TABLE I

DIARYLSTIBINIC ACIDS AND PYRIDINIUM DIARYLCHLOROANTIMONATES

R_2SbO_2H	Yield, %	Formula	Sb analyses, % Calcd.	Found	Pyridinium diarylchloroantimonate formula	Sb analyses, % Calcd.	Found
C_6H_5-[a]	5	$C_{12}H_{11}O_2Sb$	39.41	39.45	$C_{17}H_{16}Cl_4NSb$	24.46	24.24
p-$CH_3C_6H_4-$[b]	8	$C_{14}H_{15}O_2Sb$	36.13	35.93	$C_{19}H_{20}Cl_4NSb$	23.15	22.88
m-ClC_6H_4-	6	$C_{12}H_9Cl_2O_2Sb$	32.22	32.19	$C_{17}H_{14}Cl_6NSb$	21.48	20.78
p-ClC_6H_4	12	$C_{12}H_9Cl_2O_2Sb$	32.22	32.30	$C_{17}H_{14}Cl_6NSb$	21.48	21.48
p-$O_2NC_6H_4-$[c]	20	$C_{12}H_9N_2O_6Sb$	30.52	30.40	$C_{17}H_{14}Cl_4N_2O_4Sb$	20.71	20.60

[a] Previously prepared by A. Michaelis and A. Reese, *Ann.*, **233**, 39 (1886), and other workers. [b] Previously prepared by A. E. Goddard and V. E. Yarsley, *J. Chem. Soc.*, 719 (1928). [c] Calcd.: N, 7.02. Found: N, 6.99.

and catalyst used. The results were generally comparable to those obtained with arsenic trichloride, except that the presence of water in the solvent did not materially increase the yields of stibinic acids. The best yield of arylstibonic acid was obtained by the use of absolute alcohol as the solvent and cuprous chloride as the catalyst; the yield of *p*-nitrobenzenestibonic acid was 65% under these conditions.[3] The best yield of diarylstibinic acid was obtained by the use of isopropyl or *t*-butyl alcohol and copper bronze.

Since it has been shown that the crystalline pyridinium arylchloroantimonates serve as useful derivatives for the characterization of primary stibonic acids,[2] the corresponding derivatives of the secondary acids were prepared and recrystallized. However, these compounds did not give sharp, reproducible m.ps.

Experimental

Antimony trichloride (0.1 mole) was dissolved in 100 ml. of the solvent and the solution added to 0.1 mole of the diazonium fluoride in a 2-necked flask. The subsequent procedure to the end of the steam distillation was similar to that used with arsenic trichloride.[1] After steam distillation the residual liquid in the flask was treated with 150 ml. of concentrated hydrochloric acid. A crystalline precipitate of the diarylstibine trichloride separated after several hours. This was removed by filtration and dissolved in 100 ml. of ethanol and 10 ml. of concentrated hydrochloric acid. The solution was treated with Darco and filtered. Ten ml. of pyridine reagent (*cf.* ref. 2) was added to the clear filtrate to precipitate the pyridinium chloroantimonate. The latter was then recrystallized from ethanol acidified with hydrochloric acid. The purified pyridinium salt was dissolved in 2% sodium hydroxide solution, and the clear solution acidified to congo red. The diarylstibinic acid which separated was thoroughly washed with water on a buchner funnel and air dried.

The filtrate, after removal of the diarylstibine trichloride, was treated with pyridine reagent in order to precipitate the pyridinium salt of the primary acid. This salt was then recrystallized and hydrolyzed by the procedure described in a previous paper.[2] Regardless of the solvent or catalyst used, the resulting arylstibonic acid was not analytically pure. Similar results were obtained when the ammonium chloroantimonate was used.

Table I lists the diarylstibinic acids and the corresponding pyridinium chloroantimonates prepared in this study. These results were obtained by the use of anhydrous isopropanol as the solvent and copper bronze as the catalyst. Athough previous workers have reported m.ps. for some diarylstibinic acids, the compounds listed in the present paper softened on heating but in no case was a sharp m.p. observed.

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(3) The ratio between nitrogen and antimony in this sample was 1.11 after attempted purification.

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The Synthesis of Ketones from Di-*t*-butyl Malonates

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Attempts to prepare ketones of the type $RCO-CH_2R'$ by the acylation of diethyl alkylmalonates with acid chlorides, followed by hydrolysis and decarboxylation with acidic or alkaline reagents, have been almost uniformly unsuccessful, because the intermediary acylalkylmalonates preferentially undergo hydrolysis of the acyl–carbon bond to, in effect, reverse the process.[2] Bowman[3] has utilized the benzyl esters of alkylated malonic acids to circumvent this difficulty elegantly. The acylmalonic esters formed from these compounds were cleaved to ketones by catalytic hydrogenolysis followed by thermal decarboxylation.

In the present note we wish to report the use of *t*-butyl esters of malonic acids for the preparation of ketones.[4] Di-*t*-butyl malonate, prepared in 60% yield by the acid-catalyzed reaction between malonic acid and isobutylene, was alkylated with benzyl chloride, cyclohexyl bromide and *n*-octyl bromide to give the corresponding di-*t*-butyl alkylmalonates. Conversion of these compounds to the sodio derivatives by treatment with sodium hydride in an inert solvent, followed by reaction of the sodio compound with an acid chloride, gave oily di-*t*-butyl acylalkylmalonates which were not purified, but treated directly with *p*-toluenesulfonic acid in refluxing toluene or anhydrous acetic acid to effect cleavage of the carbo-*t*-butoxy groups to give isobutylene, carbon dioxide and the ketone. The following ketones have been prepared in this manner: phenyl β-phenylethyl ketone (70–85% yield from benzoyl chloride), *p*-nitrophenyl β-phenylethyl ketone (81% from *p*-nitrobenzoyl chloride), *o*-nitrophenyl β-phenylethyl ketone (71%

(1) Allied Chemical and Dye Corp. Fellow, 1950; Sterling-Winthrop Research Institute Fellow, 1950–1951. The Upjohn Co., Kalamazoo, Mich.

(2) See R. E. Bowman, *J. Chem. Soc.*, 322 (1950), for discussion and leading references. An exception is the case where R′ = H; *i.e.*, the use of unsubstituted malonic esters gives good yields of methyl ketones. H. G. Walker and C. R. Hauser, THIS JOURNAL, **68**, 1386 (1946).

(3) R. E. Bowman, *J. Chem. Soc.*, 325 (1950).

(4) *Cf.* the preparation of keto esters by the use of *t*-butyl ethyl malonates, D. S. Breslow, E. Baumgarten and C. R. Hauser, THIS JOURNAL, **66**, 1286 (1944).

from *o*-nitrobenzoyl chloride), styryl β-phenylethyl ketone (79% from cinnamoyl chloride), *n*-heptyl *n*-nonyl ketone (65% from capryloyl chloride), phenyl cyclohexylmethyl ketone (56%, as the 2,4-dinitrophenylhydrazone, from benzoyl chloride), *o*-tolyl β-phenylethyl ketone (70% from *o*-toluyl chloride), and *o*-tolyl cyclohexylmethyl ketone (56% from *o*-toluyl chloride).

The present method offers an advantage over the Bowman method[3] in that it is possible to prepare ketones with easily reducible groups. The two nitro ketones described above, for example, could not be prepared by the Bowman method, because the nitro groups would not be expected to survive the hydrogenation step. The styryl ketone is another case in point.

In order to test the steric limitations of the reaction an attempt was made to prepare mesityl β-phenylethyl ketone by the acylation of di-*t*-butyl benzylmalonate with mesitoyl chloride. It was found necessary to allow the acylation to proceed for 20 hours to bring about appreciable reaction. The intermediary di-*t*-butyl benzylmesitoylmalonate was isolated in crystalline form in 26% yield and was cleaved to mesityl β-phenylethyl ketone in 84% yield. Thus although the introduction of one hindering group appears to exert relatively little effect as shown in the preparation of *o*-tolyl β-phenylethyl ketone, a second hindering group results in a marked decrease in the rate and yield of the acylation step.

Experimental[5]

Di-*t*-butyl Malonate.—The following procedure is essentially that developed in these laboratories by McCloskey.[6] A mixture of 50.0 g. (0.48 mole) of malonic acid, 120 ml. (about 1.5 moles) of liquid isobutylene, 100 ml. of ether and 5 ml. of concentrated sulfuric acid was shaken in a pressure bottle until all of the malonic acid had dissolved (about 6 hours). The bottle was cooled to −10°, opened, and the contents were washed with a solution of 70 g. of sodium hydroxide in a mixture of 250 ml. of water and 250 g. of ice. The organic layer was separated, dried over anhydrous potassium carbonate, and distilled in equipment which had been previously washed with alkali. After removal of the ether, 62.0 g. (60%) of di-*t*-butyl malonate was collected at 112–115° (31 mm.), $n^{25}D$ 1.4172 (reported[7] b.p. 93° (10 mm.), $n^{20}D$ 1.4184).

Di-*t*-butyl Alkylmalonates.—Di-*t*-butyl benzylmalonate was prepared by adding a solution of 6.96 g. (0.055 mole) of benzyl chloride in 25 ml. of dry *t*-butyl alcohol to a solution of di-*t*-butyl sodiomalonate, prepared from 35.57 g. (0.165 mole) of di-*t*-butyl malonate and 2.54 g. (0.11 mole) of sodium hydride in 75 ml. of *t*-butyl alcohol, in a 200-ml. three-necked flask equipped with a glass stirrer, a dropping funnel, and a reflux condenser capped with an Ascarite drying tube. After stirring for 1.5 hours at about 65° the mixture was cooled and diluted with 350 ml. of water. The organic layer was separated and the aqueous layer was extracted three times with ether. The combined extracts and organic layer were dried over anhydrous potassium carbonate. After removal of the ether and *t*-butyl alcohol by distillation at atmospheric pressure, a trace of magnesium oxide was added (to inhibit decomposition of the alkylmalonic ester) and the liquid was distilled in alkali-washed equipment. The first fraction consisted of 15.45 g. of di-*t*-butyl malonate, b.p. 50–58° (0.5 mm.), $n^{25}D$ 1.4171. After an intermediate fraction (3.45 g.) the **di-*t*-butyl benzylmalonate** distilled at 105–120° (0.5 mm.); yield 13.41 g. (80% based on benzyl chloride), $n^{25}D$ 1.4678. Redistillation afforded material, b.p. 115–117° (0.9 mm.), $n^{25}D$ 1.4682.

Anal. Calcd. for $C_{18}H_{26}O_4$: C, 70.56; H, 8.56. Found: C, 70.54; H, 8.72.

Di-*t*-butyl cyclohexylmalonate was prepared similarly from 18.5 g. (0.113 mole) of cyclohexyl bromide, 49.1 g. (0.227 mole) of di-*t*-butyl malonate and 5 g. of sodium hydride. An alkylation time of 63 hours at 90° gave 25.7 g. (76.5% yield based on cyclohexyl bromide) of di-*t*-butyl cyclohexylmalonate, b.p. 100–102° (0.1 mm.), $n^{25}D$ 1.4422. Shorter alkylation times gave much lower yields.

Anal. Calcd. for $C_{17}H_{30}O_4$: C, 68.42; H, 10.13. Found: C, 68.51; H, 10.19.

The preparation of **di-*t*-butyl *n*-octylmalonate** in the same way from 9.7 g. (0.05 mole) of *n*-octyl bromide, 21.6 g. (0.1 mole) of di-*t*-butyl malonate, and 1.8 g. (0.075 mole) of sodium hydride (alkylation time 48 hours) gave 11.7 g. (71% yield based on octyl bromide) of redistilled diester, b.p. 113–115° (0.5 mm.), $n^{25}D$ 1.4284.

Anal. Calcd. for $C_{19}H_{36}O_4$: C, 69.47; H, 11.05. Found: C, 69.43; H, 11.22.

Preparation of Ketones.—The following description of the preparation of phenyl β-phenylethyl ketone serves as an example of the general method. The other ketones were prepared similarly, except that in the preparations of styryl β-phenylethyl ketone and *n*-heptyl *n*-nonyl ketone the acylations were allowed to proceed for 2 minutes rather than one hour. In these cases the longer acylation time led to intractable oily products.

To a solution of 1.22 g. (0.004 mole) of di-*t*-butyl benzylmalonate in 25 ml. of dry benzene in a 200-ml. three-necked flask equipped with a glass stirrer (rubber slip-seal) and a reflux condenser capped with an Ascarite drying-tube was added 0.15 g. (0.006 mole) of sodium hydride. The mixture was stirred gently and heated at about 80° until gas evolution stopped (about 2.5 hours), and a solution of 0.56 g. (0.004 mole) of benzoyl chloride in 10 ml. of benzene was added. Heating and stirring were continued for one hour, the mixture was cooled to room temperature, and the excess sodium hydride was destroyed by the addition of 0.35 g. (0.002 mole) of anhydrous *p*-toluenesulfonic acid.[8] The salts were removed by filtration and washed with a little benzene. Evaporation of the benzene solution left a clear yellow oil which was refluxed for one hour with 0.1 g. of anhydrous *p*-toluenesulfonic acid in 25 ml. of glacial acetic acid containing about 2% acetic anhydride by volume. The reaction was followed by means of a constant-pressure eudiometer, and was found to be complete after 45 minutes, 83.5% of the theoretical amount of gas being evolved. The pale-brown solution was poured over crushed ice, neutralized by the addition of 5% sodium hydroxide solution, and the white crystalline precipitate of phenyl β-phenylethyl ketone was recovered by filtration. After drying, it weighed 0.67 g. (80% yield), m.p. 68.3–70.3°. On recrystallization from ethanol the m.p. was raised to 70–72° and was undepressed on admixture with authentic phenyl β-phenylethyl ketone. The semicarbazone melted at 144–144.8° (reported m.p. 143°,[9] 144°[10]). The **2,4-dinitrophenylhydrazone** crystallized from benzene–ethanol in clusters of stocky orange needles, m.p. 186.6–187.2° (reported,[11] 166°).

Anal. Calcd. for $C_{21}H_{18}O_4N_4$: C, 64.61; H, 4.65. Found: C, 64.65; H, 4.64.

Treatment of the sodio derivative from 1.20 g. of di-*t*-butyl benzylmalonate and 0.15 g. of sodium hydride with 0.75 g. (0.004 mole) of *p*-nitrobenzoyl chloride followed by decomposition as described above gave 0.83 g. (81% yield) of ***p*-nitrophenyl β-phenylethyl ketone**, m.p. 69–73°. Recrystallization from ethanol gave colorless plates, m.p. 74.5–75°.

Anal. Calcd. for $C_{15}H_{13}O_3N$: C, 70.58, H, 5.13. Found: C, 70.58; H, 4.98.

The 2,4-dinitrophenylhydrazone crystallized from benzene in the form of orange micro crystals, m.p. 235.9–236.7°.

(5) All melting points are corrected.

(6) A. L. McCloskey, Ph.D. Dissertation, University of Wisconsin, 1951.

(7) H. J. Backer and J. D. H. Homan, *Rec. trav. chim.*, **58**, 1048 (1939).

(8) K. H. Slotta and W. Franke, *Ber.*, **63**, 678 (1930).

(9) S. Jacobson and B. Ghosh, *J. Chem. Soc.*, 959 (1915).

(10) T. S. Stevens, *et al.*, *ibid.*, 3193 (1928); C. W. Shoppee, *ibid.*, 2567 (1928).

(11) J. F. J. Dippy and R. H. Lewis, *Rec. trav. chim.*, **56**, 1000 (1937).

Anal. Calcd. for $C_{21}H_{17}O_6N_5$: C, 57.93; H, 3.94. Found: C, 57.93; H, 3.75.

Treatment of the sodio derivative from 2.44 g. of di-*t*-butyl benzylmalonate and 0.29 g. of sodium hydride with 1.50 g. (0.008 mole) of *o*-nitrobenzoyl chloride as described above gave 1.44 g. (71% yield) of crude **o-nitrophenyl β-phenylethyl ketone**. Purification of the oil was effected by distillation (b.p. 163.5–166° (0.5 mm.) with some decomposition) followed by chromatography on alumina. The ketone was eluted by benzene and was then evaporatively distilled at 85–95° (0.02–0.04 mm.); $n^{25}D$ 1.5833.

Anal. Calcd. for $C_{15}H_{13}O_3N$: C, 70.58; H, 5.13. Found: C, 70.03; H, 4.90.

Treatment of the sodio derivative from 1.22 g. of di-*t*-butyl benzylmalonate and 0.15 g. of sodium hydride with 0.67 g. (0.004 mole) of cinnamoyl chloride as described above gave 0.75 g. (79% yield) of **styryl β-phenylethyl ketone**, m.p. 49–52°. Recrystallization from petroleum ether (b.p. 90–100°) raised the m.p. to 52.5–53.8° (reported 53°,[12] 53–54°[13]).

Treatment of the sodio derivative from 1.32 g. of di-*t*-butyl *n*-octylmalonate and 0.15 g. of sodium hydride with 0.65 g. (0.004 mole) of caprylyol chloride as described above gave after crystallization from methanol 0.59 g. of ***n*-heptyl *n*-nonyl ketone**, m.p. 40.8–41.6° (reported,[8] 42°). A second crop amounting to 0.07 g., m.p. 37–39.5°, was obtained, raising the yield to 65%. The hydantoin, 5-heptyl-5-nonylhydantoin, prepared from the ketone by the procedure of Henze and Speer,[14] crystallized from methanol in clusters of white needles, m.p. 116.5–117.2° (reported,[8] 123°).

Anal. Calcd. for $C_{19}H_{36}O_2N_2$: N, 8.64. Found: N, 8.41.

Treatment of the sodio derivative from 1.20 g. of di-*t*-butyl cyclohexylmalonate and 0.15 g. of sodium hydride with 0.56 g. (0.004 mole) of benzoyl chloride as described above afforded an oil which was converted to the **2,4-dinitrophenylhydrazone of phenyl cyclohexylmethyl ketone**. The crude derivative, m.p. 145–150°, was obtained in 56% yield. Recrystallization from benzene–petroleum ether raised the m.p. to 148.3–148.6°.

Anal. Calcd. for $C_{20}H_{22}O_4N_4$: N, 14.65. Found: N, 15.00.

Treatment of the sodio derivative from 2.44 g. of di-*t*-butyl benzylmalonate and 0.29 g. of sodium hydride with 1.24 g. (0.008 mole) of *o*-toluyl chloride as described above gave ***o*-tolyl β-phenylethyl ketone**[15] in 70% yield. The product was purified by evaporative distillation at 125–130° (0.05 mm.), $n^{25}D$ 1.5720.

Anal. Calcd. for $C_{16}H_{16}O$: C, 85.67; H, 7.19. Found: C, 85.26; H, 7.36.

Treatment of the sodio derivative from 14.95 g. of di-*t*-butyl cyclohexylmalonate and 1.6 g. of sodium hydride with 7.75 g. (0.05 mole) of *o*-toluyl chloride as described above afforded 6.02 g. (56% yield) of ***o*-tolyl cyclohexylmethyl ketone**, b.p. 126–130° (0.5 mm.), $n^{25}D$ 1.5278. An analytical sample was obtained by redistillation; b.p. 109.5–110° (0.04 mm.), $n^{25}D$ 1.5290.

Anal. Calcd. for $C_{15}H_{20}O$: C, 83.28; H, 9.32. Found: C, 83.16; H, 9.06.

An attempt to prepare the 2,4-dinitrophenylhydrazone of this ketone was unsuccessful.

Di-*t*-butyl Benzylmesitoylmalonate.—The sodio derivative from 4.88 g. (0.016 mole) of di-*t*-butyl benzylmalonate and 0.6 g. (0.025 mole) of sodium hydride, was heated at 80° in 150 ml. of benzene with 2.92 g. (0.016 mole) of freshly distilled mesitoyl chloride for 20 hours. The gelatinous precipitate was removed by filtration and evaporation of the filtrate under reduced pressure gave a brown oil which was dissolved in petroleum ether (b.p. 90–100°) and chromatographed on activated alumina. Development with petroleum ether eluted a small amount (1.33 g.) of a yellow oil. Further development with a 10% solution of chloroform in petroleum ether yielded from the least strongly adsorbed fraction, after extrusion of the column and elution with chloroform, a crystalline product contaminated with traces of oil. The oil was washed from the crystals with a small amount of cold petroleum ether (b.p. 40–60°) to yield 1.86 g. (26%) of almost pure di-*t*-butyl benzylmesitoylmalonate, m.p. 104.5–107.5°. Three recrystallizations from petroleum ether (b.p. 90–100°) gave glistening white crystals, m.p. 106.8–107.6°.

Anal. Calcd. for $C_{28}H_{36}O_5$: C, 74.31; H, 8.02. Found: C, 74.39; H, 7.98.

Mesityl β-Phenylethyl Ketone.—A solution of 4.60 g. (0.01 mole) of di-*t*-butyl benzylmesitoylmalonate in 35 ml. of propionic acid containing a trace of anhydrous *p*-toluenesulfonic acid was refluxed for about ten hours, and 95% of the calculated amount of gas was evolved. The reaction mixture was worked up as described above to yield 2.13 g. (84% yield) of mesityl β-phenylethyl ketone, b.p. 140–141° (0.05 mm.), $n^{25}D$ 1.5547 (reported[16] b.p. 167–169° (1.5 mm.), $n^{25}D$ 1.5520.)

Anal. Calcd. for $C_{18}H_{20}O$: C, 85.67; H, 7.98. Found: C, 85.42; H, 7.99.

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(13) C. Paal, *Ber.*, **45**, 2221 (1912).
(14) H. R. Henze and R. J. Speer, THIS JOURNAL, **64**, 522 (1942).
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(16) J. M. Sprague and H. Adkins, THIS JOURNAL, **56**, 2669 (1934).

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On the Infrared Spectrometry of N^{15}-Labeled Phthalyl Glycine Ethyl Ester

BY FELIX FRIEDBERG AND LAWRENCE M. MARSHALL

The analysis of deuterium-containing compounds by means of infrared spectrometry has been described recently.[1,2] In the course of a study on the spectra–structure correlation in simple peptides, we observed, that phthalyl glycine ethyl ester labeled with N^{15} exhibited a characteristic shift of its spectrum to the right in the region, from 1430 to 1350 cm.$^{-1}$ if compared to the N^{14} control (see graph).

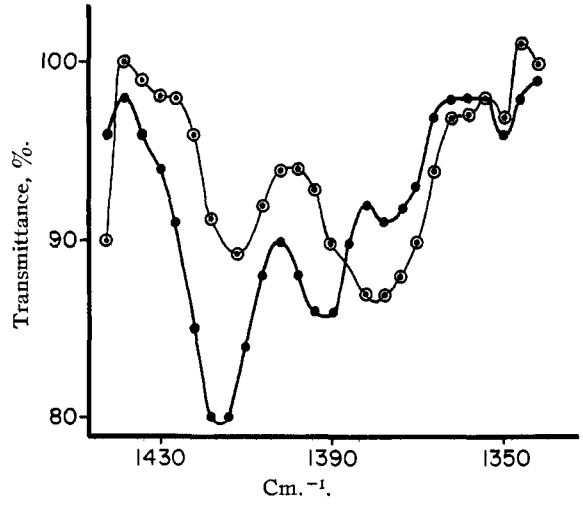

Fig. 1.—Absorption for 5 mg. of phthalyl glycine ethyl ester dissolved in 1 ml. of CCl_4, examined at one-half maximum gain: ●, N^{14} containing compound; ⊙, N^{15} containing compound.

Hence, especially in physiological investigations, infrared spectrometry may be of value in the detection and identification of compounds labeled with N^{15}.

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