stirring 605 g. (5 moles) of allyl bromide. During the addition of allyl bromide the reaction mixture was maintained at reflux temperature. After stirring for an additional two hours, the reaction mixture was cooled and the Grignard addition product decomposed with cold 6 *N* hydrochloric acid. The ether layer was separated, the aqueous layer extracted, and the combined extracts were dried and distilled; yield 387.5 g. (70.5%), b. p. 121–125° $n^{22}D$ 1.4398.

γ-Bromopropylcyclopentane.—Oxygen gas was bubbled into 693 g. (6.3 moles) of allylcyclopentane at 0° for thirty minutes with stirring. The passage of oxygen was continued, and hydrogen bromide[8] was passed in rapidly for three and one-half hours. At the end of this time, the theoretical amount and 52 g. in excess of hydrogen bromide had been absorbed. The reaction mixture was allowed to stand at 0° overnight, and the excess hydrogen bromide was distilled off at 50 mm. pressure. The mixture was washed with dilute carbonate solution, dried over anhydrous potassium carbonate, and distilled at atmospheric pressure through a partial take-off helices-packed column. More than 100 g. of lower boiling material distilled before the pure γ-bromopropylcyclopentane was collected at 204–207° (741 mm.), yield 786.3 g. The change in the index of refraction of the distillate was also used as an indication of the point at which to begin collection of the pure γ-bromopropylcyclopentane. This material was redistilled through a 70-cm. Vigreux column at reduced pressure before using; b. p. 99–100° (22 mm.), yield 714 g. (59.2%), $n^{25}D$ 1.4819.

Ethyl γ-Cyclopentylpropylmalonate.—(A) Alkylation of malonic ester was carried out in the usual manner[9] using 18.5 g. (0.126 mole) of γ-chloropropylcyclopentane and refluxing for sixteen hours; yield 22.4 g. (66%), b. p. 139–146° (2 mm.), $n^{25}D$ 1.4470. (B) In the same manner the malonic ester synthesis was carried out using 713 g. (3.73 moles) of γ-bromopropylcyclopentane and refluxing for thirteen hours; yield 839 g. (83%), b. p. 138–144° (2 mm.), $n^{25}D$ 1.4470.

δ-Cyclopentyl-*n*-valeric Acid.—Hydrolysis and decarboxylation of the ethyl γ-cyclopentylpropylmalonate was carried out according to the general method of "Organic Syntheses"[10] except that the oily layer of crude organic acid was separated in a funnel and the aqueous solution extracted with ether or benzene instead of using an automatic separator. (A) From 22.4 g. (0.08 mole) of γ-cyclopentylpropylmalonic ester, prepared as indicated in (A) above, was obtained 12.4 g. (84%) of δ-cyclopentyl-*n*-valeric acid; b. p. 137–137.5° (4.5 mm.), m. p. 12.5–14°, $n^{20}D$ 1.4596; m. p. of amide derivative after one recrystallization, 135–136° (uncor.). (B) From 838 g. (3.1 moles) of γ-cyclopentylpropylmalonic ester, prepared as indicated in (B) above, was obtained 448.8 g. (85%) of δ-cyclopentyl-*n*-valeric acid; b. p. 149–150° (9 mm.), m. p. 14–15, $n^{20}D$ 1.4595; m. p. of amide after one recrystallization 135–136° (uncor.).

In one run a mixture of cyclopentylvaleric acids prepared from an unfractionated bromopropylcyclopentane product was separated by careful fractionation through a 12-in. helices-packed partial take-off column: the fractions boiling 159–164° (19 mm.) ($n^{20}D$ 1.4587 to 1.4592) were rejected as probably containing a high percentage of the undesired isomer, and δ-cyclopentyl-*n*-valeric acid was collected at 164–165° (19 mm.), $n^{20}D$ 1.4594. None of the fractions boiling 159–164° (19 mm.) solidified upon cooling to 0°.

Summary

δ-Cyclopentyl-*n*-valeric acid was prepared through a malonic ester synthesis from γ-bromopropylcyclopentane and from γ-chloropropylcyclopentane.

The γ-bromopropylcyclopentane was prepared by the addition of hydrogen bromide in the presence of oxygen to allylcyclopentane. The chloro compound was prepared by the alkylation of γ-chloropropyl *p*-toluenesulfonate with cyclopentylmagnesium bromide. In view of the respective yields, synthesis through the bromo compound was preferable.

(8) "Organic Syntheses," Coll. Vol. II, John Wiley and Sons, Inc., New York, N. Y., 1943, p. 338.

(9) "Organic Syntheses," Coll. Vol. I, John Wiley and Sons, Inc., New York, N. Y., 1941, p. 250.

(10) "Organic Syntheses," Coll. Vol. II, John Wiley and Sons, Inc., New York, N. Y., 1943, p. 416.

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[CONTRIBUTION FROM THE CHEMISTRY LABORATORY OF INDIANA UNIVERSITY]

The Skraup Reaction with *p*-Methoxyacetanilide

BY C. E. KASLOW AND SAMUEL RAYMOND[1]

The preparation of 6-methoxyquinoline from *p*-anisidine by the Skraup reaction is well-known. By using the modification of Manske[2] the yield of 6-methoxyquinoline has been increased and by using an improved method of isolation it has been shown that an important side reaction is the formation of 6-quinolinol, which may amount to as much as one-third of the product. It is probable that this compound is formed by demethylation of 6-methoxyquinoline, since the yield of the quinolinol increases with time at the expense of the 6-methoxyquinoline.

Sucharda and Mazonski[3] have reported that 6-quinolinol is a by-product in the Skraup method for preparation of quinoline itself. Its formation was ascribed to reduction of the nitrobenzene to phenylhydroxylamine which rearranges to *p*-aminophenol. The latter substance then undergoes a Skraup reaction yielding 6-quinolinol. A corresponding substance, 6-methoxy-8-hydroxy- or 6,8-dihydroxyquinoline, could not be isolated in the present case. The yields are recorded in Table I.

Experimental

The following procedure was used for the preparation and isolation of 6-methoxyquinoline and 6-quinolinol.

6-Methoxyquinoline and 6-Quinolinol.—A mixture of 120 g. of anhydrous glycerol, 30 g. of boric acid, 36 g. (0.225 mole) of *p*-methoxyacetanilide, and 22 g. (0.14 mole) of *p*-nitroanisole was heated in a three-necked 500-ml. flask, fitted with a mechanical stirrer in an oil-bath

(1) The William S. Merrell Company Post Doctorate Research Fellow, 1945–1946.

(2) Manske, Ieger and Gallagher, *Can. J. Research*, **19B**, 318 (1941).

(3) Sucharda and Mazonski, *Ber.*, **69**, 2719 (1936).

TABLE I

Time at 135°,[a] hr.	6-Methoxyquinoline yield, %	6-Quinolinol yield, %	Total yield, %
8	63	2.5	65.5
10[b]	43	21	64
17	63[c]	..[d]	63
40	57	7	64
60	55	11	66
120	52	17	69
48[e]	43	12	55

[a] Maximum internal temperature, then as the reaction subsided, the bath temperature was allowed to rise to this value. [b] The boric acid was omitted. [c] Isolated by the procedure of Cromwell, Caughlin and Gilbert, THIS JOURNAL, **66**, 401 (1944). [d] Not isolated. [e] Twelve hours at a bath temperature of 155°.

until the internal temperature was 110–115°, then 25 ml. of concentrated sulfuric acid was added dropwise to the stirred reaction mixture over a period of fifteen to twenty minutes. The temperature of the reaction mixture rose gradually to 133–135° and after it started to drop, the temperature of the oil-bath was allowed to rise to 135°. After heating for forty hours, the reaction mixture was poured in 1 liter of ice and water, and the *p*-nitroanisole removed by filtration. Fifty per cent. sodium hydroxide solution was added to the filtrate until it was almost neutral then enough sodium bicarbonate was added to make the solution neutral. The mixture was extracted with benzene in a continuous extractor of the type described by Aston, *et al.*[4] This apparatus was modified by using a three-necked flask with a mechanical stirrer which speeded up the extraction process. After extraction for two days the benzene was removed by distillation, the oily residue was dissolved in 100 ml. of absolute ethanol, 12 ml. of concentrated sulfuric acid dissolved in 50 ml. of cold absolute ethanol added to precipitate the 6-methoxyquinoline as 6-methoxyquinolinium acid sulfate[5] and the mixture digested on a steam-bath for 1–1.5 hours. After cooling, the white solid was removed by filtration, washed with 25 ml. of absolute ethanol and the solid digested with 50 ml. of hot absolute ethanol, filtered and dried. The 6-methoxyquinoline was obtained from the acid sulfate by the usual procedure, as a water-clear liquid, b. p. 101–103° at 0.5 mm.; yield, 20.4 g. (57%).

The combined alcohol filtrates, after testing for complete removal of 6-methoxyquinoline by adding 1 ml. of sulfuric acid, were concentrated by distillation on a steam-bath. The residue was extracted with four 50-ml. portions of dilute ammonium hydroxide[6] (11:), the ammoniacal solution extracted once with benzene to remove any *p*-anisidine and the aqueous portion exactly neutralized with dilute hydrochloric acid. The yield of 6-quinolinol was 2.3 g. (7%); m. p. 187–188°; recrystallized from dilute ethyl alcohol, m. p. 192–193°.[7]

(4) Aston, Newkirk, Jenkins, and Dorky, "Organic Syntheses," Vol. 23, John Wiley and Sons, Inc., New York, N. Y., 1943, p. 49.

Summary

6-Quinolinol as well as 6-methoxyquinoline was obtained by the Skraup reaction on *p*-methoxyacetanilide. An improved method for isolation of 6-methoxyquinoline and 6-quinolinol by a continuous extraction process has been described.

(5) Skraup, *Monatsh.*, **6**, 763 (1885), reported that the acid sulfate was insoluble in 50% ethyl alcohol but tests proved it to be slightly soluble even in 95% ethyl alcohol.

(6) The use of sodium hydroxide at the point gave mostly tars.

(7) Hargreaves, *J. Am. Pharm. Assoc.*, **25**, 975 (1936), reported a melting point of 193°.

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Isomerization of Alkyl Phosphites. V. The Synthesis of Phosphonoacetic and Phosphonomalonic Esters

BY GENNADY M. KOSOLAPOFF

The synthesis of triethyl phosphonoacetate has been accomplished through condensation of ethyl chloroacetate with triethyl phosphite by Arbuzov and Dunin,[1] and through the condensation of ethyl chloroacetate with sodium diethyl phosphite by P. Nylen[2] and by Arbuzov and Kamai.[3]

The latter reaction was reported by Nylen to give yields of about 50% using dry ether for the reaction solvent, while Arbuzov and Kamai reported the following effect of solvent on the yield: ligroin 56%, dry ether 59% and absolute ethanol 94.6%.

The startling improvement of the yield with the use of absolute ethanol appeared to be puzzling when the conditions under which such a reaction is run are considered. The co-presence of diethyl phosphite and sodium ethoxide may be represented by the equation

$$HPO(OC_2H_5)_2 + NaOC_2H_5 = NaPO(OC_2H_5)_2 + HOC_2H_5,$$

with a conceivable degree of equilibrium conditions, in which the proportion of sodium being linked with the phosphorus compound and with the ethanol may be varied depending on the conditions. Thus, it may be expected that the presence of an excess of ethanol would tend to push the reaction equilibrium condition considerably to the left. If this hypothesis is correct, the yields of triethyl phosphonoacetate should be lower when the reaction is run in the presence of an appreciable amount of ethanol, since in such a case the chloroacetate may tend to react to a considerable extent with the sodium ethoxide.

Accordingly, experiments were set up in which ethyl chloroacetate was treated with sodium diethyl phosphite in dry ethanol and in hexane. The results of the experiments appear to show the correctness of the above hypothesis, in that the best yield was obtained in hexane in the absence of ethanol. However, in no case could the yields

(1) Arbuzov and Dunin, *J. Russ. Phys.-Chem. Soc.*, **46**, 295 (1914).

(2) P. Nylen, Studien über Phosphororg. Verb., Upsala, 1930.

(3) Arbuzov and Kamai, *J. Russ. Phys.-Chem. Soc.*, **61**, 619 (1929).