20 °C (0.5 mm).[5] We thank Fluka AG for the gift of this reagent.
(7) T. Mukaiyama and M. Hayashi, *Chem. Lett.*, 15 (1974); T. Mukaiyama, K. Banno, and K. Narasaka, *J. Am. Chem. Soc.*, **96**, 7503 (1974).
(8) See ref 5 of ref 1.
(9) Review: J. K. Rasmussen, *Synthesis*, 91 (1977).
(10) S. Murai, Y. Kuroki, K. Hasegawa, and S. Tsutsumi, *J. Chem. Soc., Chem. Commun.*, 946 (1972).
(11) A mixture of cyclohexanone diethyl acetal and 4-*tert*-butylcyclohexanone dimethyl acetal was treated with 2 equiv of **4** and a catalytic amount of $SnCl_4$, and the analysis of the reaction mixture revealed that little crossover occurred in the reaction. The conclusion was made on the basis of the comparison of the mass spectrum of the reaction mixture with those of the authentic samples and their mixture. The fact that trimethylchlorosilane which might trap free alkoxide anion did not prevent the rearrangement also supports intramolecular alkoxyl migration.
(12) H. G. Richey, Jr., *Carbonium Ions*, **3**, 1201–1294 (1972).

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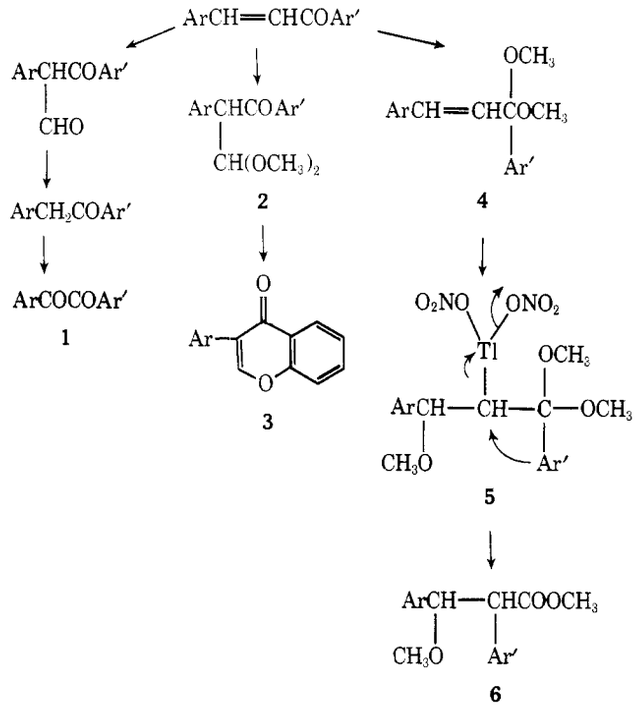
Thallium in Organic Synthesis. 49. Oxidative Rearrangement of Chalcone Dimethyl Ketals to Methyl 2,3-Diaryl-3-methoxypropanoates with Thallium(III) Trinitrate in Trimethyl Orthoformate[1]

Summary: Treatment of chalcones (ArCH=CHCOAr') with thallium(III) trinitrate (TTN) in acidic methanol gives 3,3-dimethoxy-1,2-diarylpropan-1-ones (**2**) by rearrangement of the Ar group. However, prior conversion of chalcones to their dimethyl ketals (which can be carried out in situ in trimethyl orthoformate as solvent), followed by reaction with TTN, yields methyl 2,3-diaryl-3-methoxypropanoates (**6**) by rearrangement of the Ar' group.

Sir: During the past decade, thallium(III) trinitrate (TTN)

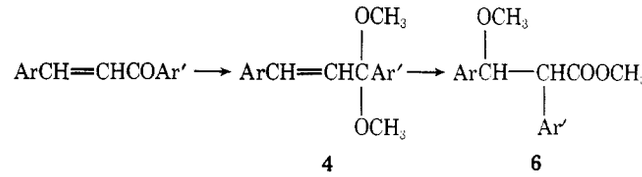
Scheme I



has been shown to be a versatile reagent in organic synthesis and has been used to effect many useful and unique transformations.[2] As an example, the readily accessible and phytochemically significant chalcones are converted to benzils (**1**)[3] by oxidation in acidic aqueous glyme, while oxidation in acidic methanol gives 3,3-dimethoxy-1,2-diarylpropan-1-ones (**2**),[3] key intermediates (Ar′ = 2-ROC$_6$H$_4$) in the synthesis of isoflavones (**3**).[4] In the formation of both **1** and **2** from chalcones, it is the Ar ring which migrates during the oxidative rearrangement.

We have recently observed that the reaction of chalcone with TTN *in trimethyl orthoformate* (TMOF) gives a 50:50 mixture of 3,3-dimethoxy-1,2-diphenylpropan-1-one (**2**, Ar = Ar′ = C$_6$H$_5$) and methyl 2,3-diphenyl-3-methoxypropanoate (**6**, Ar = Ar′ = C$_6$H$_5$) (Scheme I). The keto acetal **2** is formed by normal Ar ring migration, but the ester **6** clearly must have resulted from migration of the Ar′ ring. This unique Ar′ ring migration can be rationalized as follows. Since the reaction of chalcone with TTN is slow due to deactivation of the carbon–carbon double bond by the carbonyl group, and since both aldehydes and ketones are rapidly converted to acetals and ketals with TMOF in the presence of TTN (acting as a Lewis acid),[5] ketalization of chalcone presumably competes with normal oxidative rearrangement to **2**. This would have two consequences: (i) removal of the deactivating carbonyl would make the double bond more reactive to electrophilic attack by TTN, and (ii) the *gem*-methoxy groups in the intermediate **5** should greatly favor migration of the Ar′ group rather than the Ar group. It would thus be expected that methyl 2,3-diphenyl-3-methoxypropanoate (**6**, Ar = Ar′ = C$_6$H$_5$) should be the exclusive product of TTN-mediated oxidative rearrangement of the preformed chalcone dimethyl ketal (**4**, Ar = Ar′ = C$_6$H$_5$), and this indeed proved to be the case (see above). This reaction pathway cannot be followed, however, if the reaction of chalcone with TTN is carried out under conditions which exclude rapid ketal formation; this is consistent with our previous observation that oxidative rearrangement of chalcone with TTN in acidic aqueous methanol led exclusively to the keto acetal **2** (Ar = Ar′ = C$_6$H$_5$).[3]

Table I. Methyl 2,3-Diaryl-3-methoxypropanoates from Chalcones



Ar	Ar′	Mp, °C
C$_6$H$_5$	C$_6$H$_5$	93.5–95.5
C$_6$H$_5$	4-CH$_3$C$_6$H$_4$	97.0–98.5
C$_6$H$_5$	4-CH$_3$OC$_6$H$_4$	80.5–82.0
4-ClC$_6$H$_4$	4-CH$_3$OC$_6$H$_4$	91.5–93.0
4-O$_2$NC$_6$H$_4$	C$_6$H$_5$	91.0–93.0
4-O$_2$NC$_6$H$_4$	4-CH$_3$OC$_6$H$_4$	97.0–99.0

Thus, the in situ preparation of chalcone dimethyl ketals followed by reaction with TTN in TMOF constitutes a convenient synthesis of methyl 2,3-diaryl-3-methoxypropanoates (see Table I), provided, however, that the migratory aptitude (ma) of the Ar′ group is moderate to good.[6] When maAr ≫ maAr′, complex mixtures of products are obtained from the preformed ketals, and their reactions with TTN have no synthetic significance. Full details of a study of the effects of substrate modification, relative migratory aptitudes of the Ar and Ar′ groups, and solvents on these oxidative rearrangements will be reported in the full paper.

The general procedure for the preparation of methyl 2,3-diaryl-3-methoxypropanoates is as follows. The chalcone ketals are prepared in situ by stirring the chalcone (0.01 mol) with 2–6 g of Dowex 50W-X4 cation-exchange resin in 35 mL of TMOF at room temperature. After ketal formation is complete (15–24 h, monitored by TLC using $HCCl_3$ and silica gel), the mixture is filtered into a solution of 5.0 g (0.011 mol) of TTN·3H$_2$O in 20 mL of TMOF. When the oxidative rearrangement is complete (6–24 h), a small amount of solid sodium bisulfite is added to ensure complete reduction of Tl(III), 200–300 mL of diethyl ether is added, and the reaction mixture is chilled. The precipitated thallium(I) nitrate is removed by filtration and the ether layer is washed with saturated sodium chloride (2 × 50 mL), followed by saturated sodium bicarbonate (2 × 50 mL) and saturated sodium chloride (1 × 50 mL), and dried over $MgSO_4$. Removal of the ether gives the esters in almost quantitative yield (90–98% purity by NMR). All products are best recrystallized from methanol. The esters all exhibit carbonyl bands (IR) at 1730–1740 cm^{-1} and methinyl protons (NMR) at approximately δ 3.75 and 4.70 (J = 9.5–11.0 Hz).[7]

References and Notes

(1) For the previous paper in this series, see E. C. Taylor, J. G. Andrade and A. McKillop, *J. Chem. Soc., Chem. Commun.*, 538 (1977). We gratefully acknowledge financial support for this work from the National Science Foundation (Grant No. CHE7616506).

(2) For a recent review, see A. McKillop and E. C. Taylor, *Endeavor*, **35**, 88 (1976).

(3) A. McKillop, B. P. Swann, M. E. Ford, and E. C. Taylor, *J. Am. Chem. Soc.*, **95**, 3641 (1973).

(4) (a) L. Farkas and A. Wolfner, *Acta Chim. Acad. Sci. Hung.*, **88**, 173 (1976); (b) A. Levai and L. Balogh, *Pharmazie*, **30**, 747 (1975); (c) L. Farkas, S. Antus, and M. Nogradi, *Acta Chim. Acad. Sci. Hung.*, **82**, 225 (1974).

(5) E. C. Taylor, R. L. Robey, K.-T. Liu, B. Favre, H. T. Bozimo, R. A. Conley, C.-S. Chiang, A. McKillop, and M. E. Ford, *J. Am. Chem. Soc.*, **98**, 3037 (1976).

(6) Even with the last three compounds in Table I, where maAr′ ≫ maAr, prior ketal formation was essential for synthetically useful transformations to the esters **6**. In TTN/TMOF (i.e., without prior ketal formation), isolation of pure **6** proved to be extremely difficult because of the simultaneous formation under these reaction conditions of degradation products of the initial chalcone.

(7) Satisfactory analytical and spectroscopic data were obtained for all new compounds.

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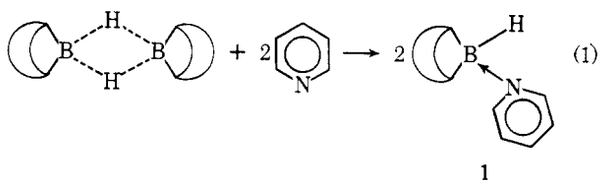
A New Reagent, 9-Borabicyclo[3.3.1]nonane–Pyridine, for the Selective Reduction of Aldehyde Groups in the Presence of Keto and Other Functional Groups

Summary: The exceptionally mild, highly selective, new reducing agent, 9-borabicyclo[3.3.1]nonane–pyridine (9-BBN·py), cleanly reduces the aldehyde group in the presence of keto and many other functional groups, making possible the clean, selective reduction of aldehyde groups in complex molecules.

Sir: The selective reduction of one carbonyl group in the presence of other such groups is a frequent synthetic problem. It has been solved in various ways.[1] A difficult, yet commonly encountered, problem in organic synthesis is the clean reduction of aldehyde in the presence of keto groups. Although aldehydes are reduced faster than ketones, the absolute rates are often too fast to take advantage of the favorable difference in the relative reduction rates. Consequently, in recent years, various reagents have been developed for such selective reductions. These include tetrabutylammonium cyanoborohydride,[2] sodium triacetoxyborohydride,[3] lithium tri-*tert*-butoxyaluminohydride,[4] 9-borabicyclo[3.3.1]nonane (9-BBN),[5] and Li-*n*-Bu_2-9-BBN "ate" complex.[6] More recently, diisopropylcarbinol on dehydrated alumina has been reported to be superior to all of these earlier reagents in its ability to distinguish effectively between an aldehyde and unhindered cyclohexanone.[7] However, this method requires large amounts of alumina with a tedious workup procedure resulting from the presence of both diisopropylcarbinol and diisopropyl ketone in the reaction mixture.

In this communication, we report application of the newly synthesized reagent, 9-borabicyclo[3.3.1]nonane–pyridine (9-BBN·py, **1**),[8] for the selective reduction of aldehydes in the presence of ketones. The reagent **1** is conveniently prepared by a simple reaction between the readily available 9-BBN dimer[9] and pyridine in pentane solution (eq 1).[8] The product



(1)

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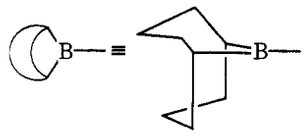
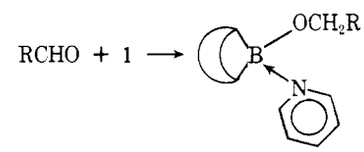


thus obtained is a stable crystalline solid, indefinitely stable under nitrogen.[10]

The selectivity in reduction and the functional group tolerance exhibited by **1** is quite remarkable, far better than that exhibited by the parent 9-BBN itself.[5] Thus a wide variety of aldehydes are reduced almost completely in 2 h at 25 °C in THF or Et_2O solutions (eq 2), whereas, under similar experimental conditions, even unhindered ketones are not reduced significantly (Table I). Competition experiments carried out by adding 10 mmol of **1** to a mixture of 10 mmol of aldehyde and 10 mmol of ketone in Et_2O reveal that **1** is highly selective toward aldehydes (Table II).[11] Also, various representative functional groups, such as ester, lactone, *N,N*-dialkylamide,



(2)

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Table I. Reduction of Aldehydes and Ketones by 9-BBN·py in THF Solutions[a] at 25 °C

Compd	Time, h	% reduced[b]
Benzaldehyde	1.0	95
	1.5	100
Cinnamaldehyde	1.0	86
	1.5	98
Cyclohexylcarboxaldehyde	1.0	91
	3.0	100
Octanal	1.0	91
	2.0	99
Hexanal	1.0	94
	2.0	100
Propanal	1.0	85
	1.5	97
Cyclohexanone	1.0	0
	1.5	3
2-Methylcyclohexanone	2.0	0
2-Hexanone	1.0	5
	12.0	43
Dicyclopropyl ketone	1.5	8
3-Pentanone	1.0	5
	7.0	10
Acetophenone	1.0	3
	9.0	5
Phenylacetone	1.0	6
	8.0	46

[a] The reaction mixture was 0.25 M in the substrate and 0.25 M in 9-BBN·py. [b] Progress of the reaction was followed by the measurement of residual hydride in the aliquot; for details of the procedure, see H. C. Brown, "Organic Syntheses via Boranes", Wiley, New York, N.Y., 1975, Chapter 9.

Table II. Relative Reactivities of Aldehydes with Respect to Ketones toward 9-BBN·py in Et_2O at 25 °C. Competition Experiments

Compd used	Product	Mol %[a]
Cyclohexanone	Cyclohexanone	98.5
+	Cyclohexanol	1.5
Benzaldehyde	Benzaldehyde	6.0
	Benzyl alcohol	93.0
Acetophenone	Acetophenone	96.0
+	1-Phenylethanol	2.0
Benzaldehyde	Benzaldehyde	4.0
	Benzyl alcohol	94.0
3-Pentanone	3-Pentanone	96.0
+	3-Pentanol	2.5
Octanal	Octanal	4.5
	1-Octanol	94.5

[a] Determined by GLC (ref 11) from the response ratios determined for authentic samples.