Lewis Acid Promoted Reactions of n-(1-Phenylcyclopropyl)alkanoyl Chlorides. Ring-Size Effects in Competitive Intramolecular Acylation of Phenyl and Cyclopropyl Substituents

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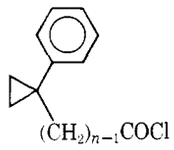
Exclusive intramolecular acylation of the phenyl ring occurs in aluminum chloride and stannic chloride promoted reactions of 3-(1-phenylcyclopropyl)propanoyl chloride (**1**, $n = 3$). Treatment of **1** ($n = 3$) with stannic chloride in benzene or with aluminum chloride in acetonitrile results in the production of spiro[cyclopropane-1,4′-tetral-1′-one]. In methylene chloride aluminum chloride effectively converts **1** ($n = 3$) to 4-ethyl-1-naphthol, and in benzene the aluminum chloride promoted reaction results in the production of 4-ethyl-4-phenyl-1-tetralone. In contrast, aluminum chloride promoted reactions of 4-(1-phenylcyclopropyl)butanoyl chloride (**1**, $n = 4$) result in exclusive intramolecular acylation of the cyclopropane ring; 4-phenylcycloheptanone is formed from reactions performed in methylene chloride, and both 4-phenylcycloheptanone and 4,4-diphenylcycloheptanone are produced in benzene. These results indicate that, although the phenyl ring is more susceptible to electrophilic attack than is the cyclopropyl ring in intermolecular acylation reactions, ring-size effects dominate these reactivity differences in the intramolecular process.

We have recently reported that cyclopropylalkanoyl chlorides undergo Lewis acid catalyzed intramolecular acylation reactions to form five-, six-, and seven-membered ring ketones.[2] The facility of these intramolecular rearrangements, which are analogous to Lewis acid catalyzed cyclizations of alkenoyl and arylalkanoyl chlorides,[3,4] has led us to investigate the reactivity of the cyclopropane ring relative to the benzene ring in Lewis acid promoted intramolecular cyclizations of n-(1-phenylcyclopropyl)alkanoyl chlorides (**1**). Although



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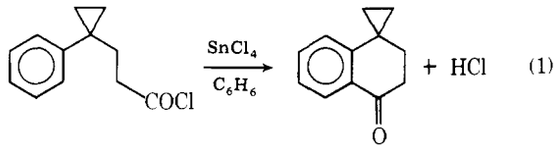
intermolecular acylation of phenylcyclopropane with acetyl chloride–aluminum chloride occurs exclusively at the para position of the benzene ring,[5] ring-size effects in intramolecular acylation of **1**, due to the positioning of the electrophilic acyl group relative to the phenyl and cyclopropyl rings, may be expected to have a dominant influence on acylation selectivity.[3d,6] Intramolecular acylation of the cyclopropane ring of **1** is expected to occur through an intermediate state that connects $n + 2$ carbon atoms, whereas intramolecular acylation of the benzene ring should occur through an intermediate state that joins $n + 3$ carbon atoms.

Exclusive intramolecular acylation of the phenyl ring occurs in aluminum chloride promoted reactions of 2-phenylcyclopropanecarbonyl chloride.[7] In addition, (1-phenylcyclopropyl)acetyl chloride (**1**, $n = 2$) has recently been reported to undergo intramolecular cyclization to form spiro[cyclopropane-1,3′-indan-1′-one].[8] Although cyclopropane ring opening is observed subsequent to acylation of the phenyl ring, reaction products resulting from intramolecular acylation of the cyclopropyl ring have not been detected. However, ring-size effects are expected to inhibit competitive acylation in these systems.

Results and Discussion

Treatment of 3-(1-phenylcyclopropyl)propanoyl chloride with stannic chloride in benzene at 25 °C results in the production of spiro[cyclopropane-1,4′-tetral-1′-one] (**2**, eq 1), which was isolated in 84% yield. Corresponding products from intramolecular acylation of the cyclopropane ring are not observed, nor, surprisingly, are products resulting from intermolecular acylation of the solvent benzene. Considering the reported sensitivity of the cyclopropane ring to ring opening under reaction conditions from which hydrogen chloride is produced,[2,8] the formation of **2** in high yield is notable and suggests that alteration of the Lewis acid and conditions employed with **1** ($n = 3$) could effectively lead to designed structural modifications of the product formed by intramolecular acylation of the phenyl ring. This expectation is realized in the results from reactions of **1** ($n = 3$) promoted by the stronger Lewis acid aluminum chloride.



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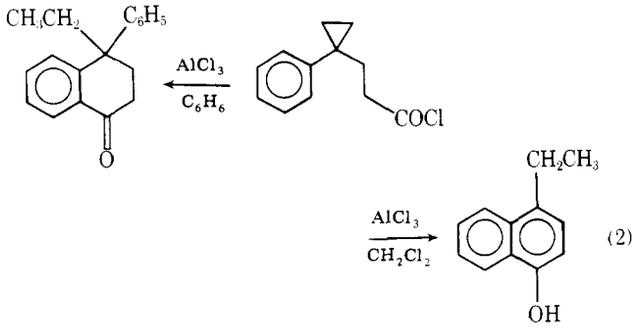
Reaction of 3-(1-phenylcyclopropyl)propanoyl chloride with aluminum chloride (eq 2) in methylene chloride at 25 °C



(2)

produces 4-ethyl-1-naphthol as the sole identifiable product (59% isolated yield). Under similar conditions in benzene, 4-ethyl-1-phenyl-1-tetralone is formed (71% isolated yield). These results are consistent with a reaction scheme in which proton addition to the cyclopropane ring of **2** produces the corresponding benzylic cation that undergoes elimination to 4-ethyl-1-naphthol or is effectively trapped through electrophilic substitution with benzene. In acetonitrile, a basic medium for aluminum chloride, cyclopropane ring opening that results from proton addition is not observed and **2** is formed nearly exclusively.

Intramolecular acylation of the phenyl ring of 3-(1-phenylcyclopropyl)propanoyl chloride produces a benzenonium ion intermediate that possesses an electron-deficient center adjacent to the cyclopropane ring. Due to geometrical con-

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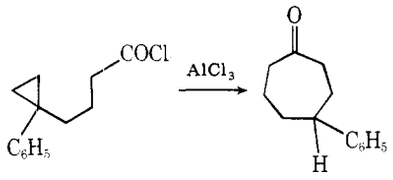
straints, this cyclopropylcarbinyl cation is formed in the bisected geometry that is preferred for conjugation with the cyclopropane ring.[9] However, the cyclopropylcarbinyl ring opening process that could be expected during intramolecular acylation of *n*-(1-phenylcyclopropyl)alkanoyl chlorides (**1**, *n* = 2, 3) is not observed, presumably due to the stability of the delocalized benzenonium ion intermediate.

In contrast to the intramolecular cyclization reactions reported for 3-(1-phenylcyclopropyl)propanoyl chloride, the aluminum chloride promoted reactions of 4-(1-phenylcyclopropyl)butanoyl chloride (**1**, *n* = 4) result in exclusive, molecular acylation of the cyclopropane ring. Products from intramolecular acylation of the phenyl ring that correspond to those observed in reactions of the next lower homologue are not detected. However, 4-phenylcycloheptanone (**3**, eq 3) is



(3)

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the only detectable monomeric substance from reactions performed in methylene chloride, and this unexpected product is formed in relatively low yield (32% isolated yield). The residual material is a relatively insoluble, high melting substance that does not exhibit ^{1}H NMR absorption characteristic of either a cyclopropane ring or a benzosuber-1-one structure, and it was not further characterized. In benzene, however, 4-(1-phenylcyclopropyl)butanoyl chloride forms both **3** (26% yield) and 4,4-diphenylcycloheptanone (48% yield), indicating the dominant preference for intramolecular acylation of the cyclopropane ring in reactions of **1** (*n* = 4) with aluminum chloride. Products from intermolecular acylation of the solvent benzene were not detected. In contrast, 4-cyclopropylbutanoyl chloride has been observed to react with aluminum chloride under similar conditions to form 4-chlorocycloheptanone and 3-chloromethylcyclohexanone; cycloheptanone and 3-methylcyclohexanone were not detected.[2]

The production of **3** is attributable to hydrogen abstraction by the carbocation formed through intramolecular acylation of the cyclopropane ring of **1** (*n* = 4).[10] However, attempts to increase the yield of **3** from reactions performed in methylene chloride through the addition of an equivalent amount of triphenylmethane did not result in a substantial improvement in the yield of 4-phenylcycloheptanone (36% isolated yield). Since methylene chloride is not an effective hydride donor, the reactants or products from intramolecular cyclization must serve in this capacity for the production of **3**. Surprisingly, **3** is also formed in reactions that occur in benzene; competition with electrophilic substitution apparently does not markedly affect the relative rate for hydride abstraction.[11]

The dramatic effect of ring size in intramolecular acylations of **1** (*n* = 3, 4) indicates the substantial reactivity of the cyclopropane ring. Although intramolecular acylations with 5-phenylalkanoyl chlorides that result in the formation of seven-membered ring benzosuber-1-ones are well known,[3] competing intramolecular acylation of the cyclopropane ring in **1** (*n* = 4), requiring an intermediate state that joins six carbon atoms, is preferred. Thus, although the phenyl ring is more susceptible to electrophilic attack than is the cyclopropyl ring in intermolecular acylation reactions,[5] ring-size effects dominate these reactivity differences in the intramolecular processes.

Aluminum chloride promoted reactions of the next higher homologue of **1** (*n* = 4), 5-(1-phenylcyclopropyl)pentanoyl chloride (**1**, *n* = 5), were investigated in both chloroform and benzene. Under conditions identical with those employed for ring expansion of **1** (*n* = 4), and even with a 10-fold dilution of reactants, intractable materials were obtained. Although as many as seven distinct products were observed by GLC analysis, none of the products was formed in greater than 3% yield and the reaction mixtures were not further analyzed.[12]

Experimental Section

General. Instrumentation has been previously described.[13] Mass spectra were obtained using a Finnigan Model 1015 gas chromatograph–mass spectrometer operated at 70 eV. For GC analyses use was made of 5 ft columns of 20% SE-30 and 20% Carbowax 20 M and a 6 ft column of 10% DEGS, each on Chromosorb P. The syntheses of 3-(1-phenylcyclopropyl)propanoic acid, 4-(1-phenylcyclopropyl)-butanoic acid, 5-(1-phenylcyclopropyl)pentanoic acid, and their respective acid chlorides (**1**, *n* = 3–5) have been described.[14] Finely powdered aluminum chloride was stored in a desiccator over phosphorus pentoxide. Stannic chloride was distilled prior to use. Reagent grade acetonitrile, benzene, and methylene chloride were distilled from calcium hydride prior to their use as reaction solvents. All glassware was oven-dried and assembled in a dry atmosphere.

Spiro[cyclopropane-1,4′-tetral-1′-one] (2). 3-(1-Phenylcyclopropyl)propanoyl chloride (0.209 g, 1.00 mmol) in 2 mL of dry benzene was added to a continuously stirred, ice-bath cooled solution of stannic chloride (0.96 g, 3.7 mmol) in 10 mL of anhydrous benzene. The rate of addition was sufficiently slow so that the reaction temperature did not rise above 10 °C. After addition was complete, the light yellow reaction solution was allowed to warm to room temperature. The reaction solution was again cooled in an ice bath after a reaction time of 12 h, and 20 mL of 6 M hydrochloric acid was slowly added to the homogeneous reaction medium. The acid layer was separated and washed 3 times with 20-mL portions of ether. The combined ether–benzene solution was washed successively with 20-mL portions of 6 M hydrochloric acid, saturated aqueous sodium bicarbonate, and water and then dried over anhydrous magnesium sulfate. The organic solvent was removed under reduced pressure, and 0.167 g of a dark colored liquid was obtained that, by GC and ^{1}H NMR analyses, contained 92% of **2** (0.84 mmol, 84% yield) and 8% of an unidentified component.[15] Purified **2** was obtained by GC collection using a 10% DEGS column: mp 51–52 °C; NMR ($CDCl_3$) δ 7.97 (1 H, d of d, J_o = 7 Hz, J_m = 2 Hz, H ortho to carbonyl), 7.25 (2 H, d of q, J = 7.2 Hz, β hydrogens), 6.75 (1 H, d of d, J_o = 7 Hz, J_m = 2 Hz, H ortho to cyclopropyl), 2.67 (2 H, dist t, J = 6.5 Hz), 1.92 (2 H, dist t, J = 6.5 Hz), and 1.10–0.85 (4 H, m, cyclopropane ring H); IR (CCl_4) 1685 cm^{-1} (C=O).

Anal. Calcd for $C_{12}H_{12}O$: C, 83.69; H, 7.02. Found: C, 83.54; H, 7.06.

Similar treatment of 3-(1-phenylcyclopropyl)propanoyl chloride (0.209 g, 1.00 mmol) with anhydrous aluminum chloride (0.44 g, 3.3 mmol) in freshly distilled acetonitrile afforded, after workup, 0.11 g of a light yellow liquid that, by GC and ^{1}H NMR analyses, consisted of 83% of **2** (0.53 mmol, 53% yield) and 17% of two unidentified products.[15]

4-Ethyl-4-phenyl-1-tetralone. 3-(1-Phenylcyclopropyl)propanoyl chloride (2.00 g, 9.6 mmol) in 20 mL of dry benzene was added to a continuously stirred, ice-bath cooled mixture of aluminum chloride (1.50 g, 11.2 mmol) in 30 mL of anhydrous benzene. The rate of addition was sufficiently slow so that the reaction temperature did not rise above 10 °C. After addition was complete, the homogeneous reaction solution was allowed to warm to room temperature. The reaction solution was again cooled in an ice bath after a reaction time of 2 h. Following the workup procedure described for the synthesis of **2**, 1.70 g of a white crystalline solid was obtained (6.8 mmol, 71% yield): mp 92–93 °C; NMR ($CDCl_3$) δ 8.35–8.10 (1 H, m, H ortho to carbonyl), 7.85–6.95 (8 H, m), 2.80–2.40 (4 H, m), 2.26 (2 H, q, J = 7 Hz), and 0.93 (3 H, t, J = 7 Hz); IR (KBr) 1680 cm^{-1} (C=O).

Anal. Calcd for $C_{18}H_{18}O$: C, 86.36; H, 7.24. Found: C, 86.15; H, 7.21.

4-Ethyl-1-naphthol. 3-(1-Phenylcyclopropyl)propanoyl chloride (0.209 g, 1.00 mmol) in 2 mL of dry methylene chloride was added to a continuously stirred, ice-bath cooled mixture of aluminum chloride (0.33 g, 2.5 mmol) in 10 mL of anhydrous methylene chloride. The rate of addition was sufficiently slow so that the reaction temperature did not rise above 10 °C. After addition was complete, the homogeneous reaction solution was allowed to warm to room temperature. The brown reaction solution was again cooled in an ice bath after a reaction time of 2 h. Following the workup procedure described for the synthesis of **2**, 0.12 g of a light green liquid was obtained that, by GC and

^{1}H NMR analyses, contained 85% of 4-ethyl-1-naphthol (0.59 mmol, 59% yield) and 15% of unidentified components.[15] Purified 4-ethyl-1-naphthol[16] was obtained following extraction with 5% aqueous sodium hydroxide: NMR (CCl_4) δ 8.3–7.8 (2 H, m), 7.6–7.3 (2 H, m), 7.04 (1 H, AB d, J = 7.5 Hz), 6.61 (1 H, AB d, J = 7.5 Hz), 6.1–5.6 (1 H, br, phenolic OH), 3.02 (2 H, q), and 1.32 (3 H, t); IR (CCl_4) 3600 (free O–H), 3600–3100 (associated O–H), 3070, 2970, 2940, 2880, 1590, 1508, 1452, 1380, 1270, 1258, 1140, 1048, and 880 cm^{-1}.

4-Phenylcycloheptanone (3). 4-(1-Phenylcyclopropyl)butanoyl chloride (0.223 g, 1.00 mmol) in 2 mL of dry methylene chloride was added to a continuously stirred, ice-bath cooled mixture of aluminum chloride (0.35 g, 2.6 mmol) in 10 mL of anhydrous methylene chloride. The rate of addition was sufficiently slow so that the reaction temperature did not rise above 10 °C. During the addition the reaction solution turned orange and a black solid formed at the bottom of the reaction flask. After addition was complete, the reaction mixture was allowed to warm to room temperature and became progressively darker. The dark brown reaction mixture was again cooled in an ice bath after a reaction time of 12 h. Following the workup procedure described for the synthesis of **2**, 0.18 g of a dark brown solid was obtained that, by GC and ^{1}H NMR analyses, contained 0.32 mmol (32% yield) of **3**. Purified **3** was obtained by GC collection using a 20% SE-30 column, and its physical and spectral properties were identical with those reported for **3**.[17]

4,4-Diphenylcycloheptanone. 4-(1-Phenylcyclopropyl)butanoyl chloride (0.223 g, 1.00 mmol) in 2 mL of dry benzene was added to a continuously stirred, ice-bath cooled mixture of aluminum chloride (0.45 g, 3.4 mmol) in 10 mL of anhydrous benzene. The rate of addition was sufficiently slow so that the reaction temperature did not rise above 10 °C. During the addition the reaction solution turned yellow and a dark colored solid formed at the bottom of the reaction flask. After 1 h the reaction mixture was allowed to warm to room temperature, and after a reaction time of 12 h the resulting dark brown reaction mixture was again cooled in an ice bath. Following the workup procedure described for the synthesis of **2**, 0.32 g of a dark oil was obtained that, by GC and ^{1}H NMR analyses, contained 0.26 mmol (26% yield) of **3** and 0.48 mmol (48% yield) of an additional product identified as 4,4-diphenylcycloheptanone: mp 100.5–101.5 °C; NMR ($CDCl_3$) δ 7.27 (10 H, s), 2.8–2.3 (2 H, m), 2.56 (4 H, s), and 2.3–1.5 (4 H, m); IR (CCl_4)[18] 3084, 3062, 3028, 2940, 2872, 1702 (C=O), 1597, 1492, 1444, 1333, 1060, and 908 cm^{-1};[19] mass spectrum, *m/e* (relative intensity)[20] 264 (47, parent ion), 236 (37, M − C_2H_4), 200 (40), 199 (28), 194 (43), 182 (37), 167 (25), and 91 (23).

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Registry No.—1 (n = 3), 67688-25-9; 1 (n = 4), 67688-26-0; **2**, 67688-27-1; **3**, 67688-28-2; 4-ethyl-4-phenyl-1-tetralone, 67688-29-3; 4-ethyl-1-naphthol, 10240-09-2; 4,4-diphenylcycloheptanone, 67688-30-6.

References and Notes

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(11) The corresponding reaction of **1** (n = 4) with aluminum chloride in benzene that contained 1.2 molar equiv of triphenylmethane produced **3** (34% yield), 4,4-diphenylcycloheptanone (31% yield), and triphenylmethanol (14% yield based on **1**). Thus, hydride transfer from triphenylmethane, even in the nucleophilic benzene solvent, occurs at the expense of electrophilic substitution. These results and the difference in product-forming steps from aluminum chloride promoted reactions of 4-cyclopropylbutanoyl chloride[2] and **1** (n = 4) may reflect the nature of the reaction intermediates involved in these processes. The results from intramolecular acylation reactions of 4-cyclopropylbutanoyl chloride have been interpreted by invoking a protonated cyclopropane intermediate from which the observed chloro ketones could be formed directly. In contrast, the additional stabilization from the phenyl substituent may promote either direct formation of the stabilized benzyl cation or collapse of the protonated cyclopropane intermediate to the benzyl cation on a time scale in which migration of the tetrachloroaluminate ion to the developing cationic center is slower than hydride transfer.
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(18) Spectral bands from 4000 to 800 cm^{-1} with intensities ≥ 20% that of the carbonyl stretching frequency are given.
(19) Observed spectral band positions closely match those reported for **3**.[17]
(20) Relative intensities of molecular fragments above *m/e* 91, relative to base peak at *m/e* 40.

Influence of Some Metal Salts on the Electroreduction of Aryl Ketones[1]

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The electrolytic reduction of 2,3:6,7-dibenzotropone was studied in aprotic solvent in the presence of various anhydrous metal salts. While the cyclic voltammogram shows this reaction to be a reversible one-electron reduction in CH_3CN and DMF, the presence of salts such as $CoCl_2$ and $Ni(acac)_2$ is found to affect the reversibility of the electrochemical reaction without influencing the reduction potential.

Few reports appear which describe the influence of metal cation salts on the electrolytic reductions of ketones in aprotic solvents. The reduction in these solvents does provide some technical disadvantages over the reactions carried out in protic media. Some of the differences are the higher overpotentials required and the greater amounts of dimeric product formed in aprotic solvents. Since metal cations can be quite efficient in promoting the ionization reactions of alkyl halides in aprotic solvents by acting as Lewis acids (eq 1),[2] it seemed appropriate to study their influence in the electroreduction reactions of

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