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SYNTHESIS OF *N*-FUNCTIONALIZED CARBODIIMIDES, HYDANTOINS, 1,3-DIAZETIDINES, AND IMIDAZOLIDINE DERIVATIVES FROM *N*-VINYLIC PHOSPHAZENES DERIVED FROM ß-AMINO ACIDS

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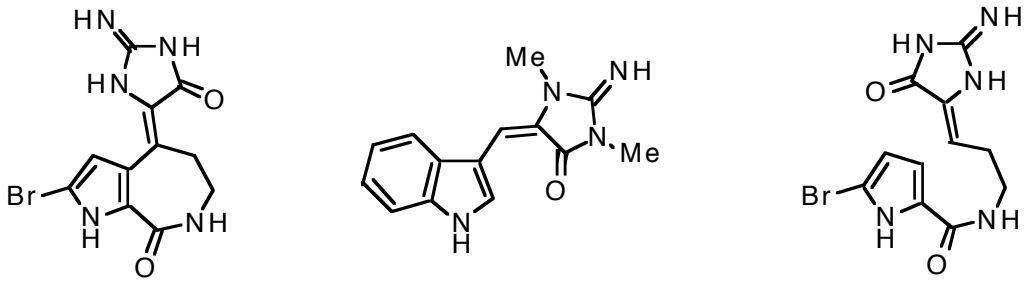
Abstract- Synthesis of *N*-vinylic carbodiimides through Aza-Wittig reaction of *N*-vinylic phosphazenes with isocyanates is reported. These heterocumulenes are used for the preparation of unsymmetrical ureas and nitrogen heterocycles such as hydantoins, 1,3-diazetidines, imidazolidinones, and bis-imidazolidinone azines.

The utility of *N*-vinylic phosphazenes[1] has been demonstrated as key intermediates in the preparation of heterocycles[2-4] and for the construction of the framework of pharmacologically active alkaloids.[5] In this context, we have used the Aza-Wittig reaction of *N*-vinylic phosphazenes with carbonyl compounds leading to a very efficient method for the preparation of 2-azadienes derived from α-[2e] and β-amino acids.[2a,d] Following on from our studies of the reactivity and synthetic utility of phosphazenes, here we wish to explore the reactivity of *N*-vinylic phosphazenes (**1**) derived from β-amino acids or dehydroaspartic esters, towards isocyanates to obtain *N*-functionalized carbodiimides[6] and unsymmetrical ureas and to explore their usefulness in the synthesis of heterocyclic compounds such as 1,3-diazetidines and C-5 unsaturated 2-iminoimidazolones. The presence of an alkoxycarbonyl group as substituent on the exocyclic double bond of these heterocycles could allow the synthesis of cyclic or acyclic derivatives of these compounds through well known transformations of the alkoxycarbonyl group.

It is well known that the reaction of carbodiimides with an appropriate nucleophile such as H_2O and NH_3 or their derivatives leads to ureas or guanidines, respectively.[7] Unsymmetrically substituted urea is a frequent structural feature of many biologically active compounds such as enzyme inhibitors[8a] and peptide analogues.[8b] Recently, compounds containing this functional group have been tested showing many other biological activities.[8c] Moreover, unsymmetrically substituted ureas have been used as key

intermediates in the synthesis of acyclic[9a,b] and heterocyclic compounds[9c,d] and several methods for the preparation of unsymmetrical ureas in solution or solid phase have been published.[9e-g] On the other hand, guanidines with an ester group on the α position can undergo cyclization to give 2-aminoimidazolone or 2-iminoimidazolone,[10] which are a structural feature of several marine products such as hymenialdisine (**2**),[11a-c] aplysinopsine (**3**),[11d] and dispacamide (**4**) alkaloids (Figure 1)[11e] isolated from marine sponges. These metabolites exhibit an interesting pharmacological activity[12] and have been the subject of several syntheses.[13] The common characteristic of this group of natural products is the presence of a ring of C-5 unsaturated 2-iminoimidazolone connected through an exocyclic double bond to other heterocyclic and acyclic systems.

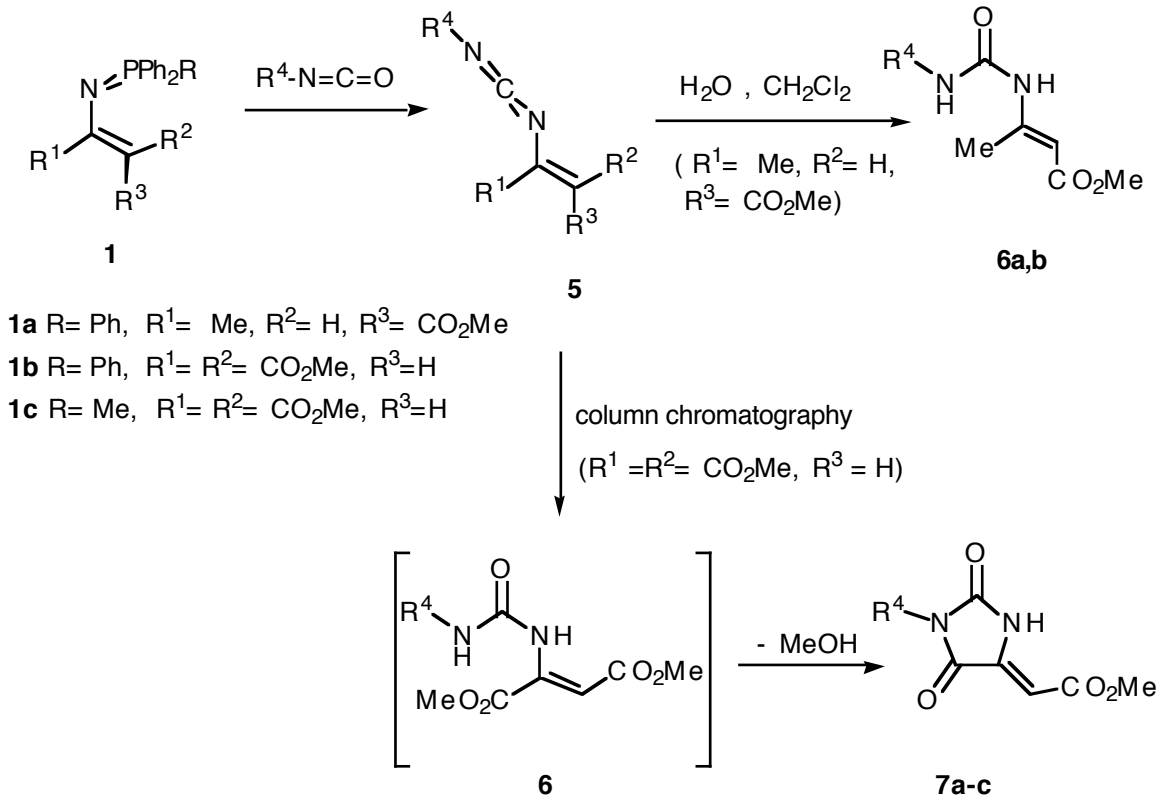


2: Hymenialdisine **3**: Aplysinopsine **4**: Dispacamide

Figure 1

The Aza-Wittig reaction of phosphazene (**1a**) with isocyanates in $CHCl_3$ afforded the α, β-unsaturated carbodiimides (**5a-c**) derived from β-amino esters (Scheme 1) in high yields (Table 1, Entries 1-3). Vinylic heterocumulenes (**5a-c**) were isolated after column chromatography as a single isomer that was assigned as *E* according to configuration of *N*-vinylic phosphazene (**1a**). However, small amounts of ureas (**6a**) and (**6b**) were obtained (~10%) during purification of compounds (**5a**) and (**5b**). Complete transformation of these carbodiimides (**5a,b**) into unsymmetrically substituted ureas (**6a,b**) (Scheme 1) was achieved by stirring the former in CH_2Cl_2/H_2O (Table 1, Entries 4,5).

When phosphazenes (**1b,c**) derived from dehydroaspartic esters[14] were used, carbodiimides (**5d-f**) could be observed by ^{1}H-NMR. But all attempts to purify the heterocumulenes (**5d-f**) by column chromatography were unsuccessful, as they were readily converted into hydantoin derivatives (**7a-c**) (Scheme 1) in high yields (Table 1, Entries 6-8). Compounds (**7**) were characterized on the basis of their NMR spectroscopic data and MS spectrometry and were consistent with hydantoin structures. Formation of hydantoins (**7**) can be explained by addition of water to heterocumulenes (**5d-f**) during the column chromatography purification process to give the intermediate ureas (**6**) and subsequent cyclocondensation. Consequently, carbodiimides (**5d-f**) were not isolated and crude reaction mixtures were satisfactorily used without purification for the following purposes. These carbodiimides were obtained as a single isomer that was assigned as *Z* form according to the configuration of phosphazenes (**1b,c**) and of the products obtained by subsequent reactions of *N*-vinylic carbodiimides and nucleophiles.



Scheme 1

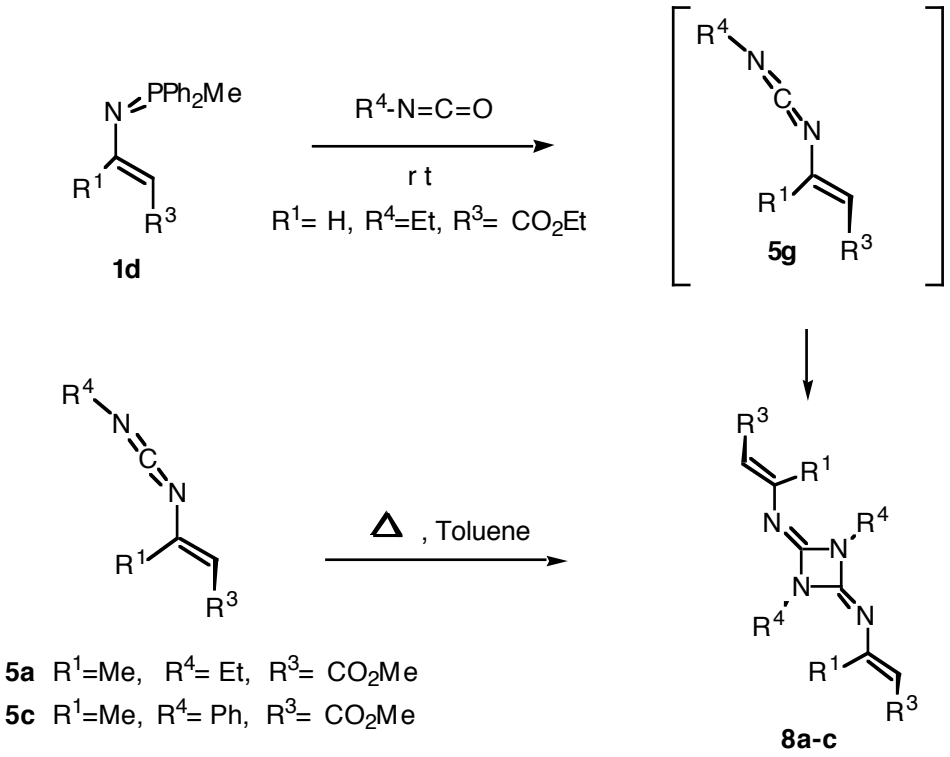
Table 1. Carbodiimides (**5**), Ureas (**6**), Hydantoins (**7**) and 1,3-Diazetidines (**8**)

Entry	Compd	R^1	R^2	R^3	R^4	Yield (%)	m p [°C][a]
1	**5a**	Me	H	CO_2Me	Et	78	oil
2	**5b**	Me	H	CO_2Me	Pr	67	oil
3	**5c**	Me	H	CO_2Me	Ph	80	oil
4	**6a**	-	-	-	Et	74	oil
5	**6b**	-	-	-	Pr	65	oil
6	**7a**	-	-	-	Et	48	156-158
7	**7b**	-	-	-	Pr	60	153-155
8	**7c**	-	-	-	Ph	40	235-237
9	**8a**	H	H	CO_2Et	Et	81	93-95
10	**8b**	Me	H	CO_2Me	Et	S79	oil
11	**8c**	Me	H	CO_2Me	Ph	73	145-147

[a] After recrystallization from CH_2Cl_2-hexane.

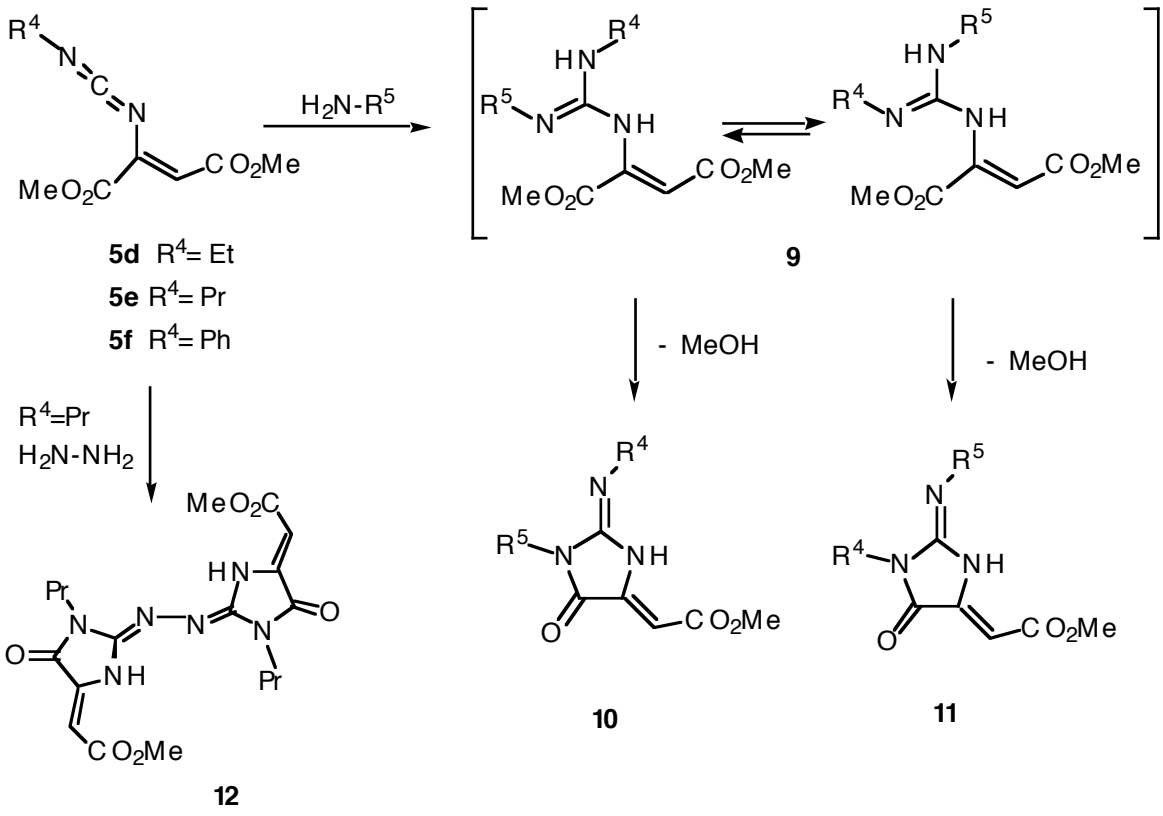
All attempts to obtain carbodiimides using phosphazene (**1d**) (Scheme 2) were unsuccessful when Phenyl isocyanate was used. However, when ethyl isocyanate was used, 1,3-diazetidine-2,4-diimine (**8a**)

(R^1=R^2=H, R^3=CO_2Et, R^4=Et) was obtained (Scheme 2, Table 1, Entry 9). Formation of this four membered hetetocycle could be explained by "*in situ*" dimerization of carbodiimide (**5g**).[15a,16] First indications of this 1,3 diazetidine structure were obtained by MS spectrometry where compound (**8a**) showed the molecular peak at m/z = 336 (M^+). ^1H and ^{13}C NMR spectra showed only two different signal for ethyl groups corresponding to CO_2Et and Et_2N and one signal for the two vinylic CH respectively, which suggest a symmetrical structure. In order to test if functionalized carbodiimides (**5**) could be precursors of 1,3-diazetidines (**8**), the dimerization of some isolated carbodiimides (**5**) was explored. When *N*-vinylic carbodiimides (**5a**) (R^4=Et) and (**5c**) (R^4=Ph) were refluxed in toluene 1,3-diazetidines (**8b**) and (**8c**) were obtained (Scheme 2, Table 1, Entries 10 and 11). In those cases, MS spectrometry of the 1,3-diazetidines (**8b**,**c**) showed a peak at $M^+/2$, which is in agreement with the literature.[16]



Scheme 2

In order to enhance the synthetic use of *N*-functionalized heterocumulenes (**5**), the reaction of crude carbodiimides (**5d-f**) with nitrogen nucleophiles such as amines was explored. Heterocumulenes (**5d-f**), generated " *in situ*" by reaction of phosphazenes with isocyanates, were allowed to react with amines at room temperature affording the iminoimidazolones (**10**) or (**11**) (Scheme 3) as single isomers (Table 2, Entries 1, 3-4), except when carbodiimide (**5d**) reacted with propylamine, where a mixture of two isomers (**10b**) and (**11b**) of vinylic iminoimidazolone was obtained in a ratio of 46:54 (**10b/11b**) (Table 2, Entry 2). The structure of both isomers will be discussed later on.



Scheme 3

The structural constitutions of iminoimidazolones (**10**) were inferred from the ^{1}H and ^{13}C NMR spectral data and confirmed for compound (**10a**) on the basis of X-Ray diffraction analysis. Figure 2 shows an ORTEP representation[17] of compound (**10a**), and the configuration between the exocyclic methoxycarbonyl group and the amino group in the ring is *cis*. Comparing with the NMR spectroscopic data found for the olefinic proton in compounds (**10**) and (**11**) and compound (**10a**), a *cis* configuration was assumed for all iminoimidazolones. These olefinic protons in all iminoimidazolones appeared at δ = 5.61-5.67 as singlets. On the other hand, the iminic structure assumed for the exocyclic N in compounds (**10**) and (**11**) is confirmed by comparing with the structure found for compound (**10a**), analyzed by X-Ray diffraction, and with the studies of Talaty *et al.*[10]

The annelation leading to iminoimidazolidinones can be explained[7b] by a cyclocondensation across the ester functionality in the intermediate (**9**) with loss of alcohol (Scheme 3). Although the cyclization could take place through both imino groups, the higher nucleophilicity of the *N*-alkylimino group could explain the selective process that leads to iminoimidazolidinones as a single isomer (**10**) or (**11**), regardless of the carbodiimides and amines used in the process. When both imino groups in the intermediate guanidine (**9**) are alkyl substituted, there is no selectivity in the cyclocondensation process and two iminoimidazolidinones (**10b**) and (**11b**) are obtained. The structure of componds (**10b**) and (**11b**) were assigned by means of their ^{1}H NMR spectral data. In compound (**10b**), the protons of N-CH_2 in the propyl group appeared at δ = 3.55 as a triplet, and the protons of N-CH_2 in the ethyl group appeared at δ = 3.29 as a quartet. Similarly, the N-CH_2 of the propyl group in iminoimidazolidinone (**10a**) shows absorptions at δ = 3.69. It

can be assumed that isomer (**10b**) has the propyl group attached to the nitrogen on the cycle. In the case of the isomer (**11b**), however, the N-CH_2 in the propyl group appeared at δ = 3.20 as a triplet whereas the N-CH_2 in the ethyl group appears as a quartet at δ =3.65, which is consistent with an ethyl group on the nitrogen of the ring.

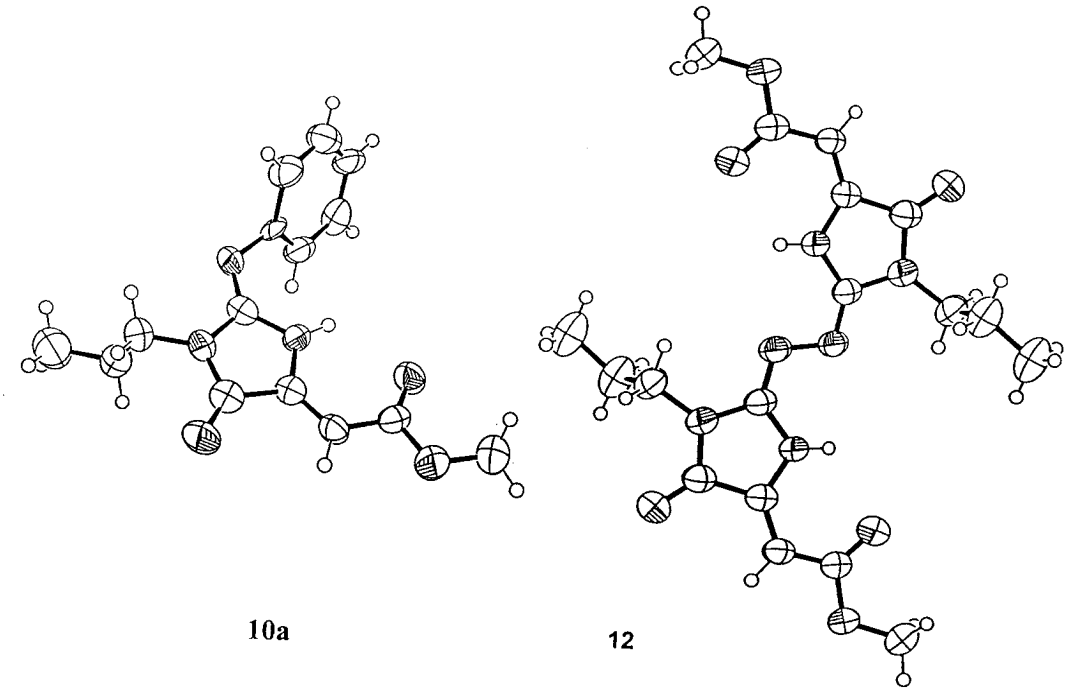


Figure 2. ORTEP view of compounds (**10a**) and (**12**)

Table 2. Iminoimidazolones (**10**) and (**11**)

Entry	Compd	Starting compound	R^4	R^5	Solvent	Time	Yield%	m p [°C][a]
1	**10a**	**5f**	Ph	Pr	$CHCl_3$	60 h	60	76-77
2	**10b/11b**	**5d**	Et	Pr	CH_2Cl_2	3 h	30/35	92-94/ 89-90
3	**10c = 11c**	**5e**	Pr	Pr	CH_2Cl_2	1 h	60	82-83
4	**11d**	**5e**	Pr	H	CH_2Cl_2	1 h	53	128-129

[a] After recrystallization from CH_2Cl_2-hexane.

Finally, we aimed to extend this methodology to the preparation of bisheterocyclic compounds by using reagents with two nucleophilic centers such as hydrazine. Reaction of *N*-vinylic carbodiimides with hydrazine could lead to symmetrical bis-imidazolidinone azines. Thus, we performed the reaction of carbodiimide (**5f**) with hydrazine in ethanol which afforded azine (**12**) in 31% yield (Scheme 3). The structure of this compound was characterized by its spectral data and was confirmed by X-Ray diffraction analysis. An ORTEP representation[17] of molecule (**12**) is given in Figure 2, where a planar disposition of

both heterocycles can be observed. These types of compounds have received considerable interest because of their potential as materials for electroluminescence purposes and in the non-linear optics (NLO) field. [18]

Table 3. Selected spectral data for compounds (**5-12**)

Compd	^{1}H-NMR ($CDCl_3$)[a] δ (ppm)	^{13}C-NMR ($CDCl_3$)[a] δ (ppm)	IR[b] υ (cm^{-1})	MS[c] (m/z)
5a	1.31 (t, 3H, $^3J_{HH}$ = 7.3 Hz, CH_3), 2.37 (s, 3H, CH_3), 3.44 (q, 2H, $^3J_{HH}$ = 7.3 Hz, CH_2), 3.64 (s, 3H, OCH_3), 5.50 (s, 1H, =CH).	16.6 (CH_3), 19.2 (CH_3), 41.5 (CH_2), 50.6 (OCH_3), 108.3 (=CH), 132.5 (C=), 155.4 (N=C=N), 167.4 (C=O)	2146 (N=C=N) 1715 (C=O)	168 (M^+, 35 %)
5b	0.96 (t, 3H, $^3J_{HH}$ = 7.3 Hz, CH_3), 1.65 (m, 2H, CH_2), 2.39 (s, 3H, CH_3), 3.35 (t, 2H, $^3J_{HH}$ = 7.3 Hz, NCH_2), 3.64 (s, 3H, OCH_3), 5.54 (s, 1H, =CH).	11.1 (CH_3), 19.3 (CH_3), 24.3 (CH_2), 48.0 (NCH_2), 50.6 (OCH_3), 108.0 (=CH), 136.9 (C=), 155.4 (N=C=N), 167.3 (C=O)	2143 (N=C=N) 1712 (C=O)	182 [M^+, 33 %]
5c	2.40 (s, 3H, CH_3), 3.63 (s, 3H, OCH_3), 5.62 (s, 1H, =CH), 7.05-7.29 (m, 5H, Ar).	20.1 (CH_3), 51.1 (OCH_3), 110.8 (=CH), 124.4, 126.3, 129.7, 133.0 (Ar), 136.9 (C=), 152.7 (N=C=N), 167.2 (C=O)	2141 (N=C=N) 1718 (C=O).	216 [M^+,100%]
5d	(**5d** + Ph_3PO): 3.76 (s, 3H, OCH_3), 3.87 (s, 3H, OCH_3), 6.41 (s, 1H, =CH), 7.18 - 7.70 (m, 20H, Ar).	(**5d** + Ph_3PO): 51.7 (OCH_3), 53.7 (OCH_3), 114.2 (=CH), 120.5-134 (Ar + C=), 138.2 (N=C=N), 163.5 (C=O), 164.6 (C=O)	2132 (N=C=N) 1742 (C=O)	260 [M^+, 37 %]
5e	(**5e** + Ph_3PO): 1.19 (t, 3H, $^3J_{HH}$ = 7.2 Hz, CH_3), 3.41 (q, 2H, $^3J_{HH}$ = 7.2 Hz, CH_2), 3.59 (s, 3H, OCH_3), 3.70 (s, 3H, OCH_3), 6.14 (s, 1H, =CH), 7.39-7.70 (m, 15 H, Ar)	(**5e** + Ph_3PO): 16.2 (CH_3), 40.9 (CH_2), 51.4 (OCH_3), 53.2 (OCH_3), 112.0 (=CH), 128-134 (Ar + C=), 140.3 (N=C=N), 163.8 (C=O), 165.3 (C=O)	2157 (N=C=N) 1736 (C=O)	212 [M^+, 78%]
5f	(**5f** + Ph_3PO): 0.93 (t, 3 H, $^3J_{HH}$ = 7.2 Hz, CH_3), 1.65 (m, 2H, CH_2), 3.43 (t, 2H, $^3J_{HH}$ = 6.8 Hz, NCH_2), 3.68 (s, 3H, OCH_3), 3.79 (s, 3H, OCH_3), 6.20 (s, 1H, =CH), 7.39-7.70 (m, 15 H, Ar)	(**5f** + Ph_3PO): 11.1 (CH_3), 23.9, (CH_2), 47.4 (NCH_2), 51.3 (OCH_3), 53.1 (OCH_3), 111.7 (=CH), 128-134 (Ar + C=), 140.4 (N=C=N), 163.8 (C=O), 164.9 (C=O)	2150 (N=C=N) 1726 (C=O)	226 [M^+, 42%]
6a	1.10 (t, 3H, $^3J_{HH}$ = 7.2 Hz, CH_3), 2.31 (s, 3H, CH_3), 3.20 (m, 2H, CH_2), 3.61 (s, 3H, OCH_3), 4.60 (s, 1H, NH), 4.73 (s, 1H, =CH), 10.50 (s, 1H, NH)	15.2 (CH_3), 21.9 (CH_3), 35.4 (CH_2), 50.9 (OCH_3), 92.5 (=CH), 153.8 (C=), 157.5 (C=O), 170.4 (C=O)	3327 (NH) 1680 (C=O)	186 [M^+, 19%]

Table 3. Continued

Compd	^{1}H-NMR ($CDCl_3$)[a] δ (ppm)	^{13}C-NMR ($CDCl_3$)[a] δ (ppm)	IR[b] υ (cm^{-1})	MS[c] (m/z)
6b	0.90 (t, 3H, $^3J_{HH}$ = 7.2 Hz, CH_3), 1.52 (m, 2H, CH_2), 2.35 (s, 3H, CH_3), 3.15 (m, 2H, NCH_2), 3.63 (s, 3H, OCH_3), 4.76 (s, 1H, =CH), 5.63 (s, 1H, NH), 10.53 (s, 1H, NH)	11.2 (CH_3), 21.6 (CH_3), 23.0 (CH_2), 42.0 (NCH_2), 50.6 (OCH_3), 92.2 (=CH), 153.8 (C=), 157.26 (C=O), 170.0 (C=O)	3318 (NH) 1671 (C=O)	200 [M^+, 19%]
7a	1.26 (t, 3 H, $^3J_{HH}$ = 7.2 Hz, CH_3), 3.67 (q, 2H, $^3J_{HH}$ = 7.2 Hz, CH_2), 3.82 (s, 3H, OCH_3), 5.91 (s, 1H, =CH), 9.05 (s, 1H, NH)	13.6 (CH_3), 34.2 (CH_2), 52.4 (OCH_3), 95.9 (=CH), 139.7 (C=), 153.6 (C=O), 162.5 (C=O), 167.4 (C=O)	3269 (NH) 1737 (C=O) 1704 (C=O) 1675 (C=O)	198 [M^+, 56%]
7b	0.87 (t, 3 H, $^3J_{HH}$ = 7.3 Hz, CH_3), 1.63 (m, 2H, CH_2), 3.50 (t, 2H, $^3J_{HH}$ = 7.3 Hz, NCH_2), 3.75 (s, 3H, OCH_3), 5.85 (s, 1H, =CH), 8.86 (s, 1H, NH)	11.1 (CH_3), 21.4 (CH_2), 40.5 (NCH_2), 52.2 (OCH_3), 95.6 (=CH), 139.5 (=C), 153.6 (C=O), 162.5 (C=O), 167.2 (C=O)	3270 (NH) 1732 (C=O) 1699 (C=O) 1673 (C=O)	212 [M^+, 31%]
7c	($CDCl_3$ + DMSO-d_6): δ = 3.79 (s, 3H, OCH_3), 5.78 (s, 1H, =CH), 7.41-7.54 (m, 5H, ar), 11.18 (s, 1H, NH)	50.3 (OCH_3), 93.9 (=CH), 125.0, 126.9, 127.5, 129.6 (ar), 137.3 (C=), 152.0 (C=O), 160.6 (C=O), 164.0 (C=O)	3280 (NH) 1739 (C=O) 1702 (C=O) 1677 (C=O)	246 [M^+, 68%]
8a	1.23 (t, 6H, $^3J_{HH}$ = 7.3 Hz, CH_3), 1.30 (t, 6H, $^3J_{HH}$ = 7.2 Hz, CH_3), 3.46 (q, 4H, $^3J_{HH}$ = 7.3 Hz, CH_2), 4.21 (q, 4H, $^3J_{HH}$ = 7.2 Hz, CH_2), 5.83 (d, 1H, $^3J_{HH}$ = 13.2 Hz, =CH), 7.85 (d, 2H, $^3J_{HH}$ = 13.2 Hz, =CH)	13.5 (CH_3), 14.3 (CH_3), 38.0 (NCH_2), 60.2 (OCH_2), 114.7 (=CH), 144.8 (=CH), 153.5 (C=N), 167.3 (C=O)	1708 (C=O) 1596 (C=N)	336 [M^+, 6%] 168 [M^+/2, 63%]
8b	1.16 (t, 6H, $^3J_{HH}$ = 7.2 Hz, CH_3), 2.11 (s, 6H, CH_3), 3.93 (s, 6H, OCH_3), 3.95 (q, 4H, $^3J_{HH}$ = 7.2 Hz, CH_2), 5.88 (s, 2H, =CH)	13.3 (-CH_2-$\underline{C}H_3$), 23.6 (CH_3), 36.1 (CH_2), 55.5 (OCH_3), 106.2 (=CH), 156.0, 162.4, 163.0	1679 (C=O) 1540 (C=N)	168 [M^+/2, 74%]
8c	2.25 (s, 6H, CH_3), 3.87 (s, 6H, OCH_3), 6.09 (s, 2H, =CH), 7.42-7.70 (m, 10H, Ar)	29.8 (CH_3), 55.8 (OCH_3), 106.8 (=CH), 128.7-134.7 (ar + C=), 155.9 (C=N), 163.4 (C=O)	1693 (C=O) 1540 (C=N)	216[M^+/2, 100%]

Table 3. Continued

Compd	^{1}H-NMR ($CDCl_3$)[a] δ (ppm)	^{13}C-NMR ($CDCl_3$)[a] δ (ppm)	IR[b] υ (cm^{-1})	MS[c] (m/z)
10a	0.93 (t, 3H, $^3J_{HH}$ = 7.5 Hz, CH_3), 1.72 (m, 2H, CH_2), 3.65 (s, 3H, OCH_3), 3.69 (t, 2H, $^3J_{HH}$ = 7.4 Hz, NCH_2), 5.66 (s, 1H, =CH), 6.90-7.35 (m, 5H, Ar.), 8.97 (s, 1H, NH)	10.8 (CH_3), 20.9 (CH_2), 40.6 (NCH_2), 51.3 (OCH_3), 90.6 (=CH), 121.3 (ar), 124.0 (ar), 129.3 (ar), 140.7 (ar), 142.9 (C=), 145.5 (C=N), 161.7 (C=O), 167.8 (C=O)	3397 (NH) 1686 (C=O) 1640 (C=O)	287 [M^+, 11%]
10b	0.85 (t, 3H, $^3J_{HH}$ = 7.4 Hz, CH_3), 1.19 (t, 3H, $^3J_{HH}$ = 7.2 Hz, CH_3), 1.61 (m, 2H, CH_2), 3.29 (q, 2H, $^3J_{HH}$ = 7.2 Hz, NCH_2), 3.55 (t, 2H, $^3J_{HH}$ = 7.3 Hz, NCH_2), 3.72 (s, 3H, OCH_3), 5.61 (s, 1H, =CH), 9.04 (s, 1H, NH)	11.1(CH_3), 16.2 (CH_3), 21.2 (CH_2), 40.8 (NCH_2), 42.0 (NCH_2), 51.7 (OCH_3), 89.6 (=CH), 141.9 and 142.5 (C= + C=N), 162.2 (C=O), 168.9 (C=O)	3104 (NH) 1730 (C=O) 1699 (C=O) 1672 (C=O)	239 [M^+, 40%]
10c= 11c	0.85 (t, 3H, $^3J_{HH}$ = 7.5 Hz, CH_3), 0.90 (t, 3H, $^3J_{HH}$ = 7.3 Hz, CH_3), 1.6 (m, 4H, CH_2), 3.19 (t, 2H, $^3J_{HH}$ = 6.9 Hz, NCH_2), 3.59 (t, 2H, $^3J_{HH}$ = 7.3 Hz, NCH_2), 3.72 (s, 3H, OCH_3), 5.61 (s, 1H, =CH), 9.04 (s, 1H, NH)	11.2 (CH_3), 11.8 (CH_3), 21.2 (CH_2), 24.3 (CH_2), 40.8 (NCH_2), 49.3 (NCH_2), 51.7 (OCH_3), 89.4 (=CH), 142.0 (C=), 142.6 (N=C), 162.4 (C=O), 169.0 (C=O)	3124 (NH) 1680 (C=O)	253 [M^+, 24%]
11b	0.91 (t, 3H, $^3J_{HH}$ = 7.4 Hz, CH_3), 1.17 (t, 3H, $^3J_{HH}$ = 7.1 Hz, CH_3), 1.60 (m, 2H, CH_2), 3.20 (t, 2H, $^3J_{HH}$ = 7.1 Hz, NCH_2), 3.64 (q, 2H, $^3J_{HH}$ = 7.1 Hz, NCH_2), 3.72 (s, 3H, OCH_3), 5.61 (s, 1H, =CH), 9.03 (s, 1H, NH)	11.8 (CH_3), 13.2 (CH_3), 24.3 (CH_2), 34.2 (NCH_2), 49.3 (NCH_2), 51.6 (OCH_3), 89.5 (=CH), 142.0 and 142.3 (C= + C=N), 162.1 (C=O), 168.9 (C=O)	3270 (NH) 1746 (C=O) 1690 (C=O) 1666 (C=O)	239 [M^+, 21%]
11d	0.89 (t, 3H, $^3J_{HH}$ = 7.4 Hz, CH_3), 1.64 (m, 2H, CH_2), 3.57 (t, 2H, $^3J_{HH}$ = 7.3 Hz, NCH_2), 3.71 (s, 3H, OCH_3), 5.67 (s, 1H, =CH)	11.18 (CH_3), 21.3 (CH_2), 40.8 (NCH_2), 53.4 (OCH_3), 91.5 (=CH), 141.5 (C=), 151.4 (N=C), 162.9 (C=O), 168.15 (C=O)	3390 (NH) 3257.5 (NH) 1673 (C=O)	211 [M^+, 8%]
12	0.92 (t, 6H, $^3J_{HH}$ = 7.4 Hz, CH_3), 1.73 (m, 4H, CH_2), 3.68 (t, 4H, $^3J_{HH}$ = 7.0 Hz, NCH_2), 3.74 (s, 6H, OCH_3), 5.69 (s, 2H, =CH)	11.3 (CH_3), 21.3 (CH_2), 41.4 (NCH_2), 51.8 (OCH_3), 91.4 (=CH), 139.8 (C=), 148.4 (N=C), 162.9 (C=O), 168.1 (C=O)	3423 (NH) 1679 (C=O) 1640 (C=O)	----

[a] Obtained on a Varian VXR 300 Spectrometer. [b] Recorded in a Nicolet FTIR Magna 550. [c] Obtained on a Hewlett Packard 5890 Spectrometer.

In conclusion, this paper describes an easy and efficient access to heterocumulenes derived from β-amino esters and dehydroaspartic esters. These carbodiimides (**5**) can serve as intermediates in the synthesis of unsymmetrical ureas as well as new nitrogen containing heterocyclic compounds such as hydantoins (**7**), diazetidines (**8**), iminoimidazolidinones (**10**) and (**11**) and symmetrical bis-imidazolidinone azine (**12**). Compounds with these substructures could be very useful in the synthesis of biologically active derivatives with interest in medicinal chemistry.[8-13]

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REFERENCES AND NOTES

1. For a review see: M. Nitta in *Reviews on Heteroatom Chemistry,* vol. 9, ed. by S. Oae, MYU Tokyo 1993, pp. 87.
2. a) F. Palacios, E. Herrán, and G. Rubiales, *J. Org. Chem*., 1999, **64**, 6239. b) F. Palacios, C. Alonso, and G. Rubiales, *J. Org. Chem.,* 1997, **62**, 1146. c) F. Palacios, D. Aparicio, and J. M. de los Santos, *Tetrahedron* , 1996, **52**, 4857. d) F. Palacios, I. Pérez de Heredia, and G. Rubiales, *J. Org. Chem*., 1995, **60**, 2384. e) J. Barluenga, M. Ferrero, and F. Palacios, *Tetrahedron Lett.,* 1988, **29**, 4863.
3. a) M. Nitta, Y. Iino, S. Mori, and T. Takayasu, *J. Chem. Soc., Perkin Trans. 1* , 1995, 1001. b) A. R. Katritzky, R. Mazurkiewicz, C. V. Stevens, and M. F. Gordeev, *J. Org. Chem.,* 1994, **59**, 2740. c) T. Oikawa, N. Kanomata, and M. Tada, *J. Org. Chem.,* 1993, **58**, 2046.
4. a) F. Palacios, M. Legido, I. Pérez de Heredia, and G. Rubiales, *Heterocycles* , 2000, **52**, 1057. b) J. Barluenga, M. Ferrero, and F. Palacios, *Tetrahedron* , 1997, **53**, 4521. c) F. Palacios, C. Alonso, and G. Rubiales, *Tetrahedron* , 1995, **51**, 3683.
5. J. A. R. Rodrigues, R. Augusto, G. C. Leiva, and J. D. F. de Sousa, *Tetrahedron Lett.,* 1995, **36**, 59.
6. For a review see: M. N. Vovk and L. I. Samarai, *Rus. Chem. Rev*., 1992, **61**, 548.
7. a) J. M. Chezal, G. Delmas, S. Mavel, H. Elakmaoui, J. Métin, A. Diez, Y. Blache, A. Gueiffier, M. Rubiralta, J. C. Teulade, and O. Chavignon, *J. Org. Chem.,* 1997, **62**, 4085 and references there cited b) T. Okawa and S. Eguchi, *Synlett* , 1994, 555.
8. a) C. T. Supuran, A. Scozzafava, B. C. Jurca, and M. A. Ilies, *Eur. J. Med. Chem*., 1998, **33**, 83. b) D. Limal, V. Semetey, P. Dalbon, M. Jolivet, and J.-P. Briand, *Tetrahedron Lett*., 1999, **40**, 2749. c) L. Matzen, C. Van Amsterdam, W. Rautenberg, H. E. Greiner, J. Harting, C. A. Seyfried, and H. Bottcher, *J. Med. Chem*., 2000, **43**, 1149.
9. a) D. Dubé and A. A. Scholte, *Tetrahedron Lett*., 1999,**40**, 2295. b) J. Yamaguchi, Y. Shusa, and T. Suyama, *Tetrahedon Lett*., 1999, **40**, 8251. c) J. Lu and H. R. Ma, *Synlett* , 2000, 63. d) Z. Xin, Z.

Pei, T. Von Geldem, and M. Jirousek, *Tetrahedron Lett.*, 2000, **41**, 1147. e) Y. Matsumura, Y. Satoh, O. Onomura, and T. Maki, *J. Org. Chem.*, 2000, **65**, 1549. f) T. H. Kim and G.-J. Lee, *J. Org. Chem.*, 1999, **64**, 2941. g) Y. Hamuro, M. A. Scialdone, and W. F. DeGrado, *J. Am. Chem. Soc.*, 1999, **121**, 1636.

10. E. R. Talaty, M. M. Yusoff, S. A. Ismail, J. A. Gomez, C. E. Keller, and J. M. Younger, *Synlett*, 1997, 683.
11. a) D. H. Williams and D. J. Faulkner, *Nat. Prod. Lett.*, 1996, **9**, 57. b) G. Cimino, S. De Rosa, S. De Stefano, L. Mazzarella, R. Puliti, and G. Sodano, *Tetrahedon Lett.*, 1982, **23**, 767. c) G. M. Sharma, J. S. Buyer, and M. W. Pomerantz, *J. Chem. Soc., Chem. Commun.*, 1980, 435. d) R. Kazlauskas, P. T. Murphy, R. J. Quinn, and R. J. Wells, *Tetrahedron Lett.,* 1977, 61. e) F. Cafieri, E. Fattorusso, A. Mangoni, and O. Taglialatela-Scafati, *Tetrahedon Lett.*, 1996, **37**, 3587.
12. a) A. M. Badger, M. N. Cook, B. A. Swift, T. M. Newman-Tarr, M. Gowen, and M. Lark, *J. Pharmacol. Exp. Ther.*, 1999, **290**, 587. b) J. T. Backer and R. J. Well in *Natural Products as Medicinal Agents* . ed. by J.L. Beal, E. Reinhard, Hippokrates Verlag, Stuttgart, 1981, pp 299.
13. a) A. C. Barrios Sosa, K. Yakushijin, and D.A. Horne, *J. Org. Chem.*, 2000, **65**, 610. b) M. Fu, M. Fernandez, M. L. Smith, and J. A. Flygare, *Org. Lett.,* 1999, 1351. c) T. Lindel and H. Hoffmann, *Tetrahedron Lett.,* 1997, **38**, 8935. e) Y. Xu, K. Yakushijin, and D. A. Horne, *J. Org. Chem.*, 1997, 62, 456. e) H. Annoura and T. Tatsuoka, *Tetrahedron Lett.*, 1995, **36**, 413. f) P. Molina, P. M. Fresneda, and P. Almendros, *Tetrahedron Lett.,* 1992, **33**, 4491. g) A. Dalkafouki, J. Ardisson, N. Kunesch, L. Lacombe, and J. E. Poisson, *Tetrahedron Lett.*, 1991, **32**, 5325.
14. Phosphazenes derived from diphenylmethylphosphine (**1c**) required milder reaction conditions (see ref. 2a-d) than those derived from triphenylphosphine.
15. For recent contributions see: a) M. Alajarín, P. Molina, P. Sanchez-Andrada, and M. C. Foces-Foces, *J. Org. Chem.,* 1999, **64**, 1121. b) C. Shi, Q. Zhang, and K. K. Wang, *J. Org. Chem.,* 1999, **64**, 925.
16. R. M. Claramunt, M. C. Foces-Foces, F. Hernandez Cano, A. Fruchier, P. Molina, M. Alajarin, C. Lopez Leonardo, and J. Elguero, *J. Chem. Soc., Perkin Trans.* 2, 1990, 1859.
17. Crystallographic data (excluding structure factors) for the structures (**10a**) and (**12**) have been deposited with the Cambridge Crystallographic Data Centre as supplementary publication no. CCDC-147012. and CCDC-147011, respectively.
18. a) F. Bodar-Houillon, Y. Elissami, A. Marsura, N. E. Ghermani, E. Espinosa, N. Bouhmaida, and A. Thalal, *Eur. J. Org. Chem.*, 1999, 1427. b) R. Centore and C. Garzillo, *J. Chem. Soc., Perkin Trans. 2* , 1997, 79. c) D. Bethell, D.-H. Kang, and G. Zerbi, *J. Chem. Soc., Perkin Trans. 2* , 1996, 1081.