

THE REACTION OF TERTIARY AMINES WITH DICHLOROCARBENE

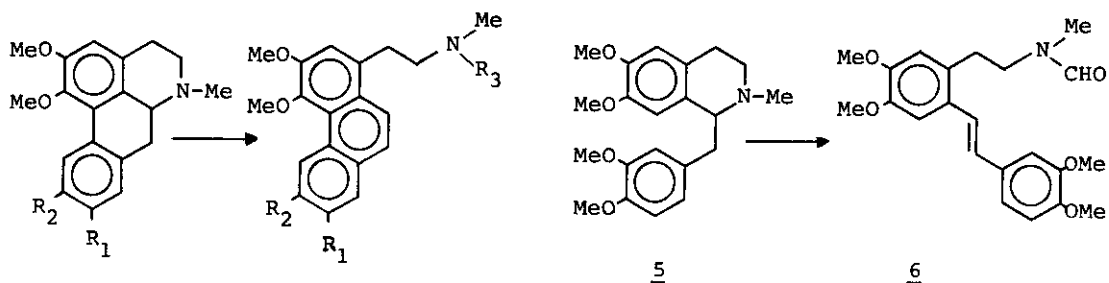
Luis Castedo*, José L. Castro and Ricardo Riguera

Departamento de Química Orgánica de la Facultad de Química e Instituto de Productos Naturales Orgánicos (Sección Alcaloides) del C.S.I.C.
Santiago de Compostela (Spain)

Abstract- Reaction of dichlorocarbene with phenethyl tertiary amines gives conjugated unsaturated compounds which are the result of a β -elimination. A similar reaction occurs with β -tertiary amino esters.

Tertiary amines have been usually considered stable towards dichlorocarbene. They have been used as phase transfer catalyst in carbene formation¹ in spite of the report by Saunders et al.² showing that dichlorocarbene reacts with aliphatic and benzylic tertiary amines. More recently a few reports³⁻⁵ on this subject have appeared. They show that the initially formed nitrogen ylide from the reaction of the tertiary amine with dichlorocarbene then suffers a decomposition with cleavage of one of the original C _{α} -N bonds by one of the following processes: a) the action of a nucleophile such as a phenoxide anion³, b) the assistance of a donor atom in a beta position such as in 1,3-diamines⁴, c) a Stevens rearrangement as occurs in benzylamines², d) a cheletropic reaction⁵, and e) a beta-elimination² where the nitrogen ylide acts in as much the same way as the N-oxide function in the Cope reaction. The latter, presumably general for tertiary amines having a beta proton, appeared to be of no practical use due to the complex reaction mixtures obtained. However, in the present study we have determined from the reaction of dichlorocarbene with a series of tertiary amines that a beta-elimination occurs when products with a well stabilized double bond resulted. This thus represents a convenient method for the preparation of this type of compounds. Thus, reaction of dichlorocarbene generated under phase-transfer conditions (TBAC, NaOH 50%, stirring at room temperature for 2 hours), with glaucine 1 and nuciferine 2 gave after tlc purification the corresponding phenanthrene formamides 3⁶ (57% yield) and 4⁷ (60% yield), respectively. They were further hydrolysed by acid treatment to the known secondary amine 3 (R₃=H)^{6,8} and to the phenanthrene alkaloid nor-

atherosperminine 4 ($R_3=H$)⁹, respectively. Similarly, laudanosine 5 was transformed (50% yield) into the trans-stilbene 6¹⁰ which by hydrolysis gave the corresponding secondary amine 11 that was treated with methyl iodide to produce the known trans methiodide 12.

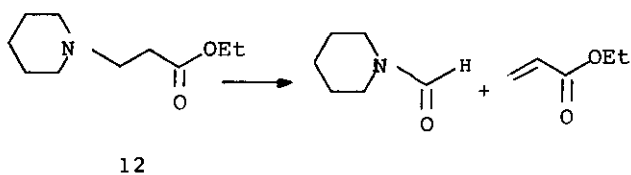
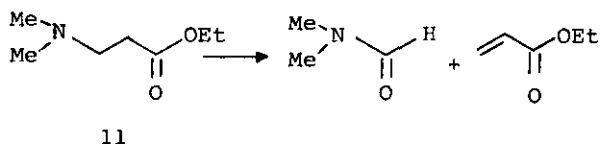
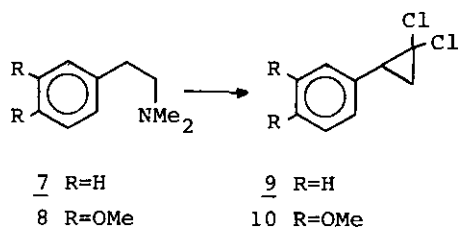


- 1 $R_1=R_2=OMe$ 3 $R_1=R_2=OMe, R_3=CHO$
2 $R_1=R_2=H$ 4 $R_1=R_2=H, R_3=CHO$

Treatment of the phenethylamines 7 and 8 with Cl_2C : (stirring at $0^\circ C$ for 15 min) resulted in the obtainment of the dichlorocarbene adducts 9 and 10¹³ in 52% and 32% yield, respectively. However, the amineborane complex derived from 8 (mp, $102-104^\circ C$) was found to be inert towards dichlorocarbene in the aforementioned conditions.

In none of the above cases the presence of any product resulting from Stevens or Sommelet rearrangements was detected as could be reasonably expected. As a test, we treated benzyldimethylamine with dichlorocarbene generated under phase-transfer conditions. A very complex mixture was obtained from which we have isolated the reported *N,N*-dimethylphenylacetamide². On the other hand, no dibenzyl could be detected by glc using an authentic sample for comparison. Similar treatment of other benzylamines such as nicotine produces an unworkable mixture of products. Analogous results were obtained with a series of tertiary anilines.

The above beta-elimination could also be extended to other tertiary amines such as 11 and 12, which gave the corresponding formamides (40-60% yield) and ethyl acrylate (70-80% yield) (by glc) after stirring at room temperature for 3 hr.



The regioselectivity of the reaction giving in all cases the more stable double bond together with former results on the decomposition of laudanosine N-oxide ¹¹ strongly suggests a five member ring concerted mechanism similar to that of the Cope reaction.

In an attempt to prove its intramolecular nature we treated glaucine-d₃ (deuterium at C_{6a} and C₇) as above, obtaining no deuterium incorporation at the formyl group of 3. However, this result could be due to an exchange with the solvent as we have found that reaction of glaucine 1 with Cl₃CD/50%NaOD/TBAC gave 3 deuterated at its formyl group.

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REFERENCES

1. "Phase transfer catalysis in Organic synthesis", W.P.Weber and G.W.Gokel Springer-Verlag, Berlin 1977.
2. M.Saunders and R.W.Murray, Tetrahedron, 11, 1 (1960).
3. M.Yonovich and Y.Sasson, Tetrahedron Letters, 21, 1875 (1980).
4. T.Sasaki, S.Eguchi, T.Kiriyama and Y.Sakito, J. Org. Chem., 38, 1648 (1973).
5. G.W.Gribble, R.W.Allen, C.S.LeHoullier, J.T.Eaton, N.R.Easton Jr., R.I.Slayton and M.P.Sibi, J. Org. Chem., 46, 1025 (1981).
6. N.Mollov, S.Philipov and H.Dutschewska, Chem. Ber., 111, 554 (1978).

7. λ_{\max} (EtOH) ($\log \epsilon$) 235(4.40), 251(4.60), 258(4.62), 280(sh,4.15), 306(4.11) and 314(4.11) nm; λ_{\min} ($\log \epsilon$) 228(4.37), 238(4.39), 292(4.03) and 344(3.63) nm; ν_{\max} (Cl_3CH) 1670, 1600 cm^{-1} ; pmr (Cl_3CD) 2.83, 2.95(s,3H,N-Me, two rotamers), 3.25-3.75(m,4H,- CH_2), 3.92, 4.02(s,3H each,-OMe), 7.10-8.02(m, 7H,Ar-H and CHO), 9.66(m,1H, H_5); m/e(%) 323(37, M^+), 264(52), 251(100), 207(16), 189(16), 178(24), 165(45).
8. J.B.Bremner and K.N.Winzenberg, Aust. J. Chem., **31**, 313 (1978).
9. M.Leboeuf, F.Bevalot and A.Cavé, Planta médica, **38**, 33 (1980).
10. mp 140-142°C(benzene-hexane); λ_{\max} (EtOH) ($\log \epsilon$) 336(4.40), 300(sh,4.22) nm; λ_{\min} ($\log \epsilon$) 266(3.86) nm; ν_{\max} (KBr) 1670, 1600, 1300, 1020 cm^{-1} ; pmr(Cl_3CD) 2.85, 2.90(s,3H,N-Me,two rotamers), 2.98(m,2H,- CH_2), 3.43(m,2H,- CH_2), 3.89, 3.93, 3.98(s,12H,-OMe), 6.59-7.45(m,7H,Ar-H), 8.03, 7.84(s,1H,CHO two rotamers), m/e(%) 385(53, M^+), 326(22), 313(31), 282(25), 175(25) and 151(100).
11. J.B.Bremner and L.van Thuc, Aust. J. Chem., **33**, 379 (1980).
12. A.R.Battersby and B.J.T.Harper, J. Chem. Soc., 3526 (1962).
- 13 K.-O.Henseling and P.Weyerstahl, Chem. Ber., **108**, 2803 (1975).

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