the presence of the surfactant cetyltrimethylammonium bromide (CTAB, cmc 9×10^{-4} m, 25 °C). Rate constants and activation parameters are listed in Table I. As anticipated,[14] the rate of hydrolysis is retarded upon binding of 1 to the CTAB micelles. Most likely the reduced micropolarity in the Stern region of the micelles should be invoked to explain the rate inhibition.[14] Plots of $\Delta^{\ddagger}H^{\ominus}$ and $-T\Delta^{\ddagger}S^{\ominus}$ as a function of [CTAB] are depicted in Figure 2. Largely compensatory changes set in around the cmc, but, interestingly, the signs of these changes are *opposite* to those found for n-Bu_4NBr above the chic. In order to understand this difference, we note that the micellar surface may be apprehended as a concentrated electrolyte solution[15] as reflected, inter alia, in the reduced dielectric constant in the Stern region ($\epsilon \sim 32$).[16] As shown in Figure 1, the changes in $\Delta^{\ddagger}H^{\ominus}$ and $-T\Delta^{\ddagger}S^{\ominus}$ reverse their sign above the so-called "magic mole fraction" (ca. 0.85 m) for aqueous n-Bu_4NBr, and this tendency extents to 1.8 m n-Bu_4NBr. Unfortunately, no reliable activation parameters could be determined beyond this concentration because of phase separation. Therefore, $\Delta^{\ddagger}H^{\ominus}$ and $\Delta^{\ddagger}S^{\ominus}$ were measured in 2.00 m aqueous Me_4NBr (Table I) and, indeed, at this high electrolyte concentration both $\Delta^{\ddagger}H^{\ominus}$ and $\Delta^{\ddagger}S^{\ominus}$ are *larger* than in pure water in accord with the results for the hydrolysis in the Stern region of the CTAB micelles.

On the basis of the present kinetic data, the difference between aqueous solutions of n-Bu_4NBr and CTAB as reaction media can be conceived as follows. At the low concentrations of CTAB below the cmc, reaction rates hardly respond to the presence of the electrolyte. At the cmc, micelles are being formed which bind the substrate effectively.[18] The substrate then reacts in a relatively concentrated electrolyte solution at micellar binding sites of reduced micropolarity, and the rate constants are substantially reduced. In the 0–1.8 m aqueous n-Bu_4NBr solutions no micelles are formed and there is no critical concentration for the initiation of rate inhibition. Instead the rate constants decrease gradually as a result of changes in hydration effects operating on the activation process. However, there is a threshold concentration for the outset of large changes in $\Delta^{\ddagger}H^{\ominus}$ and $\Delta^{\ddagger}S^{\ominus}$ which reflects overlap of hydration shells, particularly those of the hydrophobic cations. This concentration is the chic. The activation parameters then pass through extrema at ca. 0.85 m. At still higher concentrations of n-Bu_4NBr the solutions are loosing the characteristics of typically aqueous media as dominated by the presence of extensive, three-dimensional hydrogen-bond networks. The hydrolysis then proceeds in a concentrated electrolyte solution, and the rates are more and more governed by changes in $\Delta^{\ddagger}H^{\ominus}$ and $\Delta^{\ddagger}S^{\ominus}$ which are opposite in sign to those at the lower concentrations of n-Bu_4NBr.

Experimental Section

Materials. Tetra-n-butylammonium bromide and tetramethylammonium bromide were obtained from Janssen Chimica and Fluka, respectively, and were used as such. Cetyltrimethylammonium bromide (Merck) was purified by using standard procedures.[19] 1-Benzoyl-3-phenyl-1,2,4-triazole (1) was prepared as described previously.[2,7] Demineralized water (distilled twice in an all-quartz unit) was used throughout.

Kinetic Measurements. These were performed as described previously.[2,7] All pseudo-first-order rate constants (in triplicate; in the temperature range 20–40 °C) were reproducible to within 1%. A Perkin-Elmer λ5 spectrophotometer, equipped with a Perkin-Elmer 3600 data station was employed.

Acknowledgment. We thank Dr. J. R. Haak for useful discussions.

(14) Attempts to measure the chic via the temperature dependence of the Dimroth–Reichardt solvent parameter $E_T(30)$[3] failed because n-Bu_4NBr precipitated in the alkaline solutions.
(15) Fadnavis, N.; Engberts, J. B. F. N. *J. Org. Chem.* **1982**, *47*, 152.
(16) For CTAB the degree of counterion binding is ca. 0.7. For a discussion of the ion distribution around the micellar surface, see ref 5, pp 71, 72.
(17) Fernandez, M. S.; Fromherz, P. *J. Phys. Chem.* **1977**, *81*, 1755.
(18) Previously,[15] we found $K = 1.4 \times 10^5$ M^{-1}, where K is the substrate–micelle association constant divided by the aggregation number of the CTAB micelles.
(19) Duynstee, E. F. J.; Grunwald, E. *J. Am. Chem. Soc.* **1959**, *81*, 4540.

Equilibria among Anions of α-Hydroxy β-Diketones and α-Ketol Esters

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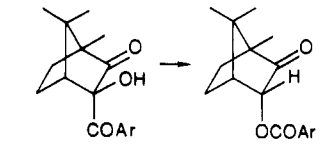
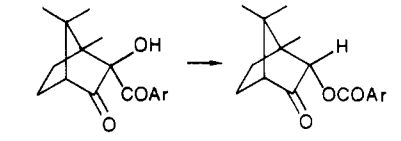
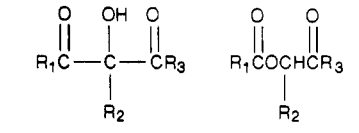
We have reported[1] thermal and base-catalyzed rearrangements of α-hydroxy β-diketones to α-ketol esters. Quantitative isomerizations of compounds **1a** to **2a**, of **1b** to **2b**, and of related compounds in the bicyclo[2.2.2]octane series resulted after 1 min at 200 °C or 10 min at room temperature in 5×10^{-3} N potassium hydroxide in methanol. Slower rearrangement of diacetylmethylcarbinol (**3a**) to acetoin acetate (**4a**) was also observed.



1a **2a**



1b **2b**



3 **4**

a, $R_1 = R_2 = R_3 = CH_3$
b, $R_1 = R_3 = C_6H_5$, $R_2 = H$
c, $R_1 = R_3 = C_2H_5$, $R_2 = CH_3$
d, $R_1 = CH_3$, $R_2 = R_3 = C_6H_4CH_2$
e, $R_1 = C_6H_5$, $R_2 = R_3 = CH_3$
f, $R_1 = R_2 = CH_3$, $R_3 = C_6H_5$
g, $R_1 = R_3 = CH_3$, $R_2 = C_6H_5$

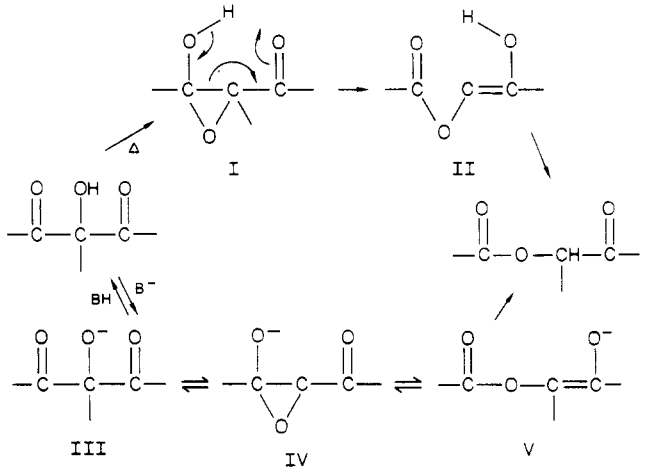
Three examples of thermal rearrangements of diacyl carbinols had been reported earlier. In 1936 Blatt and Hawkins[2] obtained α-hydroxyacetophenone benzoate (**4b**) from distillation of dibenzoylcarbinol (**3b**), a result which was repeated by Karrer et al.[3] in 1950; these authors also

(1) Rubin, M. B.; Inbar, S. *Tetrahedron Lett.* **1979**, 5021.
(2) Blatt, A. H.; Hawkins, W. L. *J. Am. Chem. Soc.* **1936**, *58*, 81.
(3) Karrer, P.; Kebrle, J.; Thakkar, H. M. *Helv. Chim. Acta* **1950**, *33*, 1711.

0022-3263/88/1953-3355$01.50/0

proposed a mechanism for the rearrangement. Subsequently, House and Gannon[4] described two additional cases in which distillation of diacylcarbinols **3c,d** provided ketol esters **4c,d** and reaffirmed the mechanistic proposal of Karrer et al. The only previous example of a base-catalysed reaction of this type was due to Karrer et al.,[3] who obtained **4b** from **3b** by reaction in the presence of sodium bicarbonate. Stronger bases afforded the carboxylic acids which could have been formed either by saponification of ester **4b** or by the well-known base-catalyzed cleavage of β-diketones. We now wish to report more complex behavior of such systems as well as observations indicating the existence of a manifold of anionic rearrangements which are accessible by action of base on either hydroxy diketones or ketol esters.

The mechanism proposed[3] for the thermal reaction appears eminently reasonable[5] and accounts for the regio- and stereochemistry observed[1] in the rearrangements of **1a,b**. Initial attack of hydroxyl oxygen on a neighboring carbonyl group affords epoxide I which, via a six-membered, cyclic transition state isomerizes to the enol II followed by ketonization to final product. An analogous

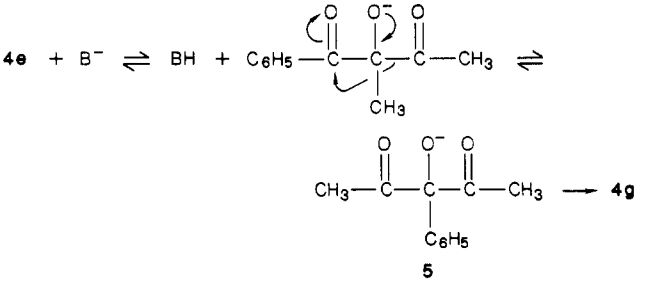


mechanism was suggested for the base-catalyzed reaction, as illustrated, in which reversible formation of alcoholate anion III is followed by reversible formation of epoxide IV, which, again reversibly, can isomerize to the enolate ion V of product ester. In the absence of a suitable proton donor, such a system could be in an equilibrating state until workup. Our attempts to trap intermediate anions as their products of reaction with added trimethylchlorosilane were not successful. Formation of ketol esters in reactions of diphenyl triketone[6] with Grignard reagent or with malonate ion presumably proceed via initial attack on the central carbonyl group of trione followed by α-hydroxy β-diketone rearrangement. A limiting factor in such mechanisms could be the stereoelectronic requirement[7] for back-side attack of a hydroxyl group or of its anion on one of the neighboring carbonyl groups.

Reactions of the unsymmetrical compound, acetylbenzoylmethylcarbinol[8] (**3e**) were more complex, as reported.[1] Heating at 200 °C for 2 h or reaction with sodium hydride in ether[9] produced the two expected ketol esters acetoin *O*-benzoate (**4e**) and α-hydroxypropiophenone acetate (**4f**). However, in both reactions a third product, identified as 1-phenyl-1-hydroxyacetone acetate (**4g**), was obtained. It should be noted that the ratio **4e**:**4f**:**4g**, as determined by NMR analysis, was 1:2:1 in the thermal reaction and 1:0.1:1 in the sodium hydride reaction.

Formation of **4g** may be explained by a known isomerization process[10] of ketol esters in which a pseudoester (or its anion) is formed from enol (or enolate ion) of starting material. Ring opening then can lead to regeneration of starting ester or to formation of its isomer. In the case of the thermal reaction of **3e**, this process would be subject to kinetic control,[11] whereas base-catalyzed reaction in the absence of a proton donor should lead to the thermodynamically more stable product.

An intriguing alternative mechanism for formation of **4g** in the base-catalyzed reaction is rearrangement of alcoholate ion III in a manner analogous to the benzilic acid rearrangement. Such a process is well-known with tertiary



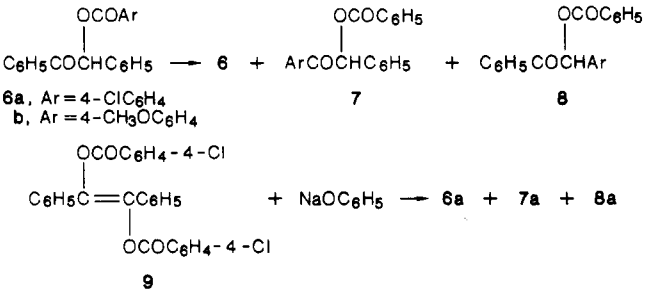
ketols[12] and has been shown to be reversible. It has also been demonstrated with α-hydroxy-β-keto acids[13] and amides,[14] where the migrating group was shown by tracer studies to be the carboxylate ion or carboxamide group. Also relevant is the base-catalyzed rearrangement of cyclic *vic*-triketones or their hydrates,[15] which proceed via formation of an alcoholate ion and produce ring-contracted α-hydroxy-β-keto acids. Returning to **3e**, one of its two possible benzilic acid type rearrangements is degenerate but the other provides alcoholate ion **5** of diacetylphenylcarbinol, as illustrated. Subsequent isomerization of **5** via an epoxy intermediate would produce the enol (thermal reaction) or enolate anion of **4g**. Extension of the behavior of **3e** to an α-hydroxy β-diketone moiety bearing three (**3**, $R_1 \neq R_2 \neq R_3$), instead of two, different

(4) House, H. O.; Gannon, W. F. *J. Org. Chem.* **1958**, *23*, 879.
(5) A similar mechanism involving an aziridine intermediate has been suggested to account for the formation of *o*-hydroxyanilides in the reaction of *o*-hydroxy aromatic aldehydes or ketones with monochloramine in base by: Crochet, R. A.; Sullivan, F. R.; Kovacic, P. *J. Org. Chem.* **1974**, *39*, 3094. For a recent example invoking a similar anion, see: Cullis, P. M.; Arnold, J. R. P.; Clarke, M.; Howell, R.; DeMira, M.; Naylor, M.; Nicholls, D. *J. Chem. Soc., Chem. Commun.* **1987**, 1088.
(6) Kohler, E. P.; Erikson, J. L. E. *J. Am. Chem. Soc.* **1931**, *53*, 2301. Sharp, D. B.; Hoffmann, H. A. *J. Am. Chem. Soc.* **1950**, 4311.
(7) Burgi, H. B.; Dunitz, J. D.; Lehn, J.-M.; Wipff, G. *Tetrahedron* **1970**, *30*, 1563.
(8) Ramirez, F.; Bahtia, S. B.; Bigler, A. J.; Smith, C. P. *J. Org. Chem.* **1968**, *33*, 1192.
(9) Rapid hydrolysis of acetates **4f** and **4g** in KOH/MeOH precluded investigations in this medium. However, formation of a mixture of **4e**, **4f**, and **4g** could be demonstrated by drawing a sample of **3e** into a hypodermic syringe followed by a sample of KOH/MeOH solution and analyzing immediately by gas chromatography.
(10) (a) Fieser, L. F.; Fieser, M. *Steroids*; Reinhold: New York, 1959; pp 229, 230. (b) Wendler, N. . In *Molecular Rearrangements*; de Mayo, P., Ed.; Interscience: New York, 1964; Vol. 2, 1124. Formation of mixtures of **4f** and **4g** (see Experimental Section) may involve such a mechanism.
(11) It should be noted that all three products were recovered unchanged after thermal treatment under the conditions of the isomerization reaction in which they were formed.
(12) Reference 10b, pp 1114–1121. This rearrangement has sometimes been referred to as the acyloin rearrangement or the tertiary ketol rearrangement.
(13) Armstrong, F. B.; Hedgecock, C. J. R.; Reary, J. B.; Whitehouse, D.; Crout, D. H. G. *J. Chem. Soc. Chem. Commun.* **1974**, 351. Crout, D. H. G.; Hedgecock, C. J. R. *J. Chem. Soc., Perkin Trans. 1* **1979**, 1982.
(14) Gowal, H.; Spiess, A.; Ballenegger, M.; Duc, L.; Moll, H.; Schlunke, H.-P.; Dahn, H. *Helv. Chim. Acta* **1985**, *68*, 2132 and references therein.
(15) Rubin, M. B. *Chem. Rev.* **1975**, *75*, 177.

substituents suggests that such a compound coul be converted to a mixture of up to six isomeric ketol esters!

A further consequence of the system of equilibrating anions involved in base-catalyzed rearrangements is that entry into this system need not be restricted to α-hydroxy β-diketones. Generation of the enolate ion (V) of an α-ketol ester could lead to intermediate IV, which would be in equilibrium with anion III previously derived from reaction of base with an α-hydroxy β-diketone.[16] Thus a suitably substituted ketol ester could isomerize to a mixture of six different ketol esters under appropriate reaction conditions. We decided to test this hypothesis in cases where only three isomers would be formed in order to simplify isolation and analysis.

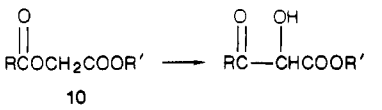
Esters of benzoin with aromatic acids were chosen for this investigation since they offer only a single proton to an attacking base, thereby minimizing possible side reactions. Refluxing benzoin *p*-chlorobenzoate (**6a**) with sodium hydride in benzene for 6 h afforded an ester mixture in 60% yield. Pure samples of **6a**, *p*-chlorobenzoin benzoate (**7a**), and *p'*-chlorobenzoin benzoate (**8a**) were separated in approximately equal amounts from this mixture by tedious thick-layer chromatography. Analysis of NMR



spectra suggested that the crude product consisted largely of a 1:1:1 mixture of all three esters. Minor products were benzil and desoxybenzoin. A similar experiment was performed with benzoin *p*-methoxybenzoate (**6b**). The chromatographic procedure was only partly successful in separation of pure benzil, desoxybenzoin, and benzoin benzoate as minor products plus an ester fraction. Accordingly, this ester fraction was saponified with dilute KOH/MeOH at room temperature, which allowed isolation of pure samples of methyl benzoate *and* methyl *p*-methoxybenzoate, thereby showing that exchange of the aryl ester moiety had occurred. Pure samples of benzoin and *p*-methoxybenzoin were also obtained. Analysis of NMR spectra of the ester mixture before saponification suggested that the ratio of esters **6b**:**7b**:**8b** was 1:0.1:1 in the original reaction product although no definite proof for the presence of **7b** was obtained.

The reactions described above demonstrate that scrambling of the substituents does occur when the anion of an α-ketol ester is formed. However, the long reaction times required to generate anions resulted in considerable loss of material. A much more quantitative result was obtained under very much milder conditions when the enolate anion of **6a** was generated by reaction of sodium phenoxide with α,β-stilbenediol bis(*p*-chlorobenzoate) (**9**) in benzene solution containing a trace of dimethylformamide. Workup after *35 min at room temperature* gave phenyl *p*-chlorobenzoate and a 90% yield of an ester mixture from which pure samples of **6a**, **7a**, and **8a** were isolated. NMR analysis of the mixture again indicated the presence of approximately equal amounts of all three esters as had been observed in the reaction of **6a** with sodium hydride.

Thus, rapid scrambling of the groups attached to an α-ketol ester moiety occurs when the anion is generated under very mild conditions. In all the known examples of base-catalyzed reactions of α-hydroxy β-diketones and the related α-ketol esters, the only detectable products were the esters. However, replacement of one keto function by a carboxyl group appears to reverse the direction of isomerization. As noted above, these reactions include isomerizations of α-hydroxy-β-keto acids and amides as well as the racemization of optically active α-methyl-α-hydroxyacetoacetic acid. After our work was completed, a report appeared describing[16] the isomerization of esters of (acyloxy)acetic acids **10** to α-hydroxy-β-keto esters, exactly the reverse of the process observed with diketones. However, it should be noted that these reactions were shown, by trapping with trimethylchlorosilane, to involve the dianions of products.



10

Experimental Section

Melting points are uncorrected. Infrared spectra were determined in potassium bromide pellets unless stated otherwise, and NMR spectra were measured at 60 MHz in deuteriochloroform with tetramethylsilane as internal standard. Mass spectra were determined at 70 eV.

Thick-layer chromatography was performed with 20 × 20 cm glass plates coated with a 2-mm layer of silica gel containing a fluorescent indicator. In difficult separations, plates were developed and removed from the apparatus, and the solvent was allowed to evaporate while the underside of the plate was warmed gently to prevent condensation of moisture. The plate was replaced in the chamber and developed one or more additional times. Bands were scraped from the plates, and the silica gel was eluted with chloroform to obtain products. Gas chromatographic analyses were performed with 5 ft × $^1/_8$ in. glass columns packed with 1% XE-60 on 100/120 mesh Gaschrom Q and an FID detector.

Acetoin Benzoate (4e). This compound was prepared by the procedure of Diels and Stephan.[17] The NMR spectrum [δ 7.9–8.1 (m, 2 H), 7.3–7.6 (m, 3 H), 5.25 (q, *J* = 6 Hz, 1 H), 2.20 (3 H), 1.50 (d, *J* = 6 Hz, 3 H)] was in full agreement. The substance was recovered unchanged after heating in a sealed tube at 200 °C for 3 h in the presence or absence of an equivalent amount of benzoic acid.

α-Hydroxypropiophenone Acetate (4f) and 1-Phenyl-1-hydroxyacetone Acetate (4g). These compounds were prepared by reaction of the corresponding bromo ketones with potassium acetate in ethanol according to the procedures of von Auwers et al.[18,19] In both cases NMR spectra indicated that a mixture of expected product contaminated with about 20% of the isomer was formed. Separation into pure compounds could not be achieved by fractional distillation; pure samples were obtained by thick-layer chromatography as described below. NMR data for the pure compounds were as follows: **4f**, δ 7.8–8.1 (m, 2 H), 7.3–7.6 (m, 3 H), 5.90 (q, *J* = 6 Hz, 1 H) 2.10 (3 H), 1.50 (d, *J* = 6 Hz, 3 H); **4g**, δ 7.4 (5 H), 5.95 (1 H), 2.15 (3 H), 2.10 (3 H).

Each compound was recovered unchanged after heating at 200 °C for 2 h in the presence or absence of an equivalent amount of benzoic acid.

Rearrangement of Acetylbenzoylmethylcarbinol (3e). A sample (325 mg) of **3e** was heated in an oil bath at 210 °C for 2 h. The NMR spectrum of the resulting light-colored oil indicated the presence of a mixture of **4e**, **4f**, and **4g** in the ratio 1:2:1. Preparative TLC was performed on 150 mg of the crude product with five 20 × 20 cm plates. Each plate was developed twice with

(16) Such a mechanism has been proposed to account for isomerizations of α-(acyloxy)acetates: Lee, S. D.; Chan, T. H.; Kwon, K. S. *Tetrahedron Lett.* **1984**, *25*, 3999.

(17) Diels, O.; Stephan, E. *Ber.* **1908**, *40*, 4336.
(18) von Auwers, K. *Ber.* **1917**, *50*, 1177.
(19) von Auwers, K.; Mauss, H. *Biochem. Z.* **1928**, *192*, 200.

2:3 chloroform–hexane and twice with 7:3 chloroform–hexane. The resulting broad zone was divided into three equal parts. The top third was predominantly **4e**, the center was **4f**, and the bottom was **4g**. Rechromatography of each fraction gave pure samples (by IR and NMR comparison) of **4e** (13 mg), **4f** (12 mg), and **4g** (15 mg). In addition, benzoic acid (20 mg) was isolated.

B. With Sodium Hydride. Sodium hydride (55% dispersion in mineral oil, 4.4 mg) was added to a solution of **3e** (20 mg) in anhydrous ether and allowed to stand at room temperature for 15 min. Excess formic acid was added and the cloudy solution was filtered and concentrated to give a light-colored oil (16 mg). NMR analysis indicated the presence of a mixture of **4e**, **4f**, and **4g** in the ratio 1:0.1:1. The presence of the three esters was further confirmed by gas chromatographic analysis.

Benzoin *p*-Methoxybenzoate (6b). *p*-Methoxybenzoyl chloride (8.7 g) was added to a stirred solution of benzoin (11.1 g) in dry pyridine (50 mL). After being stirred for 2 h at room temperature, the solution was poured into cold, dilute sulfuric acid and worked up in the usual way to give crude ester (17.8 g, 95%). Crystallization from methanol gave **6b**, mp 99–100 °C, unchanged by further crystallization. IR 1720, 1690 cm^{-1}; UV (MeOH) 257 (ϵ 30000), 313 nm (350); NMR δ 7.9–8.3 (m, 4 H with superimposed doublet, J = 8 Hz), 7.2–7.7 (m, 8 H), 7.10 (1 H), 6.90 (d, J = 8 Hz, 2 H), 3.85 (3 H).

Anal. Calcd for $C_{22}H_{18}O_4$: C, 76.28; H, 5.24. Found: C, 76.18; H, 5.30.

Benzoin *p*-Chlorobenzoate (6a). Pure **6a** was obtained by reaction of *p*-chlorobenzoyl chloride with benzoin in pyridine using the procedure described above for **6b** followed by crystallization from ethanol, mp 112–113 °C: IR 1740, 1690 cm^{-1}; UV max (MeOH) 248 (ϵ 32000), sh 315 nm (400); NMR δ 7.9–8.3 (m, 4 H with superimposed doublet, J = 8 Hz, at 8.10), 7.3–7.7 (m, 10 H), 7.15 (1 H).

Anal. Calcd for $C_{21}H_{15}ClO_3$: C, 71.89; H, 4.37; Cl, 10.01. Found: C, 71.78; H, 4.33; Cl, 10.13.

***p*-Chlorobenzoin Benzoate (7a).** *p*-Chlorobenzoin[20] and benzoyl chloride in pyridine afforded **7a** by using the procedure described above. The pure sample was crystallized from methanol, mp 93–94 °C: IR 1720, 1690 cm^{-1}; NMR δ 7.9–8.3 (m, 4 H, with superimposed doublet at δ 8.00, J = 8 Hz), 7.3–7.7 (m, 10 H), 7.10 (1 H); MS, m/e (relative intensity) 350.0727 (M^+, 6), 211.0764 (100); $C_{21}H_{15}ClO_3$ requires 350.0744.

α,β-Stilbenediol Bis(*p*-chlorobenzoate) (9). The preparation was based on the procedure of Bauld[21] for the dibenzoate. A solution of benzil (2.1 g) in dry benzene (50 mL) was added dropwise to stirred magnesium turnings (0.24 g, activated with iodine) under nitrogen, and the resulting suspension was refluxed for 24 h. The dark solution was then treated with *p*-chlorobenzoyl chloride (5.0 g) and refluxed for an additional 30 min. Filtration and concentration afforded a crude product, which crystallized on standing. Two crystallizations from methanol gave **9** (1.3 g), mp 153–154 °C: IR 1740 cm^{-1}; NMR δ 7.3–8.1 (m); MS, m/e (relative intensity) 492.0562 (M^+ + 4, 3.2), 490.0580 (M^+ + 2, 16.5), 488.0594 (M^+, 27.1), 138.9929 (100); $C_{28}H_{18}Cl_2O_4$ requires 488.0605.

Reaction of Benzoin *p*-Chlorobenzoate (6a) with Sodium Hydride in Benzene. A solution of **6a** (1 g) in benzene (70 mL) was boiled down to 50 mL and cooled under nitrogen, and sodium hydride (127 mg of 55% dispersion in mineral oil) was added. After a 12-h reflux under nitrogen, the brown solution was cooled and acidified with excess acetic acid. A small amount of insoluble material was filtered off and the filtrate concentrated to give a yellow oil (0.9 g). A portion (490 mg) was run twice on preparative plates with 4:1 hexane–chloroform, twice with 3:1 hexane–chloroform, and twice with 5:2 hexane–chloroform to give desoxybenzoin (45 mg), unidentified material (95 mg), a mixed fraction (150 mg) consisting, by NMR analysis, of a mixture of **6a**, **7a**, and **8a**, and pure samples of **7a** (48 mg; identity by comparison of IR and NMR spectra) and **8a** (105 mg).

The analytical sample of *p'*-chlorobenzoin benzoate (**8a**) was obtained by two crystallizations from methylene chloride–hexane, mp 119 °C: IR (chloroform) 1720, 1700 cm^{-1}: NMR δ 7.9–8.3 (m, 4 H), 7.3–7.7 (m, 10 H), 7.10 (1 H); MS, m/e (relative intensity) 352 (M^+ + 2, 2), 350 (M^+, 7), 105 (100).

Anal. Calcd for $C_{21}H_{15}ClO_3$: C, 71.89; H, 4.37. Found: C, 71.72; H, 4.29.

Reaction of Benzoin *p*-Methoxybenzoate (6b) with Sodium Hydride in Benzene. The reaction of **6b** (1 g) was run and worked up as described above for the *p*-chloro isomer to give a yellow oil (0.75 g). Preparative chromatography as described above in the reaction of **6a** gave benzil (14 mg), desoxybenzoin (17 mg), benzoin benzoate (20 mg), an unidentified fraction (15 mg), a fraction (120 mg) containing **6b**, **7b**, and **8b** (by NMR analysis), and a fraction (270 mg) containing **6b** and **8b** by NMR. A portion (108 mg) of the last fraction in methanol (5 mL) under nitrogen was treated with 2 mL of 2.8×10^{-2} N methanolic potassium hydroxide for 2 h at room temperature, then acidified, and concentrated. The residue was taken up in methylene chloride and filtered and the filtrate concentrated to give an oil (100 mg). This oil was chromatographed on two plates by running 4 times with 1:1 chloroform–hexane to give methyl benzoate (10 mg), benzil (4 mg), methyl *p*-methoxybenzoate (22 mg), benzoin (29 mg), *p*-methoxybenzoin (32 mg), and a trace (2 mg) of a yellow material, possibly *p*-methoxybenzil. The *p*-methoxybenzoin had mp 105–106 °C (lit.[22] mp 105.5 °C); other compounds were identified by TLC and spectral comparison with authentic samples.

Reaction of α,β-Stilbenediol Bis(*p*-chlorobenzoate) (9) with Sodium Phenoxide. A solution of **9** (225 mg) in dry benzene containing sodium phenoxide (160 mg) under nitrogen was treated with a few drops of dimethylformamide and stirred at room temperature. The solution darkened and then became yellow-orange. After 35 min, it was acidified with excess acetic acid, a small amount of insoluble material was filtered off, and the filtrate was concentrated under reduced pressure on a water bath. The crude material was run twice on three plates with chloroform to give phenyl *p*-chlorobenzoate (88 mg), phenol (90 mg), and a fraction (152 mg, 90%) consisting by NMR of a mixture of **6a**, **7a**, and **8a**. The ester fraction was run 5 times on four plates with 2:3 chloroform–hexane. A narrow bottom streak gave **8a** (32 mg). The broad upper streak was arbitrarily divided in half. The lower half was run 5 times with 20:1 hexane–ethyl acetate to give three separate streaks. The upper one gave **7a** (12 mg), the center streak gave **6a** (25 mg), and the lower streak gave additional **8a** (7 mg). Compounds were identified by spectral comparison with samples as described above.

Registry No. **3e**, 15138-21-3; **4e**, 21478-63-7; **4f**, 19347-08-1; **4g**, 19275-80-0; **6a**, 114678-98-7; **6b**, 114678-99-8; **7a**, 114679-00-4; **7b**, 38828-29-4; **8a**, 114679-01-5; **8b**, 38828-30-7; **9**, 114679-02-6; benzoic acid, 65-85-0; *p*-methoxybenzoyl chloride, 100-07-2; benzoin, 119-53-9; *p*-chlorobenzoyl chloride, 122-01-0; *p*-chlorobenzoin, 39774-18-0; benzoyl chloride, 98-88-4; benzil, 134-81-6; desoxybenzoin, 451-40-1; methyl benzoate, 93-58-3; methyl *p*-methoxybenzoate, 121-98-2; *p*-methoxybenzoin, 4254-17-5; *p*-methoxybenzil, 22711-21-3; phenyl *p*-chlorobenzoate, 1871-38-1; phenol, 108-95-2.

(20) Arnold, R. T.; Fuson, R. C. *J. Am. Chem. Soc.* **1936**, *58*, 1295.
(21) Bauld, N. L. *J. Am. Chem. Soc.* **1962**, *84*, 4345. We assume this compound to be the trans isomer.
(22) Kinney, C. R. *J. Am. Chem. Soc.* **1929**, *51*, 1592.

α-Methoxy-α-(trifluoromethyl)benzyl Isocyanate. A Convenient Reagent for the Determination of the Enantiomeric Composition of Primary and Secondary Amines

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Several methods have been found for the determination of the enantiomeric composition of chiral amines by NMR analysis. These methods are based on the fact that diastereotopic nuclei have different chemical shifts. In order

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