J. Org. Chem. **1982**, *47*, 5393–5395

of reducing agent. It may be that the additional mole of 8 serves to complex the $AlH(OEt)_2$ formed on initial hydride transfer, lowering its Lewis acidity and ability to interact with acetal. The use of a twofold molar excess of 8 in THF constitutes the second useful procedure for formation of 2.

We have also briefly explored the use of $LiAlH(OEt)_3$ in THF but find that it offers no advantage compared to 8 and even leads to traces (1–2%) of 5.

The use of 1 ($R = CH_3$) gave similar results with the various reducing agents described, in somewhat lower yields. Because of the greater difficulty in preparing the methylated salt, it is preferable in this system to make ethylated 2 and transacetalize to obtain other derivatives.

A few experiments were carried out with 1 as the $SbCl_6^-$ salt. While acetal is formed, the counterion is also reduced (e.g., vigorous reaction with $NaBH_4$) to a black solid, presumably antimony. Other counterions have not been examined.

The procedures described here for the reduction of 1 have also been successfully applied to some naphthalene analogues and should have wide generality.

Experimental Section

Dichloromethane was distilled from $LiAlH_4$,[9] ether from CaH_2, and THF from sodium and benzophenone ketyl. Reagent grade DMF was stored over Linde 3A molecular sieve, and pyridine was stored over KOH pellets.

The *O*-ethylphthalidium tetrafluoroborate, 1 was prepared by Meerwein's procedure.[7]

For small-scale reactions, stock solutions of $LiAlH_4$ in ether and THF were prepared by refluxing for 3 h and using the clear supernatant without filtration. Mixed hydride reagents were formed by addition of anhydrous ethanol (distilled from Mg) and measuring H_2 evolution by gas buret.

The following procedures illustrate the preferred methods for formation of 2.

(A) $NaBH_4$. To a 50-mL three-necked flask equipped with a magnetic stirrer, thermometer, and condenser with N_2 inlet was added 10 mL of DMF, 0.78 mL (9.6×10^{-3} mol) of pyridine, and 0.38 g (1.0×10^{-2} mol) of $NaBH_4$. Brief stirring at room temperature effected solution. The mixture was then immersed in an ice bath, and 2.0 g (8.0×10^{-3} mol) of 1 ($R = CH_2CH_3$) was added (powder funnel, N_2 flow) over a period of 20 min. After the mixture was stirred an additional 10 min, 5 mL of water was added dropwise (some H_2 evolution) followed by 30 mL of saturated NaCl solution. This mixture was extracted four times with 20-mL portions of pentane; the combined pentane phase was washed with water and brine, dried over K_2CO_3, and rotary evaporated to give 1.2 g (89%) of 2. The ^1H NMR of this material was identical with that of an analytically pure sample, and VPC gave no indication ($\leq 1\%$) of 5.

(B) $LiAlH_2(OEt)_2$. A 1-L three-necked flask was fitted with a mechanical stirrer, condenser with N_2 inlet, and addition funnel. THF, 450 mL, was added, followed by 9.3 g (0.24 mol) of $LiAlH_4$. The cloudy solution was cooled in an ice bath and 25.7 mL (0.44 mol) of anhydrous ethanol in 50 mL of THF was added over a period of 1 h. With continued cooling and stirring, 25 g (0.10 mol) of 1 ($R = CH_2CH_3$) was added rapidly through a powder funnel. The ice bath was removed, and stirring was continued for 2 h. Again with cooling, the excess hydride was quenched by the dropwise addition of 150 mL of 10% NaOH, after which the liquid phase was decanted from the precipitated aluminum salts and rotary evaporated to remove most of the THF. The residue was taken up in 50 mL of ether, washed with water and brine, dried over K_2CO_3, and again rotary evaporated to give 16.0 g of crude material, which contained only traces of 5 by VPC analysis. Distillation gave 14.3 g (87%) of pure 2, bp 77–79 °C (2.0 Torr).[10]

Acknowledgment. Support by a grant from the University of California Cancer Research Coordinating Committee is gratefully acknowledged.

Registry No. 1 ($R = C_2H_5$), 487-97-8; 2 ($R = C_2H_5$), 75802-19-6; 3, 270-75-7.

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[9] A referee has questioned our use of dichloromethane as a solvent (when so specified) for reductions of the salt 1 and also the use of $LiAlH_4$ to dry this solvent, stating "Halogenated hydrocarbons are known to react with explosive violence with reactive complex metal hydrides." On the first point, CH_2Cl_2 is the only common solvent that will dissolve a moderate amount of 1 without potentially or in practice reacting with it. On the second point, we shared the referee's concern but have now used this technique for over a year without experiencing any difficulty, after first learning of it as a method for preparing ultra-dry CH_2Cl_2 from Professor W. C. Kaska of this department. While a still pot of CH_2Cl_2 to which solid $LiAlH_4$ has been added has been maintained at reflux for weeks without incident, we do not advocate this as a general procedure for drying halogenated hydrocarbons.

[10] Some decomposition of 2 may occur when distillation is done at higher temperatures, evidenced by the formation of viscous pot residue.

Use of Ethylaluminum Dichloride as a Catalyst for the Friedel–Crafts Acylation of Alkenes

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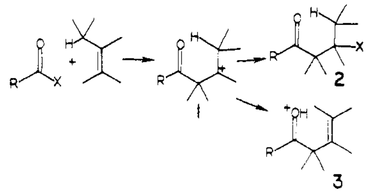
Introduction

Friedel–Crafts acylation of alkenes is an old and well-known reaction.[1,2] A reactive acylating agent reacts with an alkene to give an intermediate cation 1, which can react with nucleophiles, usually chloride, to give 2 or undergo a 1,5-proton shift to give the protonated β,γ-unsaturated ketone 3. Since both the starting alkenes and product β,γ-unsaturated ketones are sensitive to the protic acid produced in this reaction, aliphatic Friedel–Crafts acylation has been much less useful than its aromatic counterpart.



(1)

Reaction of acid halides with alkenes in the presence of Lewis acids usually leads to β-chloro ketones. Treatment of the crude reaction mixture with base provides a good yield of α,β-unsaturated ketone.

The best synthesis of β,γ-unsaturated ketones involves the reaction of acylium salts with alkenes in the presence of a hindered base[3,4] or the reaction of alkenes with zinc chloride in a large excess of acyl anhydride as solvent.[5-7] Acylium salts are not attractive starting materials, and the zinc chloride procedure is only applicable to acetic anhy-

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[2] Groves, J. K. *Chem. Soc. Rev.* **1972**, *1*, 73.

[3] (a) Smit, V. A.; Semenovsky, A. V.; Kucherov, V. F.; Chernova, T. N.; Krimer, M. Z.; Lubinskaya, O. V. *Tetrahedron Lett.* **1971**, 3101. (b) Smit, V. A.; Semenovsky, A. V.; Lubinskaya, O. V.; Kucherov, V. F. *Dokl. Akad. Nauk SSSR* **1972**, *203*, 604.

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[6] Dubois, M.; Cazaux, M. *Bull. Soc. Chim. Fr.* **1975**, 265.

[7] Beak, P.; Berger, K. R. *J. Am. Chem. Soc.* **1980**, *102*, 3848.

0022-3263/82/1947-5393$01.25/0 © 1982 American Chemical Society

dride and other anhydrides that can be used in excess as solvent. β,γ-Unsaturated ketones are therefore not readily available by Friedel–Crafts acylation.

We have recently initiated a program to explore the use of alkylaluminum halides as Lewis acids.[8] These readily available compounds, and the aluminates derived from them, are Bronsted bases and, therefore, allow Lewis-acid-catalyzed reactions to be carried out under aprotic conditions. Since addition of HCl to alkenes is often a problem in Friedel–Crafts acylation, we decided to explore the use of alkylaluminum halides as catalysts in these reactions.

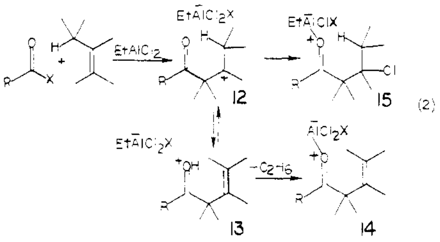
Results and Discussion

Our initial studies suggested that $EtAlCl_2$, in dichloromethane as solvent, was the most effective alkylaluminum halide catalyst for these reactions. The results of a survey of acylating agents and alkenes are shown in Table I. Individual reaction conditions were not optimized.

1-Methylcyclohexene, which is a reactive substrate,[5-7] was chosen for a survey of acylating agents. With $EtAlCl_2$ as catalyst, β,γ-unsaturated ketones are obtained from both acyl chlorides and anhydrides. The use of acyl chlorides is more economical in the case of complex acyl moieties. The reaction requires only 1 equiv of Lewis acid and is compatible with anhydrides that cannot be used as solvent. In contrast, succinic and benzoic anhydride do not react when $ZnCl_2$ is used as catalyst.[7] The reaction with dimethylacryloyl chloride with $SnCl_4$ as catalyst has been reported to give a complex mixture of **4b**, the β-chloro ketone, and 1-chloro-1-methylcyclohexane, which results from addition of HCl, produced as a byproduct in the formation of **4b**, to 1-methylcyclohexene.[9] We have never observed the formation of chloroalkane as a byproduct using $EtAlCl_2$, since the HCl is scavenged as it is produced ($EtAlCl_2$ + HCl → ethane + $AlCl_3$).

The scope of the reaction with less nucleophilic alkenes was explored with acetyl chloride and acetic anhydride as acylating agents. Reaction of 2-methyl-2-butene with acetyl chloride gave a 66% yield of a 4:1 mixture of 3,4-dimethyl-4-penten-2-one (**5**) and 4-chloro-3,4-dimethyl-2-pentanone (**6**). Use of acetic anhydride gave a 71% yield of a 1:1 mixture of **5** and **6**. Similar results were obtained with 1-hexene. Acetyl chloride gave a 81% yield of a 4:1 mixture of 4-octen-2-one (**7**) (as a 70:30 trans–cis mixture) and 4-chloro-2-octanone (**8**). Acetic anhydride gave a 42% yield of a 1:1 mixture of **7** and **8**. Reaction of acetyl chloride with cyclohexene gave a 90% yield of a 4.5:1 mixture of 3-acetylcyclohexene (**9**) and 2-chloro-1-acetylcyclohexane (**10**), as a 3:1 trans–cis mixture. Acetic anhydride gave a more complex mixture. These reactions proceed in higher yield with fewer byproducts than previously reported with other Lewis acid catalysts.[10-12] The one side reaction is the addition of the ethyl group to the acid chloride to give ethyl ketone. This is significant with nonnucleophilic alkenes or benzoyl chloride and dimethylacryloyl chloride.

Our results with acyl chlorides, in conjunction with many earlier studies, provide a clearer picture of the reactions of the intermediate cation **12** (eq 2). The 1,5-proton shift to give **13** is readily reversible, since β,γ-unsaturated ketones are minor products when normal Lewis acids are used and a major product when $EtAlCl_2$ is used. Deprotonation of **13** by $EtAlCl_3^-$ to give **14** makes the 1,5-proton shift irreversible and allows the isolation of β,γ-unsaturated ketones. The greater percentage of chloride formed from acyl anhydrides is due to either enhanced chloride delivery from or decreased basicity of acetoxyethyldichloroaluminate as compared to ethyltrichloroaluminate.



As has been previously noted,[12c] the formation of *trans*-2-chloro-1-acetylcyclohexane requires an intermolecular chloride delivery. This is in marked contrast to the addition of $CH_2O{\cdot}Me_2AlCl$ to cyclohexene, which gives *cis*-2-chlorocyclohexanemethanol via intramolecular chloride delivery.[13] The delivery of chloride to **12** is irreversible, since **15** is not converted to **14** in the presence of $EtAlCl_2$.[14]

Reaction of isoprene with dimethylacrylolyl chloride gave a complex mixture. Reduction of the mixture and chromatographic purification gave a 12% yield of ipsdienol (**11**), an aggregation pheromone of *Ips paraconfusus*. The low yield in this case appears to be due to the instability of the diene to Lewis acids. Use of $SnCl_4$ as catalyst gave only the chloro ketone.[16]

These results demonstrate that $EtAlCl_2$ is a useful catalyst for the Friedel–Crafts acylation of alkenes and makes β,γ-unsaturated ketones more accessible by this reaction.

Experimental Section

All reactions were conducted in anhydrous solvents under nitrogen in flame-dried glassware. $EtAlCl_2$ was obtained from Texas Alkyls as the pure reagent in a lecture bottle or as a 1.54 M solution in heptane. A 3.54 M solution in dichloromethane was prepared by dispensing a known quantity of $EtAlCl_2$ from the cylinder and dilution with solvent to the appropriate volume. Dichloromethane and 1,2-dichloroethane were distilled from calcium hydride. Acetic anhydride was refluxed over calcium carbide for 5 days and then distilled. GC was carried out on a 10 ft × 0.25 in. 10% Carbowax 20 M column.

General Procedure. $EtAlCl_2$ (2.6 mL of a 1.54 M solution in heptane *or* 1.13 mL of a 3.54 M solution in dichloromethane, 4 mmol) was added to a stirred solution of alkene (4 mmol) and acyl chloride *or* anhydride (4 mmol) in dichloromethane (10 mL) at 0 °C. The solution was allowed to warm to room temperature and stirred for 1 h. The reaction was quenched by the addition of water and ether. The aqueous layer was separated and extracted twice with ether. The combined organic extracts were washed twice with saturated $NaHCO_3$ solution and twice with

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[8] Snider, B. B.; Rodini, D. J.; Karras, M.; Kirk, T. C.; Deutsch, E. A.; Cordova, R.; Price, R. T. *Tetrahedron* **1981**, *37*, 3927.

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[11] 1-Hexene: ref 7 and 3b.

[12] Cyclohexene: ref 3a, 4, and (a) Royals, E. E.; Hendry, C. M. *J. Org. Chem.* **1950**, *15*, 1147; (b) Dubois, M.; Lallemand, J. Y.; Cazaux, M. *C. R. Hebd. Seances Acad. Sci., Ser. C.* **1974**, *279*, 759; (c) Ötvös, L.; Tüdos, H.; Radics, L. *Chem. Ind. (London)* **1970**, 597.

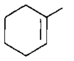
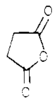
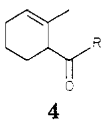
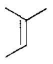
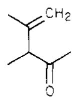
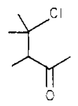
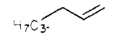
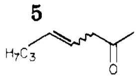
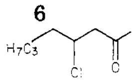
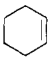
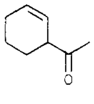
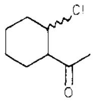
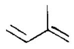
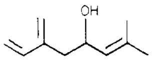
[13] Snider, B. B.; Rodini, D. J.; Kirk, T. C.; Cordova, R. *J. Am. Chem. Soc.* **1982**, *104*, 555.

[14] Treatment of **8** with 1 equiv of $EtAlCl_2$ under the reaction conditions led to only slight decomposition after 20 h. Addition of a large excess of $EtAlCl_2$ caused extensive decomposition. Reaction of 1-hexene with acetyl chloride for 20 h gave a 56% yield of **7**, a 25% yield of **8**, and an 18% yield of 3-octen-2-one. Use of a slight excess of $EtAlCl_2$ caused extensive decomposition over this extended reaction time.

[15] Mori, K. in "The Total Synthesis of Natural Products"; Apsimon, J., Ed.; Wiley-Interscience: New York, 1981; Vol. 4, pp 1–185.

[16] Adams, D. R.; Bhatnagar, S. P.; Cookson, R. C.; Tuddenham, R. M. *J. Chem. Soc., Perkin Trans 1* **1975**, 1741. See also: Garbers, C. F.; Scott, F. *Tetrahedron Lett.* **1976**, 1625.

Table I. $EtAlCl_2$ Catalyzed Friedel-Crafts Acylation of Alkenes[a]

alkene	acylating agent	products (% yield)			
	CH_3COCl $(CH_3CO)_2O$ $(CH_3)_2C{=}CHCOCl$ $[(CH_3)_2C{=}CHCO]_2O$ $PhCOCl$ 	a (54) a (55) b (64) b (60) c (40)[b] d (20)[c]	 4	a, R = CH_3 b, R = $(CH_3)_2C{=}CH$ c, R = Ph d, R = $CH_2CH_2CO_2H$	
	CH_3COCl $(CH_3CO)_2O$	(53) (36)	 5	(13) (35)	 6
	CH_3COCl $(CH_3CO)_2O$	(65)[d] (21)[d]	 7	(16) (21)	 8
	CH_3COCl	(73)	 9	(16)[e]	 10
	$(CH_3)_2C{=}CHCOCl$	(12)[c,f]	 11		

[a] Reaction for 1 h in CH_2Cl_2 at 25 °C unless otherwise specified. [b] Propiophenone was isolated in 23% yield. [c] See Experimental Section for reaction conditions. [d] 70:30 *E-Z*. [e] 75:25 trans-cis. [f] Yield after reduction with $NaBH_4$.

saturated brine, dried ($MgSO_4$), and evaporated in vacuo (at 0 °C in the case of volatile products).

The spectral data for ketones **4a**,[6] **4b**,[9] **4c**,[17] **5**,[7] **6**,[18] **7**,[3b] **9**,[4] and **10**[12c] and alcohol **11**[19] are identical with those previously reported.

Enone 4a was purified by evaporative distillation (75 °C, 8 Torr).

Enone 4b was purified by evaporative distillation (70 °C, 0.1 Torr).

Enone 4c was purified by chromatography on silica gel with 9:1 hexane-ether as eluent. Propiophenone was also isolated in 23% yield.

Reaction with succinic anhydride was carried out in 15 mL of 1,2-dichloroethane for 16 h at room temperature. The reaction was quenched with water, dichloromethane, and 10% hydrochloric acid. The aqueous layer was separated and extracted twice with dichloromethane. The combined organic layers were washed with brine, dried (Na_2SO_4), and evaporated to give 474 mg of an oil, which crystallized slowly. Recrystallization from petroleum ether gave pure **4d** as white needles (159 mg, 20%): mp 61-61.5 °C; NMR ($CDCl_3$) δ 5.67 (m, 1), 3.14 (m, 1), 2.55-3.0 (m, 4), 1.62 (s, 3), 1.4-2.2 (m, 6); IR (KBr) 2500-3500, 1707 cm^{-1}. Anal. (C, H).

The ratio of 5:6 was determined by analysis of the NMR spectrum. Evaporative distillation gave a mixed fraction (50 °C, 20 Torr), followed by pure **6** (75 °C, 14 Torr).

The ratio 7:8 was determined by analysis of the NMR spectrum and GC data. Pure samples were obtained by preparative GC. The data for **7** follow: NMR ($CDCl_3$) δ 3.15 (d, 0.3 × 2, J = 6 Hz, cis isomer[20]) and 3.08 (d, 0.7 × 2, J = 6 Hz, trans isomer[20]); GC t_R = 4.4 min (140 °C, 45 mL/min). The data for **8** follow: NMR ($CDCl_3$) δ 4.32 (tt, 1, J = 7 and 7 Hz), 2.93 (dd, 1, J = 8 and 16 Hz), 2.75 (dd, 1, J = 6 and 16 Hz), 2.19 (s, 3), 0.8-1.9 (m, 9); GC t_R = 12.2 min (140 °C, 45 mL/min).

The ratio of 9:10 and the stereochemistry of **10** was determined by analysis of the NMR spectrum and GC data. **9**: GC t_R = 8.0 min (140 °C, 40 mL/min). **10**: GC t_R = 22.1 min (140 °C, 40 mL/min).

Reaction of isoprene and dimethylacryloyl chloride was carried out for 1 h at -20 °C. Normal workup gave 526 mg of crude product. Sodium borohydride (0.19 g, 5 mmol) was added to a solution of this material (347 mg) in 2-propanol (15 mL) and water (5 mL). The solution was stirred for 4.5 h at 20 °C and poured into saturated brine. This mixture was extracted with 3 portions of pentane, which was dried (Na_2SO_4) and evaporated to give 328 mg of crude **11**. Chromatography on silica gel with 1:1 hexane-ether as eluent gave 47 mg (12%) of pure ipsdienol (**11**).

Acknowledgment. We thank the National Institutes of Health for generous financial support.

Registry No. 4a, 15564-32-6; **4b**, 83632-87-5; **4c**, 32704-48-6; **4d**, 83632-84-2; **5**, 54678-04-5; **6**, 684-02-6; (*E*)-**7**, 37720-70-0; (*Z*)-**7**, 28362-73-4; **8**, 83632-85-3; **9**, 29372-98-3; *cis*-**10**, 83632-86-4; *trans*-**10**, 81568-11-8; **11**, 35628-00-3; $(CH_3CO)_2O$, 108-24-7; $(CH_3)_2C{=}CHCOCl$, 3350-78-5; $[(CH_3)_2C{=}CHCO]_2O$, 34876-10-3; $PhCOCl$, 98-88-4; $EtAlCl_2$, 563-43-9; CH_3COCl, 75-36-5; 1-methylcyclohexene, 591-49-1; 2-methyl-2-butene, 513-35-9; 1-hexene, 592-41-6; cyclohexene, 110-83-8; isoprene, 78-79-5; succinic anhydride, 108-30-5.

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[18] Hart, H.; Schlosberg, R. H. *J. Am. Chem. Soc.* **1968**, *90*, 5189.

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[20] Hine, J.; Linden, S.-M.; Wang, A.; Thiagarajan, V. *J. Org. Chem.* **1980**, *45*, 2821.

Palladium-Catalyzed Synthesis of Cinnamylamines

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Received May 11, 1982

Cinnamylamines are useful intermediates in organic synthesis but as a class cannot be synthesized by one general procedure. We recently had need for a series of various substituted cinnamylamines and tried some of the