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HYPERVALENT IODINE IN ORGANIC SYNTHESIS.

ACETAL FORMATION UNDER BASIC CONDITIONS AND CARBON DEUTERIATION OF THE ALDEHYDO GROUP

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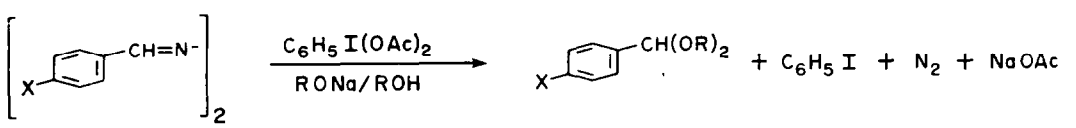
Summary - Aldazines upon treatment with phenyliodosyl diacetate in CH_3OH or CH_3OD and $NaOCH_3$ are converted smoothly into two equivalents of the corresponding aldehyde dimethylacetal with deuterium incorporation at the aldehydic carbon atom in the case of CH_3OD.

Acetal derivatives of aldehydes are valuable in synthesis either as intermediates or as protecting groups.[1a,b] Most commonly acetals are formed in acidic media although specialized methods exist which use metal catalysis,[2,3] photochemical,[4,5,6] and reaction via the oxime[7]. A general synthesis of aldehyde acetals under non-acidic conditions is desirable and we now report such a reaction. The aldehyde is first converted to the aldazine and treated at room temperature with $NaOCH_3/CH_3OH$ and phenyliodosyl diacetate. The ratio of aldazine: $C_6H_5I(OAc)_2$:$NaOCH_3$ is 1:2:10[8]. If $CH_3CH_2OH/NaOCH_2CH_3$ is used the diethylacetal of the aldehyde is obtained. The yields shown below represent isolated product and in each case comparison was made with either literature or an authentic sample.

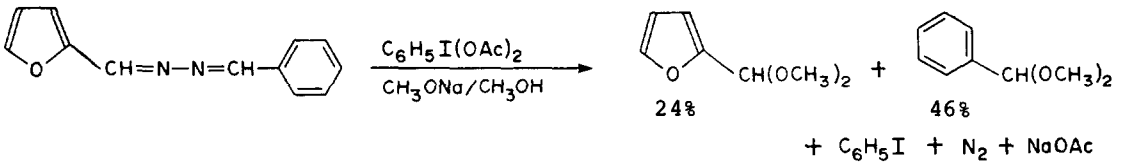


X = H, Cl, OCH_3, OC_2H_5

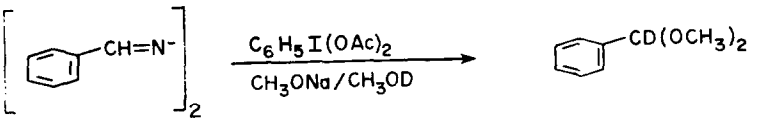
R = CH_3, CH_3CH_2

R=CH_3, X=H(88%); Cl(90%); OC_2H_5(50%); OCH_3(55%
R=C_2H_5, X=H(67%), Cl(95%); OCH_3(70%)

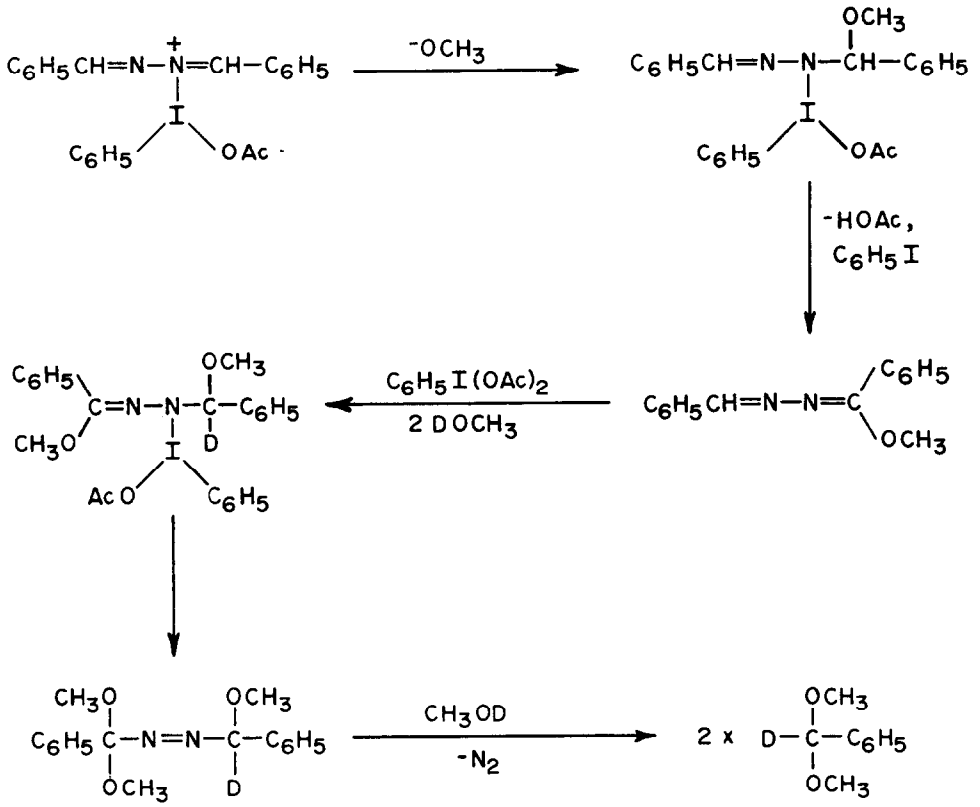
The reaction also proceeds well with heteroaromatic carboxaldazines, e.g. furfuralazine yields the dimethylacetal in 36%, and pyridine 4-carboxaldazine yields the dimethylacetal in 43%. Furfural pyridine-4-carboxaldazine is of interest because it is a mixed system. Treatment with $C_6H_5I(OAc)_2$, CH_3ONa/CH_3OH proceeds as below:



Deuteriation of the aldehydic carbon in aryl aldehydes occurs in quantitative yield (by n.m.r.) in the reaction ($CH_3OD/NaOCH_3/C_6H_5I(OAc)_2$). No deuterium exchange occurs in the absence of $C_6H_5I(OAc)_2$. Hydrolysis of the dimethyl acetal is effected using 2% HCl under nitrogen.



Finally, the deuteriation results places some restriction on the mechanism of the reaction. Based on our previous observations with reactions of $C_6H_5I(OAc)_2$, which characteristically proceed with initial nucleophilic attack at iodine, it appears likely that the initial step in the present reaction is nucleophilic attack of the aldazine upon $C_6H_5I(OAc)_2$[9,10,11,12]. Several pathways may be envisioned which account for the products. The following appears reasonable:



This acetal synthesis works best with arylaldazines. Azines possessing α-hydrogens and arylmethylketazines give mixtures of products and very low yield of acetals.

Finally, oxidation of aldehyde hydrazones under the conditions used for the aldazine →acetal conversion leads to the diazo compound and dinitrogen.[14]

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8. Sodium (1.15g, 0.05 mole) was dissolved in 50 ml of CH_3OH, then the solution was cooled to 0°C and the aldazine (0.005 mole) was added. After 5 min, phenyliodosyl diacetate (0.011 mole) was added and the reaction mixture was stirred at room temperature 2 days. After the solvent was removed in vacuo, 30 ml of water was added. Then the resulting solution was extracted with CH_2Cl_2. The dimethylacetal was isolated either by fractional distillation or column chromatography on silica gel. Dinitrogen evolution as measured eudiometrically indicated 89% yield.

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