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N-Vinylation of lactams with calcium carbide water system

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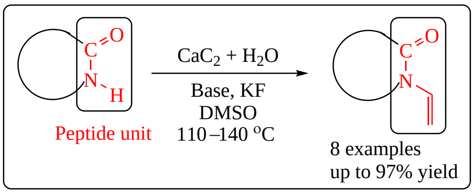
Direct *N*-vinylation of lactams with calcium carbide water system was performed under super-basic conditions. The vinylation occurred exclusively at NH group leaving C=O function intact to afford cyclic *N*-vinyl amides in yields up to 97%. The obtained products are prospective monomers for the preparation of synthetic peptides.



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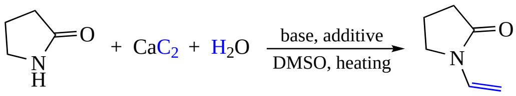
N-Vinyl carboxamides can be considered as promising monomers for synthetic peptides due to the presence of polymerizable $–N(CH=CH_2)–C(O)–$ unit. Apparently, they can be further polymerized according to standard (free radical or cationic) polymerization techniques. After polymerization, the structure of thus resulted poly(vinyl amides) looks somewhat similar to peptides and even to polynucleotides. Recently, vinyl purines were used for insertion into DNA chain,[1–4] for prevention of formation of gas hydrates in oil industry,[5] in pharmaceutical industry and cosmetics.[6] The scope of vinyl amide-based polymers is very wide.[7–11] Vinyl derivatives are generally obtained through metal-catalyzed substitution, free radical vinyl exchange or addition elimination reactions.[12–15] However, these methods require expensive catalysts and are accompanied by the formation of significant amounts of by-products. Nucleophilic addition to triple acetylene bond is an atom-economic scheme.[16–18] Direct *N*-vinylation of lactams with gaseous acetylene under elevated pressure was described earlier; however, it required Ru-based catalysts[19] or Bu^n_3P ligands.[20] Herein, we want to present metal free direct *N*-vinylation of lactams with calcium carbide as a source of acetylene. Calcium carbide is known for its efficient insertion into a series of SH, NH, OH compounds[21–27] and it found valuable applications in organic chemistry.[28–35]

The reaction of calcium carbide with water results in gaseous acetylene that can be immediately involved in a target reaction. A mixture of DMSO and an inorganic base was chosen as a reaction medium for nucleophilic addition to unsaturated bonds, that is a common medium for vinylation.[36–40] Initially, various bases and additives as well as reagent ratios were tested for optimization of the reaction conditions. 2-Pyrrolidone **1a** was chosen as a model compound for optimization (Scheme 1, Table 1) due to simple detection of product **2a** in the NMR spectra.[†]



1a **2a**

Scheme 1

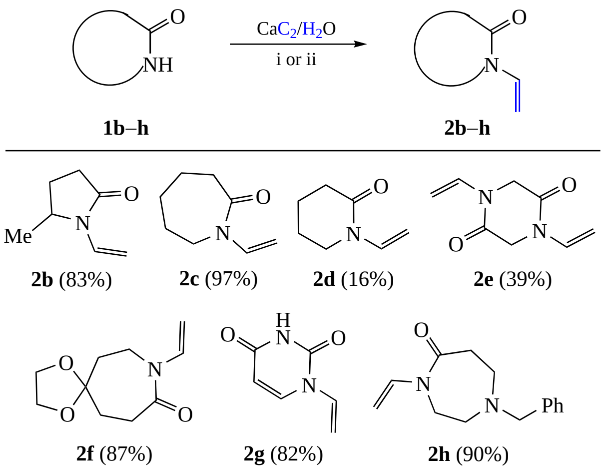
No product was observed in the presence of only KOH (Table 1, entry 1). Therefore, KF and CsF additives were applied since their use was successful in similar reactions with the very acetylene.[41–43] Only traces of the desired product **2a** were observed in the presence of KF (entry 2). The desired product was also not formed when the base/additive ratio was altered and CsF was used as an additive (entries 3–5). The same result was obtained, when Cs_2CO_3 was attempted as a base (entry 6). Interestingly, the reaction started in the presence of the additive only and in the absence of any base (entry 7); most probably, $Ca(OH)_2$ formed upon CaC_2 decomposition could act as the base. Then, the yield was increased using potassium carbonate as a base and KF as an additive (entries 8–10). Variation of the

Table 1 Optimization of vinylation of 2-pyrrolydone **1a** with CaC_2/H_2O system.

Entry	Base (mmol)	Additive (mmol)	CaC_2 (mmol)[a]	*T*/°C	*t*/h	Yield of **2a** (%)
1	KOH (1.1)	–	3	110	4	n.r.[b]
2	KOH (1.1)	KF (2.0)	3	110	4	traces
3	KOH (1.0)	KF (1.1)	3	110	4	n.r.[b]
4	KOH (1.1)	CsF (1.1)	3	110	4	n.r.[b]
5	–	CsF (1.1)	4	110	4	n.r.[b]
6	Cs_2CO_3 (0.5)	KF (1.1)	4	110	4	traces
7	–	KF (2.0)	3	110	4	45
8	K_2CO_3 (1.0)	KF (1.1)	4	110	4	61
9	K_2CO_3 (1.0)	KF (2.0)	3	110	4	92
10	K_2CO_3 (1.0)	KF (2.0)	3/4	100	4	43/64

[a] Stoichiometric amount (6 mmol) of water was applied in each case. [b] No reaction.

[†] *Synthesis of vinyl amides.* A lactam (1 mmol), K_2CO_3 or Cs_2CO_3 (1 mmol), KF (116 mg, 2 mmol), CaC_2 (192 mg, 3 mmol) and DMSO (3 ml) were placed in a tube with a screw cap. Then, water (110 μl, 6 mmol) was added and the tube was immediately capped. The mixture was heated at 110–140 °C for 4 h. The mixture was then cooled to room temperature, filtered and extracted with diethyl ether and methyl *tert*-butyl ether. The organic layer was washed with water and brine, dried over Na_2SO_4, and the residue was subjected to chromatography. In case of uracil **1g**, the reaction mixture was not extracted and was directly chromatographed on silica gel.



Scheme 2 *Reagents and conditions*: i, lactam **1b**–**d**,**f**,**h** (1 mmol), K_2CO_3 (1 mmol), KF (2 mmol), CaC_2 (3 mmol), H_2O (110 μl, 6 mmol), DMSO (3 ml), 110–120 °C; ii, lactam **1e**,**g**, the reagent ratio is the same but with Cs_2CO_3 and at 140 °C.

base/additive ratio and temperature allowed us to obtain the target product **2a** in 92% yield (entry 9).

The optimized conditions were further used to obtain other *N*-vinyl lactams **2b**–**h** (Scheme 2). 5-Methylpyrrolidone smoothly reacted with calcium carbide giving **2b** in 83% yield. Azepane-based compounds **1c**,**f**,**h** and 2-piperidone **1d** were converted into the corresponding vinyl products at higher temperature (120 °C). Cesium carbonate was required for successful vinylation of piperazine-2,5-dione **1e**. The vinylation of uracil required heating to 140 °C resulting in **2g** in 82% yield. The stronger base and higher temperature were required for vinylation of lactams **1e** and **1g** due to the presence of two C=O functions and lower nucleophilicity.

In conclusion, a series of lactams was vinylated using calcium carbide water system as a source of acetylene to produce the corresponding *N*-vinyl derivatives in moderate to good yields. In this procedure calcium carbide seems to be an expedient substitute for gaseous acetylene. Since the vinylation of lactams resulted in polymerizable monomers with C(O)–N– unit, the procedure developed can be considered as a step towards synthetic peptides. The polymerization of vinylated lactams is under progress.

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Online Supplementary Materials

Supplementary data associated with this article can be found in the online version at doi: 10.1016/j.mencom.2024.09.034.

References

1 E. Colacino, G. De Luca, A. Liguori, A. Napoli, C. Siciliano and G. Sindona, *Nucleosides, Nucleotides Nucleic Acids*, 2003, **22**, 743.
2 M. Kubota, S. Nainar, S. M. Parker, W. England, F. Furche and R. C. Spitale, *ACS Chem. Biol*., 2019, **14**, 1698.
3 M. Gupta, S. R. Levine and R. C. Spitale, *Acc. Chem. Res*., 2022, **55**, 2647.
4 R. Dalpozzo, A. D. Nino, L. Maiuolo, A. Procopio, R. Romeo and G. Sindona, *Synthesis*, 2002, 172.
5 R. Kawatani, M. A. Kelland and H. Ajiro, *J. Appl. Polym. Sci*., 2020, **137**, 49154.
6 N. A. Cortez-Lemus and A. Licea-Claverie, *Prog. Polym. Sci*., 2016, **53**, 1.
7 W. Fan and S. Yamago, *Angew. Chem., Int. Ed.*, 2019, **58**, 7113.
8 R. Kawatani, T. Hamawaki, T. Waku, N. Tanaka and H. Ajiro, *Macromol. Chem. Phys*., 2023, **224**, 2200386.
9 E. F. Panarin, *Russ. Chem. Bull*., 2015, **64**, 15.
10 A. K. Teotia, H. Sami and A. Kumar, in *Switchable and Responsive Surfaces and Materials for Biomedical Applications*, ed. Z. Zhang, Woodhead Publishing, Oxford, 2015, pp. 3–43.
11 S. V. Kurmaz and A. N. Pyryaev, *Mendeleev Commun*., 2010, **20**, 52.
12 K. Mondal, S. Patra, P. Halder, N. Mukhopadhyay and P. Das, *Org. Lett*., 2023, **25**, 1235.
13 M. Bosch and M. Schlaf, *J. Org. Chem*., 2003, **68**, 5225.
14 B. Spiegelberg, H. Jiao, R. Grauke, C. Kubis, A. Spannenberg, A. Brandt, A. Taden, H. Beck, S. Tin and J. G. de Vries, *Adv. Synth. Catal*., 2022, **364**, 1251.
15 D. Alavez-Rosas, M. Maldonado-Domínguez, O. González-Antonio, M. Romero-Ávila, J. Méndez-Stivalet and B. Flores-Pérez, *Chem. Heterocycl. Compd*., 2017, **53**, 526.
16 I. P. Beletskaya and V. P. Ananikov, *Chem. Rev*., 2022, **122**, 16110.
17 N. V. Semenova, E. Yu. Schmidt, I. A. Ushakov and B. A. Trofimov, *Mendeleev Commun*., 2023, **33**, 164.
18 A. A. Kurokhtina, E. V. Larina, N. A. Lagoda and A. F. Schmidt, *Mendeleev Commun*., 2024, **34**, 215.
19 E. Semina, P. Tuzina, F. Bienewald, A. S. K. Hashmi and T. Schaub, *Chem. Commun*., 2020, **56**, 5977.
20 N. A. Sitte, M. Menche, P. Tužina, F. Bienewald, A. Schäfer, P. Comba, F. Rominger, A. S. K. Hashmi and T. Schaub, *J. Org. Chem.*, 2021, **86**, 13041.
21 Z. Zhang, F. Wen, H. Liu and Z. Li, *ChemistrySelect*, 2022, **7**, e202201463.
22 Y. Wang, F. Wen and Z. Li, *Chem. – Asian J.*, 2022, **17**, e202200698.
23 H. Liu, X. You, F. Wen, Z. Zhang and Z. Li, *Asian J. Org. Chem*., 2022, **11**, e202200204.
24 T. Jing, N. Liu, C. Xu and Q. Bu, *Eur. J. Org. Chem*., 2022, e202200178.
25 K. A. Lotsman, K. S. Rodygin, I. Skvortsova, A. M. Kutskaya, M. E. Minyaev and V. P. Ananikov, *Org. Chem. Front*., 2023, **10**, 1022.
26 Y. Gyrdymova, D. Samoylenko and K. Rodygin, *Chem.– Asian J*., 2023, **18**, e202201063.
27 S. A. Metlyaeva, K. S. Rodygin, K. A. Lotsman, D. E. Samoylenko and V. P. Ananikov, *Green Chem*., 2021, **23**, 2487.
28 H. Wang, W. Xu, M. Sharif, X. Wu, G. Cheng, X. Cui and Z. Zhang, *Appl. Energy*, 2022, **327**, 120139.
29 P.-W. Yang, X.-X. Liu, X.-Q. Li and M.-X. Wei, *Org. Chem. Front*., 2021, **8**, 2914.
30 X. Ma, Z. Wang, Z. Liu and Z. Li, *Chin. J. Chem*., 2021, **39**, 2990.
31 X. Ma and Z. Li, *Synlett*, 2021, **32**, 631.
32 K. A. Lotsman and K. S. Rodygin, *Green Chem*., 2023, **25**, 3524.
33 K. S. Rodygin, D. E. Samoylenko, M. M. Seitkalieva, K. A. Lotsman, S. A. Metlyaeva and V. P. Ananikov, *Green Chem*., 2022, **24**, 1132.
34 K. S. Rodygin, Y. V. Gyrdymova and V. P. Ananikov, *Russ. Chem. Rev*., 2022, **91**, RCR5048.
35 A. N. Lebedev, K. S. Rodygin, R. M. Mironenko, E. R. Saybulina and V. P. Ananikov, *J. Catal*., 2022, **407**, 281.
36 S. P. Teong, J. Lim and Y. Zhang, *ChemSusChem*, 2017, **10**, 3198.
37 B. A. Trofimov, L. A. Oparina, L. N. Parshina, M. Y. Khil'ko, A. P. Tantsyrev and G. P. Aleksandrova, *Cellulose*, 2013, **20**, 1201.
38 N. M. Vitkovskaya, V. B. Orel, V. B. Kobychev, A. S. Bobkov, D. Z. Absalyamov and B. A. Trofimov, *Int. J. Quantum Chem*., 2020, **120**, e26158.
39 I. A. Bidusenko, E. Y. Schmidt, N. I. Protsuk, I. A. Ushakov, A. V. Vashchenko, A. V. Afonin and B. A. Trofimov, *Org. Lett*., 2020, **22**, 2611.
40 D. Z. Absalyamov, N. M. Vitkovskaya, V. B. Orel, E. Y. Schmidt and B. A. Trofimov, *Asian J. Org. Chem*., 2023, **12**, e202300042.
41 G. Werner, K. S. Rodygin, A. A. Kostin, E. G. Gordeev, A. S. Kashin and V. P. Ananikov, *Green Chem*., 2017, **19**, 3032.
42 H. Liao and Z. Li, *Tetrahedron Lett*., 2023, **120**, 154445.
43 L. A. Oparina, M. Ya. Khil'ko, N. A. Chernyshova, S. I. Shaikhudinova, L. N. Parshina, Th. Preiss, J. Henkelmann and B. A. Trofimov, *Russ. J. Org. Chem*., 2005, **41**, 661.

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