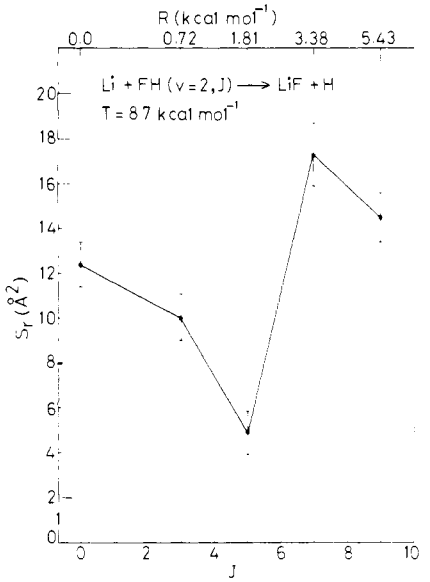

Figure 1. Reaction cross section S_r as a function of the rotational state J (lower scale) for HF (v = 2) at T = 8.7 kcal mol^{-1}. The corresponding rotational energies (in kcal mol^{-1}) are shown in the upper scale. The error bars correspond to a 95% confidence level.

The results of the QCT study are plotted in the form of S_r as a function of J in Figure 1. With increase in J from 0 to 5, there is a monotonic decrease in S_r; further increase in J to 7 and 9 results in a dramatic increase in S_r.

For reaction 1, ab initio studies[3] show that an angular approach of Li to FH at an LiFH angle of 74° has the lowest barrier, ~10 kcal mol^{-1}, for the reaction. Also, detailed analysis of the initial conditions of the reactive trajectories shows that there is a preferred cone of reaction at the F end of the HF molecule. Therefore it is understandable that an increase in J from 0 to 3–5 disrupts the preferred orientation of the reaction, resulting in a drop in the magnitude of S_r. In the absence of any additional effect, we would have expected a leveling off of S_r. However, in this particular case, because of the large vibrational energy present in the molecule, increase in J results in substantial centrifugal distortion. This means a stretching of the FH bond under attack, and the result would be similar to increasing the vibrational energy. For example, when v is changed from 0 to 1 to 2, S_r increases from 0.8 ± 0.2 to 8.7 ± 0.9 to 12.4 ± 1.0 Å^2 at T = 8.7 kcal mol^{-1} for J = 0. This is explained on the basis of the *sudden* character of the PES.[3,11,13] It must be added that such an explanation for the observed dependence of S_r on J was suggested earlier by Blackwell et al.[9] although no dynamical results were available at that time.

At large J, even though the effect of reagent rotation on S_r is qualitatively similar to that of reagent vibration, there is a quantitative difference between the two. In the energy range we have studied, $\Delta S_r/\Delta V$ = 0.5 Å^2/(kcal mol^{-1}) and $\Delta S_r/\Delta R$ = 2.7 Å^2/(kcal mol^{-1}); that is, rotation is nearly 4 times more efficient than vibration in enhancing the reaction cross section. Reagent translation is the least effective in this case with a $\Delta S_r/\Delta T$ value of 0.086 Å^2/(kcal mol^{-1}).

In summary our findings are significant for these reasons: (1) Ours is the first dynamical study of the effect of reagent rotation for a prototype alkali atom–hydrogen halide reaction, on an ab initio PES. (2) Increase in J results in a substantial decrease followed by a rapid increase in S_r, with a minimum occurring around J = 5. The results are in qualitative accord with the experimental results on the related alkali atom–hydrogen halide exchange reactions. (3) For the first time we have shown that reagent rotation can be more effective than reagent vibration in enhancing a reaction.

Registry No. Li, 7439-93-2; FH, 7664-39-3.

(13) Polanyi, J. C.; Sathyamurthy, *N. Chem. Phys.* **1978**, *33*, 287. NoorBatcha, I.; Sathyamurthy, N. *J. Chem. Phys.*, in press.

Total Synthesis of (±)-Pleuromutilin[1]

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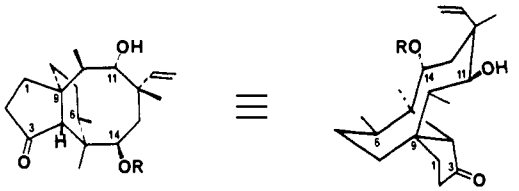
Received December 7, 1981

Pleuromutilin (**1**), an antibiotic isolated from *Pleurotus mutilus*



pleuromutilin (**1**), R = $COCH_2OH$
mutilin (**2**), R = H

and other basidiomycetes, was first reported by Kavanagh in 1951.[2] Derivatives of **1** are currently used as important antimycoplasmal agents in veterinary medicine.[3] Structurally, pleuromutilin is a most intriguing diterpene due to its intricate tricyclic skeleton and rare eight-membered ring.[4–6] Unusual chemistry arising from these structural features has been described by Arigoni in his detailed elucidation of the biogenesis of **1**.[4,7] In this communication we report the first total synthesis of (±)-pleuromutilin (**1**) by an efficient stereoselective route.

Our approach to this tricyclic ring system is based on a sequential Michael strategy which produces in one step the indane nucleus with four of the eight stereocenters of **1**.[8] Thus, treatment of the kinetic enolate of **3**[8] at −70 °C in THF with **4**[9,10] gave the sequential Michael adduct **5** (mp 73–74 °C) as the sole product in 62% yield[11] (see Chart I for structures). Homologation of **5** to the α,β-unsaturated methyl ketone **6** was carried out by means of a four-step sequence. Selective addition of vinyl lithium (THF–Et_2O, −40 °C, 67%), followed by oxidative rearrangement (PCC, CH_2Cl_2, 79%)[12] produced the α,β-unsaturated aldehyde, which was then transformed to **6** by methyl lithium addition (THF, −93 to −80 °C, 82%) and subsequent allylic oxidation (MnO_2, CH_2Cl_2, 88%).[13] Catalytic hydrogenation of **6** (H_2, 10% Pd/Al_2O_3, MgO, 25:1 $CH(OCH_3)_3$–EtOAc, 1 atm)[14] gave the desired

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(1) Abstracted from: Gibbons, E. G. Ph.D Thesis, Harvard University, Cambridge, Massachusetts, 1982.

(2) (a) Kavanagh, F.; Hervey, A.; Robbins, W. J. *Proc. Natl. Acad. Sci. U.S.A.* **1951**, *37*, 570. *Ibid.* **1952**, *38*, 555. (b) For a review of terpenoid metabolites of mushrooms and related basidiomycetes, see: Ayer, W. A.; Browne, L. M. *Tetrahedron* **1981**, *37*, 2199.

(3) Dreyfuss, J.; Singhvi, S. M.; Shaw, J. M.; Egli, P.; Ross, J. J., Jr.; Czok, R.; Nefzger-Biessels, M.; Battig, F.; Schuster, I.; Schmook, F. *J. Antibiot.* **1979**, *32*, 496 and references therein. Riedl, K. *Ibid.* **1976**, *29*, 132 and references therein.

(4) Arigoni, D. *Gazz. Chim. Ital.* **1962**, *92*, 884; *Pure Appl. Chem.* **1968**, *17*, 331. See also: Nageli, P.; Dissertation, ETH 3206, 1961; Bonavia, G. Dissertation, ETH 4189, 1968; Hasler, H. Dissertation, ETH 6359, 1979.

(5) Birch, A. J.; Cameron, O. W.; Holzapfel, C. W.; Rickards, R. W. *Chem. Ind. (London)* **1963**, *374*. Birch, A. J.; Holzapfel, C. W.; Rickards, R. W. *Tetrahedron* **1966**, *22*, 359.

(6) X-ray structure: Dobler, M.; Dürr, B. G. *Cryst. Struct. Commun.* **1975**, *4*, 259.

(7) See also ref 5 for a discussion of the biogenesis of **1**.

(8) Gibbons, E. G. *J. Org. Chem.* **1980**, *45*, 1540.

(9) **4** was synthesized in four steps from 3-methyl-2-cyclohexen-1-ol: (i) $PhCH_2Br$, KH, THF; (ii) O_3, CH_2Cl_2–MeOH, −78 °C; (iii) $(MeO)_3P$, −78 °C; (iv) 5% aqueous NaOH, Et_2O, 24 h, 50% overall.

(10) Satisfactory combustion analyses and spectroscopic data were obtained for all new compounds with the exceptions of **6–8** and **13–25** where the elemental composition was confirmed by high-resolution mass spectrometry. IR and NMR spectra are available as supplementary material.

(11) See ref 8 for a discussion of stereochemistry in the sequential Michael reaction. The stereochemistry at C(3) was later established by correlation with reduced derivatives of mutilin (**2**).[5]

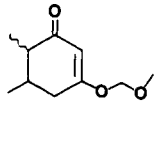
(12) Dauben, W. G.; Michno, D. M. *J. Org. Chem.* **1977**, *42*, 682.

(13) Fatiadi, A. J. *Synthesis* **1976**, 65. Attenburrow, J. et al. *J. Chem. Soc.* **1952**, 1094.

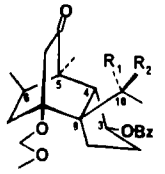
(14) The use of MgO buffer prevented loss of the benzyl group by hydrogenolysis, while the $CH(OCH_3)_3$–EtOAc solvent mixture provided the best stereoselectivity.

0002-7863/82/1504-1767$01.25/0

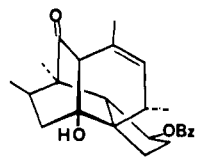
Chart I



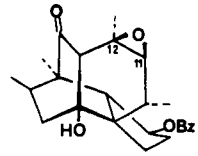
3



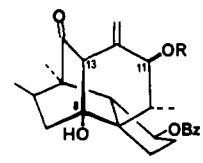
5 R_1, R_2 = O
6 R_1, R_2 = $CHCOCH_3$
7 R_1 = CH_2COCH_3, R_2 = H
8 R_1 = H, R_2 = CH_2COCH_3



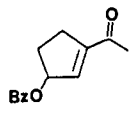
9



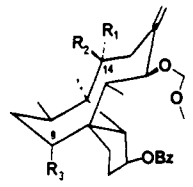
10



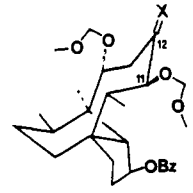
11a R = H
11b R = CH_2OCH_3



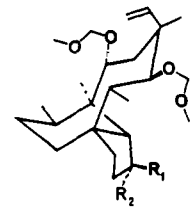
4 Bz = CH_2Ph



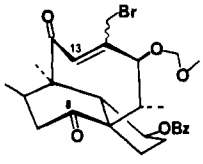
14 R_1 = H, R_2 = OH, R_3 = OH
15 R_1 = H, R_2 = OH, R_3 = OMs
16 R_1 = H, R_2 = OH, R_3 = H
17 R_1, R_2 = O, R_3 = H
18 R_1 = OH, R_2 = H, R_3 = H
19 R_1 = OCH_2OCH_3, R_2 = H, R_3 = H



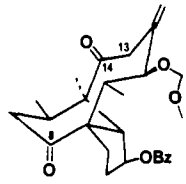
20 X = O
21 X = CHCHO
22 X = $CHCH_2OH$



23 R_1 = OBz, R_2 = H
24 R_1 = OH, R_2 = H
25 R_1, R_2 = O



12



13

methyl ketone **7** (61%) in addition to 22% of the epimer **8**.[15]

Transformation of **7** to the bridged aldol product (K_2CO_3, MeOH, 92%) followed by dehydration to the endo olefin ($POCl_3$, DMAP, pyridine–CH_2Cl_2, 35 °C)[16] and subsequent deprotection of the tertiary hydroxyl (CF_3COOH, CH_2Cl_2, room temperature) gave the homoallylic alcohol **9** (mp 88.5–89.5 °C) in 80% yield. Stereoselective epoxidation of **9** using Sharpless's procedure (*t*-BuOOH, $VO(acac)_2$, benzene, 25 °C) afforded the epoxide **10** (mp 122–123 °C) in 97% yield.[17,18] The required C(11) hydroxyl group was generated by a facile, base-induced elimination (*t*-BuOK, *t*-BuOH–THF, −30 °C) of epoxide **10**, giving the diol **11a** (mp 215 °C dec) in near quantitative yield. Protection of the C(11) hydroxyl as its methoxymethyl ether was carried out at low temperature (KH, $ClCH_2OCH_3$, 3:5.5 DMF–THF, −30 to −20 °C) to give the key tetracyclic intermediate **11b** (mp 134–135 °C) in 71% yield.[19]

Attention was then focused on the next stage of the synthesis, the fragmentation of the C(8)–C(13) bond to generate the required tricyclic skeleton of the natural product.[20] Although initial attempts to effect a direct retroaldol ring opening to the diketone **13** were unsuccessful,[21] further investigation revealed a two-step sequence that resulted in the desired transformation. Treatment of the olefin **11b** with *N*-bromoacetamide (3:1 MeOH–H_2O, NaOAc, 25 °C, 8.5 h) produced the allylic bromide **12** (mp 120–121 °C) as an amorphous white solid.[22] Reduction with zinc dust (1:1 HOAc–MeOH, −20 °C, 0.75 h) afforded the diketone **13** (^{13}C NMR ($CDCl_3$, Me_4Si) δ 212.9, 212.0) in 81% overall yield, thus producing the pleuromutilin ring system.[23,24]

The removal of the carbonyl group at C(8) and the generation of the required hydroxyl at C(14) were carried out in a five-step sequence. Treatment of the diketone **13** at −60 °C with DIBAH (5 equiv, CH_2Cl_2, 10 min) gave the diol **14** (mp 126–127.5 °C) in quantitative yield. Selective mesylation of the hydroxyl at C(8) (5 equiv of MsCl, CH_2Cl_2–pyridine, 0 °C, 2 h) followed by reduction (4 equiv of $LiAlH_4$, Et_2O, 0–25 °C, 2 h) afforded the epialcohol **16** in 68% yield over two steps.[25] Inversion of the hydroxyl group at C(14) to the desired configuration was accomplished by oxidation (PCC,[26] CH_2Cl_2, 12 h) and subsequent reduction (excess Na wire, 5% Na/Hg catalyst, EtOH, 25 °C, 2 h) to give **18** in 88% yield.[27] Alcohol **18** was then protected as its methoxymethyl ether **19** ($BrCH_2OCH_3$, *i*-Pr_2NEt, CH_2Cl_2, reflux, 24 h) in 95% yield.

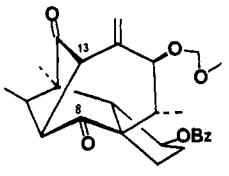
The final stage of the synthesis, the incorporation of the quaternary vinyl methyl center at C(12), required extensive experimentation.[28] It was found that alkylation methods proceeding through a carbanion at C(12) resulted in quantitative elimination

(15) This assignment of stereochemistry at C(10) was confirmed at a later stage by an analysis of NMR coupling constants in the epoxides **10** and i; see reference 18.

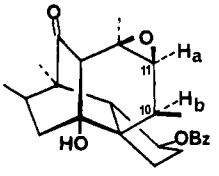
(16) Greenlee, M. L. *J. Am. Chem. Soc.* **1981**, *103*, 2425 (footnote 23 therein).

(17) Sharpless, K. B.; Michaelson, R. C. *J. Am. Chem. Soc.* **1973**, *95*, 6136. Sharpless, K. B.; Verhoeven, T. R. *Aldrichimica Acta* **1979**, *12*, 63.

(18) Dreiding models indicate a C(10)–H_b/C(11)–H_a vicinal angle of 90° in **10** which is consistent with the observed coupling constant $J_{a,b}$ = 0 Hz. Similarly, in the methyl epimer i (derived from **8**—see ref 15) there is a 28° vicinal angle, with the coupling constant $J_{a,b}$ = 4.7 Hz.



i



ii

(19) In addition, 22% of recyclable di-O-alkylated product and diol **11a** were recovered.

(20) For a review of fragmentation reactions see: Grob, C. A. *Ang. Chem., Int. Ed. Engl.* **1969**, *8*, 535. Grob, C. A.; Schiess, P. W. *Ibid.* **1967**, *6*, 1.

(21) It would appear that the closed form **11b** is the thermodynamic product; see ref 24.

(22) The actual mechanism of this Grob fragmentation sequence and its general applicability are unknown. The reaction was observed in the course of an attempted epoxidation of olefin **11b** via the bromohydrin, cf.: Carlson, R. G.; Ardon, R. *J. Org. Chem.* **1971**, *36*, 216. Although the bromide **12** appears to be a pure compound, the stereochemistry has not been determined. Treatment of **12** with KOH/MeOH afforded the bridged diketone ii (mp 130–131 °C, 89%).

(23) The use of NH_4Cl instead of HOAc as a proton source resulted in substantial amounts of **11b** in addition to **13**.

(24) Diketone **13** can be cyclized quantitatively to the aldol product **11b** on treatment with KOH/MeOH at room temperature (8 h).

(25) An examination of Dreiding models supports the feasibility of the intramolecular delivery of hydride in the reduction of **15**.

(26) Corey, E. J.; Suggs, J. W. *Tetrahedron Lett.* **1975**, 2647.

(27) Only 2–4% of the epialcohol **16** was obtained under these conditions. Other reducing agents were either unreactive or gave **16** exclusively.

(28) For a recent review on the formation of quaternary centers, see: Martin, S. F. *Tetrahedron* **1980**, *36*, 419. Magid, R. M. *Ibid.* **1980**, *36*, 1901.

of the adjacent alkoxy group at C(11).[29] Conversely, quaternization methods requiring carbonium ion character at C(12) were unsuccessful, possibly due to the inductive nature of the C(11) alkoxy group.[30] The quaternization problem was solved by a two-part sequence which we feel should prove useful in other hindered and sensitive cases of this type. Ozonolysis of **19** (MeOH–CH_2Cl_2, −78 °C), followed by immediate reduction of the hydroperoxide ($P(OCH_3)_3$, −78 °C), produced the ketone **20** (mp 109–110 °C) in near quantitative yield. Addition of **20** to (*Z*)-[2-ethoxyvinyl]lithium (50 equiv, THF, −35 to −30 °C, 0.5 h), followed by acid hydrolysis (1:2 20% H_2SO_4(aq)–THF) gave the α,β-unsaturated aldehyde **21** in 50% yield.[31] Reduction with DIBAH (CH_2Cl_2, 0 °C, 95%) yielded the allylic alcohol **22** (mp 122–123 °C). By means of Murahashi's γ-alkylation procedure (CuI, MeLi, n-$Bu_3P^+N(CH_3)Ph\ I^-$, THF), the allylic alcohol **22** was converted exclusively to the desired epimer **23** in 50% yield.[32] Transformation of **23** to mutilin (**2**) was carried out in three steps. Removal of the benzyl group (Li, NH_3(liq)), followed by oxidation of **24** (PCC, CH_2Cl_2) produced the ketone **25**. Finally, deprotection of **25** (3% HCl–EtOH, 25 °C) gave (±)-mutilin (**2**) as a white crystalline solid (mp 187–189.5 °C, CH_2Cl_2/hexane, 80% overall yield), spectroscopically indistinguishable (IR, ^1H NMR, ^{13}C NMR, MS) from the naturally derived material.[4,5] Mutilin was converted to pleuromutilin (**1**) by diesterification ($AcOCH_2COOH$, MsCl, DMAP, pyridine–THF, 25 °C)[33] and mild hydrolysis (5% KOH–MeOH, 25 °C, 12 h).[34]

Acknowledgment. The author is indebted to the late Professor R. B. Woodward for his guidance and support (National Science Foundation Grant CHE 78-25699), to Professor Y. Kishi for valuable advice and encouragement, and to Professor D. Arigoni for generous assistance and a gift of pleuromutilin.

Registry No. 1, 80924-94-3; **2**, 80924-95-4; **3**, 73192-77-5; **4**, 80878-23-5; **5**, 80878-24-6; **5**, α,β-unsaturated aldehyde derivative, 80878-25-7; **6**, 80890-19-3; **7**, 80890-20-6; **7**, bridged aldol product, 80890-21-7; **7**, endo olefin product, 80906-62-3; **8**, 80951-30-0; **9**, 80890-22-8; **10**, 80878-26-8; **11a**, 80878-27-9; **11b**, 80878-28-0; **12**, 80890-23-9; **13**, 80878-29-1; **14**, 80878-30-4; **15**, 80878-31-5; **16**, 80878-32-6; **17**, 80878-33-7; **18**, 80924-96-5; **19**, 80878-34-8; **19**, hydroperoxide derivative, 80878-35-9; **20**, 80878-36-0; **21**, 80878-37-1; **22**, 80878-38-2; **23**, 80878-39-3; **24**, 80878-40-6; **25**, 80878-41-7; i, 80878-42-8; ii, 80924-97-6.

Supplementary Material Available: NMR and IR spectra of new compounds described in this paper (32 pages). Ordering information is given on any current masthead page.

(29) For example, (a) Alkylation of the C(12) carbaldehyde, cf.: Groenewegen, P.; Kallenberg, H.; van der Gen, A. *Tetrahedron Lett.* **1978**, 491 and references therein. Dietl, H.; Brannock, K. C. *Ibid.* **1973**, 1273. (b) Alkylation of C(12) carbaldimine and metalloenamine equivalents, cf.: House, H. O.; Liang, W. C.; Weeks, P. D. *J. Org. Chem.* **1974**, *39*, 3102. Stork, G.; Dowd, S. R. *J. Am. Chem. Soc.* **1963**, *85*, 2178. Martin, S. F.; Phillips, G. W.; Puckette, T. A.; Colapret, J. A. *Ibid.* **1980**, *102*, 5866 and references therein. (c) Quaternization via 2,3-sigmatropic rearrangement of the vinyl sulfonium ylides was unsuccessful, resulting in E2′ elimination of the C(11) alkoxy group, cf.: Evans, D. A.; Sims, C. L.; Andrews, G. C. *J. Am. Chem. Soc.* **1977**, *99*, 5453 and references therein.

(30) See for example: Felkin, H. et al. *J. Am. Chem. Soc.* **1978**, *100*, 6445. Nagata, W.; Mitsuru, Y.; Okumura, T. *Tetrahedron Lett.* **1966**, 847. Cantacuzene, J.; Normant, J. *Ibid.* **1970**, 2947. Namy, J. L.; Boireau, G.; Abenhaim, D. *Bull. Soc. Chim. Fr.* **1971**, 3191 and references therein.

(31) Lau, K. S. Y.; Schlosser, M. J. *J. Org. Chem.* **1978**, *43*, 1595. Ketone **20** was found to be practically unreactive with $(MeO)_2PO$–$CH^-COOMe\ Li^+$ and TMS–$CH^-COOEt\ Li^+$ even under forcing conditions: Shimoji, K.; Taguchi, H.; Oshima, K.; Yamamoto, H.; Nozaki, H. *J. Am. Chem. Soc.* **1974**, *96*, 1620.

(32) Tanigawa, Y.; Ohta, H.; Sonoda, A.; Murahashi, S. *J. Am. Chem. Soc.* **1978**, *100*, 4610. Approximately 20% of **22** was recovered in addition to ~20% of the α-alkylation product. Assuming the boat-chair conformation for the eight-membered ring[6] (as drawn), γ alkylation was anticipated from an examination of models to occur from the less hindered pseudoequatorial face of the olefin.

(33) Anschütz, R.; Bertram, W. *Ber. Dtsch. Chem. Ges.* **1903**, *36*, 466. Brewster, J. H.; Ciotti, C. J. *J. Am. Chem. Soc.* **1955**, *77*, 6214.

(34) Cf. Riedl, K. *J. Antibiot.* **1976**, *29*, 132. Egger, H.; Reinshagen, H. *Ibid.* 915.

Oxidation of Ketals to Orthocarbonates: A Double Baeyer–Villiger Reaction

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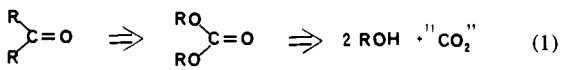
In contrast to the classical Baeyer–Villiger oxidation[1] of ketones to esters, no simple methodology exists for the double oxidation of ketones to carbonates. Herein we report that the formal equivalent of a "double" Baeyer–Villiger reaction is easily accomplished under mild conditions by oxidation of diethyl ketals with peroxycarboxylic acid. This facile double oxidation of ketals to orthocarbonates provides an efficient method for the removal of a carbonyl function from a ketone (see eq 1).



(1)

The oxidation of the symmetrical ketal 3,3-diethoxypentane[2] (**1**) is illustrative of the general reaction.[3] Addition of **1** to a well-stirred suspension of excess (3–4 molar equiv) *m*-chloroperoxybenzoic acid (MCPBA) in dry CH_2Cl_2 (200–250 mL for a 50-mmol scale oxidation) results in an exothermic reaction in which virtually all of the ketal is consumed. The oxidation may become very vigorous following an induction period of 10–30 min (vide infra) and it is often necessary to use an ice-water bath to moderate the exotherm and maintain the reaction temperature between 15–30 °C. After complete oxidation,[4] the entire reaction mixture was poured into a large excess of rapidly stirred, ice-cold 5% aqueous NaOH (ca. 1 L for a 50-mmol scale oxidation). The organic layer was separated, washed successively with 15% aqueous Na_2SO_3 and brine, dried (K_2CO_3), and concentrated. The oxidation of **1** afforded a mixture of products consisting chiefly of diethyl carbonate (**3**), tetraethyl orthocarbonate (**2**), and ethyl *m*-chlorobenzoate along with a small amount of ethyl propionate and 3-pentanone. The carbonate and orthocarbonate may be isolated in a combined yield of 70% (Table I). The low yield of **2** is not unexpected since ortho esters are known to esterify carboxylic acids, producing carbonates and alcohol:[5] $R'CO_2H + (RO)_4C \rightarrow R'CO_2R + (RO)_2C{=}O + ROH$.

The destruction of orthocarbonates via reaction with *m*-chlorobenzoic acid generated from MCPBA is unavoidable.[6] Thus, when less symmetric ketals are oxidized, product separation is often difficult since a mixture of all possible carbonates, benzoates, and alcohols is produced. Although carbonates and esters constitute the bulk of the product mixture, moderate yields (25–40%) of pure orthocarbonates[7] not generally available by other routes[8]

(1) For reviews of the Baeyer–Villiger reaction see: (a) Hassall, C. H. *Org. Reactions* (*N.Y*) **1957**, *9*, 73. (b) Smith, P. A. In "Molecular Rearrangements"; de Mayo, P., Ed.; Wiley-Interscience: New York, 11963, Vol. 1, p 577. (c) Lee, J. B.; Uff, B. C. *Q. Rev., Chem. Soc.* **1967**, *21*, 429. (d) Plesnicar, B. In "Oxidation in Organic Chemistry"; Trahanovsky, W. S., Ed.; Academic Press: New York, 1978; part C, p 254.

(2) Carswell, H. E.; Adkins, H. *J. Am. Chem. Soc.* **1928**, *50*, 235.

(3) Diethyl ketals were prepared in high yield from equimolar amounts of ketone and triethyl orthoformate dissolved in excess anhydrous ethanol containing a catalytic quantity of anhydrous HCl generated by addition of acetyl chloride to the dry ethanol.

(4) Oxidations were run until virtually no ketal remained as adjudged by GC or TLC. It should be noted that prolonged reaction times may lead to a variety of secondary products derived from further reaction of the acid labile orthocarbonates, alcohols, etc.

(5) (a) Cohen, H.; Mier, J. D. *Chem. Ind.* (*London*) **1965**, 349. (b) Kantlehner, W.; Funke, B.; Haug, E.; Spek, P.; Kienitz, L.; Maier, T. *Synthesis* **1977**, 73.

(6) Obvious benefit would derive from the use of an oxidant whose reduced form does not react with the orthocarbonate product, and we are actively evaluating other oxidizing agents for use in the ketal → orthocarbonate conversion.

(7) Satisfactory C and H analyses and/or exact mass spectroscopic molecular weights have been obtained for all new compounds (**6**, **9**, **11**, **16**), and their IR, ^1H NMR and ^{13}C NMR spectra are in accord with the assigned structures.

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