Pergamon

Tetrahedron Letters 40 (1999) 7985–7986

TETRAHEDRON
LETTERS

Dramatic solvent effect in the multicomponent reaction of nitro compounds with isocyanides

Paul Dumestre and Laurent El Kaim *

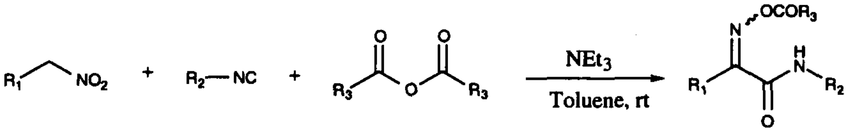
Laboratoire Réacteurs et Processus, Ecole Nationale Supérieure de Techniques avancées, 32 Bd Victor, 75015 Paris, France

Received 2 August 1999; accepted 31 August 1999

Abstract

Nitro compounds, triethylamine, acetic anhydride and isocyanides react together in toluene giving α-oximinoamides in low to moderate yields. Much faster and higher yielding reactions are obtained when DMSO is chosen as solvent. © 1999 Published by Elsevier Science Ltd. All rights reserved.

We recently published a new preparation of α-oximinoamides by a multicomponent reaction between nitro derivatives and isocyanides.[1] Using this very simple experimental procedure, ready access to complex biologically active structures was possible (Scheme 1).



Scheme 1.

However, the first results obtained on this reaction were rather disappointing as moderate to good yields were only obtained with *t*-butylisocyanide and rather acidic nitro derivatives (allylic compounds). Moreover, the reaction requires a very long time for completion, diminishing its synthetic interest even more. In an effort to improve the scope of this reaction, we examined the effect of base strength and solvent. If DBU in toluene significantly improved the result obtained with acetic anhydride, nitropropane and *t*-butylisocyanide,[1] other isocyanides and nitro derivatives tested gave much lower yields. The results obtained in a polar solvent were more convincing as DMSO significantly improved both yield and reaction time for aliphatic and allylic nitro derivatives. The results are collected in Table 1; in such a polar solvent, triethylamine is sufficiently basic to be used efficiently for aliphatic and allyllic nitro derivatives. DBU did not increase the yields and even gave on several occasions a fast reaction difficult to control.

---

* Corresponding author. Fax: 1 45 52 83 22; e-mail: elkaim@ensta.fr

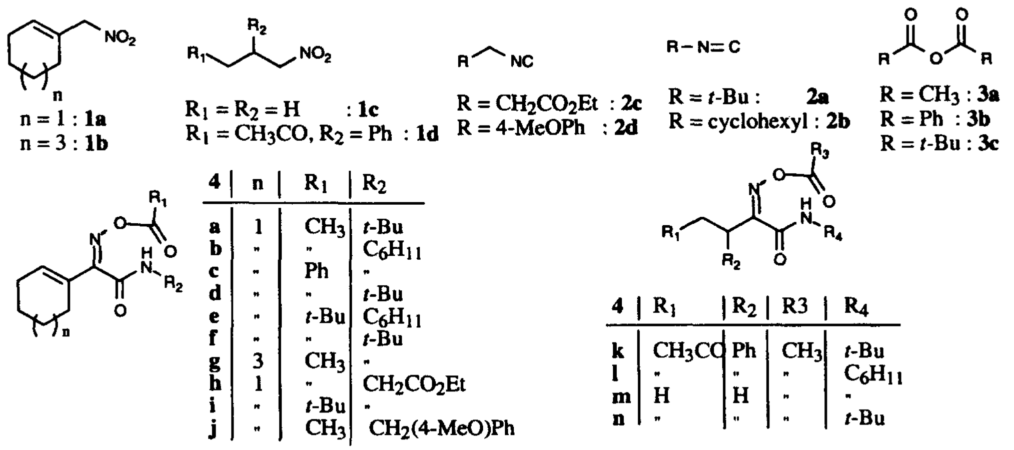
PII: S0040-4039(99)01669-X

Table 1
Nitro/isocyanide multicomponent reaction in DMSO

Nitro compound 1	Isocyanide 2	Anhydride 3	Product** 4	Time h	Yield %
a	**a**	**a**	**a**	3 (12 *)	70 (63 *)
"	**b**	"	**b**	1	52
"	"	**b**	**c**	4	55
"	**a**	"	**d**	3	68
"	**b**	**c**	**e**	20	51
"	**a**	"	**f**	5 (48 *)	53 (28 *)
b	"	**a**	**g**	2 (2 *)	68 (63 *)
a	**c**	"	**h**	20 (48 *)	38 (30 *)
"	"	**c**	**i**	20	30
"	**d**	**a**	**j**	24 (24 *)	58 (51 *)
d	**a**	"	**k**	4 (120 *)	35 (34 *)
"	**b**	"	**l**	20	26
c	"	"	**m**	20	54
"	**a**	"	**n**	36 (200 *)	68 (20 *)

* : Reaction performed in toluene

**: A typical experimental procedure is as follows: to a solution of nitro compound (2 mmol) in dry DMSO (2 ml) were added triethylamine (2.2 mmol), isocyanide (3 mmol) and acetic anhydride (2.2 mmol). The mixture was stirred at room temperature under an inert atmosphere until completion, followed by water addition and extraction.



n = 1 : **1a**
n = 3 : **1b**

$R_1 = R_2 = H$: **1c**
$R_1 = CH_3CO$, $R_2 = Ph$: **1d**

$R = CH_2CO_2Et$: **2c**
R = 4-MeOPh : **2d**

R = *t*-Bu : **2a**
R = cyclohexyl : **2b**

$R = CH_3$: **3a**
R = Ph : **3b**
R = *t*-Bu : **3c**

4	n	R_1	R_2
a	1	CH_3	*t*-Bu
b	"	"	C_6H_{11}
c	"	Ph	"
d	"	"	*t*-Bu
e	"	*t*-Bu	C_6H_{11}
f	"	"	*t*-Bu
g	3	CH_3	"
h	1	"	CH_2CO_2Et
i	"	*t*-Bu	"
j	"	CH_3	CH_2(4-MeO)Ph

4	R_1	R_2	R3	R_4
k	CH_3CO	Ph	CH_3	*t*-Bu
l	"	"	"	C_6H_{11}
m	H	H	"	"
n	"	"	"	*t*-Bu

Structures for Table 1

As shown in Table 1, these new conditions may be applied successfully to various anhydride derivatives (**3a**, **3b**, **3c**). The results observed with pivalic acid anhydride demonstrate here again the interest of DMSO over toluene: the highly encumbered oxime is obtained with a poor 25% yield after two days in toluene, whereas in DMSO, a 53% yield is obtained after 5 h.

Further work is in progress to study the stereochemical features of this reaction and apply it to more complex nitro and isocyanide derivatives.

References

1. Dumestre, P.; El Kaim, L.; Gacon, A. *Chem. Commun.* **1999**, 775–776.