gave III in 80% yield, and diphenylcadmium gave IV in 70% yield. The melting points of known phthalides II and IV agreed with published values. The infrared spectra of II, III, and IV showed an intense single carbonyl band near 5.65 μ, as expected for α,β-unsaturated lactones. Other features of the spectra strongly supported the assignment of these structures.

Among the numerous phthalide syntheses that have been reported are several that are adaptable to synthesis of phthalides which bear unlike substituents in the 3-position. Certain alkylations of 3-sodio-3-phenylphthalide afford such compounds in good yields.[3] Ethyl o-benzoylbenzoate affords II (among other products) on treatment with methylmagnesium iodide.[4] Friedel-Crafts reaction of I with aromatic compounds affords 3,3-diarylphthalides.[5,6]

However, in cases for which the required organocadmium reagent is available, the present method appears to be equal or superior in yield and convenience to the above methods for synthesis of 3,3-disubstituted phthalides in which at least one substituent is aromatic.

Experimental[7]

3-Methyl-3-phenylphthalide (II).—By the procedure of Koelsch,[8] 56.5 g. (0.25 mole) of o-benzoylbenzoic acid was stirred with 100 g. of thionyl chloride overnight at room temperature. Excess thionyl chloride was distilled under reduced pressure on a steam bath, and three 100-ml. portions of dry benzene were added and in turn distilled, leaving 3-chloro-3-phenylphthalide (I) as a tan oil.

Methylmagnesium bromide was prepared from 47.5 g. (0.50 mole) of methyl bromide. To the ether solution of this reagent was cautiously added 40.8 g. (0.25 mole) of powdered, anhydrous cadmium chloride. The resulting mixture was stirred at reflux for 1 hr., when Gilman's test[9] of a sample indicated the absence of Grignard reagent. Ether was then distilled out of the reaction vessel, and dry benzene was added periodically to replace the solvent being removed. This process was continued until the b.p. of the solvent had reached 80°. The resulting benzene solution of dimethylcadmium was cooled to 5° on an ice bath and rapidly stirred as a solution of the 3-chloro-3-phenylphthalide in 100 ml. of dry benzene was added. The resulting reaction mixture was then stirred at reflux for 2 hr. and allowed to stand overnight. To this mixture was then added 100 ml. of water, followed by 125 ml. of 6 N hydrochloric acid. The organic layer was separated and washed in turn with 3 N sodium hydroxide and with three portions of water. The organic layer was dried over magnesium sulfate, and the solvent was removed, leaving 55.7 g. (99%) of II, m.p. 72–76°. Recrystallization of this material from a mixture of ligroin (b.p. 100–102°) and absolute ethanol gave 50.2 g. (88%) of II, in two crops of m.p. 77–78° and 73–75°, reported m.p. 76.8–78.0°.[10] The infrared spectrum of this material had a single, strong band in the carbonyl region at 5.65 μ, reported 5.65 μ.[10]

3-n-Butyl-3-phenylphthalide (III).—The above procedure was employed, using 50 g. (0.21 mole) of o-benzoylbenzoic acid, 34.8 g. (0.28 mole) of n-butyl bromide, and 27.5 g. (0.15 mole) of cadmium chloride. Distillation of the crude product (48 g.) gave 43.1 g. (80%) of III, b.p. 152–155° at 0.2 mm. The infrared spectrum had a strong band at 5.66 μ.

Anal. Calcd. for $C_{18}H_{18}O_2$: C, 81.17; H, 6.81. Found: C, 81.04; H, 7.14.

3,3-Diphenylphthalide (IV).—The procedure used for preparation of II was employed, using 56.5 g. (0.25 mole) of o-benzoylbenzoic acid, 47 g. (0.35 mole) of bromobenzene, and 34.8 g. (0.19 mole) of cadmium chloride. The partly crystalline product (77 g.) was recrystallized from a mixture of petroleum "hexane" and absolute ethanol, giving 58.0 g. (70%) of IV, m.p. 112–114°, reported m.p. 114°,[11] 115°,[12] 117.5–118.5°.[13] A sample recrystallized twice more from these solvents (94% recovery) had m.p. 116–116.5°. The infrared spectrum had a strong band at 5.65 μ.

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[3] C. R. Hauser, M. T. Tetenbaum, and D. S. Hoffenberg, *J. Org. Chem.*, **23**, 861 (1958).

[4] E. Bergmann, *ibid.*, **4**, 1 (1939).

[5] C. Friedel and J.-M. Crafts, *Compt. rend.*, **84**, 1450 (1877).

[6] M. Copisarow, *J. Chem. Soc.*, **111**, 10 (1917).

[7] Melting points were taken using a Laboratory Devices "Mel-temp" block and are corrected. Infrared spectra were recorded using a Perkin-Elmer 21 spectrophotometer. Analysis was performed by Dr. Ing. Schoeller, Kronach, West Germany.

[8] C. F. Koelsch, *J. Org. Chem.*, **25**, 642 (1960).

[9] H. W. Gilman and F. Schulze, *J. Am. Chem. Soc.*, **47**, 2002 (1925).

[10] M. S. Newman, *J. Org. Chem.*, **27**, 323 (1962).

[11] N. Maxim and A. Andreescu, *Bull. soc. chim. France*, [5], **5**, 54 (1938).

[12] J. M. Wilson, *J. Chem. Soc.*, 2297 (1951).

[13] H. Gilman, W. J. Meikle, and J. W. Morton, *J. Am. Chem. Soc.*, **74**, 6282 (1952).

A Novel Reaction of Carbodiimides

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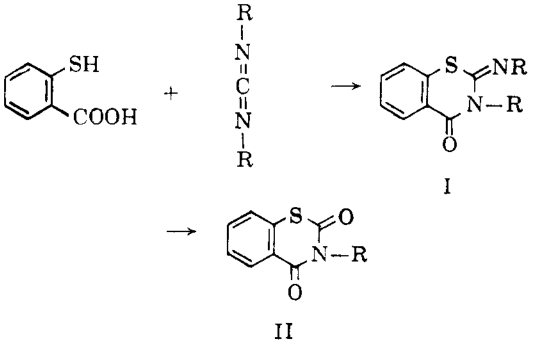
Although the use of carbodiimides as a reagent for the preparation of phosphoric and carboxylic acid amides and esters is now well known,[1] their use as starting materials has been little studied.

During the course of a study involving the reactions of carbodiimides, we discovered a novel, one-step synthesis of 2-amino-1,3-benzothiazinones (I, R = cyclohexyl and isopropyl). These were converted *via* hydrolysis to the corresponding 1,3-benzothiazinediones (II). The synthesis involves a



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[1] See for example, H. G. Khorana, *Chem. Rev.*, **53**, 145 (1953); E. Schmidt and R. Schnegg, U.S. Patent 2,686,180 (1954).

spontaneous and exothermic reaction between thiosalicylic acid and a carbodiimide in the absence of a solvent. Compound I is quite stable.

On prolonged boiling with dilute acid, the corresponding dione (II) is formed. Alkaline hydrolysis of I causes ring rupture with formation of the *sym*-disubstituted urea. Compound II is stable to prolonged treatment with acid or permanganate.

When thiosalicylic acid is replaced by its ester, the reaction product is a complex mixture containing some I.

The structures of I and II, assigned on the basis of elemental analysis, spectra, and postulated mechanism of formation, have been confirmed by the recently reported[2] synthesis of II *via* cyclization of the carbamate of thiosalicylic acid.

A study of the reduction of I and II and the reaction of carbodiimides withs alicylic, anthranilic, and β-mercaptopropionic acids is in progress.

Experimental[3]

3-Cyclohexyl-2-cyclohexylimino-2,3-dihydro-4H-1,3-benzothiazin-4-one (I, R = cyclohexyl).—To 20.6 g. (0.1 mole) of dicyclohexylcarbodiimide (Aldrich Chemical Co.) was added 7.7 g. (0.5 mole) of thiosalicylic acid. There was an immediate exothermic reaction and 20–25 ml. of dry benzene was added to make the thickening mixture more fluid. The suspension was left at room temperature for 3 hr. and then heated on a steam bath for 20 hr. The insoluble solid was filtered and proved to be dicyclohexylurea (10 g., 88% yield, m.p. 225–230°; lit.,[4] m.p. 229–230°). The filtrate was concentrated *in vacuo* and the resulting oil slowly crystallized, m.p. 80–83°. The solid was recrystallized from ethanol, m.p. 81–84°, yield 9.6 g. (56%).

Anal. Calcd. for $C_{20}H_{26}N_2OS$: C, 70.14; H, 7.65; N, 8.18. Found: C, 70.26; H, 7.81; N, 8.25.

When the reaction was carried out by adding thiosalicylic acid to a solution of carbodiimide in benzene, the yield was very low.

3-Cyclohexyl-2H-1,3-benzothiazine-2,4(3H)-dione (II, R = cyclohexyl).—A 2-g. sample (0.0058 mole) of II (R = cyclohexyl) in 20 ml. of 10% sulfuric acid and enough ethanol to dissolve the solid was refluxed for 5 hr. The solution was concentrated *in vacuo* to yield a solid which was separated by filtration, m.p. 140–145°. It was recrystallized from ethanol to give 0.95 g. of product, m.p. 150–152°, 62% yield (lit.,[2] m.p. 148°).

Anal. Calcd. for $C_{14}H_{15}NO_2S$: C, 64.34; H, 5.79; N, 5.36. Found: C, 64.72; H, 5.58; N, 5.36.

Base-Catalyzed Hydrolysis of II (R = cyclohexyl).—A solution of 2 g. of the imino compound (I) in dilute aqueous-alcoholic potassium hydroxide was refluxed for 1.5 hr. On cooling 0.7 g. (54% yield) of a white solid separated, m.p. 220–223°; a mixed melting point determination with dicyclohexylurea did not show any depression. A small amount of unidentified oil was also isolated from the filtrate.

3-Isopropyl-2-isopropylimino-2,3-dihydro-4H-1,3-benzothiazine (I, R = isopropyl).—The procedure described for the preparation of the cyclohexyl analog was followed using 15.4 g. (0.1 mole) of thiosalicylic acid and 25.2 g. (0.2 mole) of diisopropylcarbodiimide (Aldrich Chemical Co.). After the diisopropylurea had been separated by filtration, (m.p. 185–190°, 14 g., 97% yield), the filtrate was concentrated *in vacuo* to yield an oil which slowly solidified and was recrystallized from a mixture of ethanol–water, m.p. 51–52°, 11 g. (42%).

Anal. Calcd. for $C_{14}H_{18}N_2OS$: C, 64.09; H, 6.92; N, 10.68. Found: C, 63.92; H, 6.74; N, 10.83.

3-Isopropyl-2H-1,3-benzothiazine-2,4(3H)-dione (II, R = isopropyl).—The hydrolysis of the isopropylimine was carried out as described for the cyclohexyl analog, using 10% ethanolic sulfuric acid. The product was isolated as a white solid which was recrystallized from a mixture of ethanol and water, m.p. 67–68° (lit.,[1] m.p. 67°) 0.9 g. (28%).

Anal. Calcd. for $C_{11}H_{11}NO_2S$: C, 59.71; H, 5.01; N, 6.33. Found: C, 60.00; H, 4.74; N, 5.86.

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[2] K. Hasspacher, U.S. Patent 2,978,449 (1961).

[3] Analyses were carried out by Mrs. D. Rolston and her staff of these laboratories.

[4] A. Skita and H. Rolfes, *Ber.*, **53B**, 1242 (1920).

The Synthesis of 4-Substituted Cyclopentenes from 1,4-Dibromobutene-2

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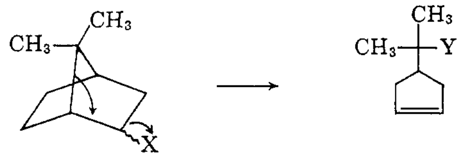
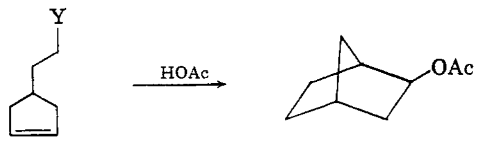
In studying the reactions of 2-substituted bicyclo[2.1.1]hexanes (I), we encountered a monocyclic, unsaturated product which appeared to arise *via* opening of the four-membered ring in the bicyclic system, giving a 4-substituted cyclopentene (II) (equation 1). To confirm the structure of II, as well as to provide material for the study of the possible reclosure of II to the original bicyclic system, in analogy to the closure of III to *exo*-norbornyl acetate (IV) (equation 2) reported independently by Lawton[4] and by Bartlett and Bank,[5] we have sought a convenient method for the synthesis of compounds of this type. The results of this search are reported below.



(1)

Ia. X = N_2^+
b. X = OTs

IIa. Y = OAc
b. Y = OH



(2)

III. Y = OTs or p-$O_3SC_6H_4NO_2$

IV

Several approaches to 4-substituted cyclopentenes are reported in the literature.[6-9] Of these

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[3] National Institutes of Health Predoctoral Fellow.

[4] R. G. Lawton, *J. Am. Chem. Soc.*, **83**, 2399 (1961).

[5] P. D. Bartlett and S. Bank, *ibid.*, **83**, 2591 (1961).