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# FACILE PREPARATION OF THE METHYL ACETAL OF METHYL PHENYLGLYOXYLATE

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Abstract. The methyl acetal of methyl phenylglyoxylate has been prepared from halophenylethynes, N-iodosuccinimide and catalytic amounts of (hydroxy(p-tosyloxy)iodo)benzene or p-toluenesulfonic acid in methanol at room temperature.

We wish to report a useful application of recent improvements in the halogenations of alkynes and aromatics to the preparation of the dimethyl acetal of methyl phenylglyoxylate[1], a potentially valuable synthetic building block via crossed Claisen condensations. This compound is formed from halophenylethynes by means of N-halosuccinimides and catalytic amounts of acids in methanol at room temperature.

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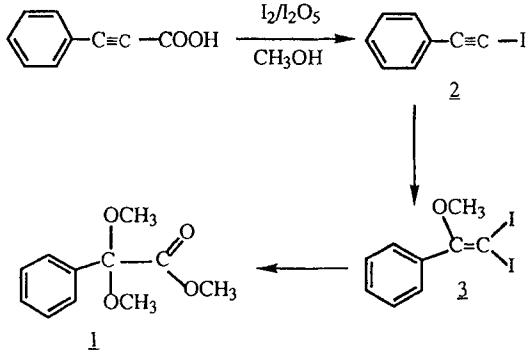
Heretofore, there was a route to ester 1 from phenylpropiolic acid in 82% yield with iodine and iodine pentoxide in methanol.[1] That oxidative decarboxylation involved ratios of alkyne/$I_2$/$I_2O_5$ of 1/6/0.5. Other ratios of oxidants afforded varying quantities of two major intermediates, 2-iodo-1-phenylethyne (2) and (2,2-diiodo-1-methoxyethenyl)benzene (3).




In this work alkyne 2 or its bromine-containing relative, $C_6H_5C{\equiv}CBr$ (4), was used as starting material with lesser quantities of iodinated reagents. Thus, alkyne 2 (2.3 mmol), which is prepared readily from phenylethyne and 1-iodo-2,5-pyrrolidinedione (N-iodosuccinimide, NIS) and catalytic amounts of siver nitrate in acetone[2], was treated with NIS (6.9 mmol) and catalytic amounts of (hydroxy(tosyloxy)iodo) benzene (Koser's reagent, HTIB) in methanol (50 mL) at room temperature for 18 hours to afford ester 1 in 86% yield.

The efforts to extend this system on a broader scale are shown in the Table. The ratios of $C_6H_5C{\equiv}CX$ to NXS were 1 to 2. These stoichiometric ratios still gave rise to intermediates

Table

Cross combinations: $2NX^1S + C_6H_5C{\equiv}CX^2$ [a]

| $X^1$ | $X^2$ | yield (%) $C_6H_5C(OCH_3)_2CO_2CH_3$ | other (%) |
|---|---|---|---|
| Br | Br | 0 | $C_6H_5CBr{=}CBr_2$ (84) |
| | | | $C_6H_5C(OCH_3)_2CBr_3$ (8) |
| Br | I | 50 | $C_6H_5CBr{=}CIBr$ (11) |
| | | | $C_6H_5C(OCH_3)_2CBr_2I$ (26) |
| I | I | 45 | $C_6H_5C(OCH_3){=}CI_2$ (26) |
| | | | $C_6H_5C(OCH_3)_2CI_3$ (29) |
| I | Br | 78 | |

a) Reaction conditions: $C_6H_5C{\equiv}CX^2$ (1 mmol), $NX^1S$ (2 mmol) and TsOH (0.2 mmol) in methanol (10 mL) at room temperature for 20 h.

and led to the use of the above ratio of 1 to 3 for synthetic purposes. In the cases of NBS, a stronger acid catalyst, p-toluenesulfonic acid (TsOH), was used on the basis of its reactions with alkynols.[3] HTIB is usually effective with NIS in alkynols and aromatic iodination but TsOH can be used.[4] The presence of trihaloethenes indicated a limitation in the use of NBS in this synthetic route. With NBS and alkyne 4 the chief product was $C_6H_5CBr{=}CBr_2$. The source of bromine might be a competing reaction with the methanol involving hypobromites. These stoichiometric results under mild conditions do demonstrate the reaction pathways and support the use of

greater quantities of NXS for purposes of high yields of the desired ester or other esters from other haloethynes. Nevertheless, the stoichiometric use of NIS and alkyne 4 is of preparative value since intermediates were detected only in trace quantities.



## EXPERIMENTAL

The following procedure is typical for these reactions: 1-iodo-2-phenylethyne (0.534g, 2.3 mmol), NIS (1.550g, 6.9 mmol) and HTIB (0.240g, 0.61 mmol) were stirred in methanol (50 mL) at room temperature for 18 hours. The solution was added to water (150 mL) and extracted with two portions (75 mL) of ether. The ether layer was washed with 5% sodium thiosulfate and water. Drying over anhydrous $MgSO_4$ and stripping of solvent followed. The product (0.41g) was a pale yellow oil with the following characteristics: IR ($CCl_4$): 3080, 3000, 2950, 2840,1750, 1570, 1490, 1470, 1450, 1440, 1270, 1240, 1200, 1180, 1120, 1080, 1040, 1030 $cm^{-1}$; $^1H$ NMR ($CDCl_3$) $\delta$: 3.27 (s, 6H), 3.72 (s, 3H), 7.31 (m, 3H), 7.60 (m, 2H); MS m/z (relative intensity): 179 (9, $M^+$-$OCH_3$), 151 (100, $M^+$-$CO_2CH_3$), 105 (67, $C_6H_5CO^+$)

For the study of the reactions involving intermediates, work-ups were as above except ether volumes were reduced for qualitative analyses with a GC/MS (Hewlett-Packard 5992, OV-1, 0.25 mm x 1.5 m) and quantitative analyses by GC

(Perkin-Elmer Sigma 3B, methyl silicone, 0.25 mm x 50 m). All products were known.

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