**Tetrahedron Letters No. 51/52, pp 4445 - 4446, 1974. Pergamon Press. Printed in Great Britain.**

# CONTROLLED PROTONATION OF TRIS-α-DIAZOKETONES

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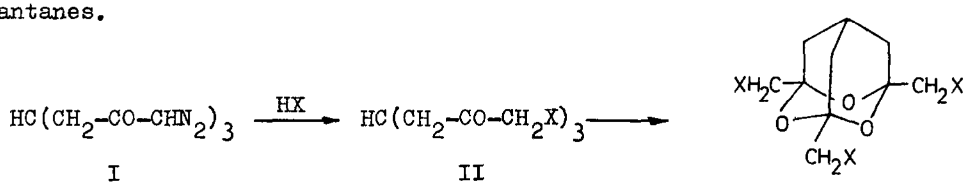
**(Received in UK 7 October 1974; accepted for publication 8 November 1974)**

Stetter and Stark[1] reported that protonation of methane(tri-α-diazoacetone)[2] (I) with either concentrated aqueous hydrochloric or hydrobromic acid gives 1,3,5-tri(halomethyl)-2,4,9-trioxaadamantanes (III) instead of the expected open-chain triketones II. These results are in agreement with that reported earlier by Stetter and Dohr[3], and that of Raasch and Krespan[4] who concluded that tricarbonyl compounds of the structure II spontaneously and irreversibly cyclize to 2,4,9-trioxaadamantanes.


$$HC(CH_2\text{-}CO\text{-}CHN_2)_3 \xrightarrow{HX} HC(CH_2\text{-}CO\text{-}CH_2X)_3 \longrightarrow$$

I II

III

In the present communication we wish to report that cyclization is an acid-catalyzed reaction and open-chain tricarbonyl compounds II can be isolated starting from methane(tri-α-diazoacetone)(I) provided protonation takes place under strictly controlled conditions; namely, in the presence of hexamethylphosphorotriamide (HMPT).

As it is well known, HMPT is a highly basic solvent that react with strong acids to form salts[5] which can even be isolated under certain circumstances[6], and we have found that they are acidic enough to protonate α-diazoketones. Therefore, dropwise addition of methane(tri-α-diazoacetone) in THF solution to an equimolecular mixture of HMPT and acid gives the corresponding triketone II (C=O st at 1740-1720 cm$^{-1}$) which, in turn, can be quantitatively cyclized to trioxaadamantane III by heating a DME solution in the presence of catalytic amounts of p-toluenesulfonic acid. As shown in Table 1 the yields of triketone decrease with the decreasing nucleophilicity of the anion ($Cl^- > Br^- \gg MsO^-$). Notice that $H_2O$ competes effectively with anions of low nucleophilicity ($MsO^-$ and $ClO_4^-$) to give the corresponding hydroxyderivative.

Table 1

Reacction of $HC(CH_2\text{-}CO\text{-}CHN_2)_3$ with acids

| Acid | Solvents | Triketone II[a] | | Trioxaadamantane III[a] | |
|---|---|---|---|---|---|
| | | m.p. | % | % | m.p. |
| HCl | HMPT/THF/$H_2O$ | 85º | 81.6 | $\xrightarrow{H^+}$ 100 | 105-6º |
| HCl | $H_2O$ | - | - | 70 | " |
| HBr | HMPT/THF/$H_2O$ | 70-1º | 60.5 | $\xrightarrow{H^+}$ 100 | 128-9º |
| HBr | $H_2O$ | - | - | 71 | " |
| MsOH | HMPT/THF | 118-20º | 19.2 | $\xrightarrow{H^+}$ 100 | 173-5º |
| MsOH | $CH_2Cl_2$ | - | - | 4.6 | " |
| MsOH | $H_2O$ | - | - | 10.8 | 170 dec[b] |
| $HClO_4$ | $H_2O$ | - | - | 13 | " |

[a] All the reported substances showed correct elemental analysis and IR and NMR spectra.

[b] As 1,3,5-tri(hydroxymethyl)-2,4,9-trioxaadamantane.

Owing to the strong basicity, HMPT can be efficiently eliminated from the reaction mixture by filtering it through a column packed with Dowex 50W, which can be regenerated and used again; the reaction product was isolated from the aqueous solution by extraction with ether.

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