[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY, IOWA STATE COLLEGE]

Optically Active Mono-substituted Succinic Acids and Derivatives

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A series of mono-substituted succinic acids was synthesized and resolved into their optical isomers in order to investigate the effect of ring closure on the magnitude of rotatory polarization. Methyl-, phenyl-, anisyl-, *o*-chlorophenyl- and cyclohexylsuccinic acids were prepared in the optically active form and were converted into several derivatives by reactions that involved no direct alteration of the asymmetric carbon atom. Of these acids only the methyl-[2] and the phenylsuccinic acids[3] had been previously prepared. A study was made of the optical rotatory powers of the acids, cyclic anhydrides, beta-amide acids, beta-N-methylamic acids, beta-anilic acids, N-methylimides and the anils. Some of the cyclic imides were also prepared but in no case could an optically active imide be obtained.

Aside from the derivatives of malic acid and the halogen substituted succinic acids, only three resolutions of mono-substituted succinic acids, additional to those included in the present study, have been described: namely, the work of Wren and co-workers on the resolution of ethylsuccinic acid[4] and hexylsuccinic acid,[5] and the recent report of the resolution of cyclopentylsuccinic acid by S. K. Ranganathan.[6] We have resolved anisylsuccinic acid by means of the fractional crystallization of the brucine salts in aqueous alcoholic solution. *o*-Chlorophenylsuccinic acid has been resolved into its optical antipodes by means of the strychnine salt in aqueous alcoholic solution. Dextro cyclohexylsuccinic acid has been prepared from *d*-phenylsuccinic acid and from *d*-*o*-chlorophenylsuccinic acid.

Ring closure of the active acids and of the open chain half-amides (prepared from the cyclic anhydrides) was accomplished by dehydration with acetyl chloride or with a mixture of acetyl chloride and a small amount of thionyl chloride. On the whole, this method of ring closure was satisfactory though the preparation of the active imides and N-methylimides failed. Several conclusive experiments have shown that high temperatures cause complete racemization. First, the distillation of the diammonium salt of *d*-phenylsuccinic acid at 168–170° under 5 mm. pressure produced racemic phenylsuccinimide. Second, the sublimation of the diammonium salt of *d*-phenylsuccinic acid at 4 mm. pressure resulted in racemization. Third, heating *d*-diammonium methylsuccinate in a sealed tube at 170° for three hours yielded a racemic imide.

The acids employed in the present investigation contained alkyl or aryl radicals and aside from methylsuccinic acid were very similar structurally. Furthermore, it was found possible to convert both *d*-phenylsuccinic acid and *d*-*o*-chlorophenylsuccinic acid into *d*-cyclohexylsuccinic acid, thus relating them configurationally. Similarity of structure might allow one to postulate the same configuration for *d*-anisylsuccinic acid. Accordingly, this group of acids was chosen for the present study.

It has been shown that ring closure of *d*-methylsuccinic acid[7] to form the anhydride increases the rotatory power, as is also the case with *l*-methoxy- and *l*-acetoxysuccinic acids,[8] while with *d*- and *l*-phenylsuccinic acids[3] the opposite is true. In the present study, if one excludes methylsuccinic acid, all the acids contain radicals of very similar structure joined carbon-to-carbon to the asymmetric carbon atom and all show great decreases in rotatory power on changing from the acid to the anhydride and from anilic acid to anil. With methylsuccinic acid the anhydride alone is exceptional.

Experimental

Synthesis and Resolution of the Substituted Succinic Acids

***dl*-Methylsuccinic acid**, m. p. 111°, was prepared by the method of Higginbotham and Lapworth.[9]

***d*-Methylsuccinic acid**, m. p. 110–111°, $(\alpha)^{28}\mathrm{D}$ +11.7° (*c* 3.07 in water) was prepared from the racemic acid by the method of Ladenberg.[2]

***dl*-Phenylsuccinic acid**, m. p. 167°, was prepared by the method of Lapworth and Baker.[10]

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[1] During part of this investigation Miss Naps held the Fannie Bullock Workman Fellowship granted by Wellesley College for the year 1936–1937.

[2] Ladenberg, *Ber.*, **28**, 1170 (1895).

[3] Wren and Williams, *J. Chem. Soc.*, **109**, 572 (1916).

[4] Wren and Crawford, *ibid.*, 230 (1937).

[5] Wren and Burns, *ibid.*, **117**, 266 (1920).

[6] S. K. Ranganathan, *J. Indian Chem. Soc.*, **16**, 107 (1939); *Current Sci.*, **6**, 277–278 (1937).

[7] Berner, Leonardsen, Grøntoft and Dahl, *Ann.*, **538**, 1 (1939).

[8] Purdie and Young, *J. Chem. Soc.*, **97**, 1527 (1910).

[9] Higginbotham and Lapworth, *ibid.*, **121**, 49 (1922).

[10] Lapworth and Baker, "Organic Syntheses," Vol. VIII, John Wiley and Sons, New York, N. Y., 1928, p. 88.

d-**Phenylsuccinic acid,** m. p. 173–174°, $(\alpha)^{26}\text{D}$ +148.1° (*c* 0.5 in ethanol) and *l*-phenylsuccinic acid, m. p. 173°, $[\alpha]^{30}\text{D}$ −147.8° (*c* 0.27 in ethanol) were both obtained by the fractional crystallization of the normal brucine salt of the racemic acid, as described by Wren and Williams.[3]

dl-**Anisylsuccinic acid,** first described by Baker and Lapworth,[11] was prepared by the same general method used to obtain phenylsuccinic acid. A yield of 11 g. of acid, m. p. 195–196°, was obtained from 20 g. of ethyl α-cyano-β-anisylacrylate.

d-**Anisylsuccinic Acid.**—Ten grams of *dl*-anisylsuccinic acid was dissolved in boiling 95% ethyl alcohol and the quantity of brucine (34.6 g.) necessary to form the normal salt was added. The solution was filtered, cooled to 20° and allowed to stand for eighteen hours. On stirring a fine, white crop of crystals melting at 185–190° was obtained. After three recrystallizations from 95% ethanol, the product had a constant melting point of 197–200° and weighed 3.8 g.

Anal. Calcd. for $C_{23}H_{26}O_4N_2{\cdot}C_{11}H_{12}O_5$: N, 4.53. Found: N, 4.55.

The dextro acid was regenerated by refluxing the *d*-acid-*l*-brucine salt with 150 cc. of 10% hydrochloric acid solution for two hours. The free acid which crystallized on cooling was filtered off, and the filtrate was then extracted four times with ether. The ether was removed by distillation and the residue was combined with the first crop. The large, glistening needles of *d*-anisylsuccinic acid were recrystallized from hot chlorobenzene containing a small amount of 95% ethanol. The compound melted at 196–197° with sublimation occurring at 191–195°. The sublimate melted sharply at 198.5–199.0°. *Optical rotations.* $[\alpha]^{32}\text{D}$ +135.8° (*c* 0.299 in ethanol), $[\alpha]^{32}\text{D}$ +161.0° (*c* 0.420 in ethyl acetate), $[\alpha]^{31}\text{D}$ +155.4° (*c* 0.869 in acetone), $[\alpha]^{31}_{5461}$ +188.7° (*c* 0.869 in acetone).

l-**Anisylsuccinic Acid.**—The mother liquor from the *d*-acid-*l*-brucine salt was evaporated to 80 cc. and then diluted with 240 cc. of water, for it was found that the alcoholic solution became sirupy on standing and showed no tendency to crystallize. The aqueous alcoholic solution, which was turbid, was heated until it became clear, then filtered and allowed to cool slowly. A crop of 19 g. of *l*-acid-*l*-brucine salt was filtered and recrystallized from a mixture of water and ethyl alcohol. Thirteen grams of salt melting at 136.5–137.0° was obtained. The analysis indicated that a normal salt containing two molecules of water of crystallization had been formed.

Anal. Calcd. for $2(C_{23}H_{26}O_4N_2){\cdot}C_{11}H_{12}O_5{\cdot}2H_2O$: N, 5.35. Found: N, 5.31.

The *l*-anisylsuccinic acid-*l*-brucine salt (13 g.) was hydrolyzed by warming to 58° in 70 cc. of water to which had been added 4 cc. of concentrated hydrochloric acid. Eight-tenths gram of *l*-anisylsuccinic acid crystallized out on cooling: m. p. 196–199°, $[\alpha]^{30}\text{D}$ −120.6° (*c* 1.044 in ethanol). After two recrystallizations from hot chlorobenzene containing approximately 2% of ethyl alcohol, a constant specific rotation of $[\alpha]^{29}\text{D}$ −122.0° was obtained. Since this value is considerably lower than the activity of the dextro isomeride, ($[\alpha]^{32}\text{D}$ (ethanol) + 135.8°), the rotations of the anhydrides prepared from the two isomers were compared: *l*-anisylsuccinic anhydride, $[\alpha]^{29.5}\text{D}$ −94.9° (*c* 0.602 in ethanol), *d*-anisylsuccinic anhydride, $[\alpha]^{29.5}\text{D}$ +95.2° (*c* 0.598 in ethanol). These data indicate that *l*-anisylsuccinic anhydride can be purified by fractional crystallization more readily than *l*-anisylsuccinic acid. After recrystallization of the two anhydrides, the resolution of *dl*-anisylsuccinic acid was complete.

In contrast to the action of hot water on optically active isomerides of phenylsuccinic acid, it was found the *d*- and *l*-anisylsuccinic acids racemized slowly in boiling water.

dl-*o*-**Chlorophenylsuccinic Acid.**—Two-tenths mole (28.1 g.) of *o*-chlorobenzaldehyde was added to 124 cc. of sodium cyanoacetate solution equivalent to 0.265 mole. To effect condensation 1.26 g. of sodium hydroxide in 100 cc. of water was added, and the solution warmed to 40°. After one-half hour the mixture solidified. The sodium salt of α-cyano-β-*o*-chlorophenylacrylic acid was filtered, washed with cold benzene, dried and then dissolved in water. The free α-cyano-β-*o*-chlorophenylacrylic acid was precipitated by the addition of concentrated hydrochloric acid. The product was filtered, washed with cold water and dried at 115°. The yield of fine, transparent needles, which melted at 208–209° with sublimation, was 25 g. or 58% of the theoretical.

Anal. Calcd. for $C_{10}H_6O_2ClN$: N, 6.56. Found: N, 6.73.

The α-cyano-β-*o*-chlorophenylacrylic acid was converted to the ethyl ester by refluxing 20 g. of the dried acid with 100 cc. of absolute ethanol containing 4 g. of dry hydrogen chloride. The mixture was heated for five and one-half hours, filtered and chilled in ice. Precipitation was started by the addition of a few lumps of ice. Sixteen grams of long transparent needles was crystallized out; m. p. 51–52°, yield, 90%. A further small quantity was obtained by working up the mother liquor.

Anal. Calcd. for $C_{12}H_{10}O_2ClN$: N, 5.94. Found: N, 5.80.

For the preparation of ethyl α,β-dicyano-*o*-chlorophenylacrylate, 15 g. of the α,β-unsaturated ester was dissolved in 27 cc. of 50% ethyl alcohol and 7.5 g. of sodium cyanide added. The mixture was heated on the steam-bath for three to four minutes, filtered and diluted with 130 cc. of water. The addition of 16.4 cc. of concentrated hydrochloric acid resulted in the formation of the colloidally dispersed, oily dicyano compound. The solution was extracted with four 50-cc. portions of ether, the ether distilled off, and the oily, red residue refluxed with 160 cc. of concentrated hydrochloric acid for twelve hours. On cooling, the solution deposited small, slightly red-colored crystals of *o*-chlorophenylsuccinic acid. The solution was filtered, extracted with ether, and the ether residue combined with the initial crop of crude acid. The combined products were decolorized with Norit and recrystallized from boiling water. The yield of pure *o*-chlorophenylsuccinic acid which melted at 173–174° with sublimation at 167° was 7.7 g. or 53% of the theoretical amount based on the weight of α,β-unsaturated ester.

Anal. Calcd. for $C_{10}H_9O_4Cl$: C, 52.53; H, 3.97; Cl, 15.50; neutralization equivalent, 114.3. Found: C, 52.75; H, 4.15; Cl, 15.36; neutralization equivalent, 115.0.

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[11] Baker and Lapworth, *J. Chem. Soc.*, **127**, 560 (1925).

d-o-**Chlorophenylsuccinic Acid.**—Attempts to fractionally crystallize the *d*- and *l*-acid-*l*-quinine salts from ethyl acetate and from ethanol were unsuccessful. The resolution was accomplished with strychnine in alcoholic solution. An equimolecular quantity (7.3 g.) of racemic *o*-chlorophenylsuccinic acid was added to 10.7 g. of strychnine dissolved in 500 cc. of hot 95% ethyl alcohol. The solution was refluxed two hours and then cooled to 20°. No deposit was formed after twelve hours, so the solution was evaporated to 130 cc. Since the sirupy residue showed no tendency to crystallize, 100 cc. of water was added and the solution stirred and then cooled overnight at 20°. A crop of 8.5 g. of transparent, monoclinic crystals which melted at 122–126° was deposited. The product was recrystallized from hot water to a constant melting point of 126–128°.

Anal. Calcd. for $C_{21}H_{22}O_2N_2 \cdot C_{10}H_9ClO_4 \cdot 2H_2O$: N, 4.67. Found: N, 4.67.

The *d*-acid-*l*-strychnine salt was hydrolyzed with dilute hydrochloric acid and the *d-o*-chlorophenylsuccinic acid extracted with ether; yield, 2.5 g., m. p. 166–168°. The acid was recrystallized once from benzene and then from 350 cc. of chlorobenzene containing 5 cc. of 95% ethanol. The pure acid melted at 167–168° and gave the following optical rotations: $[\alpha]^{28}_{\mathrm{D}}$ +115.0° (*c* 0.997 in ethanol), $[\alpha]^{28}_{5770}$ +120.0° (*c* 0.997 in ethanol), $[\alpha]^{28}_{5461}$ +136.0° (*c* 0.997 in ethanol), $[\alpha]^{30}_{\mathrm{D}}$ +133.4° (*c* 1.388 in ethyl acetate) $[\alpha]^{31}_{\mathrm{D}}$ +110.6° (*c* 0.408 in chloroform), $[\alpha]^{31}_{\mathrm{D}}$ +112.2° (*c* 0.865 in acetone), $[\alpha]^{31}_{5461}$ +126.0° (*c* 0.865 in acetone).

Anal. Calcd. for $C_{10}H_9ClO_4$: C, 52.53; H, 3.97; Cl, 15.50. Found: C, 53.10; H, 4.21, Cl, 15.30.

l-o-**Chlorophenylsuccinic Acid.**—The mother liquor from which the *d*-acid-*l*-strychnine salt was obtained was diluted with 20 cc. of water and set aside to crystallize. A crop of 2.9 g. of transparent plates melting at 135–138° was deposited. Evaporation of the solution resulted in the formation of another crop with the same melting point. The combined crops were recrystallized from hot water and yielded 2.6 g. of *l-o*-chlorophenylsuccinic acid-*l*-strychnine salt melting at 138°.

Anal. Calcd. for $C_{21}H_{22}O_2N_2 \cdot C_{10}H_9ClO_4$: N, 4.97. Found: N, 4.92.

The crop of *l*-acid-*l*-strychnine salt was hydrolyzed with dilute hydrochloric acid. The solution was cooled and extracted thoroughly with ether. After removal of the ether by distillation, the *l*-acid was washed with benzene and dried; m. p. 163–165°, yield, 2.2 g. The levo acid was further purified by recrystallization from hot chlorobenzene containing a small amount of 95% ethyl alcohol; m. p. 166–168°, $[\alpha]^{32}_{\mathrm{D}}$ −101.3° (*c* 1.005 in ethanol). The anhydride prepared from the above acid had the following rotation: $[\alpha]^{31}_{\mathrm{D}}$ −45.7° (*c* 0.835 in ethanol). This value is in good agreement with the rotation observed for pure *d-o*-chlorophenylsuccinic anhydride: $[\alpha]^{31}_{\mathrm{D}}$ +45.5° (*c* 0.907 in ethanol). The dextro anhydride was prepared from a sample of dextro acid having a specific rotation of $[\alpha]^{28}_{\mathrm{D}}$ +115.0°.

dl-**Cyclohexylsuccinic Acid.**—A convenient method of preparation of *dl*-cyclohexylsuccinic acid is the catalytic hydrogenation of *dl*-phenylsuccinic acid. Five-tenths gram of racemic phenylsuccinic acid was dissolved in 25 cc. of absolute ethanol and 0.15 g. of platinum oxide added. The catalyst was prepared by the method of Shriner and Adams.[12] Reduction was carried out for seventeen hours at room temperature and under six atmospheres gage pressure. One-tenth gram more catalyst was added after four hours. The solvent was evaporated and the residue recrystallized from benzene. Twenty-four hundredths gram of the compound melting at 146.0° was obtained.

Anal. Calcd. for $C_{10}H_{16}O_4$: C, 60.0; H, 8.03. Found: C, 60.6; H, 8.12.

The same procedure was used to reduce 0.50 g. of *dl-o*-chlorophenylsuccinic acid. The product recrystallized from benzene melted at 146.0°. A mixed melting point with the reduction product of *dl*-phenylsuccinic acid showed no depression. Ranganathan reports 143° for the melting point of the acid[6] prepared by an entirely different method.

d-**Cyclohexylsuccinic Acid.**—The active isomer was prepared from 0.50 g. of *d*-phenylsuccinic acid ($[\alpha]^{26}_{\mathrm{D}}$ +148.1° in ethanol) by catalytic hydrogenation. The procedure followed was identical to that used for the racemic compound. The oily product was crystallized by agitating an acid solution which had stood overnight. The compound melted sharply at 95.5–96.0° and weighed 0.30 g. *Optical rotations.* $[\alpha]^{30}_{\mathrm{D}}$ +26.3° (*c* 1.937 in ethanol), $[\alpha]^{30}_{5461}$ +30.5° (*c* 1.937 in ethanol), $[\alpha]^{31}_{\mathrm{D}}$ +38.3° (*c* 1.565 in acetone), $[\alpha]^{31}_{5461}$ +47.9° (*c* 1.565 in acetone).

Anal. Calcd. for $C_{10}H_{16}O_4$: C, 60.0; H, 8.03. Found: C, 59.5; H, 8.05.

d-Cyclohexylsuccinic acid was also obtained by the catalytic hydrogenation of *d-o*-chlorophenylsuccinic acid, $[\alpha]^{28}_{\mathrm{D}}$ +115.0° in ethanol. A 0.2-g. portion of the halogen compound was reduced for twelve hours using 0.1 g. of catalyst. The oily product was dissolved in dilute sodium hydroxide and the substituted succinic acid precipitated by the addition of hydrochloric acid. The compound was filtered the next day, washed with dilute hydrochloric acid and dried. After extraction and recovery from benzene, the product was recrystallized from 25% hydrochloric acid. The compound gave the following constants: m. p. 95.0–95.5°; $[\alpha]^{33}_{\mathrm{D}}$ +26.5° (*c* 1.359 in ethanol), $[\alpha]^{33}_{5461}$ +32.4° (*c* 1.359 in ethanol).

Anhydrides

d-**Methylsuccinic Anhydride.**—One-hundredth mole (7.32 g.) of *d*-methylsuccinic acid ($[\alpha]^{27}_{\mathrm{D}}$ +9.65° in water) was treated with 6.6 cc. of acetyl chloride and 0.7 cc. of thionyl chloride and refluxed gently for three hours. The excess solvents were removed under diminished pressure and the residue recrystallized from a mixture of benzene and petroleum ether (b. p. 60–68°). The transparent prisms gave the following constants: m. p. 64–65°; $[\alpha]^{29}_{\mathrm{D}}$ +31.3° (*c* 1.537 in chloroform), $[\alpha]^{29}_{\mathrm{D}}$ +32.1° (*c* 2.717 in ethanol), $[\alpha]^{28}_{\mathrm{D}}$ +31.3° (*c* 1.280 in acetone).

Anal. Calcd. for $C_5H_6O_3$: C, 52.55; H, 5.30. Found: C, 52.75; H, 5.33.

l-**Methylsuccinic Anhydride.**—From one gram of *l*-methylsuccinic acid that was only partially resolved, $[\alpha]^{22}_{\mathrm{D}}$ −5.0°, the anhydride was prepared in the same manner as for the dextro isomer. After recrystallization the anhy-

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[12] Shriner and Adams, "Organic Syntheses," Vol. VIII, John Wiley and Sons, New York, N. Y., 1928, p. 92.

dride had nearly the same rotatory power as the *d*-isomer; $[\alpha]^{30}_{\mathrm{D}}$ −32.6° (*c* 1.770 in chloroform), $[\alpha]^{31.2}_{\mathrm{D}}$ −31.3° (*c* 2.050 in ethanol).

Berner[7] prepared the anhydride of *d*-methylsuccinic acid by means of thionyl chloride alone. His product had a higher melting point, 69.5°, but the same rotatory power in ethanol, $[\alpha]^{20}_{\mathrm{D}}$ +32.1° (p. 4.074). He also noted the fact that optically impure anhydrides can be purified by crystallization while the acids cannot.

***d*-Phenylsuccinic Anhydride.**—A solution of 0.95 g. of *d*-phenylsuccinic acid in 4 cc. of acetyl chloride and 0.45 cc. of thionyl chloride was refluxed for two hours. The anhydride was recrystallized from a mixture of ethyl bromide and petroleum ether (b. p. 60–68°) and melted sharply at 82°; yield 0.83 g., $[\alpha]^{29}_{\mathrm{D}}$ +99.8° (*c* 0.751 in benzene), $[\alpha]^{29.8}_{\mathrm{D}}$ +112.2° (*c* 0.489 in acetone), $[\alpha]^{29}_{\mathrm{D}}$ +98.4° (*c* 0.681 in ethanol). Wren and Williams[3] had obtained a compound melting at 83° and having a rotation of $[\alpha]^{15}_{\mathrm{D}}$ +100.9° in benzene.

***d*-Anisylsuccinic Anhydride.**—Four-tenths gram of *d*-anisylsuccinic acid was converted to the anhydride by dehydration with an excess of acetyl chloride and an equimolecular proportion of thionyl chloride. The procedure was similar to that employed for *d*-methylsuccinic acid. The product which crystallized out on the evaporation of the excess solvents was recrystallized from a mixture of chloroform and petroleum ether (b. p. 60–68°). A beautiful crop of fine, transparent needles melting at 92.5–93.0° was obtained. The yield was 0.310 g. or 86% of the theoretical. *Optical rotations.* $[\alpha]^{31}_{\mathrm{D}}$ +93.0° (*c* 0.807 in ethyl acetate), $[\alpha]^{31}_{5461}$ +109.2° (*c* 0.807 in ethyl acetate), $[\alpha]^{31}_{\mathrm{D}}$ +95.2° (*c* 0.598 in ethanol), $[\alpha]^{31}_{\mathrm{D}}$ +87.8° (*c* 0.502 in chloroform), $[\alpha]^{31}_{5461}$ +110.0° (*c* 0.502 in chloroform), $[\alpha]^{31}_{\mathrm{D}}$ +125.7° (*c* 0.366 in acetone), $[\alpha]^{31}_{5461}$ +172.6° (*c* 0.366 in acetone).

Anal. Calcd. for $C_{11}H_{10}O_4$: C, 64.1; H, 4.89. Found: C, 64.6; H, 4.95.

***l*-Anisylsuccinic Anhydride.**—The levo anhydride was prepared in exactly the same manner as the dextro isomeride. Two recrystallizations of the product from a mixture of chloroform and petroleum ether (b. p. 60–68°) yielded a compound with a m. p. 92.5–93.0°; $[\alpha]^{29.5}_{\mathrm{D}}$ −94.9° (*c* 0.602 in ethanol), $[\alpha]^{29.5}_{5461}$ −107.9° (*c* 0.602 in ethanol).

Anal. Calcd. for $C_{11}H_{10}O_4$: C, 64.1; H, 4.89 Found: C, 64.4; H, 4.98.

***dl-o*-Chlorophenylsuccinic Anhydride.**—One gram of *o*-chlorophenylsuccinic acid was converted to the anhydride by treatment with 6.6 cc. of acetyl chloride and 0.32 cc. of thionyl chloride. The product was recrystallized twice from a mixture of benzene and petroleum ether (b. p. 60–68°). The yield of transparent needles which melted sharply at 122.0° was 0.540 g. (60% of the theoretical). *dl-o*-Chlorophenylsuccinic anhydride is insoluble in benzene and soluble in chloroform.

Anal. Calcd. for $C_{10}H_7O_3Cl$: C, 57.03; H, 3.35. Found: C, 57.6; H, 3.63.

***d-o*-Chlorophenylsuccinic Anhydride.**—One gram of *d-o*-chlorophenylsuccinic acid was dehydrated as previously described. A mass of transparent needles (0.62 g.) was obtained on recrystallization of the product from a mixture of benzene and light petroleum (b. p. 60–68°). The dextro anhydride gave the following constants: m. p. 145–146°; $[\alpha]^{31}_{\mathrm{D}}$ +45.2° (*c* 0.907 in ethanol), α^{31}_{D} 0.00° (*c* 0.964 in chloroform), α^{31}_{D} 0.00° (*c* 2.600 in chloroform), $[\alpha]^{31}_{\mathrm{D}}$ +16.8° (*c* 0.654 in benzene), $[\alpha]^{30}_{\mathrm{D}}$ +20.8° (*c* 0.863 in ethyl acetate), $[\alpha]^{29.2}_{\mathrm{D}}$ +49.7° (*c* 0.443 in acetone), $[\alpha]^{29.2}_{5461}$ +61.0° (*c* 0.443 in acetone).

A determination of the rotation in chloroform was made at two concentrations, but the value obtained in each case was zero. The *d-o*-chlorophenylsuccinic anhydride did not racemize in the solvent, however, for samples recovered from the chloroform were still active, *e. g.*, in ethanol the observed specific rotation was $[\alpha]^{30.5}_{\mathrm{D}}$ +44.3°.

Anal. Calcd. for $C_{10}H_7O_3Cl$: C, 57.03; H, 3.35. Found: C, 57.25; H, 3.68.

***l-o*-Chlorophenylsuccinic Anhydride.**—Two-tenths gram of *l-o*-chlorophenylsuccinic acid ($[\alpha]^{32}_{\mathrm{D}}$ −101.3° in ethanol) was treated by the same procedure previously described. The product melted at 145–146°, and gave the following optical rotations: $[\alpha]^{31}_{\mathrm{D}}$ −45.7° (*c* 0.832 in ethanol), $[\alpha]^{31}_{5461}$ −59.0° (*c* 0.832 in ethanol).

***d*-Cyclohexylsuccinic Anhydride.**—The preparation was performed in the usual manner with 0.275 g. of active acid. The product did not crystallize very readily, however, because of the low melting point. Large transparent prisms were obtained by chilling a solution of the product in 3 cc. of petroleum ether (b. p. 60–68°) and a few drops of ethyl bromide; yield 0.130 g.; m. p. 43.0°; $[\alpha]^{31}_{\mathrm{D}}$ +9.5° (*c* 1.390 in ethanol), $[\alpha]^{31}_{\mathrm{D}}$ +4.71° (*c* 1.912 in acetone), $[\alpha]^{31}_{5461}$ +5.75° (*c* 1.912 in acetone), $[\alpha]^{31}_{5461}$ +11.5° (*c* 1.390 in ethanol).

Anal. Calcd. for $C_{10}H_{14}O_3$: C, 65.94; H, 7.75. Found: C, 65.4; H, 7.84.

Succinamic Acids

***d*-Phenylsuccinamic Acid.**—The racemic isomer was prepared previously by Anschütz,[13] who showed that addition of ammonia to phenylsuccinic anhydride resulted in the formation of the β-amide-α-acid, the weaker carboxyl group being attached to the nitrogen. Two-tenths gram of *d*-phenylsuccinic anhydride was dissolved in 20 cc. of anhydrous ether and dry ammonia passed into the solution. After precipitation was complete, the ether was removed by evaporation and the gummy residue dissolved in 4–5 drops of water. The free amic acid was precipitated by the dropwise addition of concentrated hydrochloric acid. The product was purified by precipitation from the sodium salt, and recrystallized once from hot water: m. p. 141–145°, yield 0.130 g.; $[\alpha]^{31.8}_{\mathrm{D}}$ +52.8° (*c* 0.587 in ethanol).

Anal. Calcd. for $C_{10}H_{11}O_3N$: N, 7.24. Found: N, 7.09.

The product was again recrystallized from boiling water: m. p. 134–137°, $[\alpha]^{32.8}_{\mathrm{D}}$ +27.9° (*c* 0.897 in ethanol).

Anal. Found: N, 5.53.

The low values of melting point, rotation and nitrogen content indicated that *d*-phenylsuccinamic acid racemized in the boiling water and was partially hydrolyzed.

***d*-Anisylsuccinamic Acid.**—The same procedure employed for the preparation of the phenyl derivative was used to convert 0.150 g. of *d*-anisylsuccinic anhydride to

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[13] Anschütz, *Ann.*, **354**, 117 (1907).

the amic acid. The yield of material melting at 166–169° was 0.120 g.

Anal. Calcd. for $C_{11}H_{13}O_4N$: N, 6.27. Found: N, 5.76.

The product was recrystallized from hot water in the form of light, transparent plates, m. p. 169.0°. The nitrogen analysis (N, 5.60) showed that *d*-anisylsuccinamic acid must have undergone hydrolysis. The rotatory power of this sample was $[\alpha]^{29}_{\mathrm{D}}$ +104.3° (*c* 0.345 in ethanol).

***dl-o*-Chlorophenylsuccinamic Acid.**—The racemic amic acid was prepared from 0.140 g. of *dl-o*-chlorophenylsuccinic anhydride dissolved in anhydrous ether. The ammonium salt of the amic acid formed by the addition of excess ammonia was converted to the amic acid by treatment with concentrated hydrochloric acid. The 0.08-g. crop of transparent plates softened at 156° and melted at 164°.

Anal. Calcd. for $C_{10}H_{10}O_3ClN$: N, 6.16. Found: N, 6.22.

***d-o*-Chlorophenylsuccinamic Acid.**—An ethereal solution of 0.120 g. of *d-o*-chlorophenylsuccinic anhydride was treated with dry ammonia. The free amic acid was liberated by the procedure described previously, and recrystallized from hot water. The crop of transparent plates melted at 164–165° and weighed 0.080 g. and had a rotation of $[\alpha]^{32}_{\mathrm{D}}$ +19.0° (*c* 0.422 in ethanol).

Anal. Calcd. for $C_{10}H_{10}O_3ClN$: N, 6.16. Found: N, 6.10.

The compound was recrystallized from hot water and the optical rotation again measured. The low value indicated that *d-o*-chlorophenylsuccinamic acid racemizes in boiling water; $[\alpha]^{28}_{\mathrm{D}}$ +13.6° (*c* 0.367 in ethanol).

N-Methylsuccinamic Acids

***d*-N-Methylphenylsuccinamic Acid.**—The same general method employed for the preparation of amic acids was employed for the N-methylamic acids substituting methylamine for the ammonia. Two-tenths gram of *d*-phenylsuccinic anhydride yielded 0.110 g. of *d*-N-methylphenylsuccinamic acid which melted at 159–160° after one recrystallization from hot water. The low value of optical rotation indicated that *d*-N-methylphenylsuccinamic acid racemized in hot water; $[\alpha]^{28}_{\mathrm{D}}$ +34.8° (*c* 0.287 in ethanol), $[\alpha]^{30}_{\mathrm{D}}$ +13.9° (*c* 0.359 in ethyl acetate). Wren and Williams[3] found that esters of *d*-phenylsuccinic acid racemized readily in hot water.

Anal. Calcd. for $C_{11}H_{13}O_3N$: N, 6.76. Found: N, 6.67.

***d*-N-Methylanisylsuccinamic Acid.**—Fifty milligrams of product melting at 174–175° after one recrystallization from water was obtained from 0.20 g. of *d*-anisylsuccinic anhydride and an excess of methylamine. *Optical rotations.* $[\alpha]^{28}_{\mathrm{D}}$ +129.3° (*c* 0.263 in ethyl acetate), $[\alpha]^{31}_{\mathrm{D}}$ +119.7° (*c* 0.251 in acetone), $[\alpha]^{31}_{5461}$ +143.8° (*c* 0.251 in acetone), $[\alpha]^{29}_{\mathrm{D}}$ +143.0° (*c* 0.329 in ethanol).

Anal. Calcd. for $C_{12}H_{15}O_4N$: N, 5.90. Found: N, 5.86.

***d*-N-Methyl-*o*-chlorophenylsuccinamic Acid.**—Two-tenths gram of *d-o*-chlorophenylsuccinic anhydride was converted to 0.110 g. of the half-amide in the usual manner. The product crystallized more readily than the N-methylamic acids of phenyl- and anisylsuccinic acids. The following constants were obtained for the dextro compound: m. p. 156–158°; $[\alpha]^{29.8}_{\mathrm{D}}$ +92.5° (*c* 0.379 in acetone), $[\alpha]^{29.8}_{5461}$ +105.8° (*c* 0.379 in acetone), $[\alpha]^{34}_{\mathrm{D}}$ +104.3° (*c* 0.412 in ethanol), $[\alpha]^{34}_{5461}$ +104.2° (*c* 0.451 in ethyl acetate).

Anal. Calcd. for $C_{11}H_{12}O_3ClN$: N, 5.79. Found: N, 5.72.

N-Methylsuccinimides

Attempts to prepare the N-methylimides from the N-methylsuccinamic acids by dehydration with acetyl chloride and with mixtures of acetyl chloride and thionyl chloride resulted in compounds having indefinite composition and no rotatory power. Only in the following case was a pure product obtained.

***dl*-N-Methyl-*o*-chlorophenylsuccinimide.**—The imide was prepared from 80 mg. *d*-N-methyl-*o*-chlorophenylsuccinamic acid and 2 cc. acetyl chloride by refluxing one-half hour. The excess solvent was removed under diminished pressure and the product recrystallized from dilute acetic acid; yield 30 mg., m. p. 129–131°.

Anal. Calcd. for $C_{11}H_{10}O_2ClN$: N, 6.26. Found: N, 6.17.

The preparation was repeated with the dextro isomer but always resulted in a substance of low nitrogen content (N, 3.6), m. p. 161.5°, and possessing no rotatory power in acetone.

Succinanilic Acids

***d*-Methylsuccinanilic Acid.**—A benzene solution of 0.340 g. of *d*-methylsuccinic anhydride and 0.28 cc. (equimolecular amount) of aniline was refluxed for one-half hour. A yield of 0.400 g. of short, needle-like crystals was obtained: m. p. 143–144°; $[\alpha]^{31}_{\mathrm{D}}$ +11.4° (*c* 2.285 in ethanol), $[\alpha]^{30}_{\mathrm{D}}$ +16.6° (*c* 1.207 in acetone), $[\alpha]^{30}_{5461}$ +21.5° (*c* 1.207 in acetone).

Anal. Calcd. for $C_{11}H_{13}O_3N$: N, 6.76. Found: N, 6.82.

***l*-Methylsuccinanilic Acid.**—The same method used to prepare the dextro isomeride yielded 0.200 g. of needle-like crystals from 0.20 g. of *l*-methylsuccinic anhydride. The anilic acid gave the following constants: m. p. 143–145°; $[\alpha]^{32}_{\mathrm{D}}$ −10.9° (*c* 2.674 in ethanol).

***d*-Phenylsuccinanilic Acid.**—A benzene solution of 0.240 g. of *d*-phenylsuccinic anhydride and 0.12 cc. of aniline was refluxed for one hour. A small amount of chloroform was added to aid in dissolving the anhydride. The anilic acid could not be crystallized from the solution so it was recrystallized once through the sodium salt by the addition of a small amount of concentrated hydrochloric acid and was then purified by the dilution of a glacial acetic acid solution of the compound. The crystalline precipitate weighed 0.130 g.: m. p. 125–127°; $[\alpha]^{31}_{\mathrm{D}}$ +151.8° (*c* 0.876 in ethanol), $[\alpha]^{33}_{\mathrm{D}}$ +153.8° (*c* 0.442 in acetone), $[\alpha]^{33}_{5461}$ +169.8° (*c* 0.442 in acetone), $[\alpha]^{33}_{\mathrm{D}}$ +160.2° (*c* 0.412 in ethyl acetate), $[\alpha]^{33}_{5461}$ +208.7° (*c* 0.412 in ethyl acetate).

Anal. Calcd. for $C_{16}H_{15}O_3N$: N, 5.21. Found: N, 5.16.

The melting point of the dextro isomer is considerably lower than that of the racemic compound which melts at 167–168° as reported by Anschütz.[13] This investigator proved that the anilic acid formed on opening the ring was the β-anilide-α-acid.

d-**Anisylsuccinanilic Acid.**—The compound was prepared from 0.20 g. of *d*-anisylsuccinic anhydride and 0.1 cc. of aniline. The anilic acid was purified by precipitation from the sodium salt and recrystallization from hot benzene: yield 0.150 g.; m. p. 148–150°; $[\alpha]^{30}_{\rm D}$ +120.8° (*c* 0.323 in chloroform), $[\alpha]^{30}_{\rm D}$ +154.0° (*c* 0.318 in ethanol).

Anal. Calcd. for $C_{17}H_{17}O_4N$: N, 4.68. Found: N, 4.77.

d-*o*-**Chlorophenylsuccinanilic Acid.**—The anilic acid was prepared from 0.100 g. of dextro anhydride and 0.05 cc. of aniline. The product crystallized in fine needles: yield 0.130 g.; m. p. 169–170°; $[\alpha]^{32}_{\rm D}$ +130.7° (*c* 0.375 in ethanol), $[\alpha]^{31.5}_{\rm D}$ +160.1° (*c* 0.512 in ethyl acetate), $[\alpha]^{30}_{\rm D}$ +139.7° (*c* 0.444 in acetone), $[\alpha]^{30}_{5461}$ +173.5° (*c* 0.444 in acetone).

Anal. Calcd. for $C_{16}H_{14}O_3ClN$: N, 4.62. Found: N, 4.69.

d-**Cyclohexylsuccinanilic Acid.**—The compound was prepared from 0.128 g. of *d*-cyclohexylsuccinic anhydride and 0.07 cc. of aniline. A yield of 0.130 g. of short, needle-like crystals was obtained: m. p. 172.0–172.5°; $[\alpha]^{31}_{\rm D}$ +32.2° (*c* 0.467 in ethanol), $[\alpha]^{31}_{5461}$ +19.3° (*c* 0.467 in ethanol), $[\alpha]^{31}_{\rm D}$ +33.5° (*c* 0.626 in acetone), $[\alpha]^{31}_{5461}$ +25.6° (*c* 0.626 in acetone).

The optical activity of *d*-cyclohexylsuccinanilic acid is quite unusual in that the rotation for the 5461 line is less than the rotation for the D line in both ethanol and acetone.

Anal. Calcd. for $C_{16}H_{21}O_3N$: N, 5.08. Found: N, 5.08.

Anils

d-**Methylsuccinanil.**—Anils can be prepared from anilic acids by dehydration with acetyl chloride. The method described for the preparation of *d*-methylsuccinanil is the general procedure employed for all the anils prepared. A mixture of 0.155 g. of *d*-methylsuccinanilic acid and 2 cc. of acetyl chloride was refluxed for three-fourths hour. The excess solvent was removed under diminished pressure and the white crystalline residue recrystallized from ethanol. The product melted at 125–126° and weighed 0.130 g. The following rotations were obtained: $[\alpha]^{31}_{\rm D}$ +4.5° (*c* 2.210 in chloroform), $[\alpha]^{31}_{\rm D}$ +4.5° (*c* 1.112 in ethanol).

Anal. Calcd. for $C_{11}H_{11}O_2N$: N, 7.40. Found: N, 7.30.

l-**Methylsuccinanil.**—One-tenth gram of *l*-methylsuccinic anhydride was converted to 0.040 g. of anil: m. p 125–126°; $[\alpha]^{32.5}_{\rm D}$ −5.5° (*c* 2.354 in chloroform).

The sample was recovered from chloroform and found to have no measurable rotation in acetone.

Anal. Calcd. for $C_{11}H_{11}O_2N$: N, 7.40. Found: N, 7.46.

d-**Phenylsuccinanil.**—A mixture of 0.150 g. of *d*-phenylsuccinanilic acid and 2 cc. of acetyl chloride was refluxed for one and one-half hours. The compound was recrystallized from hot alcohol. A crop of fluffy fine needles which melted at 165–166° and weighed 0.040 g. was filtered off as soon as the solution cooled to room temperature. The filtrate soon deposited another crop which melted at 140–141° and weighed 0.070 g. The second crop also consisted of acicular crystals.

The procedure was repeated and the optical activity of the two products measured. The following constants were obtained: (m. p. 165–166°) $\alpha^{28}_{\rm D}$ 0.00° (*c* 0.254 in acetone), $[\alpha]^{28}_{5461}$ −27.5° (*c* 0.254 in acetone), $[\alpha]^{29.2}_{5461}$ +49.8° (*c* 0.382 in benzene); (m. p. 140–141°) $[\alpha]^{29.8}_{5461}$ −26.5° (*c* 0.378 in acetone), $\alpha^{29.8}_{\rm D}$ 0.00° (*c* 0.378 in acetone), $[\alpha]^{29.8}_{\rm D}$ +21.0° (*c* 0.476 in benzene), $[\alpha]^{29.8}_{5461}$ +50.4° (*c* 0.476 in benzene), $[\alpha]^{29.8}_{5461}$ −76.3° (*c* 0.406 in acetic acid).

Anal. Calcd. for $C_{16}H_{13}O_2N$: N, 5.57. Found: N (m. p. 165–166°), 5.58; N (m. p. 140–141°), 5.53.

These data indicate that *d*-phenylsuccinanil exists in two crystalline forms differing in melting point.

The rotation of the isomer melting at 140–141° had a large negative value in glacial acetic acid, but after a short time the rotation had dropped to zero.

d-**Anisylsuccinanil.**—This compound was prepared from 0.070 g. of *d*-anisylsuccinanilic acid and 2 cc. of acetyl chloride. Heating was continued for twenty minutes. The active anil (0.040 g.) melted at 165–166° and gave the following rotations: $[\alpha]^{27}_{\rm D}$ +36.6° (*c* 0.273 in acetone), $\alpha^{27}_{\rm D}$ 0.00° (*c* 0.385 in chloroform), $[\alpha]^{29}_{\rm D}$ +29.3° (*c* 0.410 in benzene), $[\alpha]^{29}_{5461}$ +26.9° (*c* 0.410 in benzene).

A second reading was made in acetone, giving the following results: $[\alpha]^{30}_{\rm D}$ +19.3° (*c* 0.413 in acetone), $[\alpha]^{30}_{5461}$ −41.1° (*c* 0.413 in acetone). After a short time, rotations for both lines had dropped to zero. These values indicate that *d*-anisylsuccinanil racemizes in acetone. The inconsistent readings obtained for the compound dissolved in benzene indicate that the sample was not optically pure. The behavior of *d*-phenylsuccinanil in acetic acid points to the fact that *d*-anisylsuccinanil probably racemized to some extent in the original reaction mixture.

Anal. Calcd. for $C_{17}H_{15}O_3N$: N, 4.98. Found: N, 5.08.

d-*o*-**Chlorophenylsuccinanil.**—A crop of 0.040 g. of transparent needles which melted at 180–181° was obtained by refluxing 0.090 g. of *d*-*o*-chlorophenylsuccinanilic acid and 2 cc. of acetyl chloride. The following rotations were obtained for the product: $[\alpha]^{31.8}_{\rm D}$ −58.8° (*c* 0.306 in chloroform), $[\alpha]^{31}_{\rm D}$ −19.2° (*c* 0.626 in acetone), $[\alpha]^{31}_{5461}$ −27.2° (*c* 0.626 in acetone), $[\alpha]^{29}_{\rm D}$ −27.6° (*c* 0.272 in ethanol), $[\alpha]^{29}_{5461}$ −38.7° (*c* 0.272 in ethanol).

Anal. Calcd. for $C_{16}H_{12}O_2ClN$: N, 4.91. Found: N, 5.01.

dl-*o*-**Chlorophenylsuccinanil.**—One-tenth gram of *dl*-*o*-chlorophenylsuccinanilic acid was heated with 2 cc. of acetyl chloride for two hours. The sirupy product was taken up in hot 95% ethanol, the solution filtered and ice added to the filtrate. The precipitate (80 mg.) was decolorized with Norit and recrystallized from dilute alcohol to yield 50 mg. of transparent needles, m. p. 143–144°.

Anal. Calcd. for $C_{16}H_{12}O_2ClN$: N, 4.91. Found: N, 4.98.

d-**Cyclohexylsuccinanil.**—One-tenth gram of the dextro anilic acid was heated with 1.7 cc. of acetyl chloride for thirty minutes. The product was recrystallized from ethyl alcohol: yield 0.040 g.; m. p. 143.5–144.5°; $[\alpha]^{31}_{D}$ −41.1° (*c* 0.584 in ethanol), $[\alpha]^{31}_{5461}$ −53.1° (*c* 0.584 in ethanol), $[\alpha]^{31}_{D}$ −44.2° (*c* 0.612 in acetone), $[\alpha]^{31}_{5461}$ −49.0° (*c* 0.612 in acetone).

Anal. Calcd. for $C_{16}H_{19}O_2N$: N, 5.45. Found: N, 5.44.

Discussion

The rotatory powers of the mono-substituted succinic acids and their anhydrides are summarized in Table I.

TABLE I

DEXTRO-ROTATORY MONO-SUBSTITUTED SUCCINIC ACIDS AND THEIR ANHYDRIDES

Compound	*[M]D in ethanol* Acid	Anhydride	*[M]D in acetone* Acid	Anhydride
Phenyl-	+287.57	+173.36	+341.93	+198.02
Anisyl-	304.47	196.3	348.4	259.2
o-Chlorophenyl-	262.9	95.20	256.05	104.68
Cyclohexyl-	52.66	16.94	76.68	8.58
Methyl-	16.12	36.63	22.85	35.71
Ethyl-			+ 30.18[4]	− 12.5[7]
Hexyl-(levo)[5]	− 53.8		− 66.54	(no
Cyclopentyl-[6]			+ 43.85	solvent)

The ring closure of the acids to form the anhydrides decreases the rotatory power except with *d*-methylsuccinic acid.

The anilic acids have higher rotatory powers than the free acids. Ring closure of the anilic acid to form the anil results in a much greater decrease in rotatory power than does ring closure of the acid to form the anhydride. In the case of *d*-phenyl-, *d*-*o*-chlorophenyl- and *d*-cyclohexylsuccinanilic acids the decrease in rotation is sufficient to cause a change in sign for the anil.

The low values for *d*-*o*-chlorophenyl-, *d*-phenyl- and *d*-N-methylphenylsuccinamic acids were due to partial racemization which occurred on recrystallization from hot water. These compounds are so easily racemized that all attempts to form the imides from them gave entirely inactive products.

Several of the compounds exhibited marked solvent effects. Thus, *d*-*o*-chlorophenylsuccinic anhydride had no rotatory power in chloroform but after recovery from this solvent it showed its normal rotatory power in ethanol, acetone, benzene and ethyl acetate. Also *d*-phenylsuccinanil had a positive rotation in benzene, $[\alpha]^{29}_{5461}$ + 49.8°, and a negative rotation in acetone, $[\alpha]^{28}_{5461}$ −27.5°, as did also a sample of partially racemized *d*-anisylsuccinanil, $[\alpha]^{30}_{5461}$ +26.9° in benzene, and $[\alpha]^{30}_{5461}$ −41.1° in acetone. In a short time this last value had dropped to zero, indicating spontaneous racemization of *d*-anisylsuccinanil in acetone. Racemization also occurred with *d*-methylsuccinanil in acetone, and with *d*-phenylsuccinanil in acetic acid.

TABLE IIa

ROTATORY POWER OF MONO-SUBSTITUTED SUCCINIC ACIDS AND DERIVATIVES [*M*]D IN ETHANOL

	Acid	Anhydride	Anilic acid	Anil	Amic acid	N-Methylamic acid
Cyclohexyl-	+ 52.66	+ 16.94	+ 88.65	−105.75		
Methyl-	16.12	36.63	23.62	+ 8.51		
Anisyl-	304.5	196.3	460.9	[a]	+232.8	+339.2
Phenyl-	287.54	173.36	408.78	[a]	102.0[a]	72.1[a]
o-Chlorophenyl-	262.9	95.2	397.0	− 78.85	43.7[a]	252.3

[a] Partial racemization known to have occurred.

TABLE IIb

[*M*]D IN ACETONE

	Acid	Anhydride	Anilic acid	Anil	N-Methylamic acid
Cyclohexyl-	+ 76.68	+ 8.58	+ 92.50	−117.73	
Methyl-	22.85	35.71	34.4	[a]	
Anisyl-	348.4	259.2		+102.95[a]	+283.9
Phenyl-	341.93	198.02	414.16	0 (D) − 69.1 (5461)	
o-Chlorophenyl-	256.05	104.68	424.3	− 54.86	223.5

[a] Partial racemization known to have occurred.

The rotatory powers of all the derivatives of the dextro acids studied in this investigation are given in Table IIa and Table IIb.

Summary

1. A study of the optical activity of methyl-, phenyl-, *o*-chlorophenyl-, anisyl- and cyclohexylsuccinic acids and anhydrides and of their anilic acids and anils has shown that ring closure results in a marked decrease in rotatory power, except in the case of the methyl anhydride.

2. The following new compounds have been described: *d*- and *l*-anisylsuccinic acids, *dl*-, *d*-

and *l*-*o*-chlorophenylsuccinic acids, *d*-cyclohexylsuccinic acid; β-anilide-α-acid and anil of *d*- and *l*-methyl-, *d*-cyclohexyl-, *d*-phenyl-, *d*-anisyl- and *d*-*o*-chlorophenylsuccinic acid; anil of *dl*-*o*-chlorophenylsuccinic acid; β-amide-α-acid of *d*-phenyl-, *d*-anisyl-, *dl*- and *d*-*o*-chlorophenylsuccinic acids; β-N-methylamide-α-acid of *d*-phenyl-, *d*-anisyl- and *d*-*o*-chlorophenylsuccinic acids; anhydrides of *d*-cyclohexyl-, *d*- and *l*-anisyl-, *dl*-, *d*- and *l*-*o*-chlorophenylsuccinic acids; imide of *dl*-N-methyl-*o*-chlorophenylsuccinic acid.

3. *d*-Phenyl-, *d*-*o*-chlorophenyl- and *d*-cyclohexylsuccinic acids have been proven to have the same configuration.
4. Several cases of unusual effects of solvents on rotatory power and of spontaneous racemization have been pointed out.

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[CONTRIBUTION FROM THE CHEMISTRY DEPARTMENT OF DUKE UNIVERSITY]

Condensations. XIII. The Alkylation of Ethyl Isobutyrate and of Certain other Esters by Means of Sodium Triphenylmethyl and Alkyl Halides

BY BOYD E. HUDSON, JR., AND CHARLES R. HAUSER

Esters of diphenylacetic acid have been alkylated by converting them into their sodium enolates by means of sodium triphenylmethyl,[1] sodium amide,[2] potassium amide,[3] or potassium ethoxide[4] and treating the enolates with certain alkyl halides. Scheibler and Schmidt[5] have reported that ethyl acetate (or ethyl phenylacetate) reacts with potassium to give the potassium enolate which reacts with ethyl bromide to give ethyl butyrate; however, the yield of this product was very low, and there is some doubt whether the intermediate potassium enolate of the ester was obtained as claimed by these workers.[6]

This paper describes the successful alkylation of ethyl isobutyrate and of ethyl methylethylacetate. These esters are converted into their sodium enolates by means of sodium triphenylmethyl and the enolates treated with alkyl halides. In this way ethyl isobutyrate has been alkylated with benzyl chloride and with ethyl and methyl iodides, while ethyl methylethylacetate has been alkylated with *n*-propyl iodide. With one exception the yields obtained were approximately 60% of the theoretical amount. The alkylation of ethyl isobutyrate may be illustrated by the following equations in which RX represents an alkyl halide

$$\mathrm{H{-}C(CH_3)_2CO_2C_2H_5 + (C_6H_5)_3CNa \rightleftharpoons Na[C(CH_3)_2CO_2C_2H_5] + (C_6H_5)_3CH}$$

$$\mathrm{RX + Na[C(CH_3)_2CO_2C_2H_5] \longrightarrow R{-}C(CH_3)_2CO_2C_2H_5 + NaX}$$

This type of reaction serves as a direct and convenient method for the synthesis of tri-substituted acetic acid esters or of the corresponding acids, which may be obtained readily from the esters by hydrolysis. The alkylation of esters of the type of ethyl methylethylacetate may be of value for the synthesis of optically active acids or their esters.

The method of alkylation described above appears to be entirely satisfactory only with disubstituted esters. The ethylation of ethyl isovalerate gave only a fair yield (22%) of the corresponding alkylated ester, while an attempt to benzylate ethyl acetate was unsuccessful, apparently because of the relatively rapid rate at which this ester undergoes self-condensation.[7]

Experimental[8]

Alkylation of Ethyl Isobutyrate with (a) Ethyl Iodide.—To an ether solution of sodium triphenylmethyl[9] containing 0.18 mole of the base was added 21 g. (0.18 mole) of ethyl isobutyrate (Eastman Kodak Co.). The mixture was shaken, and at the end of nine minutes 28.3 g. (0.18 mole) of ethyl iodide (Eastman) was added. The reaction vessel was shaken, stoppered, and allowed to stand overnight. The mixture was acidified with 3 cc. of glacial acetic acid and extracted with a small amount of water. The resulting ether solution was washed with 10% sodium carbonate solution and dried with anhydrous sodium sulfate followed by "Drierite." The solution was filtered and the ether distilled off up to 50°. The residue was vacuum-

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[1] Schlenk, Hillemann and Rodloff, *Ann.*, **487**, 147 (1931).

[2] Ramart, *Bull. soc. chim.*, **4**, 35, 196 (1924); *Compt. rend.*, **178**, 396 (1924); Ramart and Amagat, *Ann. chim.*, **10**, 8, 273 (1927).

[3] Staudinger and Meyer, *Helv. Chim. Acta*, **5**, 670 (1922).

[4] See ref. 3, p. 669.

[5] Scheibler and Schmidt, *Ber.*, **58**, 1191 (1925).

[6] In this connection see ref. 1, p. 135.

[7] See Hudson, Dick and Hauser, THIS JOURNAL, **60**, 1960 (1938).

[8] All boiling points and melting points given are corrected.

[9] Renfrow and Hauser, "Organic Syntheses," Vol. XIX, John Wiley and Sons, Inc., New York, N. Y., 1939, p. 83.