active site were used to detect the ionization of a nearby catalytically important ionizing group. An objective of experiments now in progress is to delineate further the location of ionizing groups near or in the active site of papain in solution by means of the reaction of the enzyme with reagents related to I to produce covalently bound reporter groups in which phenol functions with different ionization constants are located at various distances from the sulfur atom of Cys-25. These experiments will aid in establishing the nature of the catalytically important groups whose ionizations are reflected in the pH–rate profiles which have been measured for papain.

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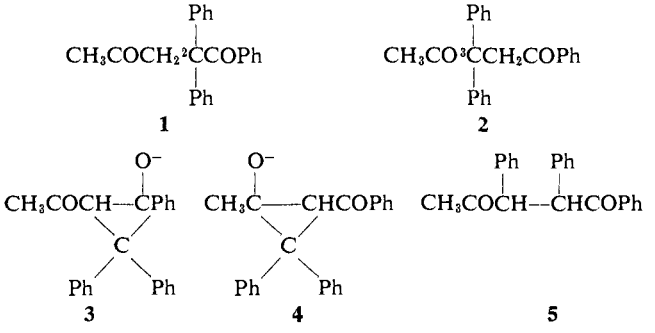
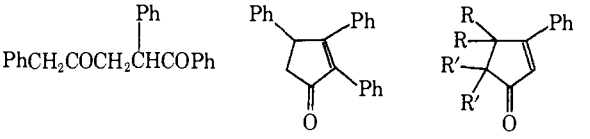
Mechanism of the Base-Catalyzed Interconversion of γ-Diketones

Sir:

The rearrangement of an enolate anion of the γ-diketone **1** to that of the γ-diketone **2**, recently reported from these laboratories, was considered to proceed *via* the two homoenolate ions **3** and **4**, rather than *via* two 1,2-phenyl migrations involving enolate anions of **5**.[1] We now present two pieces of evidence that confirm this view.

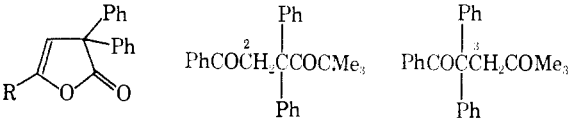


Treatment of deoxybenzoin in tetrahydrofuran with sodium hydride followed by 1-bromo-1-phenyl-2-propanone gave a mixture of the diastereoisomers of **5**, which were separated by fractional crystallization [**5a**: mp 153.5–154°; $\lambda_{max}^{CCl_4}$ 5.85, 5.96, 7.41 (m), 7.79 (w), 8.02 (w), 14.32 μ; λ_{max}^{EtOH} 247 mμ (ε 14,800); δ^{CDCl_3} 2.15 (s, 3 H), 4.60 (d, J = 11 Hz, 1 H), 5.20 (d, J = 11 Hz, 1 H), 7.3 (m, 13 H), 8.05 (m, 2H); **5b**: mp 184–185°; $\lambda_{max}^{CCl_4}$ 5.85, 5.96, 7.41 (m), 7.83, 14.35 μ; λ_{max}^{EtOH} 248 mμ (ε 13,200); δ^{CDCl_3} 1.92 (s, 3 H), 4.84 (d, J = 11 Hz, 1 H), 5.60 (d, J = 11 Hz, 1 H), 7.4 (m, 13 H), 7.9 (m, 2 H)].[2] Formed together with **5a** and **5b** were the diketone **6**,[3] mp 111.5–112° [$\lambda_{max}^{CCl_4}$ 5.86, 5.97 μ; λ_{max}^{EtOH} 246 mμ (ε 13,600); δ^{CDCl_3} 2.76 (dd, J = 4, 18 Hz, 1 H), 3.62 (dd, J = 10, 18 Hz, 1 H), 3.74 (s, 2 H), 5.13 (dd, J = 4, 10 Hz, 1 H), 7.3 (m, 13 H), 8.0 (m, 2 H)] and its dehydration product **7**, mp and mmp 139.5–140.5° (lit. mp 142–143°).[4] When **5a** was treated in ether with sodium methoxide[5] for 3 days, neither **1** nor **2** nor the corresponding cyclopentenones **8a** and **8b** could be detected in the reaction mixture,[6] demonstrating that enolate anions of **5** are not intermediates in the rearrangement of an enolate anion of **1** to that of **2**.



A critical difference between the two types of mechanism under consideration is that in the double homoenolate anion pathway the geminal phenyl groups remain attached to the same carbon atom (*i.e.*, C-2 of **1** becomes C-3 of **2**) while in the pathway involving two 1,2-phenyl migrations they do not and C-2 of **1** becomes C-2 of **2**. In order to establish by labeling experiments which of these relationships in fact holds, the analogous rearrangement of a different γ-diketone was examined in order to avoid both the complexity introduced by the occurrence of cyclopentenone formation and the inefficiency of the synthetic route to **1**.[1]

Reaction of the enol lactone **9**[7,8] with *tert*-butyllithium in ether at −15° for 2 min followed by work-up with aqueous acid gave the diketone **10** (80%), mp 130–130.5° [$\lambda_{max}^{CCl_4}$ 5.93 (br) μ; λ_{max}^{EtOH} 244.5 (ε 14,900), 280 mμ (sh, ε 1480), δ^{CDCl_3} 1.01 (s, 9 H), 4.18 (s, 2 H), 7.2–7.6 (m, 13 H), 7.8 (m, 2 H)]. Treatment of **10** in ether with sodium methoxide[5] for 7 days gave the rearranged diketone **11** (63%), mp 129.5–130° [$\lambda_{max}^{CCl_4}$ 5.85, 5.92 μ; λ_{max}^{EtOH} 235 (sh, ε 9500), 310 mμ (sh, ε 360); δ^{CDCl_3} 0.85 (s, 9 H), 3.81 (s, 2 H), 7.3 (m, 15 H)].[9] The structure of **11** was established by its independent synthesis in 85% yield by treatment of the enol lactone **12**[10] with phenyllithium in ether.



(1) P. Yates, G. D. Abrams, and S. Goldstein, *J. Amer. Chem. Soc.*, 91, 6898 (1969).
(2) All melting points are uncorrected. Satisfactory elemental analyses have been obtained for all new compounds.
(3) This product could arise *via* isomerization of the bromo ketone, bromine transfer to the deoxybenzoin anion, or isomerization of the O-alkylation product; its origin is under investigation.
(4) C. P. Koelsch and T. A. Geissman, *J. Org. Chem.*, 3, 480 (1938); P. Bladon, S. McVey, P. L. Pauson, G. H. Broadhead, and W. M. Horspool, *J. Chem. Soc. C*, 306 (1966). The cyclopentenone **7** was also formed when **6** was treated with methanolic sodium methoxide.
(5) The sodium methoxide was prepared *in situ* by the addition of sodium hydride followed by sufficient methanol to convert it to sodium methoxide.
(6) Much of **5a** was recovered unchanged together with several products formed in small amount; one of these was identified as **5b** on the basis of its R_f value. Under these conditions **1** gave a mixture of **8a** and **8b**.[1]
(7) P. Yates and T. J. Clark, *Tetrahedron Lett.*, 435 (1960); W. Reid and H. Mengler, *Justus Liebigs Ann. Chem.*, 651, 54 (1962).
(8) Treatment of **9** with methyllithium gave **2**, thus confirming the earlier assignment[1] of the structure of the rearrangement product from **1**.
(9) The rearrangement of **10** to **11**, as of **1** to **2**, is essentially irreversible; this can be interpreted in terms of thermodynamic control resulting from steric effects.
(10) F. R. Japp and W. Maitland, *J. Chem. Soc.*, 85, 1496 (1904).

Preparation of **9** partially labeled with ^{13}C at C-3 was achieved by reaction of diphenylketene with 2-diazoacetophenone-2-^{13}C, itself prepared from benzoyl chloride and $^{13}CH_2N_2$; in the nmr spectrum of labeled **9** the upfield ^{13}C satellite of the vinylic proton signal at δ 6.33 ($J_{^{13}C-H}$ = 182 Hz) showed the presence of 27 ± 1% ^{13}C-3. Reaction of labeled **9** with *tert*-butyllithium gave **10** labeled at C-2; both ^{13}C satellites of the methylene proton signal at δ 4.18 could be observed ($J_{^{13}C-H}$ = 129 Hz) and showed the presence of 28 ± 1% ^{13}C-2. Rearrangement of labeled **10** with sodium methoxide gave labeled **11**, in whose nmr spectrum the methylene proton signal at δ 3.81 was accompanied by observable upfield and downfield ^{13}C satellite signals ($J_{^{13}C-H}$ = 129 Hz), showing the presence of 28 ± 1% ^{13}C-3. Thus, C-2 of **10** becomes C-3 of **11** in accord with rearrangement *via* homoenolate ions analogous to **3** and **4**,[11] but not *via* 1,2-phenyl migration.

Acknowledgment. We thank the National Research Council of Canada for generous support for this investigation.

(11) A more concerted pathway is not excluded. In this regard, it is of interest to note the relationship of the rearrangement to the acid-catalyzed rearrangement of santonic acid to parasantonide.[12]

(12) R. B. Woodward and E. G. Kovach, *J. Amer. Chem. Soc.*, 72, 1009 (1950).

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The Facile Redistribution of Trialkylboranes with Trimethylene Borate. A Simple, General Synthesis of Alkaneboronic Esters and Acids from Olefins *via* Hydroboration

Sir:

Trialkylboranes undergo a facile and clean redistribution reaction with trimethylene borate under the influence of catalytic quantities of diborane at 120°. The alkaneboronic esters, formed in this reaction in nearly quantitative yields, are stable, readily isolated, and are easily hydrolyzed to the corresponding alkaneboronic acids. Consequently, this procedure provides a convenient new synthesis of alkaneboronic acids.

Alkaneboronic acids and their esters are generally prepared by the reaction of appropriate organometallics with borate esters.[1] Previously, we attempted to provide a new route to these derivatives by achieving a partial reaction of borane in tetrahydrofuran (THF) with olefins.[2] However, with only a few exceptions, the hydroboration reaction exhibits a marked preference to proceed to the trialkylborane.[3] Attempts to redistribute the trialkylboranes with excess borane in THF were also not completely satisfactory.[2]

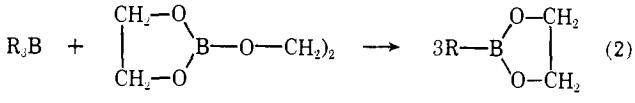
Organoboranes have been redistributed with boric oxide,[4] and with trimethoxyboroxine.[5] These reactions could provide a convenient route to the alkaneboronic acids. Unfortunately, the reactions are quite slow, requiring a temperature of 200° for a reasonable rate, so that is is not applicable to many organoboranes which can undergo isomerization at this temperature.[6]

A more promising approach appeared to be the redistribution of organoboranes with methyl borate, catalyzed by dialkylboranes[7] (eq 1).

$$n\text{-}Bu_3B + 2B(OCH_3)_3 \xrightarrow{100^\circ} 3n\text{-}BuB(OCH_3)_2 \qquad (1)$$

Indeed, this procedure appeared quite satisfactory for normal alkyl derivatives. However, the redistribution proved to be very slow with organoboranes from internal and cyclic olefins. A further difficulty appeared in storing the reaction products, $RB(OCH_3)_2$, for any length of time. They exhibited a tendency to undergo further redistribution, yielding other derivatives of boron.

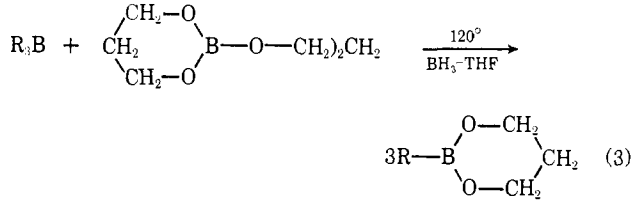
It appeared that some of these difficulties might be circumvented by preparing the ethylene glycol esters of the boronic acids through a related redistribution of the organoborane and ethylene borate[8] (eq 2). Un-



(2)

fortunately, this procedure suffered from two difficulties. First, the synthesis of ethylene borate is accompanied by the formation of considerable amount of polymer. Second, the redistribution reaction was slow and incomplete.

All of these difficulties were resolved through the use of trimethylene borate. The ester was readily synthesized in essentially quantitative yield from boric acid and trimethylene glycol. The redistribution reaction, catalyzed by 5 mol % diborane in THF, proceeded rapidly and completely at 120° (eq 3). The redistribu-



(3)

tion reaction was quite general, being equally effective for organoboranes from straight-chain olefins, such as 1-butene and 1-pentene, isoalkenes, such as isobutylene, internal olefins, such as 2-butene, cyclic olefins, such as cyclopentene and cyclohexene, and even bicyclic olefins, such as norbornene. The results are listed in Table I.[9] The products were readily recovered by distillation from the reaction mixture. Samples have been stored in ampoules for extended periods of time (up to 6 months) without detectable modification.

The esters are readily converted to the corresponding boronic acids by hydrolysis with water.

A representative redistribution reaction is that involving tri-*exo*-norbornylborane. Norbornene (14.1

(1) K. Torssell in "Progress in Boron Chemistry," Vol. 1, H. Steinberg and A. L. McCloskey, Ed., Pergamon Press, New York, N. Y., 1964, Chapter 9.

(2) H. C. Brown, A. Tsukamoto, and D. B. Bigley, *J. Amer. Chem. Soc.*, 82, 4703 (1960).

(3) H. C. Brown and G. J. Klender, *Inorg. Chem.*, 1, 204 (1962).

(4) G. F. Henion, P. A. McCusker, E. C. Ashby, and A. J. Rutkowski, *J. Amer. Chem. Soc.*, 79, 5194 (1957).

(5) P. A. McCusker and J. H. Bright, *J. Org. Chem.*, 29, 2093 (1964).

(6) H. C. Brown and G. Zweifel, *J. Amer. Chem. Soc.*, 88, 1433 (1966).

(7) R. Koster, *Angew. Chem.*, 73, 66 (1961); B. M. Mikhailov and L. S. Vasil'ev, *Izv. Akad. Nauk SSSR, Ser. Khim.*, 1756 (1962).

(8) R. Koster, *Angew. Chem.*, 71, 31 (1959).

(9) All the new compounds were analyzed by ir, nmr, and mass spectroscopy and gave satisfactory carbon and hydrogen analyses.