synthesis *via* the acetoacetic ester method often requires removal of the carboalkoxy control group under conditions requiring either high and low pH or hydrogenolysis of special esters if these conditions are to be avoided,[8] while the hydrolysis of **3** is accomplished by heating with ethanol–water under neutral or slightly basic conditions. As seen in Table I, halides containing groups threatened by acidic conditions (entries 6 and 7) are readily converted to the corresponding acetone derivative. Secondary bromides are less satisfactory for this process, however, presumably owing to their increased susceptibility to E2 elimination under the influence of highly basic nucleophiles.[9]

Experimental Section

n-Butyllithium was obtained from Matheson Coleman and Bell as a 1.6 *N* solution in hexane. Reagent grade tetrahydrofuran was distilled from $LiAlH_4$ immediately prior to use for small-scale reactions but used without purification for large-scale reactions. Starting materials were obtained from commercial sources or prepared by literature procedures. Alkyl bromides were distilled prior to use. All products were characterized by spectral and glpc comparison with authentic samples when available and through the melting points of their semicarbazone derivatives. New compounds gave satisfactory elemental analyses which were performed by the Analytical Laboratory of the University of Idaho.

The following experimental procedure is representative of the method developed for the preparation of methyl ketones from alkyl halides. Any variations in conditions are given in Table I.

2-Dodecanone from 1-Bromononane.—In 800 ml of dry THF under a nitrogen atmosphere was placed 34.4 g (0.108 mol) of acetylmethylenetriphenylphosphorane[1] (**1**). The solution was cooled by means of a Dry Ice–acetone bath and with stirring there was added 67 ml of 1.6 *N* butyllithium in hexane (0.105 mol) beyond the point where the red color of the ylide anion persisted. The intensely colored solution was stirred at −78° for 15 min, whereupon 20.7 g (0.100 mol) of 1-bromononane was added and the Dry Ice bath was replaced by an ice–water bath. The solution was stirred at 0° for 1 hr, whereupon the color of the ylide anion was nearly discharged. The solvent was removed under reduced pressure and the residue was dissolved in 300 ml of ethanol followed by the addition of water approaching the cloud point (approximately 200 ml). The resulting solution was heated (steam bath) for 22 hr and then poured into brine solution and extracted with two portions of pentane. Distillation of the oil obtained after removal of the solvent gave 17.1 g (93%) of 2-dodecanone, bp 77–78° (0.6 mm) [lit.[10] bp 120° (12 mm)].

The following procedure illustrates the preparation and isolation of the intermediate substituted phosphorane **3** obtained by alkylation of **2**.

3-Phenylpropionylmethylenetriphenylphosphine (3, R = Benzyl).—A solution containing 3.18 g (10.0 mmol) of **1** in 100 ml of THF was treated with 10.5 mmol of *n*-butyllithium at −78° as described above. The resulting solution containing anion **2** was then treated with 1.33 g (10.5 mmol) of benzyl chloride and the resulting mixture was stirred at 0° for 20 min. The mixture was warmed to room temperature whereupon the color of **2** was discharged. The reaction mixture was poured into an ice–water mixture with vigorous stirring and the product, 3.94 g (97%), was collected by filtration. Recrystallization from ethyl acetate gave 3.30 g (82%) of pure **3** (R = benzyl), mp 150–152° (lit.[6] mp 148–150°).

Acknowledgment.—We thank the Research Corporation and Washington State University for their supports through grants-in-aid.

Registry No.—**1**, 1439-36-7; **2**, 38938-34-0.

(9) J. Hine, "Physical Organic Chemistry," McGraw-Hill, New York, N. Y., 1956, p 180.

(10) T. Shenton and J. C. Smith, *Chem. Ind. (London)*, 1510 (1958).

Stereoselectivity in the Base-Catalyzed Decarboxylation of 5,5-Dicarboxy-2-isopropyl-1,3-dioxane

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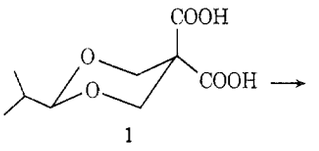
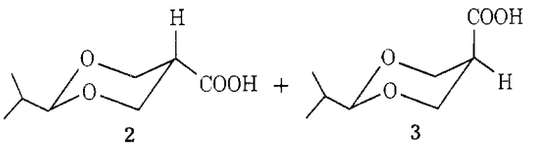
Some years ago Zimmerman and Giallombardo studied the stereochemical consequences of base-catalyzed decarboxylation of 4-phenylcyclohexane-1,1-dicarboxylic acid.[1] They found that *cis*-4-phenylcyclohexanecarboxylic acid comprises 57% of the product regardless of whether the solvent is 2,4,6-trimethylpyridine or nonbasic 1,3,5-trimethylbenzene. In striking contrast to these results, the product composition in the decarboxylation of solutions of 5,5-dicarboxy-2-isopropyl-1,3-dioxane (**1**) in pyridine and aniline derivatives depends critically on the solvent.



1



2 3

Solutions of **1** (0.1–0.2 *M*) dissolved in the desired pyridine or aniline base were decarboxylated at constant temperature. The predominant product was **2** with every base except 2,6-dimethylpyridine. The results are given in Table I.

TABLE I

PRODUCT COMPOSITION IN THE DECARBOXYLATION OF 5,5-DICARBOXY-2-ISOPROPYL-1,3-DIOXANE

Solvent	% 3 at 100.0°	% 3 at 125.0°
Pyridine	41.4 ± 0.1	
2-Methylpyridine	35.9	
2,6-Dimethylpyridine	56.3	56.3 ± 0.1
3,5-Dimethylpyridine	33.4	33.3
Aniline	24.2	27.5
N-Methylaniline	16.9	
N,*N*-Dimethylaniline	11.7	17.6

One possible mechanism for this reaction is the concerted loss of carbon dioxide and protonation, occurring with either retention or inversion of configuration. The product composition is determined by which carboxyl group departs. To test this mechanism, the kinetics of the reaction were studied using four bases at 100.0, 110.0, and 125.0°. The rate constants were all pseudo first order, and are given in Table II. If the composition of the product is determined exclusively by which diastereotopic carboxyl group is displaced, the product composition may be used to partition each rate constant into a rate constant for loss of

(1) H. E. Zimmerman and H. J. Giallombardo, *J. Amer. Chem. Soc.*, **78**, 6259 (1956).

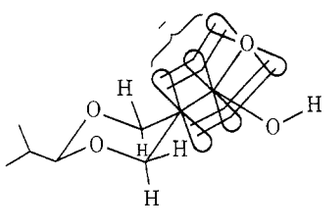
TABLE II
PSEUDO-FIRST-ORDER RATE CONSTANTS FOR DECARBOXYLATION OF 5,5-DICARBOXY-2-ISOPROPYL-1,3-DIOXANE

Solvent	Temp, °C	$10^4 k$, sec^{-1}
2,6-Dimethylpyridine	100.0	5.24
	110.0	17.0
	125.0	29.0
3,5-Dimethylpyridine	100.0	3.97
	110.0	20.6
	125.0	52.2
Aniline	100.0	7.78
	110.0	15.0
	125.0	39.4
N,N-Dimethylaniline	100.0	16.4
	110.0	27.4
	125.0	49.1

an axial carboxyl group and a rate constant for loss of an equatorial carboxyl group. For 2,6-dimethylpyridine at 100.0°, using the data of Tables I and II, the individual rate constants are $(0.563)(5.24 \times 10^{-4}) = 2.95 \times 10^{-4}$ sec^{-1} and $(0.437)(5.24 \times 10^{-4}) = 2.29 \times 10^{-4}$ sec^{-1}. The individual rate constants were calculated for each basic solvent at 100.0 and 125.0°. Arrhenius plots were then used to predict the rate constants at 110.0°, which were compared with the experimental values. The predicted rate constants at 110.0° for 2,6- and 3,5-dimethylpyridine are 36 and 34% too low, respectively; these findings are inconsistent with the proposed mechanism.

The calculated rate constants at 110.0° in the solvents aniline and *N,N*-dimethylaniline both agree with the experimental values within 5%. The entropies of activation, calculated from the individual rate constants, are −26.0 and −23.3 eu mol^{-1} in aniline and −26.5 and −42.4 eu mol^{-1} in *N,N*-dimethylaniline. These very large negative values are inconsistent with the proposed mechanism.

A second possible mechanism is that proposed by Fraenkel, Belford, and Yankwich[2] for the decarboxylation of malonic acid in quinoline. The rate-determining step is the nucleophilic attack by the basic solvent on the hydrogen bond donating or hydrogen bond accepting[3] carboxy group of the intramolecularly hydrogen bonded species. The departure of carbon dioxide is thereby facilitated, and an enediol intermediate is produced. The composition of the product is determined by which of the two faces of the intermediate is more accessible to attack by the conjugate acid of the basic solvent.[4] The upper face of the intermediate is less hindered to attack by all the conjugate acids of



the bases investigated in this study, with the exception of 2,6-dimethylpyridine. Apparently the bulk of the two methyl groups results in substantial steric interaction in approach from either side.

Comparison of the results using pyridine derivatives with those using aniline derivatives shows that the latter are more selective as proton donors. This is presumably a consequence of the more congested environment of the sp^3-hydridized nitrogen in the anilinium ions compared to the sp^2-hydridized nitrogen in the pyridinium ions. As expected, as methyl groups are substituted for hydrogen, steric interference becomes more important, and selectivity increases.

The apparent difference between the cyclohexane and 1,3-dioxane systems is puzzling, and the decarboxylation of 4-*tert*-butylcyclohexane-1,1-dicarboxylic acid is being studied in a number of basic solvents.

Experimental Section

Gas chromatographic analyses were obtained using a Hewlett-Packard research chromatograph, Model 7620A. The nmr spectra were recorded on an Hitachi Perkin-Elmer R-24 nmr spectrometer. Microanalyses were performed by Schwarzkopf Microanalytical Laboratory, Woodside, N. Y.

trans-**5-Carboxy-2-isopropyl-1,3-dioxane** (**2**).—A mixture of 20.0 g (92 mmol) of 5,5-dicarboxy-2-isopropyl-1,3-dioxane[5] and 20 ml of *N,N*-dimethylaniline was maintained at 100° for 2 hr. The reaction mixture was cooled in an ice–salt bath, and was acidified by the dropwise addition of concentrated HCl. This mixture was extracted three times with 200-ml portions of diethyl ether, and the combined ether extracts were dried over anhydrous $MgSO_4$. After filtration, the solution was concentrated on the rotary evaporator, and the last traces of ether were removed at 0.1 Torr. The residue was recrystallized from benzene to give 14.2 g (90%) of **2**: mp 141.0–141.5°; nmr ($CDCl_3$) δ 0.94 (d, 6 H, J = 10 Hz), 1.43–2.00 (m, 1 H), 2.85–3.32 (m, 1 H), 3.51–4.49 (several peaks, 5 H), 10.12 (s, 1 H).

Anal. Calcd for $C_8H_{14}O_4$: C, 55.16; H, 8.10. Found: C, 55.21; H, 8.10.

cis-**5-Carboxy-2-isopropyl-1,3-dioxane** (**3**).—The decarboxylation of **1** was effected using dimethylformamide as the solvent.[6] Recrystallization of the crude product from benzene–petroleum ether gave crystals: mp 127.0–127.5°; nmr ($CDCl_3$) δ 0.91 (d, 6 H, J = 10 Hz), 1.47–2.14 (m, 1 H), 2.24–2.50 (m, 1 H), 3.68–4.75 (several peaks, 5 H), 11.42 (s, 1 H).

Anal. Calcd for $C_8H_{14}O_4$: C, 55.16; H, 8.10. Found: C, 55.11; H, 8.07.

Decarboxylation Studies.—A sample of 0.3–0.4 g of **1** was weighed on an analytical balance (to the nearest 0.1 mg) into a small, thin-walled glass ampoule. The ampoule was sealed and placed into a 50-ml round-bottom flask, fitted with a condenser that was attached to a three-way stopcock. One arm of the stopcock was connected to a buret for measuring the evolved carbon dioxide, and the third arm was open to the atmosphere. To the flask was added 10.0 ml of the freshly distilled solvent. Dry carbon dioxide gas was bubbled slowly through the solvent for 10 min to ensure saturation.

The reaction flask was immersed in the constant-temperature bath, and the three-way stopcock was turned so that the system was open to the atmosphere until equilibrium had been established. The stopcock was then turned so that the gas buret was connected to the system. Room temperature and the barometric pressure were recorded. The reaction was initiated by fracturing the ampoule by the impact with a falling Teflon-coated magnet. The reaction vessel was shaken vigorously for 30 sec. The volume of carbon dioxide was measured at regular intervals for at least four half-lives.

After the reaction mixture was cooled, a sample of 1 ml of the solution was added to 5 g of crushed ice. Concentrated HCl was added dropwise until the mixture was acid to litmus paper. When the ice had melted, the solution was transferred to a test

(2) G. Fraenkel, R. L. Belford, and P. E. Yankwich, *J. Amer. Chem. Soc.*, **76**, 15 (1954).

(3) L. W. Clark, *J. Phys. Chem.*, **73**, 438 (1969).

(4) This explanation of the results is consistent with the finding of H. E. Zimmerman and P. S. Mariano, *J. Amer. Chem. Soc.*, **90**, 6091 (1968), that the proton donor in the ketonization of the enol of 1-acetyl-4-phenylcyclohexane, and in the tautomerization of the aci form of 4-phenyl-1-nitrocyclohexane, attacks preferentially from the less hindered, equatorial direction.

(5) E. L. Eliel and H. D. Banks, *J. Amer. Chem. Soc.*, **94**, 171 (1972).

(6) E. L. Eliel, personal communication, Nov 29, 1971; S. Mager and E. L. Eliel, *Rev. Roum. Chim.*, in press.

tube and was extracted with three 1-ml portions of diethyl ether by means of a Pasteur pipet. The combined extracts were dried over a mixture of equal parts of anhydrous $MgSO_4$ and anhydrous Na_2CO_3. The dried extract was decanted into a test tube, and excess diazomethane was added.[7] Excess diazomethane was removed by means of a stream of nitrogen, and 50- to 100-μl samples of the solution were analyzed by glpc (6-ft 10% Carbowax 20M on Chromosorb W, 80–100 mesh at 150°, He flow 60 ml/min). A correction factor for the extraction and analysis was determined using a synthetic mixture of pure **2** and **3**. Control experiments demonstrated that epimerization of the products did not occur under the conditions of the decarboxylation.

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Registry No.—1, 35113-49-6; 2, 42031-28-7; 3, 42031-29-8.

(7) H. Schlenk and J. L. Gellerman, *Anal. Chem.*, **32**, 1412 (1960).

Carboxylation Reactions Using the Reagent Lithium 4-Methyl-2,6-di-*tert*-butylphenoxide

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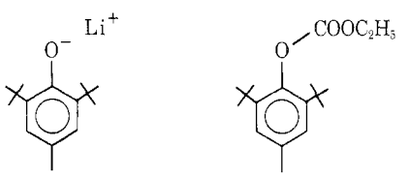
This research was initiated in order to develop a system for the carboxylation of weakly acidic substances such as ketones by the use of a base which is protected sterically from attack on carbon dioxide but able to deprotonate the substrate for carboxylation. The base chosen for initial studies was the 4-methyl-2,6-di-*tert*-butylphenoxide ion (I). It was found that the lithium salt I was readily generated from the phenol in ethereal solution by treatment with 1 equiv of *n*-butyllithium. Although solutions of I in ether did take up carbon dioxide, the rate of absorption was quite slow. It was determined, for example, that exposure of I in ethereal solution to carbon dioxide at 760 mm for 12 hr followed by quenching with triethyloxonium fluoroborate gave only 15% of the carbonated derivative II together with much recovered phenol.



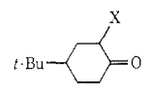
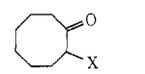
I II

The carbonation of a number of substrates was then investigated using mixtures of substrate, phenoxide base I, and carbon dioxide. Table I summarizes the results obtained for three ketones, a terminal acetylene, and a sulfone. No carbonation was observed for isoamyl acetate, *N*-acetylpiperidine, phenylacetamide, or 1-nonyne. Methyl phenylacetate, phenylacetonitrile, and γ-butyrolactone underwent carbonation to some extent with yields in the range 20–50%.

In summary, the above data would suggest that the reagent I can be used to promote the carboxylation of ketones, but that it is ineffective toward less acidic substrates. The reagent I has also been applied to dithiocarboxylation reactions using carbon disulfide as reactant.[1]

TABLE I

REACTION OF SUBSTRATES WITH CARBON DIOXIDE AND LITHIUM 4-METHYL-2,6-DI-*tert*-BUTYLPHENOXIDE[a]

Substrate registry no.	Substrate, X = H; product, X = COOH	Product registry no.	Yield, %	Reaction time, hr
98-53-3		42031-70-9	89	16
502-49-8		25731-69-7	77	16
98-86-2	$C_6H_5COCH_2X$	614-20-0	75	24
536-74-3	$C_6H_5C{\equiv}CX$	637-44-5	74	16
3112-85-4	$C_6H_5SO_2CH_2X$	3959-23-7	65	24

[a] Reaction conditions: 760 mm of CO_2, 4 equiv of I/equiv of substrate, ether solvent.

Experimental Section

2-Carboxy-4-*tert*-butylcyclohexanone.—This preparation can be used to illustrate the general procedure applied to the substrates listed in Table I. Lithium 4-methyl-2,6-di-*tert*-butylphenoxide (4 mmol) was generated by slow addition of 4 mmol (2 ml, 2 *M* in hexane) of *n*-butyllithium to 4.2 mmol (924 mg) of 4-methyl-2,6-di-*tert*-butylphenol in 25 ml of ether at −78° under argon. The resulting white precipitate dissolved completely when the mixture was allowed to warm up to room temperature. The flask containing this reagent was then attached to a hydrogenation apparatus, which was prefilled with excess carbon dioxide, and 0.9 mmol (139 mg) of 4-*tert*-butylcyclohexanone in 1 ml of ether was added. The resulting mixture was well stirred for 16 hr (the solution became turbid after 90 min). The mixture was diluted with 20 ml of ice water at 0° and extracted with ether. The aqueous layer was acidified to pH 3–4 using 0.1 *M* aqueous hydrochloric acid at 0° and extracted with two portions of ether. The ethereal extract was dried over sodium sulfate and concentrated *in vacuo* to give a thick oil (89% yield) which slowly crystallized in a cold room at 5°. Thin layer chromatographic analysis of this product revealed no impurities. The infrared spectrum ($CHCl_3$ solution) exhibited bands at 3400–2800, 1715 (m), 1660 (s), and 1598 cm^{-1} (m), indicating a predominance of the enol form. The product lost carbon dioxide upon warming with formation of 4-*tert*-butylcyclohexanone.

Acknowledgment.—This work was assisted financially by a grant from the National Science Foundation.

Registry No.—Carbon dioxide, 124-38-9; lithium 4-methyl-2,6-di-*tert*-butylphenoxide, 42031-71-0.

(1) E. J. Corey and R. H. K. Chen, *Tetrahedron Lett.*, in press.

Synthesis of Methyl 3-Hydroxybenzo[*b*]thiophene-2-carboxylate Esters by Nitro Displacement

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The first synthesis of methyl 3-hydroxybenzo[*b*]-thiophene-2-carboxylate was reported by Friedlander.[1]

(1) P. Friedlander, *Justus Liebigs Ann. Chem.*, **351**, 390 (1906).