TRIFLUOROACETYLATION OF 3-HALO-9-METHYLCARBAZoles

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Trifluoroacetylation of 3-halo-9-methylcarbazoles at 110°C proceeds at 6-position. In the case of 3-bromo- and 3-iodo-derivatives, the reaction is complicated by competing processes of dehalogenation, followed by the halogenation of the substrate, leading to 3,6-dihalo derivatives.

The development of methods for introducing fluorine-containing fragments into organic molecules is one of the important problems of fine organic synthesis [1]. We have already shown [2] that 9-methylcarbazole (Ia) is readily trifluoroacetylated, but the reaction is accompanied by considerable resin formation that decreases the yields of the required end products. In the present work, we studied the influence of electron acceptor substituents in the ring of carbazole Ia on the course of the trifluoroacetylation reaction.

It was found that in contrast to carbazole Ia, compounds Ib, c, IIa, and 9-methyl-3-nitrocarbazole do not react at 20°C with (CF₃CO)₂O and its mixtures with CF₃CO₂H in dichloroethane (DCE). The two last derivatives of carbazole are not acetylated, even at 110°C.

The chloro derivative Ib becomes smoothly acetylated by a (CF₃CO)₂O:CF₃CO₂H (1:1) mixture at 110°C, to form 9-methyl-3-trifluoroacetyl-6-chlorocarbazole (IIb) in a yield of 63% and an inappreciable amount of a resin. By using TLC and mass spectrometry, carbazole Ib and 1,1-bis(9-methyl-3-chloro-6-carbazolyl)-2,2,2-trifluoroethane (III) were also detected in the reaction mixture. We obtained a compound with a similar structure in the reaction of carbazole Ib with CF₃CO₂H [3]. At the same time, even traces of 1,1,1-tris-(9-methyl-3-chloro-6-carbazolyl)-2,2,2-trifluoroethane (IV) were not detected, although its nonchlorinated analog is formed under these conditions [2] during trifluoroacetylation of carbazole Ia.

The following compounds were chromatographically isolated from the reaction mixture obtained by trifluoroacetylation of the chloro derivative Ib under conditions of lower acidity of the medium [(CF₃CO)₂O:CF₃CO₂H, 10:1]: unreacted Ib (yield 41.5%), ketone IIb (22%), compound IV (8%), and 9-methyl-1-trifluoroacetyl-6-chlorocarbazole (V) (1.6%). Mass spectral analysis of a reaction mixture, obtained in the reaction of anhydrous (CF₃CO)₂O with compound Ib, revealed only two components - the initial Ib and ketone IIb (Table 1). It is clear that neither higher nor too low acidity of the medium favor accumulation of compound IV in the reaction mixture. At 20°C, compound IV is readily formed from compounds Ib and IIb in the presence of CF₃CO₂H:

\[
\text{Ib} + \text{IIb} \xrightarrow{\text{CF₃CO₂H}} \text{IV}, 33\%
\]

These results show that the trifluoroacetylation of compounds Ia,b proceeds in similar directions.

The trifluoroacetylation of 3-iodo-9-methylcarbazole (Id) proceeds in a different way. In this case, the main reaction product is 3,6-diiodo-9-methylcarbazole (IIf) (yield 22%), together with the expected ketone IIId (6.4%) and a considerable amount of a resin (25%). In addition, compounds Ia,d, IIa, and carbazole were recorded by mass spectrometry. Molecular
iodine was also detected. We explain the appearance of the diiodo derivative II\textsuperscript{f} by the formation of "positive iodine," probably in the form of trifluoroacetyl hypoiodite, a strong iodinating agent, in the course of the reaction [4]:

$$\text{CF}_3\text{CO}_2\text{H} \rightarrow \text{ArI} \rightarrow \text{CF}_3\text{CO}_2\text{I}$$

Here and below $\text{Ar} = \text{9-methyl-3-carbazolyl}$

This is confirmed by the fact that CF\textsubscript{3}CO\textsubscript{2}H rapidly reacts with compound II\textsubscript{d} already at 20°C to form iodine, a resin and diiodo derivative II\textsubscript{f} (yield 20%). The following scheme of the trifluoroacetylation of compound II\textsubscript{d} appears to be correct:

$$\text{II}_{\text{d}} \rightarrow \text{II}_{\text{f}} \rightarrow \text{II}_{\text{a}}$$. 

There is no path to compound II\textsubscript{a} via the deiodination of ketone II\textsubscript{d}, since the latter is not changed by the action of CF\textsubscript{3}CO\textsubscript{2}H in dichloroethane at 110°C.

The formation of molecular iodine is clearly related to the occurrence of redox processes, for example

$$\text{Ar}^+ + \text{CF}_3\text{CO}_2\text{I} \rightarrow \text{Ar}^+ + \text{CF}_3\text{CO}_2\text{I}^-$$

$$2 \text{CF}_3\text{CO}_2\text{I}^- \rightarrow 2 \text{CF}_3\text{CO}_2^- + I_2$$

During the trifluoroacetylation of O-methyl-3-bromocarbazole (I\textsubscript{c}) by an equimolar mixture (CF\textsubscript{3}CO\textsubscript{2})\textsubscript{2}O:CF\textsubscript{3}CO\textsubscript{2}H at 110°C, ketone I\textsubscript{c} (yield 40%) and the initial I\textsubscript{c} (9%) were preparatively isolated. 9-Methyl-3,6-dibromocarbazole (II\textsubscript{e}), compounds I\textsubscript{a}, II\textsubscript{a}, and carbazole were detected by mass spectrometry, indicating the occurrence of competing processes of dehalogenation and subsequent halogenation of the substrate, as in the case of the iodo derivative II\textsubscript{d}. If it is assumed that the dehalogenation is a slow stage, while the subsequent formation of the dihalo derivative proceeds rapidly, then the value of the dehalogenation/trifluoroacetylation ratio, found from the relative intensities of the corresponding peaks of M\textsuperscript{+} (Table I) and equal to 0.11 (for I\textsubscript{c}) and 12.5 (for II\textsubscript{d}), can be used to evaluate the relative rate of acylation and dehalogenation in each case. In the reaction of compound I\textsubscript{c} with the acylating agent, trifluoroacetylation predominates, while in the case of the iodo derivative II\textsubscript{d}, the main path of the reaction is dehalogenation of the substrate, and deiodination is ~100 times more rapid than debromination.