Making rings from amino acids. Shining light on possible (chemo)evolution of proline

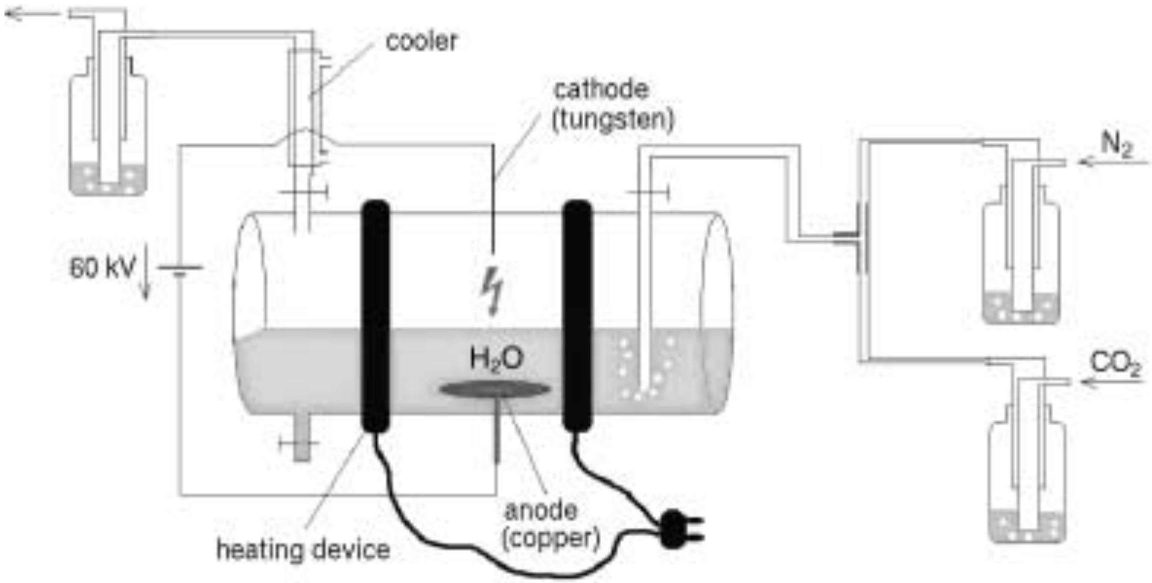
doc.dr.sc. Davor Šakić

University of Zagreb Faculty of Pharmacy and Biochemistry

Current chemical description of AA formation

- Neutral, mildly reducing, or slightly oxidising atmosphere
- Quite different from Miller's highly reducing prebiotic atmosphere
- Atmosphere 4 billion year ago - volcanic outgassing:
  - Hydrogen and helium leave the atmosphere
  - Ammonia and methane are unstable under UV-light
  - Predominant: H_2O, CO_2, N_2
  - Trace: CO, CH_4, H_2, SO_2, O_2 (decomposition of water, CO_2)
- Electrical discharge, temperature 60°C-90°C

Angew. Chem. Int. Ed. **2004**, 43, 1886



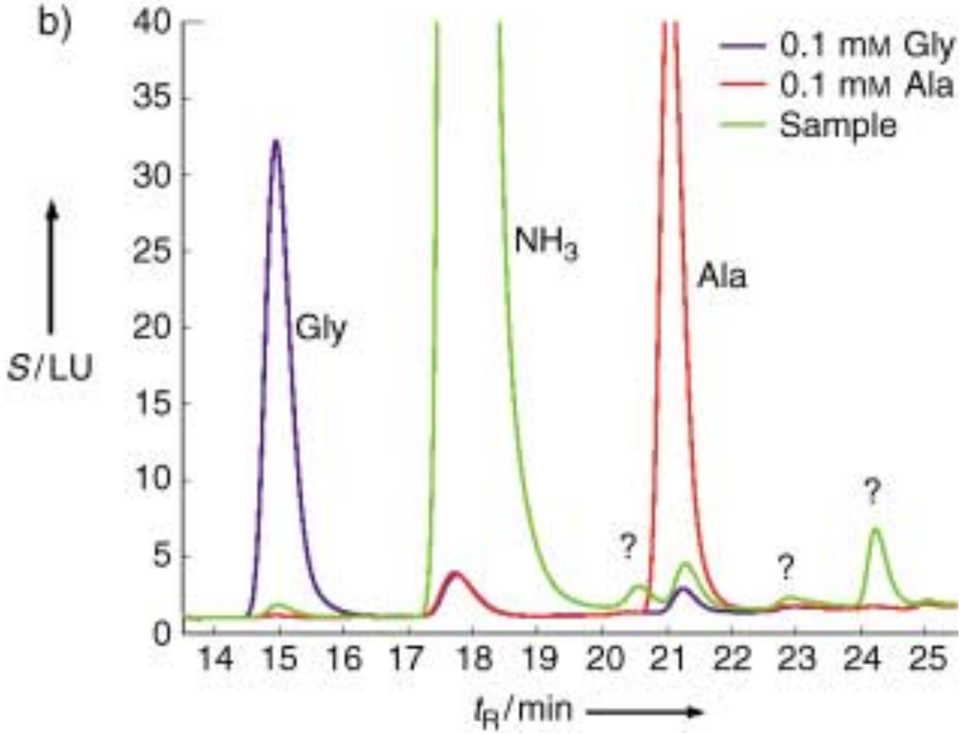
Angewandte Chemie International Edition
GDCh A Journal of the German Chemical Society

Communication

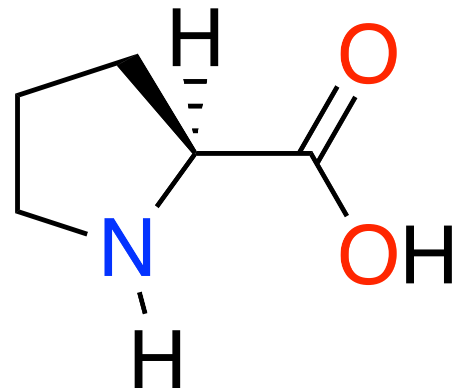
Prebiotic Formation of Amino Acids in a Neutral Atmosphere by Electric Discharge†

Kristof Plankensteiner, Hannes Reiner, Benjamin Schranz, Bernd Michael Rode Prof. Dr.

First published: 24 March 2004 | https://doi.org/10.1002/anie.200353135 | Citations: 55



Proline



The Simplest "Enzyme"

MOHAMMAD MOVASSAGHI AND ERIC N. JACOBSEN

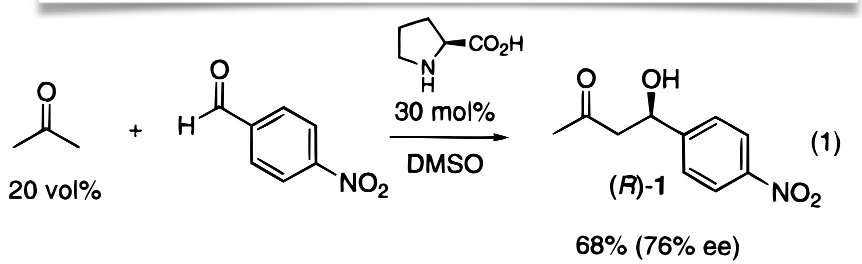
SCIENCE • 6 Dec 2002 • Vol 298, Issue 5600 • pp. 1904-1905 • DOI: 10.1126/science.1076547

- Only secondary proteinogenic amino acid
- Pyrrolidine ring is part of the backbone
- Exceptional conformational rigidity
- Hydrogen bond acceptor in peptides
- Good AA for tight turns
- Polyproline helix with hydroxyproline

J. Am. Chem. Soc. **2000,** *122,* 2395−2396

Proline-Catalyzed Direct Asymmetric Aldol Reactions

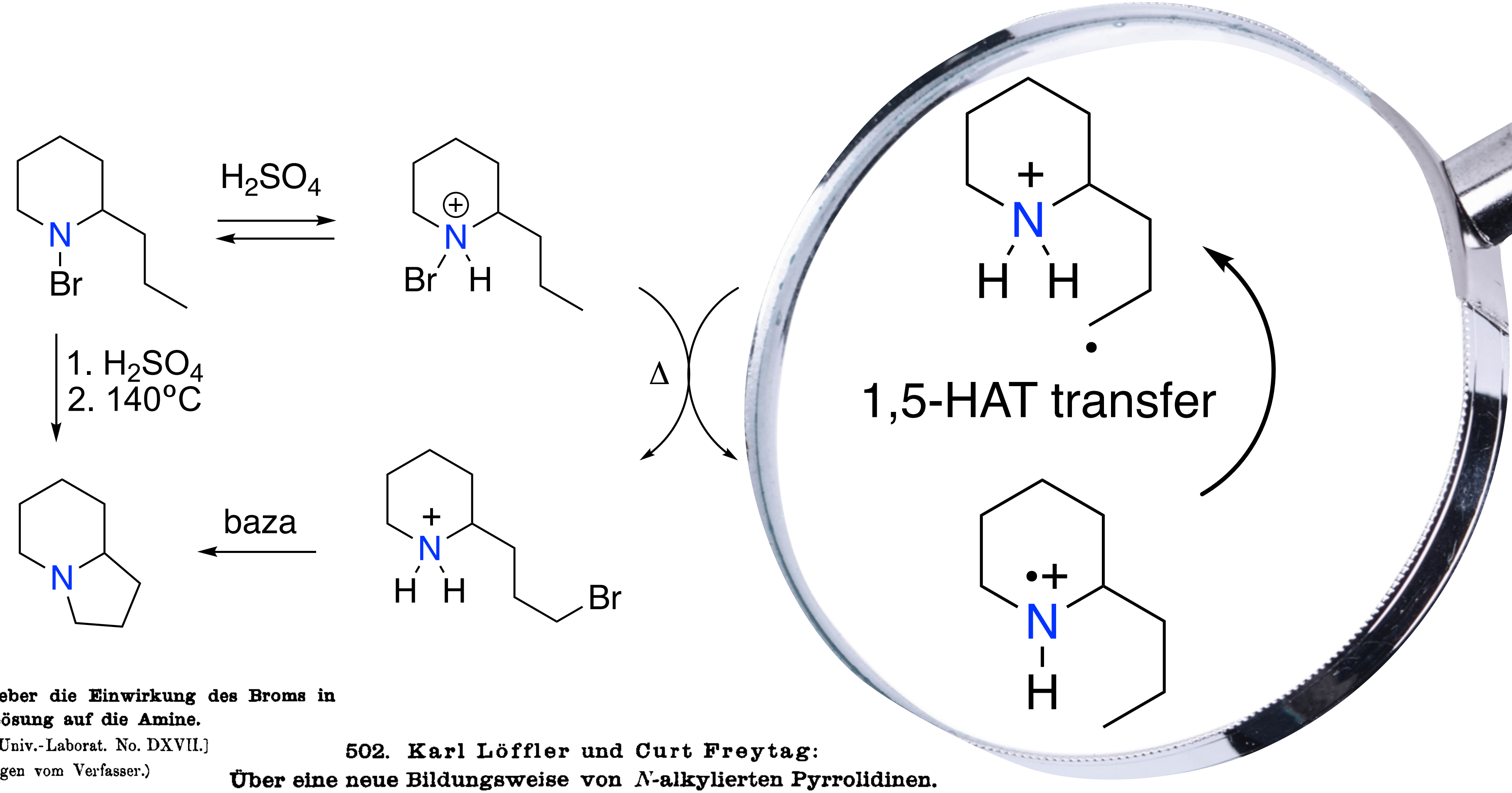
Benjamin List,* Richard A. Lerner, and Carlos F. Barbas III



How to make a pyrrolidine ring?

A possible mechanism

- Hofmann-Löffler-Freytag reaction



106. A. W. Hofmann: Ueber die Einwirkung des Broms in alkalischer Lösung auf die Amine.

[Aus dem Berl. Univ.-Laborat. No. DXVII.]

(Vorgetragen vom Verfasser.)

502. Karl Löffler und Curt Freytag: Über eine neue Bildungsweise von *N*-alkylierten Pyrrolidinen.

[Aus dem Chemischen Institut der Universität Breslau.]

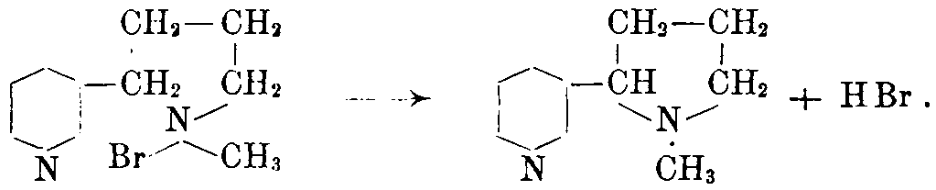
(Eingegangen am 12. August 1909.)

503. Karl Löffler und Samy Kober: Über die Bildung des *i*-Nicotins aus *N*-Methyl-β-pyridyl-butyl-amin (Dihydrometanicotin).

[Aus dem Chemischen Institut der Universität Breslau.]

(Eingegangen am 12. August 1909.)

In vorliegender Arbeit sollte die in der vorangehenden Arbeit mit Erfolg durchgeführte Reaktion zur Bildung von Pyrrolidinderivaten auf das Dihydrometanicotin angewendet werden, wobei man dann im Sinne folgender Gleichung Nicotin erwarten konnte:



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ACS Editors' Choice

OL Organic Letters

Letter

Cite This: *Org. Lett.* 2019, 21, 705–708

pubs.acs.org/OrgLett

Enantioselective Synthesis of Nicotine via an Iodine-Mediated Hofmann–Löffler Reaction

Estefanía Del Castillo[†] and Kilian Muñiz[*,†,‡]

Organic & Biomolecular Chemistry

ROYAL SOCIETY OF CHEMISTRY

PAPER

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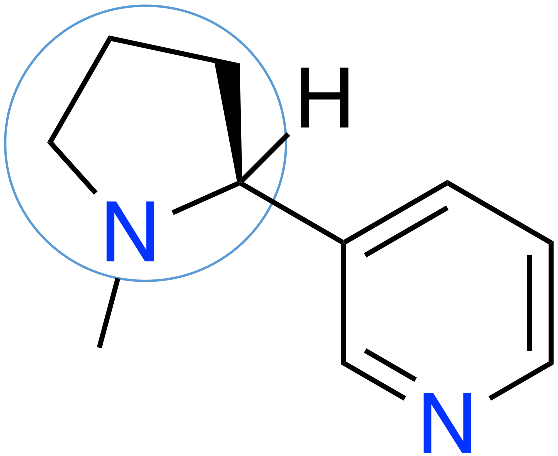
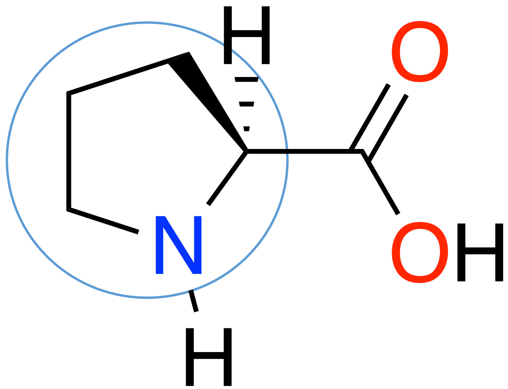
Cite this: DOI: 10.1039/d0ob02187c

Role of substituents in the Hofmann–Löffler–Freytag reaction. A quantum-chemical case study on nicotine synthesis†‡

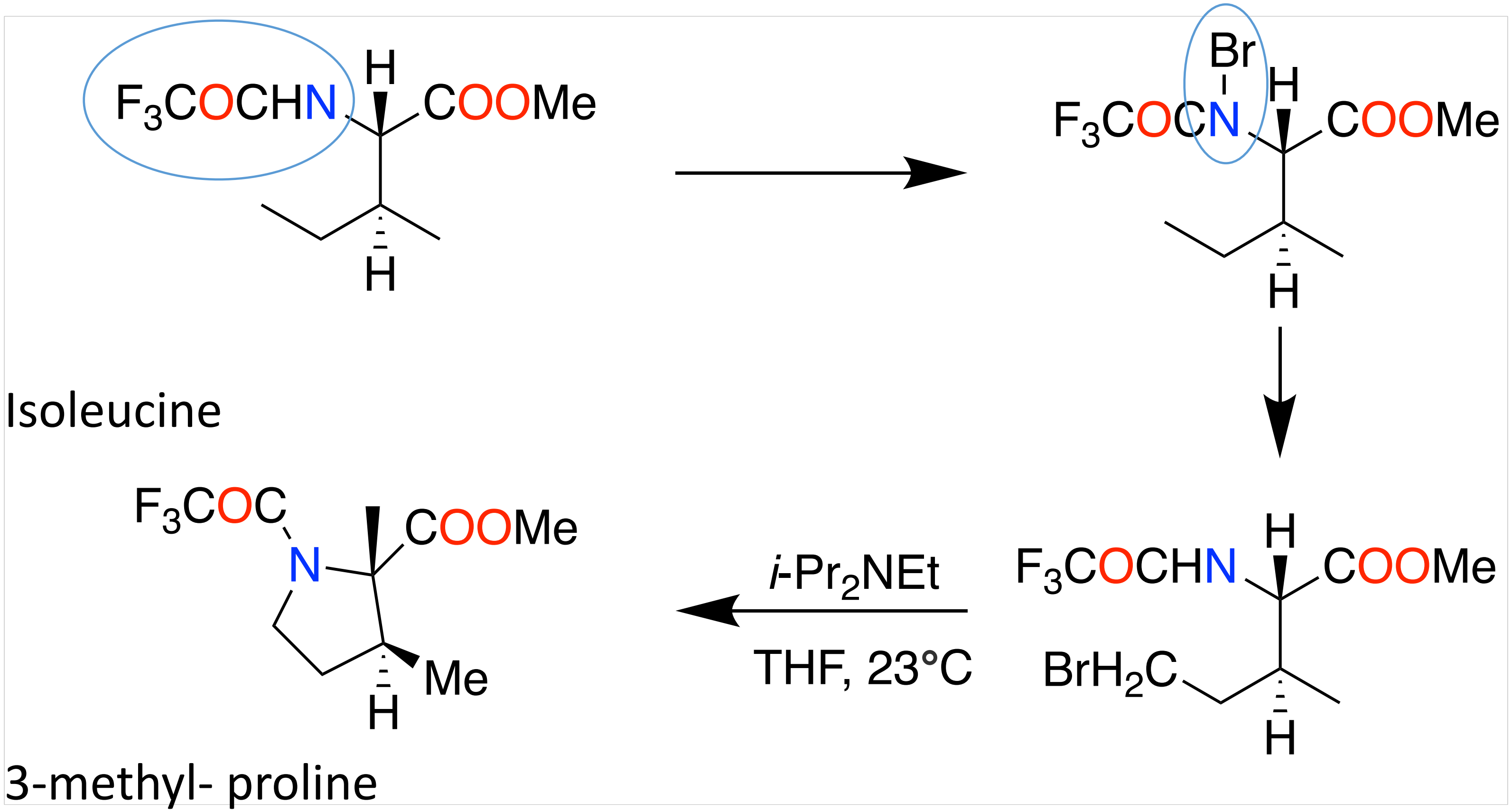
Sofia Shkunnikova,[a] Hendrik Zipse[b] and Davor Šakić[*a]



Nicotine



Proline

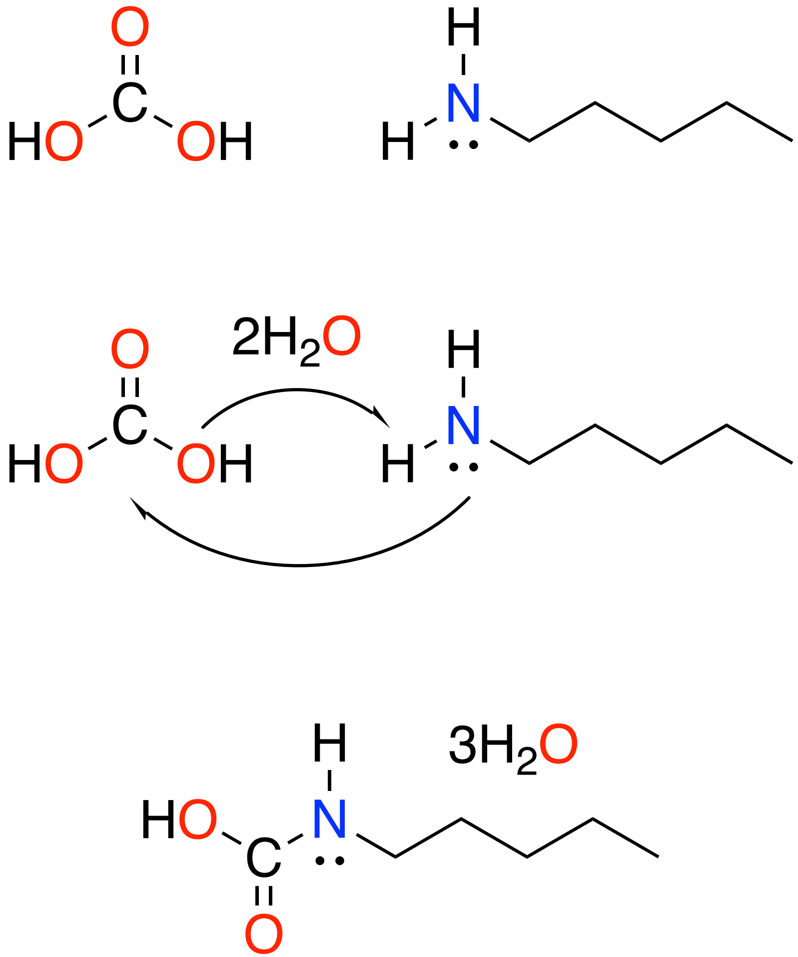


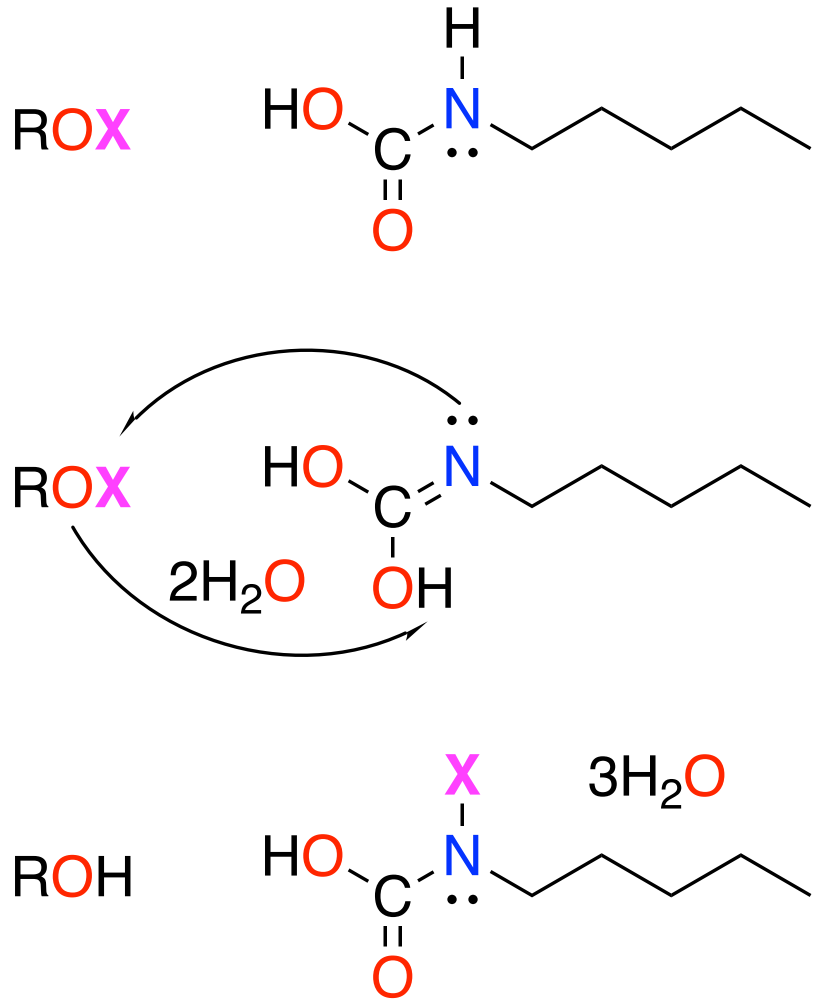
ORGANIC LETTERS
2006
Vol. 8, No. 13
2819–2821

Efficient Method for Selective Introduction of Substituents as C(5) of Isoleucine and Other α-Amino Acids

Leleti Rajender Reddy, B. V. Subba Reddy, and E. J. Corey*

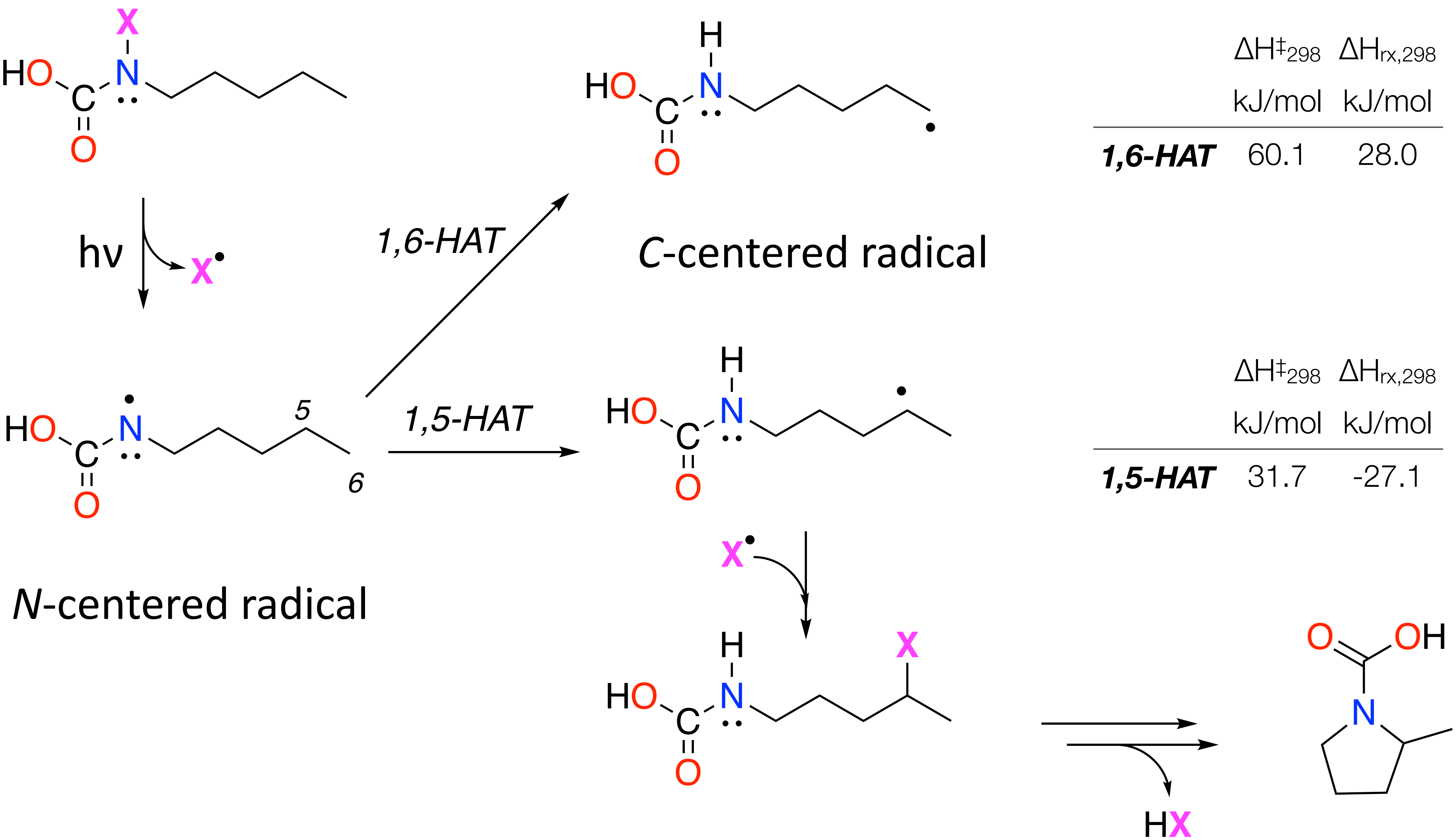
Activating amine





	$\Delta H^{\ddagger}_{298}$ kJ/mol	$\Delta H_{rx,298}$ kJ/mol
Hydroxamic acid formation	68.4	-77.7
Tautomerism & Halogenation	56.0	-11.4

Light
Molecules
Action



	$\Delta H^{\ddagger}_{298}$ kJ/mol	$\Delta H_{rx,298}$ kJ/mol
1,6-HAT	60.1	28.0

	$\Delta H^{\ddagger}_{298}$ kJ/mol	$\Delta H_{rx,298}$ kJ/mol
1,5-HAT	31.7	-27.1

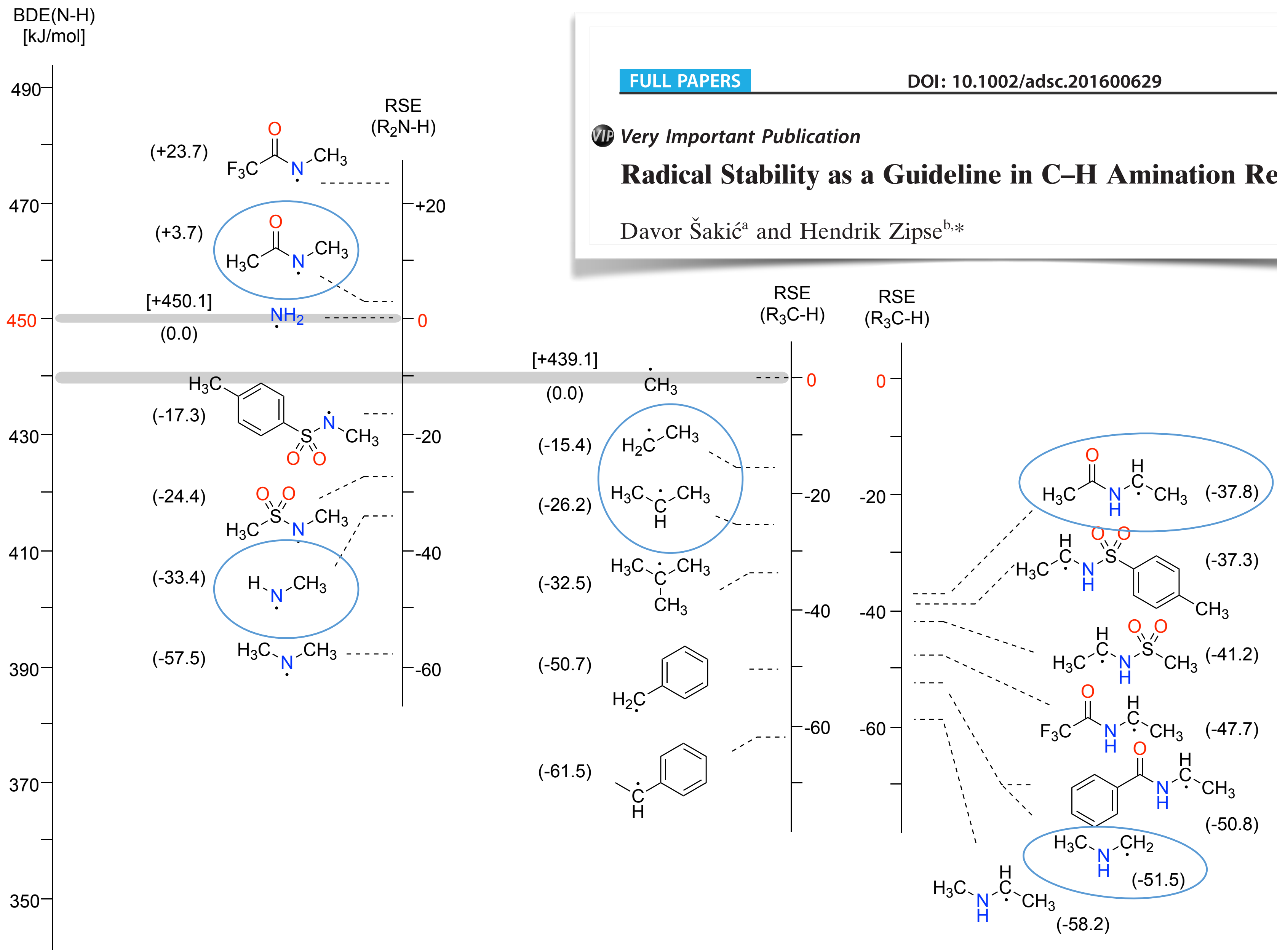
FULL PAPERS DOI: 10.1002/adsc.201600629

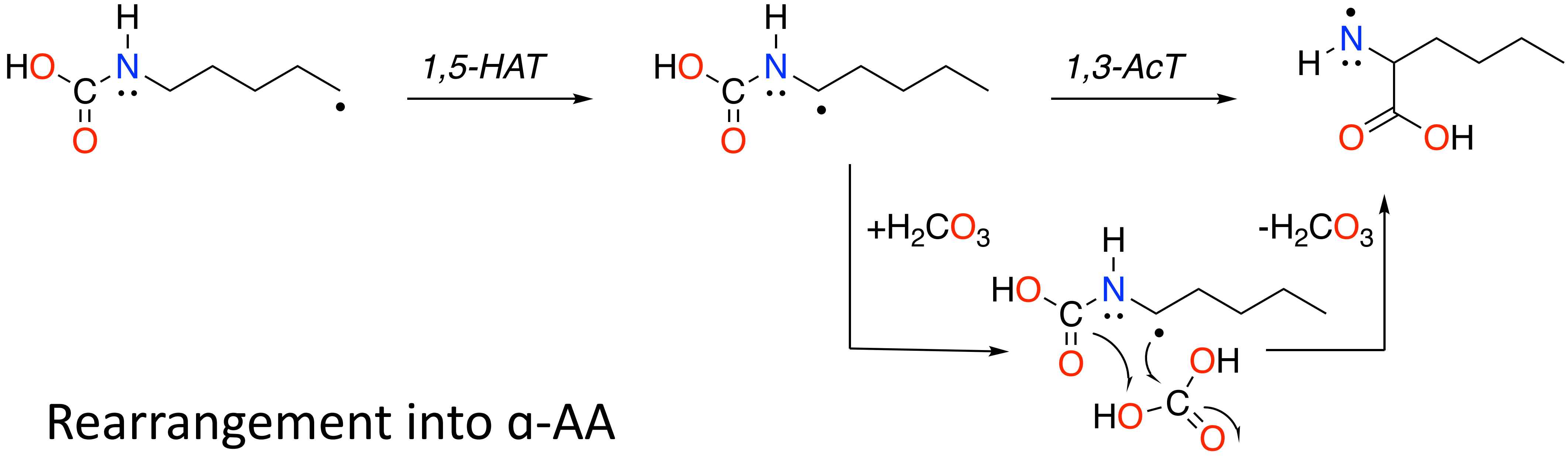
Advanced Synthesis & Catalysis

Very Important Publication

Radical Stability as a Guideline in C–H Amination Reactions

Davor Šakić[a] and Hendrik Zipse[b,*]



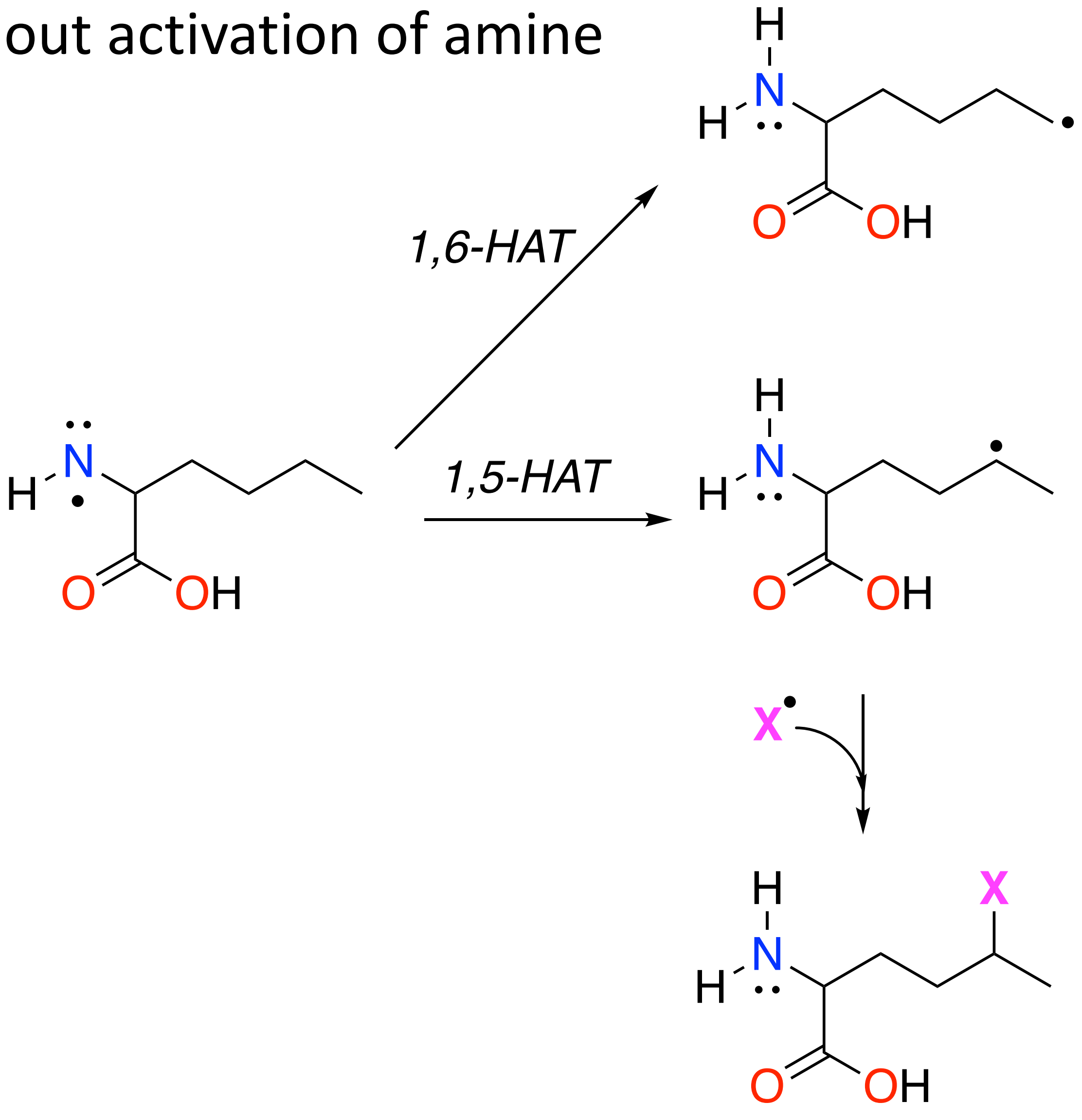


Rearrangement into α-AA

- Stabilisation of amino-acids
- Complexes
- Hydroxamic acid formation
- Transacetylation for peptide formation

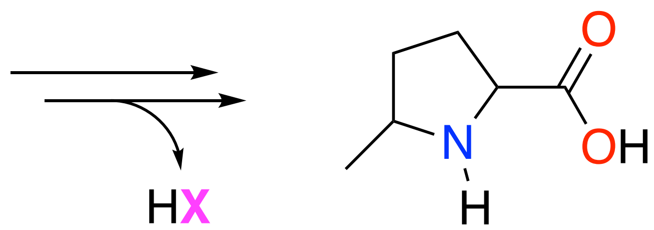
	$\Delta H^{\ddagger}_{298}$ kJ/mol	$\Delta H_{rx,298}$ kJ/mol
1,5-HAT	42.2	-39.1
1,3-AcT	146.1	18.6
1,3-AcT sup.	72.5	18.6

Without activation of amine

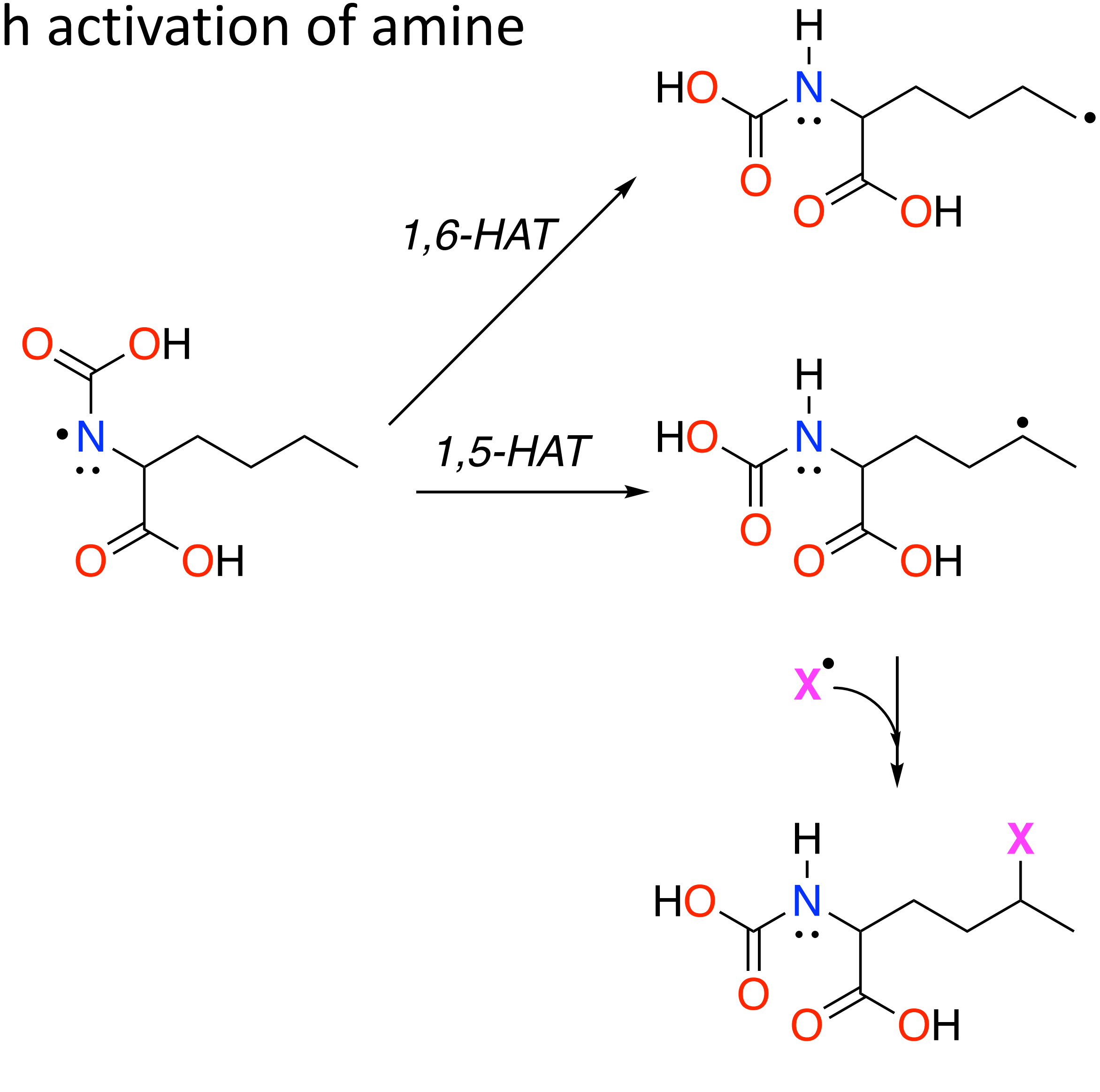


	$\Delta H^{\ddagger}_{298}$ kJ/mol	$\Delta H_{rx,298}$ kJ/mol
1,6-HAT	28.9	56.0

	$\Delta H^{\ddagger}_{298}$ kJ/mol	$\Delta H_{rx,298}$ kJ/mol
1,5-HAT	4.4	52.5

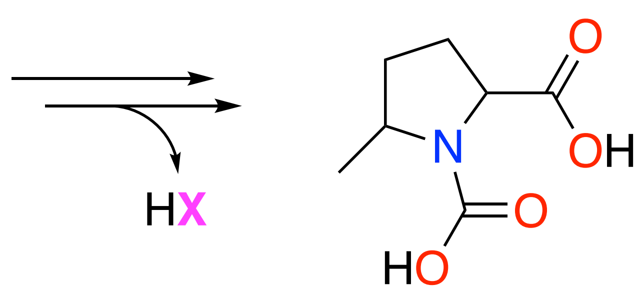


With activation of amine

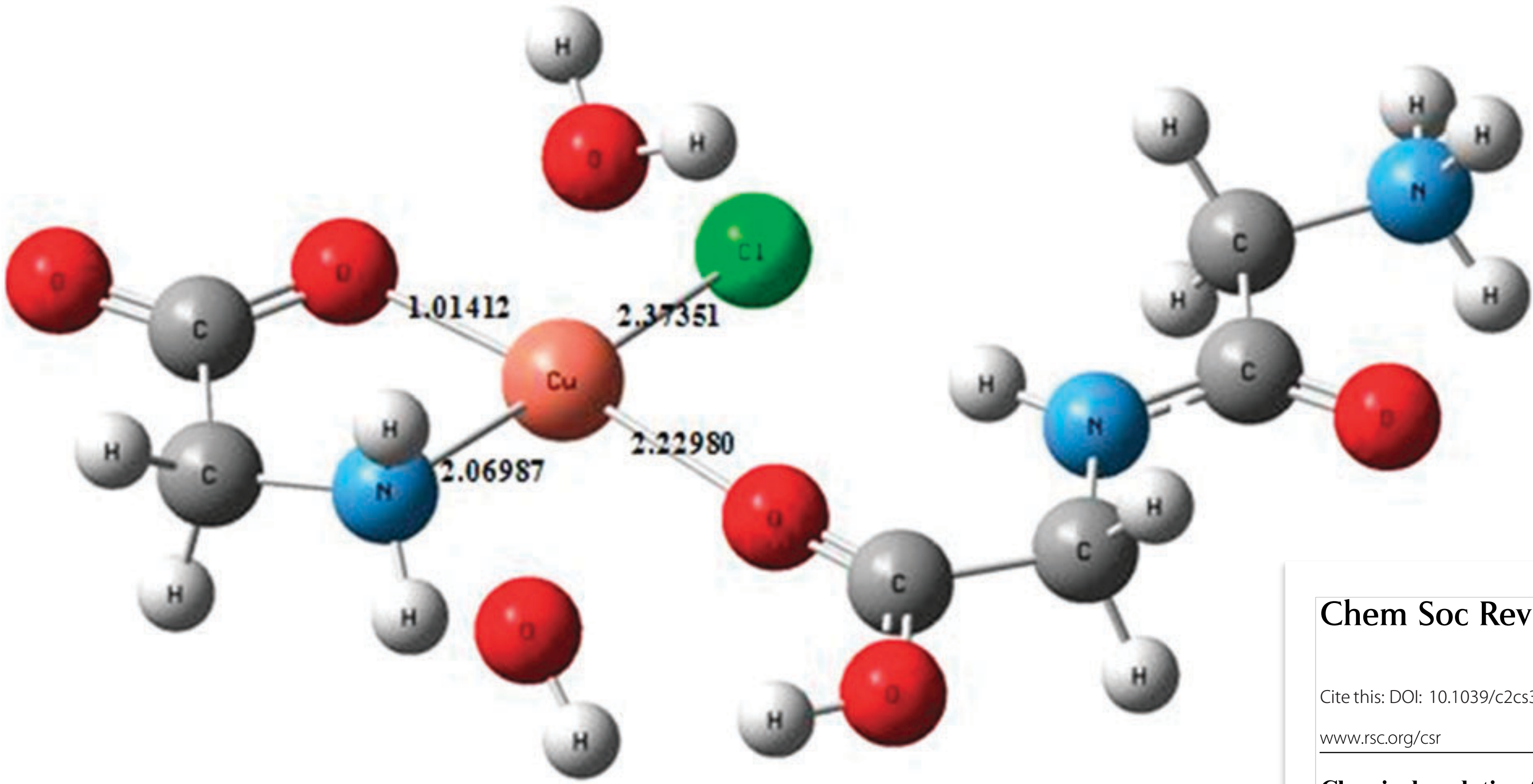


	$\Delta H^{‡}_{298}$ kJ/mol	$\Delta H_{rx,298}$ kJ/mol
1,6-HAT	27.1	-33.7

	$\Delta H^{‡}_{298}$ kJ/mol	$\Delta H_{rx,298}$ kJ/mol
1,5-HAT	21.5	-54.1



Salt induced peptide formation (SIPF)



Chem Soc Rev

Dynamic Article Links

Cite this: DOI: 10.1039/c2cs35073d

www.rsc.org/csr

TUTORIAL REVIEW

Chemical evolution from simple inorganic compounds to chiral peptides†

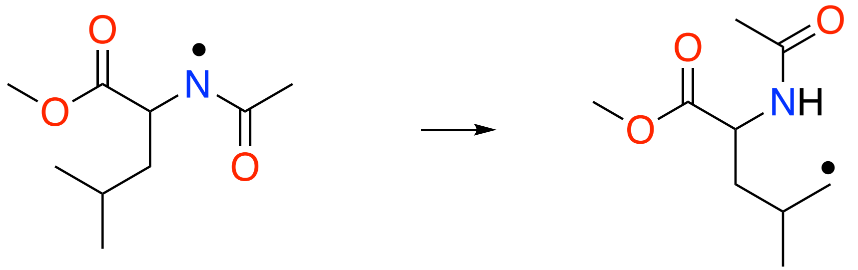
Thomas A. E. Jakschitz*[a] and Bernd M. Rode[b]

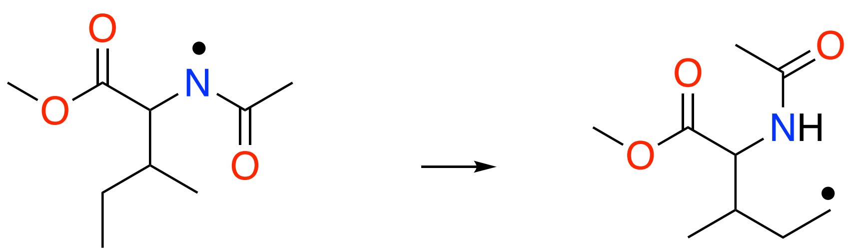
Received 12th March 2012
DOI: 10.1039/c2cs35073d

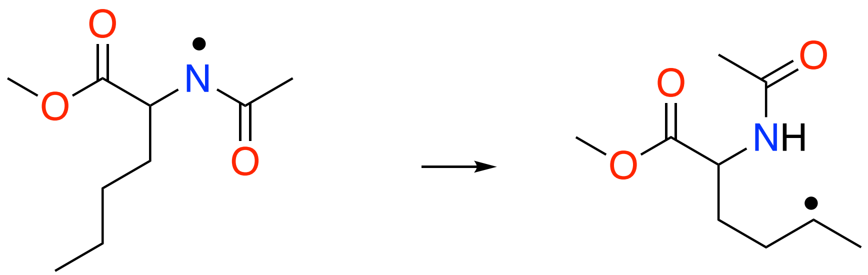
Relevance today

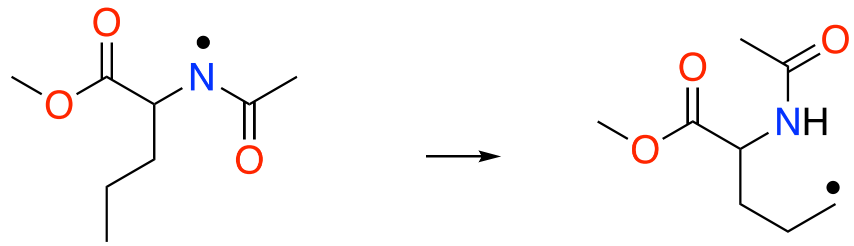
Oxidative damage leads to rings in backbone

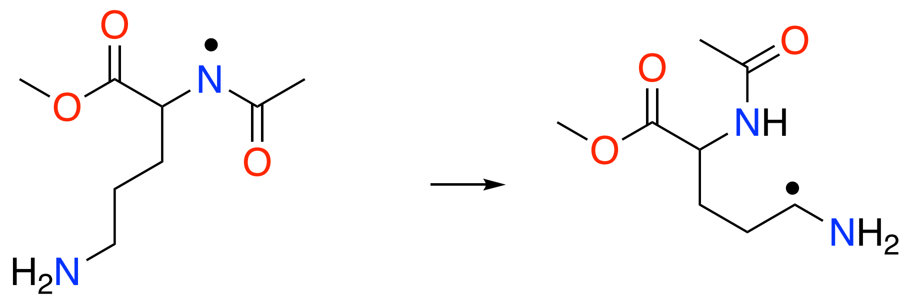
	$\Delta H^{\ddagger}$ kJ/mol	ΔH_{rx} kJ/mol
Leucine	31.3	-38.3
Isoleucine	23.4	-41.6
Norleucine	21.5	-54.1
Norvaline	36.1	-37.2
Lysine	22.3	-79.7

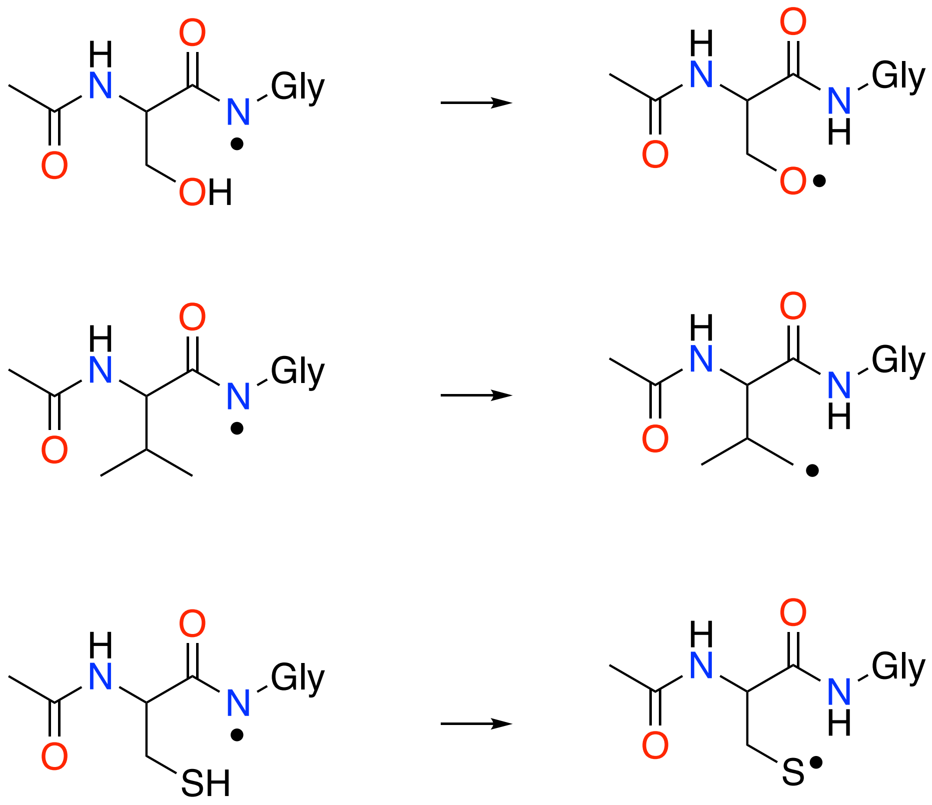


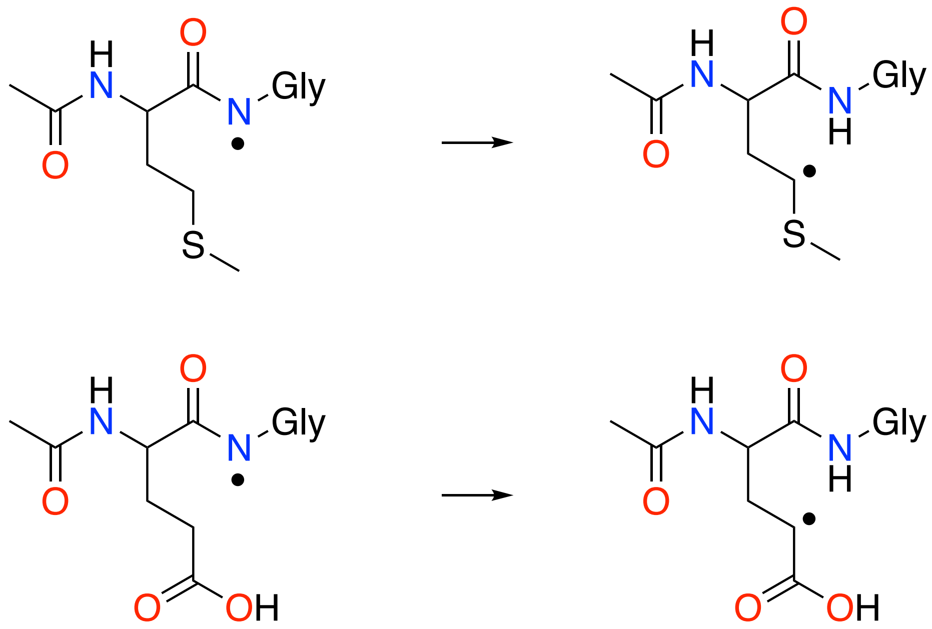






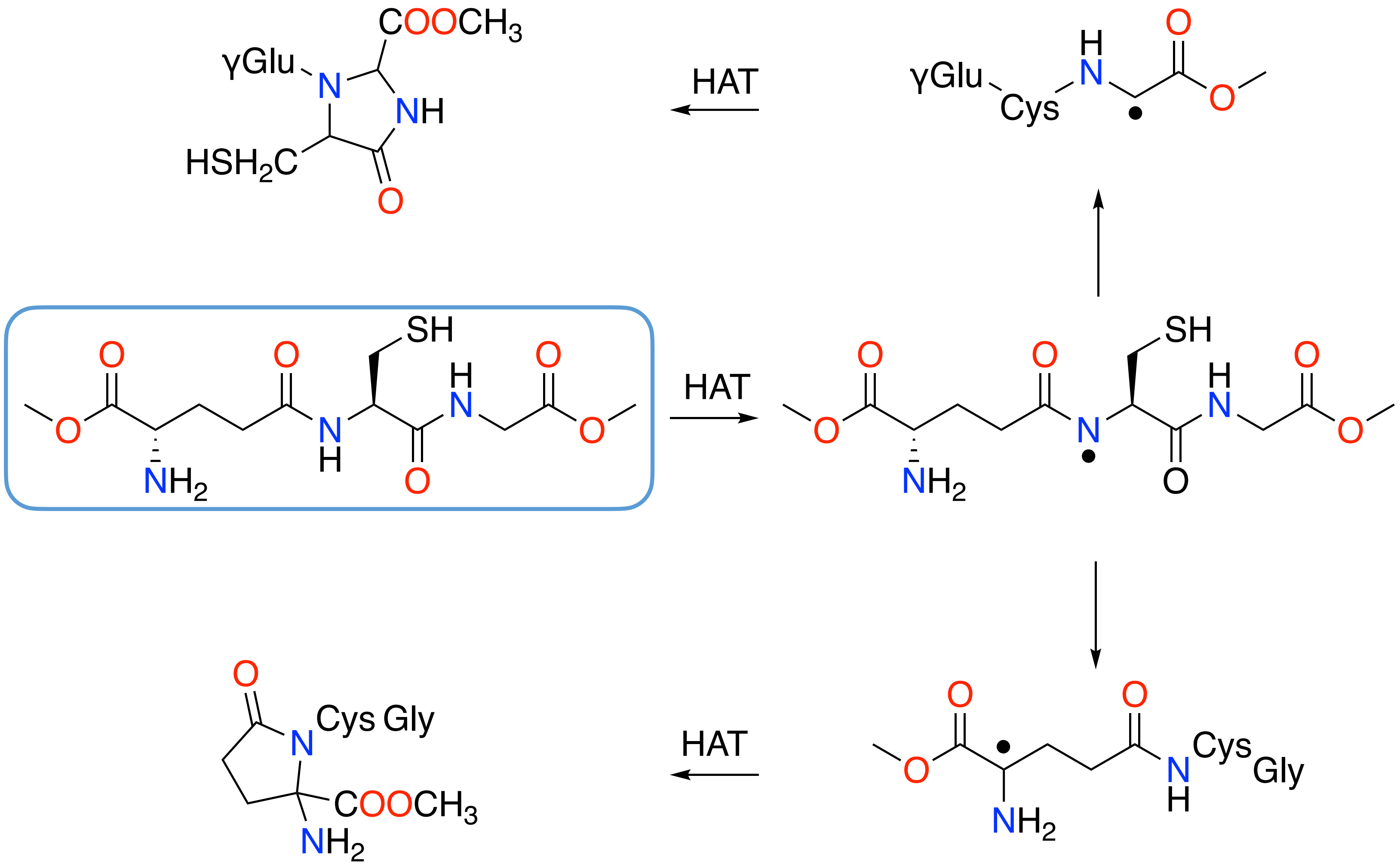






	$\Delta H^{\ddagger}$ kJ/mol	ΔH_{rx} kJ/mol
Valylglycine	33.7	-39.4
Serylglycine	31.7	-24.6
Cysteinylglycine	16.2	-95.3
Methionylglycine	3.0	-85.5
Glutamylglycine	38.9	-86.3

Oxidative damage leads to additional cross-linking of AA



COOCH3
γGlu
N
NH
HSH2C
O
HAT
H
N
γGlu
Cys
O
O
SH
O
O
O
H
N
O
O
N
H
O
NH2
HAT
O
O
SH
O
O
O
H
N
O
N
O
NH2
O
Cys Gly
N
COOCH3
NH2
HAT
O
O
O
Cys
Gly
N
H
NH2

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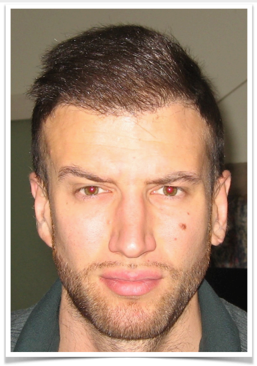
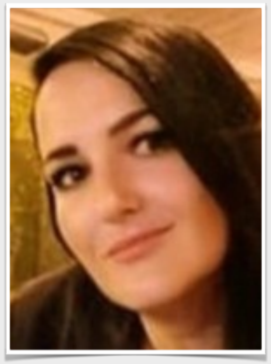
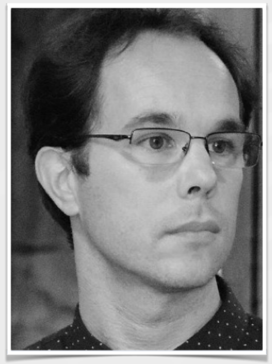
HRZZ project UIP 2020-02-4857

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Thank you!

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