[CONTRIBUTION FROM THE SCHOOL OF CHEMISTRY OF THE UNIVERSITY OF MINNESOTA]

Participation of a Neighboring Carboxyl Group in Addition Reactions. II. The Reaction of Cyanogen Iodide with γ,δ-Unsaturated Acids[1a]

BY RICHARD T. ARNOLD AND KENNETH L. LINDSAY[1b]

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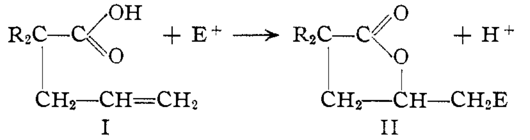
Cyanogen iodide has been shown to react with three different γ,δ-unsaturated acids (2,2-diphenylpenten-4-oic acid, 9-allyl-9-fluorenecarboxylic acid and penten-4-oic acid) to give in each case the corresponding δ-iodo-γ-pentanolactone. There was no evidence that any of the normal addition product was obtained, and no reaction was observed between cyanogen iodide and three typical olefins (cyclohexene, methylenecyclohexane and β-pinene).

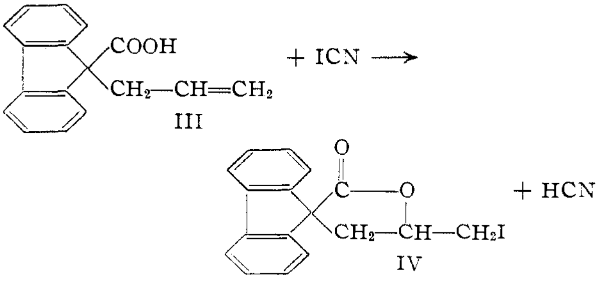
The generality of the reaction whereby a γ,δ-unsaturated acid, I, reacts with an electrophilic reagent, E^+, to give a δ-substituted-γ-pentanolactone, II, has been demonstrated thus far by the use of



I II

bromine,[2] acetyl hypobromite,[2d] acids[2a,2c] and mercuric salts[3] as electrophilic reagents. We have been able to show that iodine (both alone and catalyzed by mercuric chloride) and cyanogen iodide possess sufficient cationoid reactivity to bring about lactonization of γ,δ-unsaturated acids, the product being in each case a δ-iodo-γ-pentanolactone.

When 2,2-diphenylpenten-4-oic acid was treated with cyanogen iodide for 16 hours, a 23% yield of 2,2-diphenyl-5-iodo-4-pentanolactone was obtained. The yield was increased to 82% by increasing the time of reaction to seven days. The expected iodolactones were formed in both cases when cyanogen iodide was allowed to react with 9-allyl-9-fluorenecarboxylic acid (III) and penten-4-oic acid. In each case the reaction was considerably slower than the reaction with 2,2-diphenylpenten-4-oic acid. After sixteen days standing the yield of 2-oxa-3-iodomethyl-5,6,7,8-dibenzospiro[4,4]-nonan-1-one (IV) was 25%, while after 60 days 5-iodo-4-pentanolactone was obtained in only 20% yield. The order of reactivity of these three γ,δ-unsaturated acids toward cyanogen iodide is the same as that observed for their reactivity toward bromine[2d] and provides another illustration of the remarkable effect of substituents in facilitating ring closures.



III IV

Direct iodination was found to be inferior to the cyanogen iodide reaction for the preparation of 2,2-diphenyl-5-iodo-4-pentanolactone. When no catalyst was used, direct iodination was slower than the cyanogen iodide reaction and gave a product of extremely low purity. The use of mercuric chloride increased the rate of iodination to such an extent that a 92% yield of iodolactone was obtained in half an hour, but the product, although of higher quality, still required a number of recrystallizations before it reached analytical purity. When cyanogen iodide was employed, only one recrystallization was necessary in order to achieve a sample of analytical purity.

Cyanogen bromide, which should not be as easily polarized as cyanogen iodide, gave no appreciable reaction with 2,2-diphenylpenten-4-oic acid in 14 days. No evidence of reaction was obtained when cyanogen iodide was allowed to stand for seven days with cyclohexene or methylenecyclohexane. Recovery of unreacted cyanogen iodide was not quantitative, however (78% and 58%), because of its high volatility. Non-reactivity was quite clearly shown in the case of β-pinene by the observation that the optical rotation of the hydrocarbon was unchanged even after forty days standing with cyanogen iodide. A discussion of the mechanism of the reaction between cyanogen iodide and γ,δ-unsaturated acids will be postponed until further information is available.

Experimental

Preparation of Starting Materials.—The preparation of 2,2-diphenylpenten-4-oic acid and 9-allyl-9-fluorenecarboxylic acid was carried out as described previously.[2d] Penten-4-oic acid was prepared from allyl chloride by a standard acetoacetic ester synthesis. A sample of methylenecyclohexane was supplied by Dr. Wm. W. Lee. Cyclohexene and β-pinene were commercially available. Cyanogen iodide was prepared by Mr. H. E. Fritz according to the method of Bak and Hillebert.[4]

Reaction of Cyanogen Iodide with 2,2-Diphenylpenten-4-oic Acid.—To 1.00 g. (0.0040 mole) of 2,2-diphenylpenten-4-oic acid dissolved in 20 ml. of chloroform was added a solution of 0.62 g. (0.0040 mole) of cyanogen iodide in 20 ml. of chloroform. The solution was allowed to stand in the refrigerator overnight and then extracted with 20 ml. of 10% sodium carbonate solution. Acidification of the basic extract with concentrated hydrochloric acid precipitated 0.77 g. (77%) of 2,2-diphenylpenten-4-oic acid, m.p. 141–143°. Evaporation of the chloroform solution yielded (after one recrystallization from methanol) 0.35 g. (23%) of 2,2-diphenyl-5-iodo-4-pentanolactone, m.p. 119–120°.

Anal. Calcd. for $C_{17}H_{15}O_2I$: C, 53.98; H, 4.00. Found: C, 53.8; H, 4.14.

The above procedure was repeated except that the solution was allowed to stand in the refrigerator for seven days. The yield of iodolactone (after one recrystallization from

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[1] (a) From the Ph.D. Thesis of Kenneth L. Lindsay, 1952; (b) Ethyl Corporation, Detroit, Michigan.

[2] (a) P. N. Craig and I. H. Witt, THIS JOURNAL, **72**, 4925 (1950); (b) P. N. Craig, *ibid.*, **74**, 129 (1952); (c) R. Fittig and E. Hjelt, *Ann.*, **216**, 52 (1883); (d) See also paper I of this series, R. T. Arnold, M. M. Campos and K. L. Lindsay, THIS JOURNAL, **75**, 1044 (1953).

[3] R. L. Rowland, W. L. Perry and H. L. Friedman, *ibid.*, **73**, 1040 (1951).

[4] B. Bak and A. Hillebert, *Org. Syntheses*, **32**, 29 (1952).

methanol) was 1.25 g. (82%), m.p. 118–120°, and 2,2-diphenylpenten-4-oic acid was recovered in 11% yield.

Reaction of Cyanogen Iodide with 9-Allyl-9-fluorenecarboxylic Acid.—To a solution of 1.00 g. (0.0040 mole) of 9-allyl-9-fluorenecarboxylic acid in 20 ml. of chloroform was added a solution of 0.62 g. (0.0040 mole) of cyanogen iodide in 20 ml. of chloroform. The resulting solution was allowed to stand in the refrigerator for 16 days, washed with 10 ml. of 10% sodium carbonate solution, and evaporated in a current of air, leaving 0.37 g. (25%) of 2-oxa-3-iodomethyl-5,6,7,8-dibenzospiro[4,4]nonan-1-one, which was recrystallized for analysis from methanol to a melting point of 158–159°.

Anal. Calcd. for $C_{17}H_{13}O_2I$: C, 54.27; H, 3.48. Found: C, 54.2; H, 3.79.

Reaction of Cyanogen Iodide with Penten-4-oic Acid.—To a solution of 3.0 g. (0.030 mole) of penten-4-oic acid in 50 ml. of chloroform was added a solution of 4.6 g. (0.030 mole) of cyanogen iodide in 50 ml. of chloroform. The resulting solution was allowed to stand for 60 days in the refrigerator. It was then washed with two 100-ml. portions of 10% sodium bisulfite solution followed by two washes with 100-ml. portions of 10% sodium carbonate solution. Acidification of the basic extract with concentrated hydrochloric acid and extraction with two 100-ml. portions of ether gave (after drying and distillation of the ether solution) a 0.90 g. (30%) yield of recovered penten-4-oic acid, b.p. 91° (22 mm.), n^{25}D 1.4210, n^{20}D 1.4232. The starting penten-4-oic acid had b.p. 77–80 (11 mm.), n^{20}D 1.4240.

The chloroform solution was dried over magnesium sulfate, filtered, and distilled, giving 1.36 g. (20%) of 5-iodo-4-pentanolactone, b.p. 91° (0.2 mm.), n^{25}D 1.5385, which was colored red by traces of iodine arising from decomposition (probably of traces of cyanogen iodide not destroyed by the bisulfite treatment) during the distillation.

Anal. Calcd. for $C_5H_7O_2I$: C, 26.57; H, 3.12. Found: C, 27.25; H, 3.51.

Attempted Reaction of Cyanogen Iodide with Cyclohexene.—To a solution of 15.3 g. (0.100 mole) of cyanogen iodide in 400 ml. of chloroform was added 16.4 g. (0.200 mole) of cyclohexene and the resulting solution was allowed to stand in the refrigerator for seven days. Evaporation of the chloroform in a current of air yielded 12.0 g. (78%) of recovered cyanogen iodide. A substantial amount of cyanogen iodide was also lost through sublimation during the evaporation of the chloroform.

Attempted Reaction of Cyanogen Iodide with Methylenecyclohexane.—To a solution of 0.96 g. (0.010 mole) of methylenecyclohexane in 5 ml. of chloroform was added a solution of 1.53 g. (0.010 mole) of cyanogen iodide in 40 ml. of chloroform. The resulting solution was allowed to stand in the refrigerator for seven days. Evaporation of the chloroform in a current of air yielded 0.90 g. (58%) of recovered cyanogen iodide. A substantial amount of cyanogen iodide was also lost through sublimation during the evaporation of the solvent.

Attempted Reaction of Cyanogen Iodide with β-Pinene.—The optical rotation of a sample of β-pinene was found to be $[\alpha]^{27}$D −16.7° (*c* 5.7, chloroform, 2-dm. tube). To a solution of the same concentration of β-pinene, one-half an equivalent of cyanogen iodide was added, and the rotation of this solution was determined after it had been allowed to stand in the refrigerator for 40 days. Since the rotation thus determined was found to be $[\alpha]^{27}$D −16.6°, it was assumed that no reaction between the cyanogen iodide and the β-pinene had taken place.

Attempted Reaction of Cyanogen Bromide with 2,2-Diphenylpenten-4-oic Acid.—Cyanogen bromide was prepared by treating an aqueous suspension of bromine with sodium cyanide. It was sublimed out of the reaction mixture and used immediately. When allowed to stand in the refrigerator in chloroform solution with an equimolar amount of 2,2-diphenylpenten-4-oic acid for 14 days, cyanogen bromide did not react with the acid, which was recovered in 94% yield.

Uncatalyzed Reaction of Iodine with 2,2-Diphenylpenten-4-oic Acid.—To a solution of 1.00 g. (0.0040 mole) of 2,2-diphenylpenten-4-oic acid in 40 ml. of chloroform was added 1.00 g. (0.0040 mole) of iodine. The solution was allowed to stand in the refrigerator for seven days and extracted with 20 ml. of 10% sodium carbonate solution. Evaporation of the chloroform solution yielded 0.92 g. (61%) of crude 2,2-diphenyl-5-iodo-4-pentanolactone, m.p. 90–97°. Several recrystallizations from methanol were required to raise the melting point to 117–118°, mixed m.p. with analytical sample of m.p. 119–120°, 118–119°.

Mercuric Chloride-catalyzed Reaction of Iodine with 2,2-Diphenylpenten-4-oic Acid.—To 0.25 g. (0.0010 mole) of 2,2-diphenylpenten-4-oic acid dissolved in 20 ml. of chloroform was added a solution of 0.25 g. (0.0010 mole) of iodine in 10 ml. of chloroform, and 0.27 g. (0.0010 mole) of mercuric chloride was added. The iodine color disappeared on stirring for half an hour. The solvent was evaporated, leaving a white solid and a red precipitate (of HgI_2 or HgICl). The solid was extracted with 30 ml. of benzene, and the benzene was evaporated, leaving a white solid contaminated with only a small amount of red impurity, most of which was eliminated by repeating the benzene extraction and evaporation. The resulting pale pink solid was washed with 10 ml. of cold methanol and filtered, yielding 0.35 g. (92%) of crude 2,2-diphenyl-5-iodo-4-pentanolactone, m.p. 109–113°, which was recrystallized several times from methanol to a melting point of 116–117° and mixed m.p. with analytical sample of m.p. 119–120°, 118–119°.

Minneapolis, Minnesota