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Polynitrogen Strong Bases : 1- New Syntheses of Biguanides and their Catalytic Properties in Transesterification Reactions

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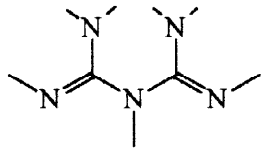
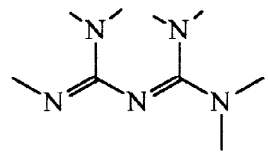
Abstract : A new and convenient method has been developed for the synthesis of soluble and polystyrene-supported biguanides by the nucleophilic addition of guanidines such as TMG and TDB to diisopropyl- , dicyclohexyl- and polymericarbodi-imide. These biguanides are excellent catalysts for the transesterification.

The most common organic strong bases are bicylic amidines such as 1,8-diazabicyclo[5.4.0]undec-7-ene and 1,4-diazabicyclo[4.3.0]non-5-ene (DBU and DBN respectively)[1] and the bicylic guanidines 1,5,7-triazabicyclo[4.4.0]dec-5-ene and its 7-methyl analog (TBD and MTBD respectively)[2]. In the course of a study on the base-catalysed transesterification of vegetable oils, we examined some soluble and polymer-supported guanidines [3]. In order to increase the efficiency of the catalysts, stronger bases were required such as highly N-substituted biguanides of type **1** or **2,** the higher homologs of guanidines (Fig.1).



1



2

Figure 1: Cross-conjugated (type **1**) and fully conjugated (type **2**) biguanides.

The increased basicity of these compounds vs guanidines resulted from the higher conjugation of the protonated form, i.e. from the extended delocalisation of the positive charge: protonated type **1** biguanides are cross-conjugated and protonated type **2** are fully conjugated.

There are no satisfactory methods in the literature to prepare highly N-alkylated biguanides; lower N-substituted compounds are available from cyanamides, dicyanamides and dicyandiamides [4-8] or described in a host of patents deprived of any synthetic value. Thus, we developped a new synthetic method for poly N-alkylated compounds.

As some guanidines can be synthesized through the nucleophilic addition of primary or secondary amines to carbodiimides [9-12] , similar additions of guanidines to carbodiimides could lead to biguanides. Thus, we prepared sucessfully N-alkylated biguanides through the addition of tetramethylguanidine (TMG) and TBD to diisopropylcarbodiimide (DiP) and dicyclohexylcarbodiimide (DCCI) as shown in Figure 2.

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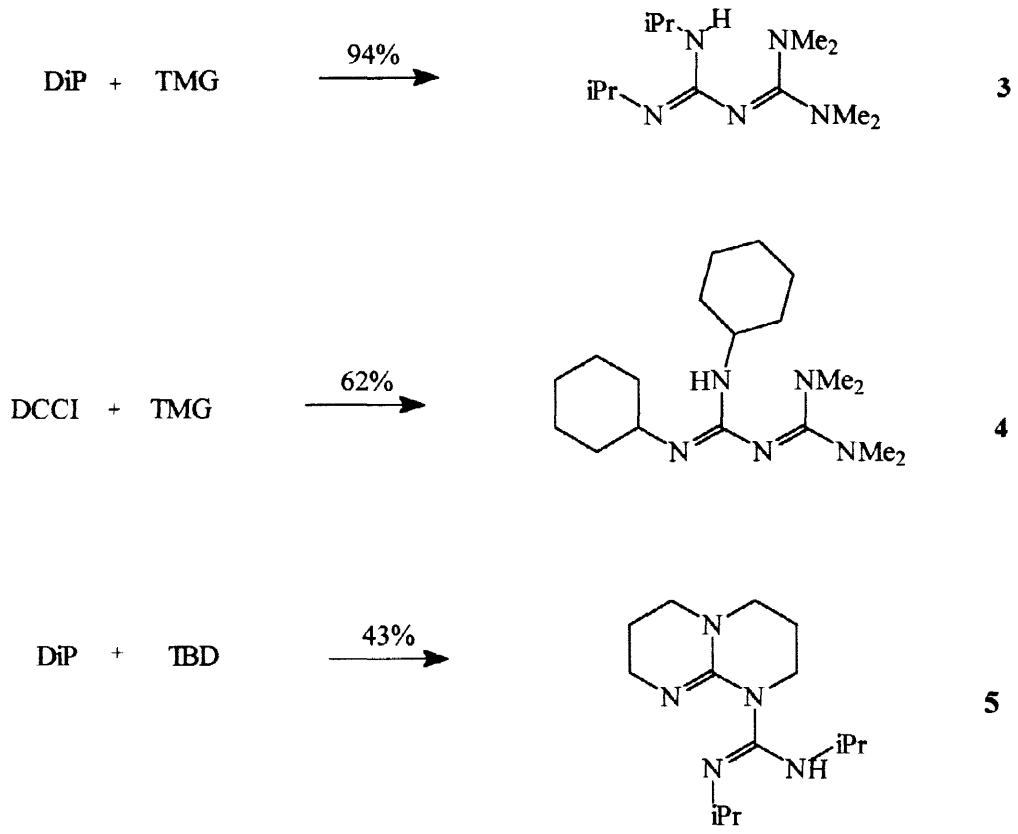


Figure 2 : Addition of guanidines on carbodiimides.

The addition occured by heating the reactants in a polar aprotic solvent; DMF is better than THF and acidic catalysis was required with the bulky TBD.

The products distilled as viscous oils or sublimed as white solids; the yields are good to excellent; compounds **3**[13] and **4**[14] are related to type **2** biguanides ; compound **5**[15] is related to type **1** biguanide. The basicities were determined by FTIR in $CDCl_3$ with $\Delta\nu$(C-D) values correlated to a $pK_A(CH_3CN)$ scale[16]. The values are six pK units above those of guanidines such as TMG.

These soluble strong bases were checked as catalysts in the transesterification of several vegetal oils such as rapeseed oil with methanol; this reaction affords a mixture of the methyl esters, used as fuel for diesel engines[17] (Figure 3).

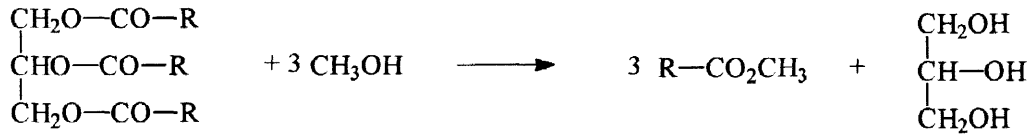
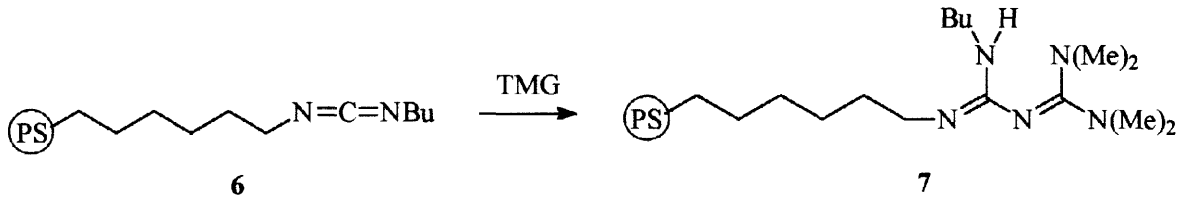


Figure 3: Transesterification of triglycerides with methanol.

As an effect of higher pK_A, the efficiency of these biguanides bases where found about thirty times higher than that given by guanidines[3] (60% yield after 5 mn instead of 180mn as shown in Table 1).

For the purpose of recycling, these strong bases where immobilized on polymers : polystyrene-supported biguanide **7**[18] were prepared in a similar manner by the reaction of TMG on carbodiimide-grafted polystyrene **6**[19]; these carbodiimides were prepared from aminoalkylated-polystyrenes[3] according to two known reaction sequences [20, 21] (Figure 3).



6 **7**

Figure 3 : Polystyrene-supported biguanide.

These supported biguanides exhibited excellent catalytic properties : the immobilization induced a very limited decrease in the reactivity of the biguanide units (Table 1). We have shown[16] that recyclings could be performed more than fifteen times without a significant alteration of the efficiency.

Table 1: Yield in the transesterification of rapeseed oil with methanol

	Reaction time (mn)					
Catalysts and yield (%)[22]	*5*	*15*	*30*	*60*	*180*	*300*
Biguanide **3**	68	90	94			
Biguanide **4**	81	85	94			
Polystyrene supported biguanide **7**	62	81	90	94		
Pentamethylguanidine[3]			30	46	60	
Polystyrene-supported guanidine[3]				63	87	92

These catalysts are, by far, more reactive and more stable than the polystyrene-supported guanidines we described previously [3].

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13. *1,2-diisopropyl-4,4,5,5-tetramethylbiguanide*; $C_{12}H_{27}N_5$ = 241.39 g/mol; $Bp_{0.2}$ = 140-150°C; Mp= 73°C; IRFT (KBr) cm^{-1} : 1601 (ν C=N); elemental analysis, calc % C 59.71, N 29.02, H 11.27, found % C 58.68, N 28.53, H 12.79; ^1H RMN($CDCl_3$) : 1.20 (d, 12H, H-1, $2(CH_3)_2$-C) ; 2.88 (s, 12H, H-3, $2(CH_3)_2$N-) ; 3.39 (sext, 2H, H-2, Me_2-*CH*-); ^{13}C MNR($CDCl_3$) 100 MHz : 23.1 (C-1, CH_3) ; 40.3 (C-3, N-CH_3) ; 45.3 (C-2, CH) ; 157.9 ; 164.7 (2C, C=N) ; $pK_{A(CH3CN)}$ 31.8.
14. *1,2-dicyclohexyl-4,4,5,5-tetramethylbiguanide*; $C_{18}H_{35}N_5$ = 321.51 g/mol; $Bp_{0.2}$ = 150-160°C; elemental analysis, calc% C 67.24, N 21.79, H 10.97, found% C 65.30, N 20.80, H 13.90; ^1H NMR ($CDCl_3$) : 1.1-1.7 (m, 12H, 4[2H-3, H-4] ; 1.7-1.9 (m, 8H, 8H-2) ; 2.85 (s, 12H, 12H-5, $2(CH_3)_2$N-) ; 3.0-3.1 (m, 2H, 2H-1); ^{13}C NMR($CDCl_3$) 100 MHz : 26.2-26.4 (C-3, C-4, CH_2) ; 34.3 (C-2, CH_2); 40.2 (C-5, N-CH_3) ; 52.5 (C-1, CH) ; 158.2 ; 164,5 (C=N); FTIR (KBr) cm^{-1} : 1600-1610, 1678 (ν C=N); $pK_{A(CH3CN)}$ 31.5.
15. *7-(N,N'-diisopropylformamidyl)-1,5,7-triazabicyclo[4.4.0]dec-5-ene*; $C_{14}H_{27}N_5$ = 265.41 g/mol; $Bp_{0.2}$ = 150-160°C; FTIR (NaCl) cm^{-1} : 1607 ,large (ν C=N); elemental analysis, C% 63.35, N 26.39, C/N 2.80, found% C 59.58, N 25.03, C/N 2.77 (contains water); ^1H NMR($CDCl_3$) : 1.0-1.2 (m, 12H, H-2) ; 1.7-2.1 (m, 4H, H-4) ; 3.1-3.4 (m, 8H, H-3); 3.7-3.9 (sext, 2H, H-1); ^{13}C NMR ($CDCl_3$) 200 MHz : 20.8 ; 21.9 ; 22.3 ; 22.9 (C-4, CH_2) ; 23.1 ; 23.5 (2C-2, CH_3) ; 37.8 ; 39.6 ; 42.9 ; 46.9 ; 48.6 ; 49.2 (C-3, N-CH_2) ; 41.6 ; 42.1 (C-1, CH) ; 149.9 ; 157.7 (C=N); $pK_A(CH_3CN)$ 31.7.
16. To be published.
17. Known as Diester® or Biodiesel®
18. *1-(6'-polystyrylhexyl)-2-n-butyl-4,4,5,5-tetramethylbiguanide*; FTIR (NaCl) cm^{-1} : 1664, νC=N).
19. *N-(n-butyl)-N'-(6'-polystyrylhexyl)carbodiimide*; FTIR (NaCl) cm^{-1} : 2122, ν(N=C=N).
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22. At 70°C; molar ratio of methanol /ester/catalyst : 2.3/1 / 0.02.