Reactions of Phenylacetaldehydes in Fluorosulfuric Acid

Jacques Kagan,* Dalmacio A. Agdeppa, Jr., Arthur I. Chang, Shyi-An Chen, Michael A. Harmata, Bennett Melnick, Gayatri Patel, Carol Poorker, and Shiv P. Singh

Department of Chemistry, University of Illinois, Chicago, Illinois 60680

William H. Watson, Jenn S. Chen, and Volker Zabel

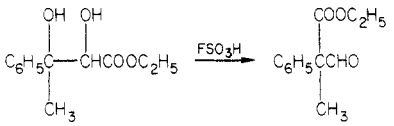
Department of Chemistry, Texas Christian University, Fort Worth, Texas 76129

Received April 9, 1981

The treatment of phenylacetaldehydes in fluorosulfuric acid generates 2,3,6,7-dibenzo-9-oxabicyclo[3.3.1]-nona-2,6-dienes. The generality of this reaction was tested on several derivatives which were substituted either at the 2-position or on the ring. Diastereoisomers, whenever obtained, were characterized by a combination of X-ray analysis and NMR data. Phenylacetone reacted differently and afforded the products of electrophilic aromatic substitution by fluorosulfuric acid. The structure of the unexpected minor reaction products was elucidated.

The treatment of saturated enolizable aldehydes with acids is known to result in aldol condensation,[1] cyclic trimerization,[2] or isomerization into ketones.[3] We describe here how bicyclic ethers may also be formed, although usually in poor yield, when phenylacetaldehydes are treated with a very strong acid such as fluorosulfuric acid. Two other types of products resulting from bimolecular reaction were also encountered.

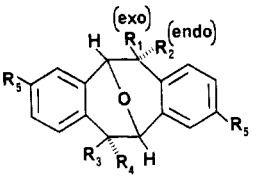
In a study of molecular rearrangements occuring with ethoxycarbonyl group migration, 2-phenyl-2-(ethoxycarbonyl)propionaldehyde (1) was obtained when ethyl 2,3-dihydroxy-3-phenylbutyrate was treated for 3 min with fluorosulfuric acid at 0 °C.[4]



1

Longer exposure to the acid led to further transformation of 1. The reaction was monitored by ^1H NMR, and the disappearance of 1 was found to be complete after 1 h at 0 °C. A mixture of three products was obtained, which was readily fractionated by chromatography over silica gel. One very minor product was ethyl 2-phenylpropionate, resulting from the decarbonylation of 1. The other two products were isomers, which showed a parent peak in their mass spectra at m/e 394, 18 units less than that for a dimer of 1. The ^1H NMR spectrum was interpreted in terms of the presence of one aromatic group, one aliphatic hydrogen which showed no coupling, one methyl, and one ethoxycarbonyl group, or some multiple thereof. The absence of any carbonyl groups other than that of the ester was also confirmed by ^{13}C NMR and by IR spectroscopy. Finally, these reaction products were not simple acetal or ketal derivatives of carbonyl compounds, since they failed to yield any new derivatives when treated with either (2,4-dinitrophenyl)hydrazine in acid or ferric chloride in acetic anhydride.[5]

The X-ray crystallographic analysis of the lower melting isomer A, melting at 116 °C, proved that it had the structure expressed in 2.[6] Although two other diastereoisomers are possible for this molecule, only one was detected and isolated. The crystals obtained for this higher melting isomer (B, mp 155–157 °C) were not suitable for an X-ray analysis, so that an unambiguous assignment of its structure was not possible. The ^1H and ^{13}C NMR spectra showed that the like substituents in B were in the same magnetic environment, consistent with a molecule having a twofold rotational axis. Assuming the deshielding effect of the bridge oxygen in the ^1H NMR to be stronger on the exo than on the endo methyl groups located at the positions 4 and 8 in A, one concludes that the methyl groups in B are exo (δ 1.80 in B vs. 1.77 and 1.57 in A) and that its structure must be therefore 3 rather than 4.



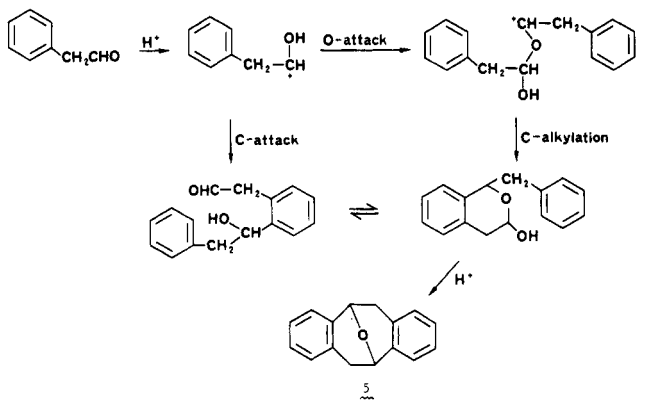
2, $R_1 = R_4 = COOC_2H_5$; $R_2 = R_3 = CH_3$; $R_5 = H$
3, $R_1 = R_3 = CH_3$; $R_2 = R_4 = COOC_2H_5$; $R_5 = H$
4, $R_1 = R_3 = COOC_2H_5$; $R_2 = R_4 = CH_3$; $R_5 = H$
5, $R_1 = R_2 = R_3 = R_4 = R_5 = H$
6, $R_1 = R_3 = C_6H_5$; $R_2 = R_4 = R_5 = H$
7, $R_1 = R_3 = Br$; $R_2 = R_4 = R_5 = H$
8, $R_1 = R_3 = CH_3$; $R_2 = R_4 = R_5 = H$
9, $R_1 = R_3 = R_5 = H$; $R_2 = R_4 = CH_3$
10, $R_1 = R_4 = R_5 = H$; $R_2 = R_3 = CH_3$
12, $R_1 = R_2 = R_3 = R_4 = H$; $R_5 = CH_3$

Phenylacetaldehyde itself reacted under similar conditions. The parent product was obtained, which also had its structure fully established by X-ray crystallography.[7,8] The ^1H NMR spectrum of this compound 5 featured three nonequivalent hydrogens, with signals at 2.5, 3.5, and 5.2 ppm, in addition to aromatic signals centered at 7 ppm. Two different coupling constants were expressed, 6 Hz for the lowest field aliphatic proton and 16 Hz for the highest field one. Both coupling constants were present in the signal at 3.5 ppm. It is clear that the signal at 5.2 ppm must be due to the bridgehead hydrogens, which appeared at 4.90 ppm in 3 and at 4.96 and 5.40 ppm in 2. Since each

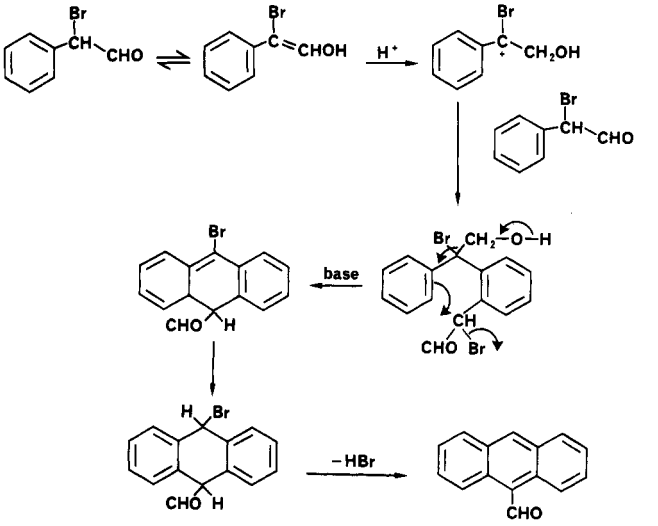
(1) Nielsen, A. T.; Houlihan, W. J. *Org. React.* **1968**, *16*, 1.
(2) Bayer, O. In "Methoden der Organischen Chemie (Houben-Weyl)"; Müller, E., Ed.; Georg Thieme Verlag: Stuttgart, 1954; Vol 7/1, p 428.
(3) Collins, C. J.; Eastman, J. F. In "The Chemistry of the Carbonyl Group", Patai, S., Ed.; Interscience: 1966; p 772.
(4) Kagan, J.; Agdeppa, D. A., Jr.; Mayers, D. A.; Singh, S. P.; Walters, M. J.; Wintermute, R. D. *J. Org. Chem.* **1976**, *41*, 2355.
(5) Ganem, B.; Small, V. R., Jr. *J. Org. Chem.* **1974**, *39*, 3728.
(6) Chen, J. S.; Watson, W. H.; Kagan, J.; Agdeppa, D. A., Jr.; Chen, S.-A. *Acta Crystallogr., Sect. B.* **1978**, *B34*, 3627.
(7) Zabel, V.; Watson, W. H.; Kagan, J.; Agdeppa, D. A., Jr.; Chen, S.-A. *Cryst. Struct. Commun.* **1978**, *7*, 727.
(8) Kagan, J.; Chen, S.-A.; Agdeppa, D. A., Jr.; Watson, W. H.; Zabel, V. *Tetrahedron Lett.* **1977**, 4469.

0022-3263/81/1946-2916$01.25/0

Scheme I



Scheme II



of these hydrogens couples with only one of the adjacent hydrogens, it must have a dihedral angle close to 80° with the other.[9] The X-ray analysis showed that the dihedral angles between the bridgehead hydrogen and the adjacent ones are 76° with the endo and 41° with the exo. As seen from a molecular model, a small deformation of the molecule such as could be experienced in going from a crystalline to a solvated state easily leads to an increase of this bond angle from 76° to 80°, thereby eliminating the coupling.

A minor product of the reaction of phenylacetaldehyde in fluorosulfuric acid was identified as 2-phenylnaphthalene. This transformation had been previously observed in HCl and H_2SO_4 media and was convincingly postulated to involve an acid-catalyzed aldol condensation reaction, followed by cyclization and dehydration.[10]

A plausible mechanism for the formation of **5** features a double ortho aromatic substitution reaction. Two pathways may be recognized, depending upon whether the initial cation formed by protonation of the carbonyl group attacks the second molecule first at carbon or at oxygen (Scheme I). Conceivably, the partitioning between the pathways depends on the nature and on the number of substituents in the phenylacetaldehyde.

We failed in our attempts to isolate any intermediates, even when the reaction of phenylacetaldehyde was performed with a limited amount of fluorosulfuric acid. The major product isolated under these conditions was 2,4,6-tribenzyl-1,3,5-trioxane, besides **5** and 2-phenylnaphthalene. An independent treatment of the trioxane with an excess of fluorosulfuric acid led to **5**, but with a yield which was not greater than that observed from phenylacetaldehyde.

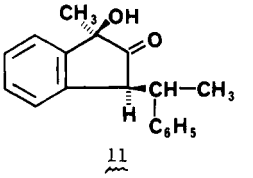
Diphenylacetaldehyde reacted with fluorosulfuric acid at −78 °C, giving **6** in addition to some deoxybenzoin, the product of isomerization of the aldehyde into a ketone.[3]

α-Bromophenylacetaldehyde also reacted similarly, and yielded **7** as a single isomer. A minor product of this reaction was identified as 9-anthranaldehyde through the comparison of its physical and spectroscopic properties with those described in the literature. Particularly noteworthy is the chemical shift of the aldehyde proton, 11.43 ppm, surely one of the most deshielded aldehyde signals on record.[11] A mechanism accounting for the formation of this aldehyde is proposed in Scheme II, where the initial acid-catalyzed aromatic substitution reaction is followed by the base-catalyzed elimination of formaldehyde and HBr, which would take place during the workup. However, the mechanism of this transformation remains to be elucidated.

The stereochemistry of both **6** and **7** was deduced from the ^1H NMR spectra. The coupling constants for the aliphatic hydrogens on adjacent carbon atoms were negligible in the case of **6** and quite small, ca. 1 Hz, in the case of **7**. As discussed earlier, this feature must be diagnostic for the presence of an endo hydrogen at positions 2 and 6.

In contrast to these two examples, the treatment of 2-phenylpropionaldehyde with fluorosulfuric acid yielded a mixture of all three isomeric products, **8**–**10**. The exo–exo isomer **8** was characterized in the ^1H NMR by a singlet for the protons at C-1 and C-5 and a clean quartet for those at C-4 and C-8, whereas a doublet and a multiplet, respectively, were observed for these protons in the endo–endo isomer **9**. In addition, the methyl signal in **8** was found significantly downfield compared to that in **9** (1.48 vs. 1.28 ppm), confirming the deshielding effect of the ether oxygen on the exo substituents.

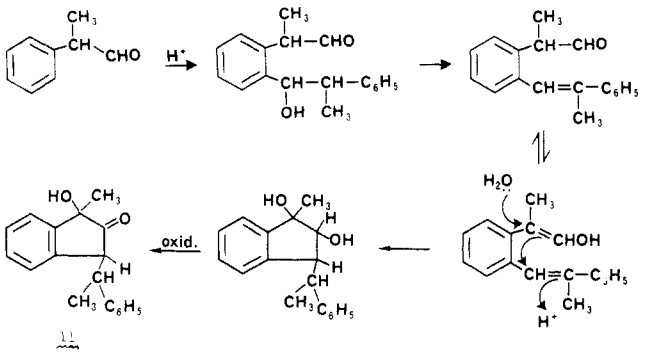
Another crystalline substance was isolated from the above reaction mixture. Its infrared spectrum disclosed the presence of a carbonyl group (1710 cm^{-1}) and a hydroxyl. The ^1H NMR in dimethyl-d_6 sulfoxide showed that the hydroxyl was tertiary,[12] and further analysis of the mass and NMR spectra led to the structure shown as **11** for this product.



The structure was in accord with the peaks at m/e 266 (M) and 248 (M − H_2O) in the mass spectrum and with the ^1H NMR spectrum in $CDCl_3$ which showed the two methyl groups, one as a singlet at 1.8 ppm and one as a doublet at 1.05 ppm (J = 6 Hz), the aliphatic ring proton at 3.9 ppm (d, J = 12 Hz), and the other benzylic proton at 3.37 ppm (dq, J = 6 and 12 Hz). There was a carbonyl signal at 213.04 ppm in the ^{13}C NMR, and since the IR showed that the carbonyl was not conjugated to an aromatic group, the data fit the structure **11** unambiguously. The stereochemistry was established by observing that the

(9) Karplus, M. *J. Chem. Phys.* **1959**, *30*, 11.
(10) Carter, H. E.; Van Loon, E. J. *J. Am. Chem. Soc.* **1938**, *60*, 1077.
(11) Pouchert, C. J.; Campbell, J. R. "The Aldrich Library of NMR Spectra"; Aldrich Chemical Co.: Milwaukee, WI; 1974; Vol. 6, No. 103D.
(12) Chapman, O. L.; King, R. W. *J. Am. Chem. Soc.* **1964**, *86*, 1256.

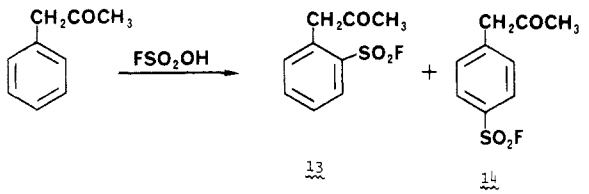
Scheme III



^{1}H NMR spectrum obtained in pyridine-d_5 could be superimposed over that obtained in $CDCl_3$, except for the benzylic multiplet which had shifted downfield by 0.1 ppm, indicating a cis relationship between this hydrogen and the hydroxyl, and the methyl singlet which had shifted downfield by 0.15 ppm, as expected for a geminal substituent.[13] This product presumably arose through ortho alkylation, followed by cyclization, hydration, and oxidation, as outlined in Scheme III. We have no evidence concerning the details of this synthesis and are therefore unable to defend the above mechanism over a similar one in which the chain extension would have preceded the aromatic substitution, as suggested by one referee. Similarly, the exact nature of the oxidizing reagent is unknown. Whether it is an air oxidation or a hydride transfer to the carbonyl group of another molecule remains to be determined.

Finally, the cyclization reaction of phenylacetaldehydes was observed on one ring-substituted molecule, (4-methylphenyl)acetaldehyde, which yielded **12** as the only isolable product.

The bicyclic ether synthesis appears to be confined to phenylacetaldehydes since phenylacetone, the simplest analogue substituted at the carbonyl carbon, did not yield the expected product. The disappearance of the starting material was much slower, and fluorosulfuric acid behaved as an electrophile to yield a mixture of the ortho- and para-substituted products **13** and **14**, which showed two



signals at 228.26 and 228.13 ppm downfield from C_6F_6 in the ^{19}F NMR. The para isomer **14** could be obtained pure by crystallization. Its structure was supported by the mass spectrum, which showed the molecular ion at m/e 216, the elemental analysis, the signal at 228.26 ppm in the ^{19}F NMR, and the ^{1}H NMR which showed the methyl and methylene groups at 2.21 and 3.85 ppm, respectively, as well as the pairs of aromatic protons at 7.5 and 8.0 ppm with the typical ortho coupling of 8 Hz. The presence of the carbonyl group was confirmed by the IR absorption at 1715 cm^{-1} and the signal at 204.12 ppm in the ^{13}C NMR. The ortho isomer **13** could not be obtained pure from the mother liquor, either by crystallization or by chromatography. However, its presence was clear from the mass spectrum of the mixture and from the ^{1}H NMR which showed the complex pattern expected for four nonequivalent protons on contiguous aromatic carbon atoms. The methyl and methylene signals were superimposed upon those of **14**. Although a basic workup was originally used for the isolation of **13** and **14**, their yield was similar whether or not a base was used.

The electrophilic substitution of aromatic compounds with fluorosulfuric acid is a well-established reaction, dating back to Steinkopf's work in 1927.[14] The reasons the course of the reaction of phenylacetone differed so completely from that of the phenylacetaldehydes is not clear. Conceivably, the steric effect due to the additional substituent at the carbonyl is responsible for making the required bimolecular alkylation reactions unfavorable.

Attempts were made to convert the bicyclic ether **5** into dibenzocyclooctatetraene without success. The starting material was recovered unchanged when treated with hydrogen iodide,[15] triphenylphosphine,[16] triphenylphosphine selenide,[17] iron pentacarbonyl,[18] and phosphorus pentasulfide.[19] Interestingly, Jung et al. have reported the results of their independent synthesis of **5** from phenylacetaldehyde[20] using trimethylsilyl iodide, a reagent which they had also shown to cleave other ethers efficiently.[21] On the other hand, these authors succeeded in performing the hydrogenolysis of one benzylic carbon–oxygen bond in **5** through a Birch reduction.[20] The yield of **5** reported in Jung's synthesis, 50%, was comparable to that initially obtained in our work.[8] However, we found that the yield in our reaction was much lower when the work was repeated later, and efforts directed at duplicating our original yield have repeatedly met with failure. Nevertheless, the yield of this type of transformation can be quite high, such as in the conversion of **1** into **2** and **3**, which proceeded in excess of 75%. More generally, however, the yields of the interesting transformations described in this work were found to be very low, and extensive decomposition accompanied the formation of the products.

Finally, in view of the small number of phenylacetaldehydes available commercially and their high sensitivity to oxidative degradation in the presence of air, it could be desirable to bypass the actual isolation of these molecules. We discovered that styrene oxide, which is known to isomerize into phenylacetaldehyde in the presence of acid catalysts,[22] could be transformed directly into **5** when it was treated with fluorosulfuric acid. In view of the relative stability of such epoxides and their ease of access, this approach might be developed into a convenient synthesis of the class of bicyclic ethers described in this account. The use of epoxides was also proved to be equivalent to that of carbonyl compounds when 2-methyl-1-phenyloxirane was treated with fluorosulfuric acid. Phenylacetone was the only product formed under mild conditions, and the desired analogue of **5** substituted at the bridgehead positions was not observed.

Experimental Section

All the NMR spectra are reported on the δ scale, in parts per million downfield from internal Me_4Si. The microanalyses were performed by Micro-Tech Laboratories.

(13) Demarco, P. V.; Farkas, E.; Doddrell, D.; Mylari, B. L.; Wenkert, E. *J. Am. Chem. Soc.* **1968**, *90*, 5480.

(14) Steinkopf, W. *J. Prakt. Chem.* **1927**, *117*, 1.
(15) Burwell, R. L. *Chem. Rev.* **1954**, *54*, 615.
(16) Weis, C. D. *J. Org. Chem.* **1962**, *27*, 3520.
(17) Clive, D. L. J.; Denyer, C. V. *J. Chem. Soc., Chem. Commun.* **1973**, 253.
(18) Alper, H.; Edward, J. T. *Can. J. Chem.* **1970**, *48*, 1543.
(19) Cava, M. P.; Scheel, F. M. *J. Org. Chem.* **1967**, *32*, 1304.
(20) Jung, M. E.; Mossman, A. B.; Lyster, M. A. *J. Org. Chem.* **1978**, *43*, 3698.
(21) Jung, M. E.; Lyster, M. A. *J. Org. Chem.* **1977**, *42*, 3761 and references cited.
(22) Breuer, A.; Zinke, T. *Ber. Dtsch. Chem. Ges.* **1878**, *11*, 1399.

Reaction of 2-Phenyl-2-(ethoxycarbonyl)propionaldehyde (1) with FSO_3H. A mixture of 206 mg of 1 and 0.45 mL of FSO_3H was allowed to stand at 0 °C for 1 h and then poured over ice. After successive extractions with 30 mL of CCl_4 and 30 mL of ether, the organic extracts were washed with 5% aqueous $NaHCO_3$, combined, dried over $MgSO_4$, and concentrated under vacuum, yielding 200 mg of an oil. Preparative TLC over silica gel, with hexane–ethyl acetate (3:1), yielded a small amount of ethyl 2-phenylpropionate, which was identified by comparison with an authentic sample, and the two products **2** (93 mg, 47%; mp 116 °C) and **3** (62 mg, 31.4%; mp 155–157 °C). Both showed a single carbonyl in the IR (CCl_4) at 1720 cm^{-1} and had a parent peak in the mass spectrum at m/e 394 (M – 18): ^1H NMR (CCl_4) for **2** 6.7–7.3 (4 H), 5.40 (s, 1 H), 4.96 (s, 1 H), 4.10 (q, J = 7 Hz, 2 H), 3.90 (q, J = 7 Hz, 2 H), 1.77 (s, 3 H), 1.57 (s, 3 H), 1.15 (t, J = 7 Hz, 3 H), 1.00 (t, J = 7 Hz, 3 H), for **3** 6.7–7.2 (m, 4 H), 4.90 (s, 1 H), 3.83 (q, J = 7 Hz, 2 H), 1.80 (s, 3 H), 0.80 (t, J = 7 Hz, 3 H); ^{13}C NMR ($CDCl_3$) for **2** 175.3, 174.3, 137.0, 134.0, 133.3, 131.2, 129.9, 128.0, 127.6, 126.1, 125.4, 77.3, 61.5, 60.8, 53.5, 50.0, 29.3, 21.7, 14.0 (the signals at 127.6 and 126.1 ppm were clearly of multiple intensity and may have included the missing aromatic carbons), for **3** 174.4, 136.2, 132.7, 129.4, 127.5, 125.6, 125.5, 77.6, 60.7, 53.3, 29.3, 13.4.

Reaction of Phenylacetaldehyde with FSO_3H. To an ice-cooled, stirred solution of 2.00 g of phenylacetaldehyde in 20 mL of CCl_4 was added 8 mL of cold FSO_3H dropwise over a period of 10 min. The brown reaction mixture was further stirred for 45 min at 0 °C and poured over ice in the presence of 200 mL of CCl_4. After separation of the organic layer, the aqueous phase was extracted with CCl_4 (2 × 250 mL) and with ether (3 × 150 mL). The extracts were washed separately with saturated $NaHCO_3$ solution followed by water, combined, dried over $MgSO_4$, and concentrated under vacuum. Silica gel column chromatography of the residue (472 mg) yielded 17 mg (1%) of 2-phenylnaphthalene [mp 103 °C (lit.[10] mp 103–104 °C); mass spectrum, m/e 204 (M^+)] and 262 mg (14.2%) of **5**: mp 141 °C; mass spectrum m/e 222 (M^+); IR no carbonyl; ^1H NMR (CCl_4) 6.7 (s, 4 H), 5.13 (d, J = 6 Hz, 1 H), 3.45 (dd, J = 6, 16 Hz, 1 H), 2.63 (d, J = 16 Hz, 1 H); ^{13}C NMR ($CDCl_3$) 137.7, 131.6, 129.1, 126.8, 125.1, 69.5, 36.1.

Reaction of Phenylacetaldehyde with a Limited Amount of FSO_3H. The acid (5 mL) was added dropwise under N_2 over 15 min to a magnetically stirred solution of 20 g of phenylacetaldehyde in 300 mL of CCl_4, which was kept at −78 °C. The red mixture was stirred 45 min longer, poured over ice, and extracted with CCl_4 (2 × 200 mL). The organic extracts were washed with saturated $NaHCO_3$ and with water, dried over $MgSO_4$, and concentrated under vacuum to yield 12.8 g of residue. A 4-g portion was chromatographed over silica gel. Elution with hexanes yielded 120 mg (2.1%) of 2-phenylnaphthalene. Further elution with mixtures of hexanes and CCl_4 and with CCl_4 yielded a mixture which was further purified by preparative TLC over silica gel and gave 28 mg (0.5%) of **5** and 416 mg (6.7%) of 2,4,6-tribenzyl-*s*-trioxane: mp 155 °C (lit.[23] mp 155–156 °C); ^1H NMR (CCl_4) 7.1 (5 H), 4.82 (t, J = 5 Hz, 1 H), 2.9 (d, J = 5 Hz, 2 H).

Reaction of Diphenylacetaldehyde with FSO_3H. A solution of 5 g of diphenylacetaldehyde (containing 7% benzophenone) in 7.5 mL of CH_2Cl_2 was added over 30 min to 12.5 mL of FSO_3H at −78 °C, with stirring under N_2. After addition of another 5 mL of solvent and stirring for 1 h, the mixture was poured over ice in the presence of 200 mL of CCl_4. The aqueous phase was again extracted with CCl_4 (2 × 125 mL) and with ether (200 mL). The organic extracts were washed with saturated $NaHCO_3$ and with water, combined, dried over $MgSO_4$, and concentrated to yield 1.8 g of residue. Preparative TLC of a 200-mg fraction over silica gel with 6% EtOAc in hexanes yielded 14 mg (2.7%) of deoxybenzoin and 76 mg (7.4%) of **6**, which was recrystallized from isopropyl ether. The pure product had the following: mp 221–222 °C; mass spectrum, m/e 392 (M^+) with base peak at 374; ^1H NMR (CCl_4) 6.9–7.3 (m, 5 H), 5.21 (s, 1 H), 4.00 (s, 1 H). Anal. Calcd for $C_{28}H_{22}O$: C, 89.84; H, 5.88. Found: C, 89.98; H, 6.04.

Reaction of 2-Phenylpropionaldehyde with FSO_3H. The experiment was performed as above by using 5 g of 2-phenylpropionaldehyde (containing ca. 10% of acetophenone). Extraction with CH_2Cl_2 yielded 3 g of residue, which was fractionated by HPLC over a silica gel column with CCl_4. Partially purified fractions were chromatographed repeatedly over Al_2O_3 preparative plates with 2% EtOAc in hexanes. The endo–exo isomer **10** was the predominant product. After recrystallization from EtOH, 155 mg (3.3%) was obtained: mp 99–101 °C; mass spectrum, m/e 250 (M^+), 235 (M – CH_3), 232 (M – H_2O) and 217 (M – CH_3 – H_2O); IR no carbonyl; ^1H NMR (CCl_4) 6.95 (m, 8 H), 4.95 (d, J = 6 Hz, 1 H), 4.82 (s, 1 H), 3.51 (m, 1 H), 2.81 (q, J = 7 Hz, 1 H), 1.45 (d, J = 7 Hz, 3 H), 1.28 (d, J = 7 Hz, 3 H); ^{13}C NMR ($CDCl_3$) 138.47–124.98, 76.46, 74.21, 41.54, 36.84, 23.75, 15.36. Anal. Calcd for $C_{18}H_{18}O$: C, 86.40; H, 7.20. Found: C, 86.40; H, 7.24. The exo–exo isomer **8** was a glassy solid: 50 mg (1.1%); no carbonyl in the IR; mass spectrum, m/e 250; ^1H NMR (CCl_4) 6.93 (s, 4 H), 4.75 (s, 1 H), 2.78 (q, J = 7 Hz, 1 H), 1.48 (d, J = 7 Hz, 3 H); ^{13}C NMR ($CDCl_3$) 137.4, 129.2, 127.1, 126.0, 125.2, 75.5, 40.2, 23.2. The endo–endo isomer **9** was obtained in a minute amount: ^1H NMR (CCl_4) 6.95 (m, 4 H), 4.90 (d, J = 7 Hz, 1 H), 3.51 (m, 1 H), 1.28 (d, J = 7 Hz, 3 H); ^{13}C NMR ($CDCl_3$) 125.0, 138.5, 76.5, 74.2, 41.5, 36.8, 23.75, 15.4. Further elution of the HPLC column with CCl_4 gave a viscous substance which was recrystallized from CCl_4/hexanes to yield **11**: 65 mg (1.45%); mp 190–192 °C (sintered at 160–162 °C); IR 1710, 3400 cm^{-1}; mass spectrum, m/e 266 (M^+), with a major peak at 248 (M – H_2O); ^{13}C NMR ($CDCl_3$) 213.0, 143.6, 143.0, 136.8, 129.2, 129.05, 127.95, 127.4, 126.75, 56.8, 45.9, 32.6, 12.3; ^1H NMR ($CDCl_3$) 7.6–6.6 (m, 9 H), 4.1 (s, 1 H), 3.9 (d, J = 12 Hz, 1 H), 3.37 (m, 1 H), 1.78 (s, 3 H), 1.1 (d, J = 6 Hz, 3 H). The signal at 4.1 ppm moved to 5.2 ppm when the spectrum was measured in Me_2SO-d_6 and disappeared when D_2O was added. The signals at 3.37 and 1.78 ppm were shifted downfield by 0.10 and 0.15 ppm, respectively, when the spectrum was measured in pyridine-d_5.

Reaction of (*p*-Methylphenyl)acetaldehyde with FSO_3H. The acid (5.5 mL) was added dropwise under N_2 over a period of 15 min to a solution of 2 g of (*p*-methylphenyl)acetaldehyde in 20 mL of CCl_4 which was kept at −5 °C. After being stirred for another 15 min, the mixture was poured over ice containing 100 mL of CCl_4, solid $NaHCO_3$ was added, the organic phase was separated, and the aqueous phase was extracted with CCl_4 (3 × 150 mL). The combined organic extracts were washed with saturated $NaHCO_3$ and with water, dried over $MgSO_4$, and concentrated to give 500 mg of residue. Recrystallization from isopropyl ether/CCl_4 yielded **12**: 165 mg (8.8%); mp 142–144 °C; mass spectrum, m/e 250 (M^+), with major peaks at 235 (M – H_2O) and 232 (M – H_2O); no carbonyl in the IR; ^1H NMR (CCl_4) 6.95–6.75 (m, 3 H), 5.16 (d, J = 6 Hz, 1 H), 3.56 (dd, J = 6, 16 Hz, 1 H), 2.20 (s, 3 H); ^{13}C NMR ($CDCl_3$) 136.4, 135.0, 131.6, 129.8, 126.95, 125.1, 69.6, 36.2, 21.0.

Reaction of α-Bromophenylacetaldehyde with FSO_3H. To 5 mL of acid kept at −78 °C was added a solution of 3.3 g of α-bromophenylacetaldehyde in 10 mL of CH_2Cl_2 over 15 min. After being stirred at this temperature for 30 min, the red mixture was warmed to room temperature and poured over ice mixed with 200 mL of CH_2Cl_2. The aqueous phase was extracted with 200 mL of CH_2Cl_2, and the combined organic layers were washed with saturated $NaHCO_3$ and water and dried over $MgSO_4$. Removal of the solvent under vacuum gave 2.1 g of dark brown residue, which was chromatographed over silica gel. Elution with CCl_4 produced 1.1 g of yellow crystals, which were recrystallized from $CHCl_3$–CCl_4 to yield **7**: 650 mg (20.6%); mp 200–202 °C; mass spectrum, m/e 378 (M^+), with isotopic peaks at 380 and 382 and major peaks at 299/301 (M – Br), 219 (M – Br – HBr), and 191 (M – Br – HBr – CO); no carbonyl in the IR; ^1H NMR ($CDCl_3$) 7.25 (s, 4 H), 5.55 (d, J = 1 Hz, 1 H), 5.18 (d, J = 1 Hz, 1 H); ^{13}C NMR ($CDCl_3$) 133.4, 131.2, 130.9, 129.05, 125.85, 75.75, 48.3. Anal. Calcd for $C_{16}H_{12}OBr_2$: C, 50.53; H, 3.16. Found: C, 50.30; H, 3.23. The mother solution was concentrated and repeatedly crystallized from EtOH to give 75 mg (4.4%) of 9-anthranaldehyde: mp 103–104 °C; mass spectrum, m/e 206 (M^+), 205 (M – H), 178 (M – CO), and 177 (M – H – CO); IR (CCl_4) 1680 cm^{-1}; ^1H NMR ($CDCl_3$) 8–6.2 (m, 9 H), 11.43 (s, 1 H).

Reaction of Phenylacetone with FSO_3H. The acid (10 mL) was added dropwise over 10 min to a stirred solution of 2.5 g of phenylacetone in 25 mL of CCl_4. The mixture was stirred for 20 h at 60 °C, poured over ice, neutralized with solid $NaHCO_3$, and

(23) Müller, A. *Fette Seifen* **1951**, *53*, 221.

extracted with EtOAc (3 × 100 mL) and with ether (3 × 100 mL). The organic extracts were combined, washed with saturated NaCl and with water, dried over $MgSO_4$, and concentrated. The dark residue (1.3 g) was chromatographed over silica gel. The fractions eluted with CCl_4–CH_2Cl_2 (1:1) gave 500 mg of syrup (12.4%) which showed a strong band at 1715 cm^{-1} in the IR. The ^1H NMR ($CDCl_3$) displayed signals at 8.05–7.3 (m, 4 H), 3.85 (s, 2 H), and 2.21 ppm (s, 3 H). Crystallization from $CHCl_3$–hexanes yielded 70 mg of **14**: mp 77–78 °C; mass spectrum, *m/e* 216 (M^+), 173, 154, 133; ^1H NMR ($CDCl_3$) 8.0 (d, J = 8 Hz, 2 H), 7.5 (d, J = 8 Hz, 2 H), 3.85 (s, 2 H), 2.21 (s, 3 H). The mother liquor after filtration of these crystals showed ^1H NMR and mass spectra very similar to those of the original syrup, indicating a mixture of **12** and **13**. In another experiment 2.5 g of phenylacetone in 5 mL of FSO_3H was stirred at room temperature for 1.75 h and added dropwise to a mixture of 75 mL of $CHCl_3$ and ice. The aqueous phase was extracted again with 75 mL of $CHCl_3$, and the combined organic extracts were washed with saturated NaCl solution (3 × 150 mL), dried over $MgSO_4$, filtered, and concentrated to yield 1.75 g of a light brown oil. The ^1H NMR disclosed that 50% of the starting material remained. The mixture was treated again with 5 mL of FSO_3H at room temperature for 20 h, yielding 1.70 g of crude product in which the starting material was absent (by NMR). After two recrystallizations from CCl_4–$CHCl_3$ and three from EtOH, 60 mg of **13** was obtained; mp 75.5–76 °C. Anal. Calcd for $C_9H_9SO_3F$: C, 49.99; H, 4.20. Found: C, 49.83; H, 4.29.

Reaction of Styrene Oxide with FSO_3H. Cold FSO_3H (8 mL) was added over 30 min to 2.2 g of styrene oxide in 30 mL of CCl_4 stirred in an ice–salt bath. The solution was stirred for 1 h, poured over ice, and extracted with CCl_4 (3 × 100 mL). The organic phase was washed with saturated $NaHCO_3$ and with water, dried over $MgSO_4$, filtered, and concentrated. The residue (500 mg) was purified by chromatography and recrystallized, yielding 120 mg (5.4%) of **5**.

Reaction of 2,4,6-Tribenzyl-*s*-trioxane with FSO_3H. Cold acid (2 mL) was added to 500 mg of the trioxane[24] in 5 mL of $CHCl_3$, which was kept at 0 °C. The mixture was stirred for 15 min, poured over ice, and extracted with $CHCl_3$ (2 × 100 mL). The extract was washed with $NaHCO_3$ and with water, dried over $MgSO_4$, and concentrated to give 100 mg of residue. Crystallization from isopropyl ether yielded 65 mg (14%) of **5**.

Reaction of 2-Methyl-3-phenyloxirane with FSO_3H. The starting material was obtained by epoxidation of β-methylstyrene (Aldrich), which contained 95% of the *E* isomer, with *m*-chloroperbenzoic acid. To 6 mL of FSO_3H cooled in an ice-bath was added 2.5 g of the epoxide dropwise in 50 min. The black reaction mixture was carefully added to ice in the presence of 200 mL of $CHCl_3$. After extraction of the aqueous phase, it was saturated with NaCl and extracted with 200 mL of $CHCl_3$. The combined organic extracts were washed with saturated NaCl solution (3 × 200 mL), dried over $MgSO_4$, filtered, and concentrated under vacuum to yield 2.2 g (88%) of an oil which had IR and ^1H NMR spectra superimposable with those of phenylacetone.

Acknowledgment. We are grateful to the National Institutes of Health (Grant No. GM 24144), the Robert A. Welch Foundation (Grant P-074), the TCU Research Foundation, the UICC Research Board, and the TCU Computer Center for partial support of this research.

Registry No. 1, 60727-92-6; 2, 77550-92-6; 3, 77550-05-1; 5, 66365-45-5; 6, 77550-06-2; 7, 77507-96-1; 8, 77550-07-3; 9, 77550-08-4; 10, 77550-09-5; 11, 77507-97-2; 12, 77507-98-3; 13, 77507-99-4; 14, 77508-00-0; fluorosulfuric acid, 15181-47-2; phenylacetaldehyde, 122-78-1; 2-phenylnaphthalene, 612-94-2; 2,4,6-tribenzyl-*s*-trioxane, 77550-10-8; diphenylacetaldehyde, 947-91-1; deoxybenzoin, 451-40-1; 2-phenylpropionaldehyde, 93-53-8; *p*-methylphenylacetaldehyde, 104-09-6; α-bromophenylacetaldehyde, 16927-13-2; 9-anthranaldehyde, 642-31-9; phenylacetone, 103-79-7; styrene oxide, 96-09-3; 2-methyl-3-phenyloxirane, 4436-22-0.

(24) Wittekind, R. R.; Lazarus, S. *J. Heterocycl. Chem.* **1971**, *8*, 495.

A Simple Method for the Efficient Synthesis of Unsaturated β-Dicarbonyl Compounds

Dennis Liotta,*[1] Christopher Barnum, Robert Puleo, George Zima, Charlene Bayer, and Hollis S. Kezar, III

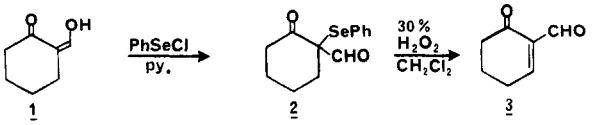
Department of Chemistry, Emory University, Atlanta, Georgia 30322

Received January 9, 1981

β-Dicarbonyl compounds which are substantially enolized can be readily converted to their corresponding unsaturated derivative by (a) selenation using a 1:1 complex of phenylselenenyl chloride/pyridine and (b) in situ oxidation with 30% H_2O_2 (after removal of the pyridine). The isolated yields of unsaturated β-dicarbonyl compounds obtained in this way are typically between 80% and 100%. If the selenation step (step a) is carried out in the presence of excess reagent, a slow "nonoxidative" elimination occurs. Synthetic and mechanistic details of this "nonoxidative" process are discussed.

Unsaturated β-dicarbonyl compounds are useful substrates for a number of important chemical reactions, including inter alia the Michael reaction and the Diels–Alder reaction. In principle, these materials can be prepared by DDQ oxidation of the corresponding saturated β-dicarbonyl compounds. In practice, the yields obtained from this procedure are usually only modest, presumably because of competitive over-oxidation.[2] In this article we report the results of a study involving reactions of a phenylselenenyl chloride/pyridine complex[3] with a variety of β-dicarbonyl compounds, which, when taken in the context of previous findings,[4] represents the simplest and most efficient method yet reported for the synthesis of unsaturated β-dicarbonyl compounds. The method is illustrated in Scheme I, using α-formylcyclohexanone. The results

Scheme I



(1) Fellow of the Alfred P. Sloan Foundation, 1980–84.
(2) Walker, D.; Hebert, J. D. *Chem. Rev.* **1967**, *67*, 153.
(3) Zima, G.; Liotta, D. *Synth. Commun.* **1979**, *9*, 697.
(4) Reich et al. have previously selenated β-dicarbonyl compounds by first reacting these compounds with sodium hydride in anhydrous THF, followed by reaction of the resulting anion with phenylselenenyl chloride. See: Reich, H. J.; Renga, J. M.; Reich, I. L. *J. Am. Chem. Soc.* **1975**, *97*, 5434.

0022-3263/81/1946-2920$01.25/0