

CYCLIC CARBAMATES AS REAGENTS FOR ALKYLAMINATION  
OF AROMATIC DERIVATIVES UNDER FRIEDEL-CRAFTS CONDITIONS

C. Jouitteau<sup>(a)</sup>, P. Le Perchec<sup>(a)\*</sup>, A. Forestière<sup>(b)</sup>, B. Sillion<sup>(b)</sup>

Laboratoire des Matériaux Organiques - C.N.R.S.<sup>(a)</sup>

Institut Français du Pétrole<sup>(b)</sup>

CEDI, BP N° 3, 69390, Vernaison, France

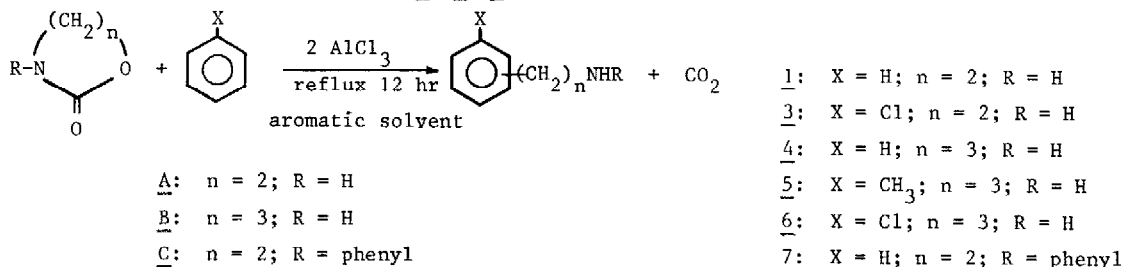
Abstract: Aryl(ethyl-) and propylamines are obtained with good yields by a decarboxylation-alkylation process applied on aluminium trichloride-cyclic carbamate complexes. The coupling of two aromatic units is observed in the case of oxazolidinone-toluene reaction.

The synthesis of arylalkylamines and particularly 3-arylpropylamines usually requires several steps (1). We report on the use of cyclic carbamates ( $n = 2, 3$ ) as being compounds that are well suited for introducing the alkylamine chain into aromatic derivatives by a decarboxylation-alkylation process using aluminium trichloride as the activator reagent.

Previous work in this field has shown that various heterocyclic compounds such as oxazolines (2), azalactones (3), and aziridines (4) lead to reactive intermediates under Friedel Crafts conditions. Oxazolidinone A itself undergoes the same process as reported earlier, although with some uncertainty (5).

Cyclic carbamates ( $n = 2, 3$ ) have been easily prepared from the corresponding aminoalcohols and ethylcarbonate under basic conditions (6, 7) and have shown good complexing properties toward Lewis acids. For example stable complexes have been isolated from reactions between carbamates A and B and  $\text{BF}_3$ ,  $\text{TiCl}_4$  and  $\text{AlX}_3$  in methylene chloride at room temperature. Among them aluminium trichloride-carbamate complexes have shown a good tendency to decompose when heated in aromatic solvents and lead to decarboxylated products. Usually the reaction is carried out by dissolving  $4 \times 10^{-2}$  mole of the carbamate in 150 ml of an aromatic solvent in an inert atmosphere and then dissolving  $8 \times 10^{-2}$  mole of aluminium trichloride. The mixture turns rapidly into a dark homogeneous solution under refluxing. Working up the mixture by a 30% NaOH solution then extracting the solution gives the products described below.

As shown in the table, the reaction occurs with tetrahydrooxazinone B ( $n = 3$ ,  $R = \text{H}$ ) in benzene, toluene or chlorobenzene, with good yields, giving rise to the corresponding substituted arylpropylamines 4, 5, 6.



Compounds	Solvent	Products (a,c,d) pNB ; BSA	Yield	bp/torr Lit. bp/torr	<sup>1</sup> H NMR (CDCl <sub>3</sub> )
Oxalidinone n = 2 (A)	Benzene	<u>1</u> + 5 % of ( <u>9</u> ) pNB (116)	65 (b)	81/14 197(760)	1.00(s, 2H, -NH <sub>2</sub> ) 2.80(m, 4H, -CH <sub>2</sub> ) 7.20(s, 5H, -C <sub>6</sub> H <sub>5</sub> )
	Toluene	<u>2</u>	74	90-101/0.5	2.25(s, 6H, -CH <sub>3</sub> ) 2.80(s, 4H, -CH <sub>2</sub> ) 7.10(m, 8H, -C <sub>6</sub> H <sub>5</sub> )
	Chlorobenzene	<u>3</u> o,p.isomers	21	60/0.2	1.10(s, 2H, -NH <sub>2</sub> ) 2.95(m, 4H, -CH <sub>2</sub> ) 7.30(m, 4H, -C <sub>6</sub> H <sub>4</sub> )
Tetrahydro-oxazinone n = 3 (B)	Benzene	<u>4</u> BSA (54)	80	98/14 (221/760)	1.05(s, 2H, -NH <sub>2</sub> ) 1.70(q, 3hz, 2H, -CH <sub>2</sub> ) 2.65(m, 4H, -CH <sub>2</sub> ) 7.25(s, 5H, -C <sub>6</sub> H <sub>5</sub> )
	Toluene	<u>5</u> o,p.isomers BSA (oil)	77	62/0.1	1.10(s, 2H, -NH <sub>2</sub> ) 1.70(q, 3.5hz, 2H, -CH <sub>2</sub> ) 2.30(s, 3H, -CH <sub>3</sub> ) 2.65(m, 4H, -CH <sub>2</sub> ) 7.30(m, 5H, -C <sub>6</sub> H <sub>4</sub> )
	Chlorobenzene	<u>6</u> o,p.isomers BSA (oil)	55	66/0.2	1.00(s, 2H, -NH <sub>2</sub> ) 1.60(m, 2H, -CH <sub>2</sub> ) 2.05(m, 4H, -CH <sub>2</sub> ) 7.00(m, 4H, -C <sub>6</sub> H <sub>4</sub> )
N-phenyl-oxazolidinone n = 2 R = phenyl (C)	Benzene	<u>7</u> BSA (80)	60	125/0.1	2.75(t, 3.5hz, 2H, -CH <sub>2</sub> ) 3.25(t, 3.5hz, 2H, -CH <sub>2</sub> ) 3.25(s, 1H, -NH) 6.55(m, 2H, -C <sub>6</sub> H <sub>5</sub> ) 7.15(1.peak, 8H, -C <sub>6</sub> H <sub>5</sub> )
	Benzene	<u>8</u> pNB (86)	48	57/0.05	3.45(octet, 2hz, 4H, -CH <sub>2</sub> ) 3.90(1.peak, 1H, -NH) 6.90(m, 4H, -C <sub>6</sub> H <sub>4</sub> , AB system, J=4hz)

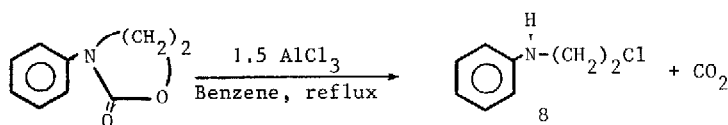
- (a) 3, 5 and 6 are mixtures of o,p.isomers - the ratio has been determined only in the case of 5 as a 3/2 o/p derivative in the light of the NMR spectra of their benzenesulfonamides.
- (b) traces of diphenylethane (~5%) were detected by VPC analysis.
- (c) pNB: p.nitrobenzamide - BSA: benzenesulfonamide.
- (d) all derivatives and products gave correct elemental analysis C, H, N, Cl and mass spectra data.

Amines 5 and 6 are obtained as a mixture of o- and p-isomers as has been shown by the NMR spectra of their corresponding sulfonamides, i.e. benzenesulfonamide of 5 clearly shows two sharp singlets in a 3:2 ratio at 2.12 and 2.20 ppm for the methyl group.

Oxazolidinone A and C ( $n = 2$ ,  $R = H$ , phenyl) lead respectively to phenethylamine (65%) and N-phenyl-phenethylamine (55%) and to a mixture of o,p.chlorophenethylamine 3 (20%) depending on the aromatic solvents used.

The reactivity of carbamates A, B, C has been found to be sensitive to the concentration of aluminium trichloride.

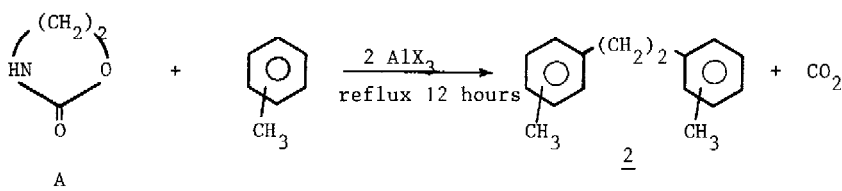
The decarboxylation process with either A or B is in fact completely inhibited if fewer than two equivalents of the Lewis acid are used. Interestingly, N-phenyl oxazolidinone C leads to 2-chloroethylphenylamine 8 if 1.5 equivalents of aluminium trichloride are used.



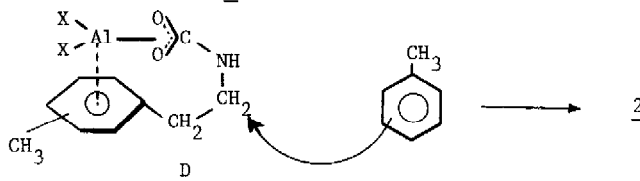
no traces of 7

Such a result suggests a general path for the decarboxylation process which involves first the incorporation of a chlorine atom coming from the  $AlX_3$ -carbamate complex followed by a classic Friedel-Crafts alkylation of the aromatics nucleus.

Another fact worth being noticed is the coupling of two aromatic units which occurs in the case of compound A. Traces of diphenylethane (9) have been detected as a side product during the synthesis of phenethylamine 1, while 1,2-ditolylethanes (2) are formed exclusively in toluene.



This difference in reactivity between A and B is probably related to the formation of a more strained intramolecular complex of type D which in turn favours the C-N bond's breaking in the case of compound A (8).



The reaction probably occurs at the amidation stage D since no incorporation of toluene is obtained if the same reaction is applied to the corresponding phenethylamine- $AlCl_3$  complex prepared independently.

REFERENCES

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It is claimed that phenethylamines have been obtained with various Lewis acids, including  $\text{FeCl}_3$ ,  $\text{ZnCl}_2$ ,  $\text{BF}_3$ , but we have observed the reaction only in the case of aluminium trichloride-carbamate derivatives. Moreover toluene and oxazolidinone A react in our hands and give rise to ditolyethane but not tolylethylamine as claimed in this patent.
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