Table I. Frequencies of the Absorption Maxima for Selected Dipolarity-Polarizability Indicators in the Gas Phase

indicator[a]	$\bar{\nu}_0$[b]	$\bar{\nu}_{gas}$[b,f]	s[c]	π^*_{gas}[d]
1	34.12[c]	36.90[e]	2.410	−1.15
6	27.52[c]	30.39[h,e]	3.182	−0.902
9	33.31[c]	34.84[e]	1.407	−1.07
14	31.10[c]	34.48[e]	3.138	−1.08
20	36.85[c]	38.14[e]	1.297	−0.995
28	28.87[c]	30.90[e]	1.741	−1.17
1b	34.97[c]	37.31[e]	2.171	−1.08
28b	26.18[c]	28.30[e]	2.212[g]	−0.958

[a] Numbered as in ref 6. [b] In kK. [c] See eq 1 and ref 6. [d] Obtained through eq 1; see text. [e] This work. [f] Estimated uncertainty: 0.15 kK. [g] See ref 9. [h] See ref 10.

atures between 25 and 72 °C in order to establish the absence of thermal decomposition and abnormal thermochromism and in "FC 75" (a mixture of the positional isomers of perfluoro-*n*-propyloxane) in order to assess the influence of the medium on the vibrational structure of the spectra. The experimental results are given in Table I. These data can be analyzed in different ways, and in a future paper we shall develop our own approach. Here, we wish to stress the following points:

(1) The gas-phase values, taken together with those from previous works[5,6] on the same PPI's, provide the widest set of medium effects on electronic transitions of polar molecules ever reported.

(2) The PPI's examined herein belong to the family of compounds used to construct the π^* scale. It has been shown[6] that for these indicators, the expression

$$\bar{\nu}_A = \bar{\nu}_0 + s\pi^*_A \quad (1)$$

holds to a high degree of precision. $\bar{\nu}_A$ stands for the wavenumber (in kK) of the near-UV absorption maximum in solvent A; within experimental error, $\bar{\nu}_0$ is the corresponding wavenumber in cyclohexane, taken as a reference ($\pi^*_{c\text{-}C_6H_{12}} = 0$), and s measures the sensitivity of the electronic transition to pority-polarizability effects. Equation 1 can be applied to the above gas-phase data to generate the values for π^*_{gas} given in Table I. Considering the enormous extrapolation involved, the agreement between the different results is quite good, and the average value, $\pi^*_{gas} = -1.06 \pm 0.10$, seems reliable.

(3) To our knowledge, the only scale covering the same range of medium effects hitherto available was Allerhand and Schleyer's G[11a] based on IR frequency shifts. We find that the already reported excellent correlation between π^* and G can be extended to the gas phase. Thus, if hydrogen-bonding acids are excluded, the following expression is obtained:

$$G = 51.52 + 51.53\pi^* \text{ cm}^{-1}$$

with number of points $n = 13$ (including the gas phase),[11b] a correlation coefficient, $r = 0.9941$, and a standard deviation $\sigma = 3$ cm^{-1}. Obviously, the extension of the scale is not detrimental to its correlational power.

(4) Finally, it is important to consider that this method can be applied to a large number of polar compounds having relatively high boiling and melting points. This opens many interesting possibilities in different fields.

Acknowledgment. We are grateful to Dr. Mortimer J. Kamlet (Naval Surface Weapons Center, Silver Spring, MD) and to Professor Louis Bellon (University of Brest, France) for generous gifts of some of the indicators used in this study.

Registry No. 1b, 100-02-7; **4**, 100-17-4; **6**, 2216-15-1; **9**, 10287-53-3; **14**, 100-01-6; **20**, 94-09-7; **28**, 99-09-2; **28b**, 619-31-8.

(9) Estimated from the data for *N,N*-dimethyl-4-nitroaniline (**13**), **14**, **6**, **3**, and *N,N*-diethyl-3-nitroaniline (**2**).

(10) The near-UV spectra of solutions of **6** show a broad, flat maximum. In the gas phase and in FC 75, this maximum is resolved into a doublet. For the sake of consistency with solution data, we have taken $\bar{\nu}_{gas}$(**6**) at the center of the doublet.

(11) (a) Allerhand, A.; Schleyer, P. v. R. *J. Am. Chem. Soc.* **1963**, *85*, 374. (b) All the available data points.

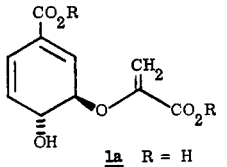
Total Synthesis of (±)-Chorismic Acid[1]

Bruce Ganem,* Nobuo Ikota, V. B. Muralidharan, Warren S. Wade, Stanley D. Young, and Yusuke Yukimoto

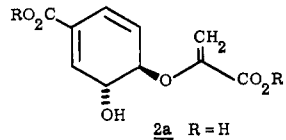
Department of Chemistry, Baker Laboratory Cornell University, Ithaca, New York 14853

Received August 2, 1982

The metabolism of shikimic acid in microorganisms and plants produces an exquisite array of biochemically important natural products.[2] Among them chorismic acid (**1a**) occupies a strategic



1a R = H
1b R = CH_3



2a R = H
2b R = CH_3

position in the shikimate pathway as the key branch point intermediate governing the biosynthesis of aromatic amino acids, isoprenoid quinones, bacterial growth promoters, and other vital compounds.[3] For some time we have been interested in the chemistry of chorismic acid[4] and in processes that affect its metabolism[5] because of the promising potential in this area for designing bacterial and plant growth regulators. We now report an efficient, stereoselective total synthesis[6] of **1a** that is suitable for preparing isotopically labeled material. Its unnatural isomer, pseudochorismic acid **2a**, has also been synthesized to probe the specificity of the enzyme chorismate mutase, which promotes the facile in vivo Claisen rearrangement of **1a**.[2a]

Bicyclic allylic alcohol **3** (Chart I) was prepared in four steps and 35% yield from 1,4-dihydrobenzoic acid.[4a] Protection of the hydroxyl as its MEM ether **4**, saponification, and esterification produced hydroxy ester **8** as a stable oil in 64% yield from **3**.[4b] Attachment of the enol pyruvate side chain proved to be difficult but was eventually achieved in stepwise fashion as follows. Coupling of **8** with dimethyl diazomalonate (1.2 equiv) was smoothly catalyzed by rhodium acetate (C_6H_6, 65 °C, 2.5 h)[7] and afforded alkoxy malonate **9** as a waxy solid (75%, mp 35–37 °C).[8] Heating unpurified **9** in moist benzene with *p*-TsOH hydrolyzed the MEM group and cyclized the malonyl side chain in one operation to bicyclic lactone **10** (mixture of epimers, 35% after flash CC). Attempts to alkylate **10** using Eschenmoser's salt [$CH_2{=}{}^+N(CH_3)_2I^-$][9] with or without triethylamine caused aromatization, probably initiated by iodide attack on the ring. The problem was circumvented by employing Potier's salt [$CH_2{=}{}^+N(CH_3)_2CF_3CO_2^-$],[10] which furnished a 4:1 mixture of Mannich base **11** and methyl *m*-enolpyruvylbenzoate. Quaternization of the amine (FSO_2OCH_3, $CDCl_3$, NMR monitoring) afforded **12**, which could be purified by extraction into H_2O (37% from **10**).

(1) Part 11 in the series "Shikimate-Derived Metabolites". For Part 10, see ref 5.

(2) For recent reviews, see: (a) Ganem, B. *Tetrahedron* **1978**, *34*, 3353–3383. (b) Weiss, U.; Edwards, J. M. "The Biosynthesis of Aromatic Compounds"; Wiley: New York, 1980. (c) Haslam, E. "The Shikimate Pathway"; Halstead Press, Wiley: New York, 1974.

(3) (a) Gibson, F. *Methods Enzymol.* **1970**, *17A*, 362–364 and references cited therein. (b) Edwards, J. M.; Jackman, L. M. *Aust J. Chem.* **1965**, *18*, 1227–1239.

(4) (a) Ikota, N.; Ganem, B. *J. Am. Chem. Soc.* **1978**, *100*, 351–352. (b) Ikota, N.; Ganem, B. *J. Chem. Soc., Chem. Commun.* **1978**, 869–870.

(5) Teng, C.-Y. P.; Ganem, B. *Tetrahedron Lett.* **1982**, *23*, 313–316.

(6) The first total synthesis of **1** was recently reported: McGowan, D. A.; Berchtold, G. A. *J. Am. Chem. Soc.* **1982**, *104*, 1153–1154.

(7) Paulissen, R.; Reimlinger, H.; Hayez, E.; Hubert, A. J.; Teyssiê, Ph. *Tetrahedron Lett.* **1973**, 2233–2236.

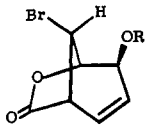
(8) Satisfactory spectral and analytical data have been obtained for all new substances described.

(9) Schreiber, J.; Maag, H.; Hashimoto, N.; Eschenmoser, A. *Angew. Chem., Int. Ed. Engl.* **1971**, *10*, 330–331.

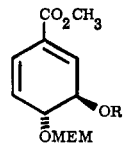
(10) Ahond, A.; Cavê, A.; Kan-Fan, C.; Husson, H.-P.; deRostolan, J.; Potier, P. *J. Am. Chem. Soc.* **1968**, *90*, 5622–5623.

0002-7863/82/1504-6787$01.25/0

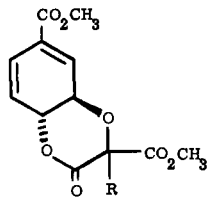
Chart I



3 R = H
4 R = MEM
5 R = $CH(CO_2CH_3)_2$
6 R = $C(CO_2CH_3)_2CH_2N(CH_3)_2$
7 R = $C(CH_2)CO_2CH_3$



8 R = H
9 R = $CH(CO_2CH_3)_2$



10 R = H
11 R = $CH_2N(CH_3)_2$
12 R = $CH_2\overset{\oplus}{N}(CH_3)_3\,{}^{\ominus}OSO_2F$

Next, a one-pot hydrolysis, decarboxylation, and β elimination in base was expected to create the enol pyruvate appendage. Indeed, when **12** was stirred with a measured quantity of base (1.5 equiv of NaOH–H_2O, 90 min, 0 °C) the initially clear solution became turbid, and $CDCl_3$ extraction gave a nearly pure sample of dimethyl chorismate **1b** in 37% yield from **12** (25% after preparative SiO_2 TLC at 5 °C). This material was spectroscopically indistinguishable from an authentic sample of the optically active diester **1b**,[11] which we and Berchtold et al.[6] have independently reconverted to **1a** (NaOH, THF–H_2O, 0 °C); 10–30%). Under fully homogeneous conditions (NaOH, THF–H_2O, 0 °C), the hydrolysis of **12** produced chorismic acid directly to complete the synthesis in 12 steps from 1,4-dihydrobenzoic acid.

Pseudochorismic acid **2a** was also readily available from allylic alcohol **3** via malonate **5** and Mannich base **6** according to the above mentioned protocol [$N_2C(CO_2CH_3)_2$, $Rh_2(OAc)_4$, 70%; $CH_2{=}{}^{+}N(CH_3)_2I^-$, CH_2Cl_2, reflux, 84%]. Quaternization of **6** (CH_3I, CH_2Cl_2, reflux), then thermolysis in Me_2SO (95 °C, 8 h) gave the bicyclic enol pyruvate **7** (mp 121–122 °C) in 73% yield from **6**. Saponification of **7** (3 equiv of NaOH, 3:1 THF–H_2O, 0 °C, 2 h; room temperature, 12 h) with concomitant HBr elimination furnished **2a** as a solid (89% yield) contaminated with variable amounts of *m*-hydroxybenzoic acid. Recrystallization from EtOAc–hexane gave pure **2a** (72%; mp 125–127 °C). As might be expected, the NMR characteristics of **1** and **2a** were remarkably similar.

Further aspects of the chemistry and biochemistry of **1a** and **2a** will be reported in due course.

Acknowledgment. We thank the National Institutes of Health, the American Cancer Society, Eli Lilly and Company, and the A. P. Sloan Foundation for generous financial assistance. Support of the Cornell Nuclear Magnetic Resonance Facility by the National Science Foundation (CHE 7904825) is gratefully acknowledged.

Registry No. (±)-**1a**, 80657-95-0; (±)-**1b**, 80631-87-4; (±)-**2a**, 83573-29-9; (±)-**3a**, 65825-61-8; (±)-**4**, 83573-19-7; (±)-**5**, 83573-26-6; (±)-**6**, 83573-27-7; (±)-**7**, 83573-28-8; (±)-**8**, 83573-20-0; (±)-**9**, 83573-21-1; (±)-**10** (β-COOMe), 83573-22-2; (±)-**10** (α-COOMe), 83602-87-3; **11**, 83573-23-3; **12**, 83573-25-5; $CH_2{=}N^+(CH_3)_2{\cdot}CF_3CD_2^-$, 25468-31-9; dimethyl diazomalonate, 6773-29-1; methyl *m*-enolypyruvylbenzoate, 16929-33-2.

Supplementary Material Available: Listing of physical and spectral data and experimental details for key intermediates (4 pages). Ordering information is given on any current masthead page.

(11) Ife, R. J.; Ball, L. F.; Lowe, P.; Haslam, E. *J. Chem. Soc., Perkin Trans. 1*, in press.

Evidence for a Single-Electron-Transfer Mechanism in Aldol Condensation Reactions

E. C. Ashby,* J. N. Argyropoulos, G. Richard Meyer, and A. B. Goel

School of Chemistry, Georgia Institute of Technology Atlanta, Georgia 30332

Received April 22, 1982

The condensation of an aldehyde or ketone in the presence of a base (Aldol condensation) is an important synthetic reaction, the mechanism of which is considered to be polar in nature.[1,2] Nevertheless, the ability of enolate anions to transfer a single electron to various organic substrates is well documented.[3-6] Recently, we reported the involvement of a single-electron-transfer (SET) mechanism in reactions of various nucleophiles with aromatic ketones.[7-9] We now report evidence consistent with the involvement of a SET mechanism in aldol condensation reactions involving enolate nucleophiles with aromatic ketones.

When the lithium enolates of 2,2-dimethyl-3-butanone (pinacolone, A) and 2,2-dimethyl-3-pentanone (B) were allowed to react with benzophenone (C), 2,4-dimethylbenzophenone (D), and mesityl phenyl ketone (E), EPR active species were generated in all cases. For example, when enolate B was allowed to react with benzophenone in a 1.5:1 mole ratio, respectively, in THF at 25 °C, a blue color appeared within a few hours. This colored solution gave rise to a well-resolved EPR spectrum, as well as a visible spectrum (λ_{max} 632 nm), both of which are similar to the EPR and visible spectra recorded for an authentic sample of lithium benzophenone ketyl (prepared by the rxn of lithium metal with benzophenone in THF). The concentration of the free ketyl (H) reached a maximum after 1 week and was calculated to be approximately 10% relative to benzophenone.[10] After this period of time when the reaction was quenched, benzophenone was recovered in nearly quantitative yield.

In contrast, the reaction of enolate A with benzophenone under exactly the same conditions gave a high yield (90%) of the condensation product, 4,4-dimethyl-1,1-diphenyl-1-penten-3-one (F) in 3 days. EPR analysis of the reaction mixture showed the existence of a paramagnetic species formed in small (~0.1%) concentration. The signal was too weak to resolve. Figure 1 shows

(1) House, H. O. "Modern Synthetic Reactions"; W. A. Benjamin; Menlo Park, CA 1972.
(2) Caine, D. S. In "Carbon–Carbon Bond Formation"; Augustine, R. L., Ed.; Marcel Dekker: New York, 1979; Vol. I.
(3) Russell, G. A.; Janzen, E. G.; Strom, E. T. *J. Am. Chem. Soc.* **1964**, *86*, 1807.
(4) Russell, G. A.; Mudryk, B.; Jawdosiuk, M. *J. Am. Chem. Soc.* **1981**, *103*, 4610.
(5) Kornblum, N. *Angew, Chem., Int. Ed.* **Engl. 1975**, *14*, 734.
(6) Bunnett, J. F.; Singh, P. *J. Org. Chem.* **1981**, *46*, 5022 and references cited therein.
(7) Ashby, E. C.; Goel, A. B.; DePriest, R. N. *Tetrahedron Lett.* **1981**, *22*, 4355.
(8) Ashby, E. C., Goel, A. B.; Park, W. S. *Tetrahedron Lett.* **1981**, *22*, 4209.
(9) Ashby, E. C.; Goel, A. B.; Argyropoulos, J. N. *Tetrahedron Lett.* **1982**, *23*, 2273.
(10) The standard used was 2,2,5,5-tetramethylpyrrolidine-3-carboxamide 1-oxy in THF. The peak heights of the ketone radical and standard were compared.

0002-7863/82/1504-6788$01.25/0