[CONTRIBUTION FROM THE CHEMICAL LABORATORY OF THE UNIVERSITY OF ILLINOIS]

The Haloform Reaction. XVI. The Action of Hypoiodite on Hindered Ketones[1]

BY ROBERT JOHNSON AND REYNOLD C. FUSON

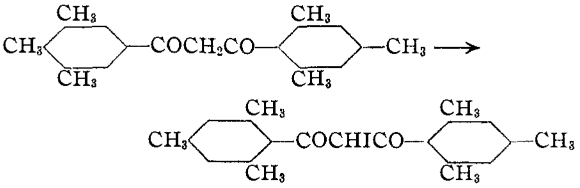
The iodination of hindered methyl ketones with hypoiodite presents an abrupt departure from the course of halogenation with hypobromite or hypochlorite. In the latter cases the mono- and dihalogen derivatives are rarely isolated and, under the influence of the reagent, apparently pass readily to the fully halogenated ketones. We have found that the action of hypoiodite, on the other hand, gives *mono-* and *diiodomethyl ketones*, and appears to be incapable of transforming these into the corresponding triiodo derivatives. Since unhindered methyl ketones very readily undergo the iodoform reaction, it is evident that the failure of hypoiodite to act upon the hindered diiodomethyl ketones is directly traceable to the presence of the hindering groups, *i. e.*, is a steric phenomenon. This is all the more noteworthy because the formation of the diiodo derivative from the methyl ketone seems to proceed very readily.

Early attempts to iodinate these ketones were carried out in aqueous media in which the ketones were insoluble, and met with little success. By using dioxane, however, as prescribed in the procedure of Fuson and Tullock,[2] we have developed a method by which the diiodomethyl ketones can be made readily.

Since this work was begun, a report has been made of a very similar result obtained by Poggi,[3] who states that pinacolone does not give iodoform, but is converted into diiodopinacolone when treated with hypoiodite. Since Fuson and Tullock had obtained iodoform from pinacolone, we reinvestigated this question, and found that both statements are correct, and that the result obtained depends on the conditions used. Whether one uses the procedure of Lieben[4] or that of Fuson and Tullock, iodoform is the only iodine-containing product obtained *when the hypoiodite is used in excess*. As might be expected, the presence of an excess of ketone leads to the formation of the mono- and diiodo compounds. That the isolation of these compounds is to be ascribed to an insufficiency of iodinating agent is supported by the fact that the *diiodopinacolone itself gives iodoform* when treated with hypoiodite.

Very similar results have been obtained with di-ortho substituted acetophenones. For example, acetomesitylene readily yields monoiodoacetomesitylene when treated with a limited amount of hypoiodite, and diiodoacetomesitylene when hypoiodite is used in excess. In a similar manner, diacetomesitylene gives di-(diiodoacetyl)-mesitylene, and 3-acetyl-2,4,6-trimethylbenzoic acid gives 3-diiodoacetyl-2,4,6-trimethylbenzoic acid. In none of these cases, however, could the triiodomethyl ketone be made, and in no case was it possible to detect any trace of iodoform among the products.

An analogous result was obtained with di-(β-isoduryloyl)-methane. This diketone gave only a monoiodo derivative, and could not be fully iodinated



It will be recalled that, with hypochlorite or hypobromite, the corresponding dihalogen compounds are obtained.[5]

Experimental

In the treatment of the ketones with solutions of hypoiodite, two general procedures were employed—one (A) involving the use of hypoiodite in excess, the other (B) a limited amount of the hypohalite.

Procedure A.—The ketone was dissolved in dioxane and this solution was added to a large volume of 10% sodium hydroxide solution. Dioxane was used in quantities sufficient to prevent the separation of the ketone from the alkaline solution. An excess of iodine (approximately twice the amount required by theory for complete iodination of the ketone) was added, with shaking, over a period of fifteen minutes. The reaction mixture was then shaken with benzene, and the resulting benzene solution was washed with water. The residue after removal of the solvent under diminished pressure was recrystallized from a mixture of ether or benzene with petroleum ether.

---

[1] For references to earlier articles of this series see Bull, Ross and Fuson, THIS JOURNAL, **57**, 764 (1935).

[2] Fuson and Tullock, *ibid.*, **56**, 1638 (1934).

[3] Poggi, *Atti della Società Italiana per il Progresso delle Scienze*, XXI Riunione, **2**, 376 (1933). See also Delange, *Bull. soc. chim.*, [4] **3**, 914 (1908).

[4] Lieben, *Ann.*, Suppl. Bd., **7**, 218 (1870).

[5] Fisher, Snyder and Fuson, THIS JOURNAL, **54**, 3665 (1932).

Procedure B.—This procedure differed from Procedure A in that the amount of iodine used was one-third to one-half of that required by theory for the formation of the monoiodo derivative of the ketone. The iodine was added in the form of an aqueous iodine–potassium iodide solution. This solution was added dropwise through the center of a rapidly revolving hollow stirrer, and required one and one-half to two hours.

The table lists the iodo derivatives prepared according to the foregoing procedures.

IODO DERIVATIVES

Iodo derivative	Ketone used, g.	Product, g.	Iodo derivative (m. p.)	Solvent	Procedure	Analysis for iodine Calcd.	Found
Iodoacetomesitylene	10	1.2	34.5–35.5	Methanol	B	44.1	44.1
Diiodoacetomesitylene[a]	10	1.2	98–99	Ether–petr. ether	A	61.3	61.5
Di-(diiodoacetyl)-mesitylene	5	0.56	160 (decomp.)	Bz.–petr. ether	A	71.7	71.7
Di-(β-isoduryloyl)-iodomethane	1	.4	191–192	Ether–petr. ether	A	29.2	29.2

[a] This compound was prepared by Mr. J. T. Walker.

3-Diiodoacetyl-2,4,6-trimethylbenzoic Acid.—To 1 g. of the acid dissolved in 20 cc. of 10% sodium hydroxide solution was added 2 g. of iodine. The solution was stirred until the iodine dissolved and, after being allowed to stand for one hour, was cooled and acidified. After further standing for one hour at 5°, the dark, gummy precipitate was separated on a filter and recrystallized three times from aqueous methanol: yield, 1.2 g. of product melting at 130–133°, with decomposition. Further recrystallization from aqueous methanol yielded a product melting at 132–133°, with decomposition.

Anal. Calcd. for $C_{12}H_{12}O_3I_2$: C, 31.45; H, 2.62; I, 55.44. Found: C, 31.29, 31.20; H, 2.65, 2.83; I, 55.05.

A neutral equivalent determination was not possible because titration gave no well-defined end-point.

Iodopinacolone.—A mixture of 80 g. of pinacolone and 800 cc. of 5% sodium hydroxide solution was cooled in an ice and salt mixture, and 80 g. of iodine, dissolved in aqueous potassium iodide, was added through a rapidly revolving hollow stirrer. The addition was complete in two hours. The solution was immediately shaken with ether, and the resulting ether solution was washed with water. The solution was dried with anhydrous sodium sulfate, and the ether was removed. The strongly lachrymatory liquid thus obtained was distilled at reduced pressure, and 6 cc. of a product boiling at 92–98° (20 mm.) was collected. This fraction was shaken with mercury to remove the iodine color, and refractionated twice; b. p. 48–49° (2 mm.); $n^{20}{}_D$ 1.5095; $d^{20}{}_4$ 1.5848; M_D, found, 42.59; calcd., 42.72.

Anal. Calcd. for $C_6H_{11}OI$: I, 56.13. Found: I, 56.47.

Diiodopinacolone.—A mixture of 10 cc. of pinacolone, 7 g. of potassium hydroxide and 100 cc. of water was cooled to 5° in an ice-bath. An aqueous solution (35 cc.), containing 11 g. of iodine and 22 g. of potassium iodide, was added dropwise over a period of two hours, with vigorous stirring. The resulting solution was extracted with petroleum ether, and the petroleum ether solution was washed with water. The residue, obtained by removal of the solvent under diminished pressure, was taken up in methanol and reprecipitated by the addition of water; yield, 1.2 g. of product melting at 72–75°. Further recrystallization gave a product melting at 76–76.5°. The melting point agrees with that reported by Poggi[3] for diiodopinacolone.

Anal. Calcd. for $C_6H_{10}OI_2$: I, 72.14. Found: I, 72.22.

Treatment of Diiodopinacolone with Sodium Hypoiodite.—A mixture of 3 cc. of dioxane, 0.14 g. of pure diiodopinacolone, and 75 cc. of 10% sodium hydroxide solution was thoroughly agitated and, with continued stirring, 8 g. of iodine was added in 2-g. lots over a period of ten minutes. The yellow solid which formed was extracted with petroleum ether, the petroleum ether solution was washed with water, and the solvent was removed under diminished pressure. Recrystallization of the residue from a methanol–water mixture gave 0.02 g. of iodoform, melting at 119–120°.

Summary

It has been shown that certain hindered methyl ketones react with hypoiodite to give mono- and diiodomethyl ketones. The corresponding triiodo derivatives could not be isolated.

URBANA, ILLINOIS RECEIVED MARCH 14, 1935