New, Diastereoselective One-Pot Synthesis of Tetrasubstituted Hydantoins

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An effective route to hydantoins is described, based on the 2:1:1 addition of arylsulfonyl isocyanates, dialkyl acetylenedicarboxylates, and dialkyl trialkylsilyl phosphites. The resulting tetrasubstituted, stable hydantoins **4**/**4′** (*Table*) were obtained in excellent yields, and their structures were corroborated spectroscopically (IR, ^{1}H-, ^{13}C-, ^{31}P-NMR, EI-MS) and by elemental analyses. A plausible mechanism for this type of cyclization is proposed (*Scheme 2*).

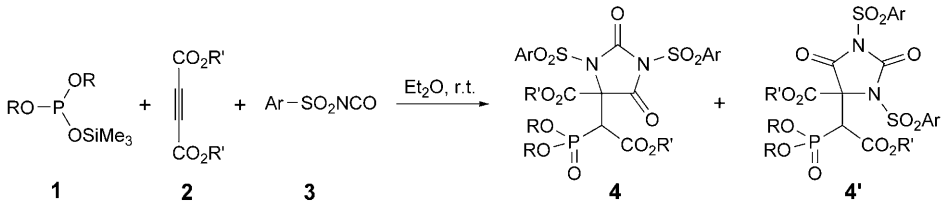
Introduction. – Hydantoins (=imidazolidine-2,4-diones) are of considerable interest both from chemical and biological points of view [1]. Several compounds of this class have shown pharmaceutically useful activities that have led, in some cases, to clinical applications. In particular, 5-substituted and 5,5-disubstituted hydantoins are important medicinal compounds: phenytoin (=5,5-diphenylhydantoin) is widely used as an anticonvulsant for the treatment of epilepsy, and as a cardiac anti-arrythmic [2][3]. Among the medicinally useful properties exhibited by other 5-substituted hydantoins, their antidepressant and antiviral activities, and the inhibition of platelet aggregation, of human aldose reductase, and of human leukocyte elastase are worth mentioning [4]. A number of other biological activities of hydantoin derivatives are known, including the possible use as herbicides and fungicides.

From an organic-synthesis point of view, hydantoins have been frequently used as precursors of unnatural α-amino acids [5][6]. In addition, they have recently received much attention as molecular scaffolds for the combinatorial synthesis of new libraries of compounds. Actually, the rigid structure of the substituted hydantoin nucleus is particularly attractive when the rapid synthesis of compounds with defined spatial structure is required. Further, the possibility to insert diverse substituents at various positions into the hydantoin nucleus renders this class of compounds very useful for studies aimed at a correlation between well-defined chemical structure and eventual biological activity [7].

Here, we report a simple one-pot reaction between dialkyl trialkylsilyl phosphites and dialkyl acetylenedicarboxylate in the presence of arylsulfonyl isocyanates for the preparation of tetrasubstituted hydantoins.

Results and Discussion. – As shown in *Scheme 1*, the dialkyl trialkylsilyl phosphites **1**, the dialkyl acetylenedicarboxylates **2**, and the arylsulfonyl isocyanates **3** underwent a

Scheme 1



1 **2** **3** **4** **4'**

4/4'	R	R'	Ar
a	Me	Me	C_6H_5
b	Et	Me	C_6H_5
c	Me	Et	C_6H_5
d	Me	Me	4-Me-C_6H_4
e	Et	Me	4-Me-C_6H_4
f	Me	Et	4-Me-C_6H_4
g	Et	Et	4-Me-C_6H_4

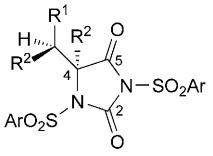
smooth 1:1:2 addition reaction in anhydrous Et_2O at ambient temperature to afford the tetrasubstituted, diastereoisomeric hydantoin derivatives **4**/**4**′.

The ^{1}H-, ^{13}C-, and ^{31}P-NMR spectra of the crude products clearly indicated the formation of the hydantoins **4a**–**g** (and their primed stereoisomers). Actually, no other product could be detected by NMR spectroscopy. The structures of compounds **4**/**4**′ were deduced from their IR, ^{1}H-, ^{13}C-, and ^{31}P-NMR spectra, and their mass spectra displayed molecular-ion peaks at appropriate *m*/*z* values. The ^{1}H-, ^{13}C-, and ^{31}P-NMR spectra were consistent with the presence of two diastereoisomers, **4** and **4**′, for each compound. Their relative proportion in $CDCl_3$ solution was determined from the corresponding ^{1}H-NMR spectra [8–10]. The diastereoisomer ratios (dr) for compounds **4a**/**4**′**a** and **4c**/**4**′**c** were found to be kinetically controlled (very fast reaction), while the dr values for **4b**/**4**′**b** and **4d**–**g**/**4**′**d**–**g** were shown to be thermodynamically controlled. Selected ^{1}H-, ^{13}C-, and ^{31}P-NMR chemical shifts and coupling constants of the major (M) and the minor (m) diastereoisomers of these compounds are collected in the *Table*.

Although the presence of the ^{31}P nucleus complicated both the ^{1}H- and ^{13}C-NMR spectra [11] of **4**/**4**′, it helped in the assignment of the signals by long-range coupling with ^{1}H and ^{13}C nuclei (see *Exper. Part*). Of particular interest were the three-bond C–P coupling constants, ^3J(C,P), providing information about the P–C–C–C torsional angles. The ^3J(C,P) value strongly depends on conformation, *transoid* couplings giving rise to larger values than *cisoid* ones. The *Karplus* relation can be derived from the data for organophosphorus compounds with tetra- and pentacoordinate phosphorus [12]. The observation of ^3J(C,P) values of 17.4–17.6 Hz for the carbonyl C(5)-atom of the hydantoin ring (see *Exper. Part*) is in agreement with the relative (1*S**,4*R**)-configuration, in which the $(MeO)_2PO$ and the C=O groups are in *anti* relation.

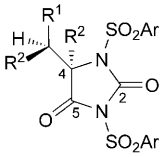
On the basis of the well-established chemistry of trivalent phosphorus nucleophiles [13–20], the hydantoin **4** may result from initial addition of the dialkyl trialkylsilyl phosphite **1** to the ester **2**, followed by subsequent addition of the resulting zwitterion **5** to the arylsulfonyl isocyanate **3** [21], to yield the betaine **6**. Then, attack of the second arylsulfonyl isocyanate would yield the extended betaine **7**. The latter then might

Table. *Selected* ^{1}*H-,* ^{13}*C-, and* ^{31}*P-NMR Chemical Shifts* (in ppm) *and Coupling Constants* (in Hz) *for the Signals of the Major* (M) *and Minor* (m) *Isomers* **4** *and* **4′**



4

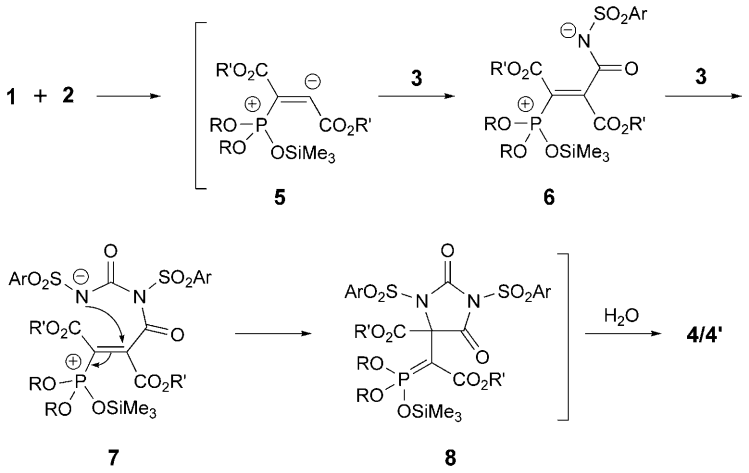
R^1 = P(O)(OR)$_2$
R^2 = COOR'



4'

Compound	**4**/**4′**	Isomer	^{1}H	^{13}C				^{31}P
			CH (^{2}J(H,P))	CH (^{1}J(C,P))	C(4) (^{2}J(C,P))	N_2CO	NCO (^{3}J(C,P))	
4a	28 : 72	M	4.53 (22.4)	48.11 (131.3)	69.58 (3.1)	147.01	163.20 (17.6)	17.40
		m	4.92 (26.4)	48.48 (127.3)	70.40 (4.9)	147.35	162.31	16.35
4b	93 : 7	M	4.94 (26.3)	49.17 (126.3)	70.43 (2.5)	147.38	162.36	13.41
		m	4.52 (22.3)					15.14
4c	8 : 92	M	4.50 (22.0)	48.25 (131.0)	69.65 (3.5)	147.06	162.61 (17.6)	17.72
		m	4.92 (26.8)					16.63
4d	51 : 49	M	4.96 (26.3)	48.10 (131.9)	69.55 (3.6)	147.08	162.48	16.59
		m	4.53 (22.3)	48.41 (126.8)	70.38 (2.1)	147.44	163.37 (17.4)	17.42
4e	91 : 9	M	4.90 (26.3)	49.10 (125.8)	70.36 (2.0)	147.41	162.50	13.43
		m	4.52 (22.7)					15.12
4f	93 : 7	M	4.93 (26.5)	48.55 (127.1)	70.50 (2.3)	147.53	161.91	16.78
		m	4.56 (22.3)					17.74
4g	82 : 18	M	4.91 (26.4)	49.09 (125.9)	70.54 (2.3)	147.54	161.94	13.74
		m	4.52 (22.3)	48.21 (131.1)	69.04 (2.0)	147.22	162.79 (17.4)	15.42

Scheme 2



cyclize under the reaction conditions to produce the ylide **8** [22], which is hydrolyzed to the hydantoin **4** (*Scheme 2*).

In conclusion, we have developed a convenient one-pot procedure for the preparation of a series of stable hydantoins by means of *in situ* generation of phosphonium betains. The present method has the advantage that the reaction can be performed under neutral conditions, and the substances can be mixed without any pre-activation or modification. The simplicity of the present method makes it an interesting alternative to more-complex multistep approaches to hydantoins.

The authors are grateful to Dr. *Akbar Heydari* and *Hossein Hamadi* for their cooperation in the synthesis of dimethyl- and diethyl trimethylsilyl phosphite.

Experimental Part

General. Dimethyl- (**2a**) and diethyl acetylenedicarboxylate (**2b**) were obtained from *Merck* (Germany) and *Fluka* (Switzerland), and were used without further purification. Dimethyl trimethylsilyl phosphite (**1a**) and diethyl trimethylsilyl phosphite (**1b**) were prepared according to a literature procedure [23]. Melting points (m.p.) were measured on an *Electrothermal 9100* apparatus; uncorrected. IR Spectra: *Shimadzu IR-460* spectrometer; in cm^{-1}. ^1H-, ^{13}C- and ^{31}P-NMR Spectra: *Bruker DRX-500 Avance* spectrometer, at 500.1, 125.7, and 202.4 MHz, resp., in $CDCl_3$ soln.; δ in ppm, J in Hz. EI-MS (20 eV): *Finnigan MAT-8430* apparatus; in m/z. Elemental analyses: *Heraeus CHN-O-Rapid* analyzer.

General Procedure for the Preparation of Hydantoins (exemplified for **4a**/**4′a**). To a magnetically stirred soln. of dimethyl acetylenedicarboxylate (**2a**; 0.14 g, 1 mmol) and phenylsulfonyl isocyanate (**3a**; 0.37 g, 2 mmol) in anh. Et_2O (5 ml) was added dropwise a soln. of dimethyl trimethylsilyl phosphite (**1a**; 0.18 g, 1 mmol) in Et_2O (3 ml) at r.t. over 10 min. The mixture was stirred for 30 min. The resulting solid was filtered off, washed with anh. Et_2O, and dried in vacuum. For isomer ratios, see the *Table*.

Methyl 4-[1-(Dimethoxyphosphoryl)-2-methoxy-2-oxoethyl]-2,5-dioxo-1,3-bis(phenylsulfonyl)imidazolidine-4-carboxylate (**4a**/**4′a**). Yield: 600 mg (98%). Colorless powder. M.p. 133–135°. IR (KBr): 1810 (hydantoin C=O); 1757 (ester C=O); 1581, 1439 (Ph); 1322 (P=O); 1397, 1188 (SO_2); 1289, 1251, 1137 (ester C–O); 1080 (P–OMe). EI-MS: 619 (10, $[M+1]^+$), 618 (2, M^+) 495 (6), 479 (4), 433 (12), 401 (8), 369 (7), 339 (12), 307 (7), 279 (17), 246 (37), 190 (13), 141 (37), 109 (20), 93 (13), 77 (100). Anal. calc. for $C_{22}H_{23}N_2O_{13}PS_2$ (618.52): C 42.72, H 3.75, N 4.53; found: C 42.7, H 3.6, N 4.5.

NMR Data of Major Isomer **4′a**. ^1H-NMR: 3.32 (*d*, ^3J(H,P) = 11.3, MeO); 3.62 (*d*, ^3J(H,P) = 11.3, MeO); 3.64 (*s*, MeO); 3.78 (*s*, MeO); 4.53 (*d*, ^2J(H,P) = 22.4, CH); 7.53–8.10 (*m*, 10 arom. H). ^{13}C-NMR: 48.11 (*d*, ^1J(C,P) = 131.3, CH); 53.17 (*s*, MeO); 53.54 (*d*, ^2J(C,P) = 6.8, MeO); 54.46 (*s*, MeO); 54.55 (*d*, ^2J(C,P) = 7.4, MeO); 69.58 (*d*, ^2J(C,P) = 3.1, C(4) of hydantoin); 129.07 (2 arom C); 129.11 (2 arom. C); 129.26 (2 arom. C); 129.30 (2 arom. C); 135.20 (1 arom. C); 135.44 (1 arom. C); 136.57 (C_{ipso}); 137.17 (C_{ipso}); 147.01 (*s*, NCON); 160.16 (*d*, ^2J(C,P) = 4.6, CO_2Me); 163.20 (*d*, ^3J(C,P) = 17.6, N–C=O); 164.70 (*d*, ^3J(C,P) = 4.9, CO_2Me). ^{31}P-NMR: 17.40 (*s*, $PO(OMe)_2$).

NMR Data of Minor Isomer **4a**. ^1H-NMR: 3.62 (*s*, MeO); 3.76 (*s*, MeO); 3.76, 3.81 (2*d*, ^3J(H,H) = 11.6 each, 2 MeO); 4.92 (*d*, ^2J(P,H) = 26.4, CH); 7.53–8.10 (*m*, 10 arom. H). ^{13}C-NMR: 48.48 (*d*, ^1J(C,P) = 127.3, CH); 53.26 (*s*, MeO); 53.66 (*d*, ^2J(C,P) = 6.5, MeO); 54.19 (*s*, MeO); 54.61 (*d*, ^2J(C,P) = 7.3, MeO); 70.40 (*d*, ^2J(C,P) = 4.9, C(4) of hydantoin); 128.88 (2 arom. H); 128.98 (2 arom. H); 129.17 (2 arom. H); 129.20 (2 arom. H); 135.26 (arom. H); 135.37 (arom. H); 136.52 (C_{ipso}); 137.16 (C_{ipso}), 147.35 (*s*, NCON); 161.41 (*d*, ^2J(C,P) = 2.5, CO_2Me); 162.31 (*s*, N–C=O); 165.77 (*d*, ^3J(C,P) = 2.5, CO_2-Me). ^{31}P-NMR: 16.35 (*s*, $PO(OMe)_2$).

Methyl 4-[1-(Diethoxyphosphoryl)-2-methoxy-2-oxoethyl]-2,5-dioxo-1,3-bis(phenylsulfonyl)imidazolidine-4-carboxylate (**4b**/**4′b**). Yield: 630 mg (98%). Colorless powder. M.p. 126–128°. IR (KBr): 1810 (hydantoin C=O); 1761 (ester C=O); 1573, 1438 (Ph); 1320 (P=O); 1397, 1189 (SO_2); 1291, 1261, 1238 (ester C–O); 1080 (P–OEt). EI-MS: 647 (5, $[M+1]^+$), 646 (2, M^+), 527 (1), 508 (2), 464 (5), 432 (9), 387 (1), 364 (4), 306 (10), 141 (33), 94 (20), 77 (100), 51 (13). Anal. calc. for $C_{24}H_{27}N_2O_{13}PS_2$ (646.57): C 44.58, H 4.21, N 4.3; found: C 44.6, H 4.3, N 4.4.

NMR Data of Major Isomer **4b**. ^{1}H-NMR: 1.23 (*t*, ^3J(H,H) = 6.9, *Me*CH$_2$O); 1.36 (*t*, ^3J(H,H) = 7.0, *Me*CH$_2$O); 3.52 (*s*, MeO); 3.62 (*s*, MeO); 4.21–4.25 (*m*, MeC*H*$_2$O); 4.94 (*d*, ^2J(H,P) = 26.3, CH); 7.54 (*m*, 4 arom. H); 7.70 (*dd*, ^3J(H,H) = 6.6, 6.8, 2 arom. H); 7.98 (*d*, ^3J(H,H) = 7.9, 2 arom. H); 8.11 (*d*, ^3J(H,H) = 7.9, 2 arom. H). ^{13}C-NMR: 16.11 (*d*, ^3J(C,P) = 2.0, *Me*CH$_2$O); 16.16 (*d*, ^3J(C,P) = 1.8, *Me*CH$_2$O); 49.17 (*d*, ^1J(C,P) = 126.3, CH); 53.11 (*s*, MeO); 54.15 (*s*, MeO); 63.44 (*d*, ^2J(C,P) = 6.2, MeCH$_2$O); 64.22 (*d*, ^2J(C,P) = 6.6, MeCH$_2$O); 70.43 (*d*, ^2J(C,P) = 2.5, C(4) of hydantoin); 128.90 (2 arom. H); 129.02 (2 arom. H); 129.14 (2 arom. H); 129.16 (2 arom. H); 135.20 (arom. H); 135.31 (arom. H); 136.61 (C$_{ipso}$); 137.27 (C$_{ipso}$); 147.38 (*s*, NCON); 161.38 (*d*, ^2J(C,P) = 2.6, *C*O$_2$Me); 162.36 (*s*, NCO); 165.96 (*d*, ^3J(C,P) = 6.7, *C*O$_2$Me). ^{31}P-NMR: 13.41 (*s*, PO(OEt)$_2$).

NMR Data of Minor Isomer **4′b**. ^{1}H-NMR: 1.01 (*t*, ^3J(H,H) = 7.0, *Me*CH$_2$O); 1.27 (*t*, ^3J(H,H) = 7.3, *Me*CH$_2$O); 3.76 (*s*, MeO); 3.79 (*s*, MeO); 4.21–4.25 (*m*, MeC*H*$_2$O); 4.52 (*d*, ^2J(H,P) = 22.3, CH); 7.50–8.07 (*m*, 10 arom. H). ^{31}P-NMR: 15.14 (*s*, PO(OEt)$_2$).

Ethyl 4-[1-(Dimethoxyphosphoryl)-2-ethoxy-2-oxoethyl]-2,5-dioxo-1,3-bis(phenylsulfonyl)imidazolidine-4-carboxylate (**4c**/**4′c**). Yield: 620 mg (96%). Colorless powder. M.p. 135–137°. IR (KBr): 1810 (hydantoin C=O); 1757 (ester C=O); 1573, 1442 (Ph); 1317 (P=O); 1391, 1186 (SO$_2$); 1288, 1252, 1222 (ester C–O); 1080 (P–OMe). EI-MS: 647 (6, $[M+1]^+$), 646 (6, M^+), 601 (2), 558 (1), 507 (13), 418 (20), 353 (13), 324 (12), 307 (10), 260 (13), 232 (13), 141 (33), 109 (17), 93 (17), 77 (100). Anal. calc. for C$_{24}$H$_{27}$N$_2$O$_{13}$PS$_2$ (646.57): C 44.58, H 4.21, N 4.33; found: C 44.6, H 4.3, N 4.4.

NMR Data of Major Isomer **4′c**. ^{1}H-NMR: 1.02 (*t*, ^3J(H,H) = 7.1, *Me*CH$_2$O); 1.32 (*t*, ^3J(H,H) = 7.1, *Me*CH$_2$O); 3.33 (*d*, ^3J(H,P) = 11.3, MeO); 3.67 (*d*, ^3J(H,P) = 11.1, MeO); 3.99–4.17 (*m*, MeC*H*$_2$O); 4.20–4.32 (*m*, MeC*H*$_2$O); 4.50 (*d*, ^2J(H,P) = 22.0, CH); 7.42 (*dd*, ^3J(H,H) = 7.4, 6.5, 4 arom. H); 7.70 (*t*, ^3J(H,H) = 7.4, 2 arom. H); 8.12 (*d*, ^3J(H,H) = 7.0, 2 arom. H); 8.13 (*d*, ^3J(H,H) = 6.5, 2 arom. H). ^{13}C-NMR: 13.36 (*Me*CH$_2$O); 13.85 (*Me*CH$_2$O); 48.25 (*d*, ^1J(C,P) = 131.0, CH); 53.39 (*d*, ^2J(C,P) = 6.9, MeO); 54.62 (*d*, ^2J(C,P) = 6.6, MeO); 62.40 (*s*, MeCH$_2$O); 64.22 (*s*, MeCH$_2$O); 69.65 (*d*, ^2J(C,P) = 3.5, C(4) of hydantoin); 129.00 (2 arom. C); 129.03 (2 arom. C); 129.25 (2 arom. C); 129.42 (2 arom. C); 135.01 (arom. C); 135.31 (arom. C); 136.84 (C$_{ipso}$); 137.35 (C$_{ipso}$); 147.06 (*s*, NCON); 160.40 (*d*, ^2J(C,P) = 5.2, *C*O$_2$Et); 162.61 (*d*, ^3J(C,P) = 17.6, N–C=O); 164.20 (*d*, ^3J(C,P) = 5.0, *C*O$_2$Et). ^{31}P-NMR: 17.72 (*s*, PO(OMe)$_2$).

NMR Data of Minor Isomer **4c**. ^{1}H-NMR: 1.14 (*t*, ^3J(H,H) = 7.1, *Me*CH$_2$O); 1.37 (*t*, ^3J(H,H) = 7.0, *Me*CH$_2$O); 3.81 (*d*, ^3J(H,P) = 11.4, MeO); 3.84 (*d*, ^3J(H,P) = 11.5, MeO); 3.99–4.17 (*m*, MeC*H*$_2$O); 4.20–4.32 (*m*, MeC*H*$_2$O); 4.92 (*d*, ^2J(H,P) = 26.8, CH); 7.54–8.14 (*m*, 10 arom. H). ^{31}P-NMR: 16.63 (*s*, PO(OMe)$_2$).

Methyl 4-[1-(Dimethoxyphosphoryl)-2-methoxy-2-oxoethyl]-1,3-bis[(4-methylphenyl)sulfonyl]-2,5-dioxoimidazolidine-4-carboxylate (**4d**/**4′d**). Yield: 630 mg (98%). Colorless powder. M.p. 143–145°. IR: 1808 (hydantoin C=O); 1757 (ester C=O); 1586, 1431 (Ph); 1321 (P=O); 1397, 1188 (SO$_2$); 1288, 1242, 1134 (ester C–O); 1080 (P–OMe). EI-MS: 647 (2, $[M+1]^+$); 646 (2, M^+), 493 (3), 447 (2), 418 (8), 386 (5), 353 (17), 321 (10), 279 (13), 246 (20), 155 (27), 108 (17), 91 (100), 65 (17). Anal. calc. for C$_{24}$H$_{27}$N$_2$O$_{13}$PS$_2$ (646.57): C 44.58, H 4.21, N 4.33; found: C 44.6, H 4.3, N 4.4.

NMR Data of Major Isomer **4d**. ^{1}H-NMR: 2.46 (*s*, Me); 2.49 (*s*, Me); 3.58 (*s*, MeO); 3.70 (*d*, ^3J(H,P) = 11.1, MeO); 3.71 (*s*, MeO); 3.85 (*d*, ^3J(H,P) = 11.6, MeO); 4.96 (*d*, ^2J(C,P) = 26.3, CH); 7.33–7.38 (*m*, 4 arom. H); 7.86–8.02 (*m*, 4 arom. H). ^{13}C-NMR: 21.80 (Me); 21.84 (Me); 48.10 (*d*, ^1J(C,P) = 131.9, CH); 53.20 (*d*, ^4J(C,P) = 3.7, MeO); 53.44 (*d*, ^2J(C,P) = 6.8, MeO); 54.27 (*d*, ^5J(C,P) = 2.2, MeO); 54.62 (*d*, ^2J(C,P) = 6.7, MeO); 69.55 (*d*, ^2J(C,P) = 3.6, C(4) of hydantoin); 129.09 (2 arom. C); 129.15 (2 arom. C); 129.73 (2 arom. C); 129.80 (2 arom. C); 133.71, 134.26, 146.60, 146.71 (4 C$_{ipso}$); 147.08 (*s*, NCON); 160.19 (*d*, ^2J(C,P) = 5.6, *C*O$_2$Me); 162.48 (*s*, NCO); 165.75 (*d*, ^3J(C,P) = 6.5, *C*O$_2$Me). ^{31}P-NMR: 16.59 (*s*, PO(OMe)$_2$).

NMR Data of Minor Isomer **4′d**. ^{1}H-NMR: 2.46 (*s*, Me); 2.50 (*s*, Me); 3.35 (*d*, ^3J(H,P) = 11.3, MeO); 3.68 (*s*, MeO); 3.82 (*d*, ^3J(H,P) = 11.4, P–OMe); 3.83 (*s*, MeO); 4.53 (*d*, ^2J(H,P) = 22.3, CH); 7.33–7.38 (*m*, 4 arom. H); 7.86–8.02 (*m*, 4 arom. H). ^{13}C-NMR: 21.78 (Me); 21.83 (Me); 48.41 (*d*, ^2J(C,P) = 126.83, CH); 53.27 (*d*, ^4J(C,P) = 3.3, MeO); 53.68 (*d*, ^2J(C,P) = 6.7, MeO); 54.47 (*d*, ^5J(C,P) = 2.9, MeO); 54.72 (*d*, ^2J(C,P) = 6.7, MeO); 70.38 (*d*, ^2J(C,P) = 2.1, C(4) of hydantoin); 129.03 (2 arom. C); 129.46 (2 arom. C);

129.66 (2 arom. C); 129.85 (2 arom. C); 133.66, 134.22, 146.52, 146.79 (4 C_{ipso}); 147.44 (*s*, NCON); 161.54 (s, CO_2Me); 163.37 (*d*, ^3J(C,P) = 17.4, NCO); 164.84 (*d*, ^3J(C,P) = 5.1, CO_2Me). ^{31}P-NMR: 17.42 (*s*, $PO(OMe)_2$).

Methyl 4-[1-(Diethoxyphosphoryl)-2-methoxy-2-oxoethyl]-1,3-bis[(4-methylphenyl)sulfonyl]-2,5-dioxoimidazolidine-4-carboxylate (**4e**/**4′e**). Yield: 660 mg (98%). Colorless powder. M.p. 143–145°. IR (KBr): 1811 (hydantoin C=O); 1757 (ester C=O); 1585, 1431 (Ph); 1319 (P=O), 1385, 1135 (SO_2); 1292, 1260, 1177 (ester C–O); 1079 (P–OEt). EI-MS: 675 (12, $[M+1]^+$), 674 (28, M^+), 551 (20), 521 (37), 492 (7), 475 (27), 446 (38), 411 (13), 367 (37), 307 (47), 274 (17), 218 (13), 155 (43), 139 (10), 107 (17), 91 (100), 65 (13). Anal. calc. for $C_{26}H_{31}N_2O_{13}PS_2$ (674.62): C 46.29, H 4.63, N 4.15; found: 46.3, H 4.6, N 4.2.

NMR Data of Major Isomer **4e**. ^{1}H-NMR: 1.19 (*t*, ^3J(H,H) = 7.0, *Me*CH_2O); 1.31 (*t*, ^3J(H,H) = 7.0, *Me*CH_2O); 2.38 (*s*, 2 Me); 3.49 (*s*, MeO); 3.61 (*s*, MeO); 4.11–4.20 (*m*, 2 MeCH_2O); 4.90 (*d*, ^2J(H,P) = 26.3, CH); 7.27 (*d*, ^3J(H,H) = 7.7, 2 arom. H); 7.29 (*d*, ^3J(H,H) = 7.6, 2 arom. H); 7.79 (*d*, ^3J(H,H) = 8.3, 2 arom. H); 7.92 (*d*, ^3J(H,H) = 8.3, 2 arom. H). ^{13}C-NMR: 16.01 (*d*, ^3J(C,P) = 1.9, *Me*CH_2O); 16.07 (*d*, ^3J(C,P) = 1.8, *Me*CH_2O); 21.69 (Me); 21.73 (Me); 49.10 (*d*, ^1J(C,P) = 125.8, CH); 53.04 (*s*, MeO); 54.09 (*d*, ^4J(C,P) = 4.1, MeO); 63.29 (*d*, ^2J(C,P) = 6.1, Me*C*H_2O); 64.10 (*d*, ^2J(C,P) = 6.3, Me*C*H_2O), 70.36 (*d*, ^2J(C,P) = 2.0, C(4) of hydantoin); 128.92 (2 arom. C); 129.01 (2 arom. C); 129.71 (2 arom. C); 129.74 (2 arom. C); 133.67, 134.28, 146.67, 146.77 (4 C_{ipso}); 147.41 (*s*, NCON); 161.39 (*d*, ^2J(C,P) = 2.6, CO_2Me); 162.50 (*s*, N–C=O); 165.94 (*d*, ^3J(C,P) = 6.7, CO_2Me). ^{31}P-NMR: 13.43 (*s*, $PO(OEt)_2$).

NMR Data of Minor Isomer **4′e**. ^{1}H-NMR: 1.01 (*t*, ^3J(H,H) = 6.8, *Me*CH_2O); 1.14 (*t*, ^3J(H,H) = 6.8, *Me*CH_2O); 2.33 (*s*, Me); 2.34 (*s*, Me); 3.60 (*s*, MeO); 3.74 (*s*, MeO); 4.11–4.20 (*m*, 2 MeCH_2O); 4.52 (*d*, ^2J(H,P) = 22.7, CH); 7.28–7.93 (*m*, 8 arom. H). ^{31}P-NMR: 15.12 (*s*, $PO(OEt)_2$).

Ethyl 4-[1-(Dimethoxyphosphoryl)-2-ethoxy-2-oxoethyl]-1,3-bis[(4-methylphenyl)sulfonyl]-2,5-dioxoimidazolidine-4-carboxylate (**4f**/**4′f**). Yield: 630 mg (94%). Colorless powder. M.p. 148–150°. IR (KBr): 1811 (hydantoin C=O); 1757 (ester C=O); 1587, 1443 (Ph); 1320 (P=O); 1388, 1170 (SO_2); 1287, 1264, 1239 (ester C–O); 1081 (P–OMe). EI-MS: 675 (19, $[M+1]^+$), 674 (15, M^+), 521 (7), 475 (7), 447 (11), 375 (9), 306 (8), 232 (13), 155 (43), 127 (13), 108 (10), 91 (100), 65 (10). Anal. calc. for $C_{26}H_{31}N_2O_{13}PS_2$ (674.62): C 46.29, H 4.63, N 4.15; found: C 46.3, H 4.6, N 4.2.

NMR Data of Major Isomer **4f**. ^{1}H-NMR: 1.06 (*t*, ^3J(H,H) = 7.1, *Me*CH_2O); 1.16 (*t*, ^3J(H,H) = 7.1, *Me*CH_2O); 2.41 (*s*, Me); 2.47 (*s*, Me); 3.82 (*d*, ^3J(H,P) = 11.6, MeO); 3.85 (*d*, ^3J(H,P) = 11.7, MeO); 3.99–4.18 (*m*, 2 MeCH_2O); 4.93 (*d*, ^2J(H,P) = 26.5, CH); 7.32 (*d*, ^3J(H,H) = 8.2, 2 arom. H); 7.35 (*d*, ^3J(H,H) = 8.2, 2 arom. H); 7.88 (*d*, ^3J(H,H) = 8.2, 2 arom. H); 8.01 (*d*, ^3J(H,H) = 8.1, 2 arom. H). ^{13}C-NMR: 13.40 (*Me*CH_2O); 13.65 (*Me*CH_2O); 21.76 (Me); 21.79 (Me); 48.55 (*d*, ^1J(C,P) = 127.1, CH); 53.59 (*d*, ^2J(C,P) = 6.3, MeO); 54.50 (*d*, ^2J(C,P) = 6.5, MeO); 62.68 (*s*, Me*C*H_2O); 63.89 (*s*, Me*C*H_2O); 70.50 (*d*, ^2J(C,P) = 2.3, C(C4) of hydantoin); 129.06 (2 arom. C); 129.13 (2 arom. C); 129.63 (arom. C); 129.77 (2 arom. C); 133.90, 134.46, 146.50, 146.67 (4 C_{ipso}); 147.53 (*s*, NCON); 161.66 (*d*, ^2J(C,P) = 2.6, CO_2Et); 161.91 (*s*, NCO); 165.12 (*d*, ^3J(C,P) = 6.5, CO_2Et). ^{31}P-NMR: 16.78 (*s*, $PO(OMe)_2$).

NMR Data of Minor Isomer **4′f**. ^{1}H-NMR: 1.10 (*t*, ^3J(H,H) = 7.0, *Me*CH_2O); 1.33 (*t*, ^3J(H,H) = 7.0, *Me*CH_2O); 2.40 (*s*, 2 Me); 3.35 (*d*, ^3J(H,P) = 11.3, MeO); 3.70 (*d*, ^3J(H,P) = 11.3, MeO); 4.11–4.20 (*m*, 2 MeCH_2O); 4.56 (*d*, ^2J(H,P) = 22.3, CH); 7.31–8.01 (*m*, 8 arom. H). ^{31}P-NMR: 17.74 (*s*, $PO(OMe)_2$).

Ethyl 4-[1-(Diethoxyphosphoryl)-2-ethoxy-2-oxoethyl]-1,3-bis[(4-methylphenyl)sulfonyl]-2,5-dioxoimidazolidine-4-carboxylate (**4g**/**4′g**). Yield: 700 mg (99%). Colorless powder. M.p. 129–130°. IR (KBr): 1808 (hydantoin C=O); 1758 (ester, C=O); 1586, 1437 (Ph); 1376 (P=O); 1398, 1134 (SO_2); 1286, 1230, 1188 (ester C–O); 1082 (P–OEt). EI-MS: 703 (2, $[M+1]^+$), 702 (5, M^+), 565 (2), 534 (2), 506 (4), 475 (3), 334 (13), 155 (47), 108 (20), 91 (100), 65 (20). Anal. calc. for $C_{28}H_{35}N_2O_{13}PS_2$ (702.68): C 47.86, H 5.02, N 3.99; found: C 48.0, H 5.0, N 4.0.

NMR Data of Major Isomer **4g**. ^{1}H-NMR: 1.05 (*t*, ^3J(H,H) = 7.1, *Me*CH_2O); 1.14 (*t*, ^3J(H,H) = 7.1, *Me*CH_2O); 1.24 (*t*, ^3J(H,H) = 7.0, *Me*CH_2O); 1.36 (*t*, ^3J(H,H) = 7.0, *Me*CH_2O); 2.43 (*s*, 2 Me); 3.95–3.99 (*m*, Me*C*H_2O); 4.02–4.08 (*m*, Me*C*H_2O); 4.11–4.16 (*m*, Me*C*H_2O); 4.16–4.27 (*m*, Me*C*H_2O); 4.91 (*d*, ^2J(H,P) = 26.4, CH); 7.30–7.35 (4 arom. H); 7.87 (*d*, ^3J(H,H) = 8.2, 2 arom. H); 7.99 (*d*, ^3J(H,H) = 7.7, 2 arom. H). ^{13}C-NMR: 13.40 (*Me*CH_2O); 13.66 (*Me*CH_2O); 16.11 (*d*, ^3J(C,P) = 6.2, *Me*CH_2O); 16.16 (*d*, ^3J(C,P) = 6.2, *Me*CH_2O); 21.73 (*s*, Me); 21.75 (*s*, Me); 49.09 (*d*, ^1J(C,P) = 125.9,

CH); 62.49 (*s*, Me*C*H$_2$O); 63.12 (*d*, ^2J(C,P) = 6.0, Me*C*H$_2$O); 63.79 (*s*, Me*C*H$_2$O); 63.99 (*d*, ^2J(C,P) = 6.2, Me*C*H$_2$O); 70.54 (*d*, ^2J(C,P) = 2.3, C(4) of hydantoin); 129.04 (2 arom. C); 129.09 (2 arom. C); 129.61 (2 arom. C); 129.72 (2 arom. C); 133.95, 134.52, 146.45, 146.59 (4 C_{ipso}); 147.54 (*s*, NCON); 161.55 (*d*, ^2J(C,P) = 2.8, *C*O$_2$Et); 161.94 (*s*, NCO); 165.32 (*d*, ^3J(C,P) = 6.8, *C*O$_2$Et). ^{31}P-NMR: 13.74 (*s*, PO(OEt)$_2$).

NMR Data of Minor Isomer **4′g**. ^{1}H-NMR: 1.00 (*t*, ^3J(H,H) = 7.1, *Me*CH$_2$O); 1.02 (*t*, ^3J(H,H) = 7.2, *Me*CH$_2$O); 1.28 (*t*, ^3J(H,H) = 7.1, MeC*H*$_2$O); 1.32 (*t*, ^3J(H,H) = 7.1, MeC*H*$_2$O); 2.42 (*s*, 2 Me); 3.71–3.76 (*m*, MeC*H*$_2$O); 3.77–3.83 (*m*, MeC*H*$_2$O); 4.11–4.16 (*m*, MeC*H*$_2$O); 4.16–4.27 (*m*, MeC*H*$_2$O); 4.52 (*d*, ^2J(H,P) = 22.3, CH); 7.29–7.99 (8 arom. H). ^{13}C-NMR: 13.28 (*Me*CH$_2$O); 13.87 (*Me*CH$_2$O); 15.63 (*d*, ^3J(C,P) = 6.0, *Me*CH$_2$O); 15.72 (*d*, ^3J(C,P) = 6.1, *Me*CH$_2$O); 21.71 (Me); 21.74 (Me); 48.21 (*d*, ^1J(C,P) = 131.1, CH); 62.17 (Me*C*H$_2$O); 62.53 (Me*C*H$_2$O); 63.57 (*d*, ^2J(C,P) = 6.1, Me*C*H$_2$O); 64.65 (*d*, ^2J(C,P) = 6.0, Me*C*H$_2$O); 69.04 (*d*, ^2J(C,P) = 2.0, C(4) of hydantoin); 129.04 (2 arom. C); 129.55 (2 arom. C); 129.57 (2 arom. C); 129.77 (2 arom. C); 134.04, 134.44, 146.36, 146.71 (4 C_{ipso}); 147.22 (*s*, NCON); 160.45 (*d*, ^2J(C,P) = 4.9, *C*O$_2$Et); 162.79 (*d*, ^3J(C,P) = 17.4, NCO); 164.18 (*d*, ^3J(C,P) = 4.9, *C*O$_2$Et). ^{31}P-NMR: 15.42 (*s*, PO(OEt)$_2$).

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