

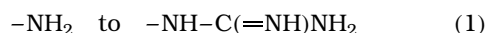
Editorial

The Terminology of Guanidine Formation

Abstract: The terminology in recent use for the conversion $-\text{NH}_2$ to $-\text{NHC}(=\text{NH})\text{NH}_2$ is surveyed and shown to be in a state of extreme confusion: a pragmatic recommendation is made that the word *guanidinylation* should be generally adopted for this conversion. Copyright © 2002 European Peptide Society and John Wiley & Sons, Ltd.

Keywords: terminology; nomenclature; guanylation; guanidination; guanidinylation; amidination; carbamimidoylation; imidoylation

There is major confusion in the literature over the terminology for the functional interconversion by which an amine (amino group) is converted to a guanidine (guanidino group)



This is an important conversion in peptide and protein chemistry — see, for example, the recent advances in Professor Goodman's laboratory, which have been reviewed by him and his colleagues [1]. The muddle over the appropriate term to use for it has come to my attention as a result of an interesting correspondence with Professor Izdebski, who has a relevant paper [2] in this issue of the Journal. In the course of trying to clarify the position, I followed up on the points made by Professor Izdebski, for which I am grateful, and realised that the terminology is in a complete mess, so I have thought it worthwhile to describe the situation here for general edification and warning. I used mainly SciFinder Scholar, Google, Altavista and the USPTO database.

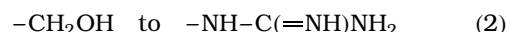
The traditional name for the group $-\text{C}(=\text{NH})\text{NH}_2$, which is the substituting group in conversion (1), was *guanyl*, but this was officially superseded [3a] many years ago by *amidino*, which has in turn more recently been officially superseded [4a] by *carbamimidoyl*.

Nitro/nitration, *amino/amination*, *nitroso/nitrosation* are all in common use. These familiar cases imply that when there is substitution of a hydrogen atom by a group with name ending in o then the name of the reaction type should generally be formed by dropping the o and replacing it by ation. When a group name ends in yl, it is well-established practice to name transformations involving substitution of

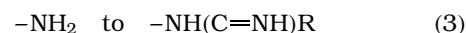
hydrogen by that group simply by adding ation to the name of the group being introduced, as in *alkyl/alkylation*.

On these premises, the strictly correct (or at any rate logically justifiable) terms for conversion (1) would have been *guanylation* in the distant past, then *amidination* and should now be *carbamimidoylation*.

Guanylation has long been, and remains, in common use for conversion (1), despite the long-standing official disapproval [3b] of *guanyl*. One recent instance [5], however, employed it for the very different direct conversion (2)



Amidination is in current use, e.g. [6], for conversion (1), but many encounters with it are when it is being used, e.g. [7], for the conversion (3)



for which the logically correct name is actually *imidoylation* because it is an *imidoyl* group $-\text{C}(=\text{NH})\text{R}$ [3c] which is replacing hydrogen in this case.

Carbamimidoylation has been used for conversion (1), e.g. [8], but only for three related mid 1970s papers, and not since then.

The correct term [3d,4b,9] for the group $-\text{NH}(\text{C}=\text{NH})\text{NH}_2$ is *guanidino*, so *guanidination* of an amino group would imply the conversion



by logical extension of the principles established by the precedents *nitro/nitration* etc. *Guanido* has also been used [9] for $-\text{NH}(\text{C}=\text{NH})\text{NH}_2$, so

guanidation would imply conversion (4) by similar reasoning.

To add to the potential confusion, the terms *guanylate* and *guanylic acid* are commonly used in biochemistry for GMP, the ribonucleotide 5'-monophosphate derived from *guanosine*, leading to the occasional appearance of *guanylation* in the biochemical literature, e.g. [10], and also *guanylylation*, e.g. [11]. Furthermore, *guanidinato* is used, e.g. [12], in coordination chemistry.

Turning to actual current practice in peptide and protein chemistry, we find that *guanylation*, *guanidinylation* and *guanidination* are all being used frequently for conversion (1) at the present time. For an example of *guanylation*, we have a report from Professor Shiori's laboratory [13] but many other recent examples by authors from all over the world could be cited. *Guanidinylation*, in rare use since 1961 [14] until the last few years, is the term adopted by Professor Murray Goodman [1] and the new Houben-Weyl peptides volume E22a [15] uses it too, no doubt under his guidance as its overall Editor. *Guanidination* seems to be the favoured term in peptide and protein chemical modification and analytical work, e.g. [16], but there is a recent case [17] of use in the field of organic synthesis from Professor Hruby's laboratory. *Guanidation* enjoyed fair currency in the past, but seems to be falling into disuse, although an important recent book [18] edited by Professor Jung used it. Keyword searching using these terms in turn produces lists which have little overlap.

Surprisingly, *guanation* has never made even a tentative appearance in the lexicon. I could not find in at all in any of the databases I explored. Shorter and more euphonious than any of the other terms which have been used for conversion (1), its first syllable proclaims the area of chemistry to which it belongs, but it cannot be logically dissected any further than that, and would thus be free of logical confusion as a stand-alone word. Assuming, that is, that nobody would construe it as a noun of action derived from the recorded verb *to guano* [9], meaning to treat with *guano* [19].

So what are we to do about naming conversion (1)? *Amidination* was correct, but has been superseded, and definitely ought to be abandoned in any case because it now has a history of ambiguity. *Carbamimidoylation* appears to be correct, but its adoption in reality seems a forlorn improbability. *Guanylation* is not approved. *Guanidation* has

almost been abandoned. *Guanidination* ought not to be used, because if logically interpreted it is a misnomer.

A pragmatic approach is needed. It appears likely to me that the combined influence of Professor Goodman's recent work on the topic and Houben-Weyl will result in slow convergence towards *guanidinylation*. It is open to the objection that *guanidinyl* appears in the literature as an unapproved uncommon (it is used about one time in fifty) synonym for *guanidino*, e.g. [20], and could therefore, like *guanidation* and *guanidination*, be misinterpreted as meaning conversion (4). But it seems the least objectionable option. **So if a one-word term is required for guanidine formation by conversion (1), then let it be *guanidinylation*, in this Journal at least.**

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19. 'guano, *n.* **1**. A natural manure found in great abundance on some sea coasts, esp. on the Chincha and other islands about Peru, consisting of the excrement of sea fowl' [9]. This is the word, first noticed in English in 1604, from which all the present confusion springs, through *guanine* (first isolated from *guano*) and *guanidine* (first isolated as an oxidation product of *guanine*).
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NOTE ADDED WHILE IN THE PRESS

As a courtesy, I sent an advance copy of the above Editorial to Dr GP Moss of the IUPAC IUBMB, and this resulted in a number of very useful comments while it was in the press. I am grateful for these. One of them, in an e-mail from Dr AD McNaught of RSC Publishing, drew attention to the possibility of employing the suffix ification, as in *ester/esterification*, leading to the word *guanidinification* for conversion (1). There would be sound logic in that. There would be similar logic in using the suffix isation, as in *polymer/polymerisation*, leading to *guanidinisation*. But I baulk at introducing novelty into such a confused and crowded arena, and we will stick to *guanidinylolation* as the least objectionable of the terms in use, for the time being.

JHJ