Tetrahedron Letters No.39, pp. 3453-3456, 1970. Pergamon Press. Printed in Great Britain.

A CLEAN SYNTHESIS OF SOME UNSTABLE BIFUNCTIONAL CARBODIIMIDES

N-METHYL-N'-VINYLCARBODIIMIDE: A NEW VINYL ALLENE ANALOGUE

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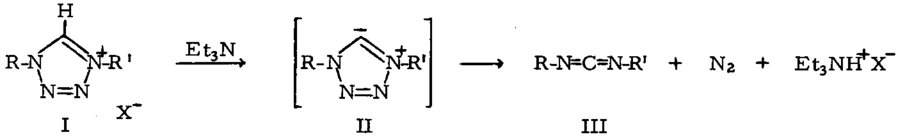
(Received in USA 19 June 1970; received in UK for publication 21 July 1970)

Carbodiimides are ordinarily prepared by the desulfurization or oxidation of N,N'-disubstituted thioureas, by the dehydration of N,N'-disubstituted ureas, by the pyrolysis or base-induced elimination of isothiourea ethers or esters, or by the catalyzed thermolysis of isocyanates.[1] Unfortunately the required reaction conditions are usually too vigorous to allow the practical synthesis by such methods of many potentially unstable and highly reactive bifunctional carbodiimides -- some of the compounds of most interest to the synthetic chemist as precursors and reagents and to the theoretical chemist as structure, reactivity, and bonding probes.

Some years ago, as a consequence of our studies on C-H acidity in heteroaromatic compounds,[2,3] we invented a very mild procedure for the conversion of the readily available 1,4-disubstituted-5-unsubstituted tetrazolium salts (I) into solutions of the carbodiimides (III).[3†]



The transformation was easily accomplished by titration of I in an appropriate solvent with one equivalent of Et_3N and in this way a few simple carbodiimides were generated as an adjunct to a study of the effect of structural variation on the rate of ylid formation (I→II).[3] One of the by-products, N_2, bubbled off as the base was added while the other, $Et_3NH^+X^-$, could be precipitated from the solution by using a non-polar solvent and thus also eliminated as a product contaminant.

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†The cations (I) are easily made by oxonium[4] or carboxonium[5] ion alkylation of 1-substituted tetrazoles which are best prepared by the acid-induced condensation of isocyanides with HN_3.[6]

Since an excess of either reagent was not required and the reaction was essentially quantitative, solutions containing only III and the solvent could thus be obtained.

In this communication we report the successful application of the reaction, I→III, to the synthesis of some new highly reactive bifunctional carbodiimides, R-N=C=N-Me (Me chosen since it should be the most unstable simple compound in each class and thus constitute a stringent test of the value of the method), and a few further reactions of these prototype systems.

The first carbodiimide we prepared was the previously unknown N-methyl-N'-vinylcarbodiimide (IV), the first and simplest member of a new class of heteroatom substituted conjugated vinyl allenes. Other members of the general class (V) rank among the most important reagents and precursors in heterocyclic and other areas of organic chemistry.*

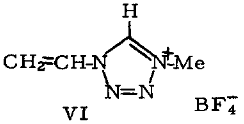
$Me\text{-}N{=}C{=}N\text{-}CH{=}CH_2$

IR: 4.59, 6.06μ (CH_2Cl_2)

IV

$V{=}W\text{-}X{=}Y{=}Z$

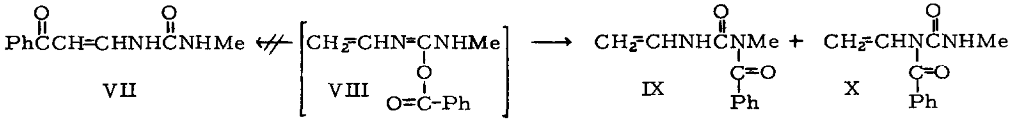
V



VI

The starting material was 1-vinyltetrazole[6] which on alkylation with trimethyloxonium fluoroborate[4] yielded the tetrazolium salt (VI) as a hygroscopic low melting solid (83%, mp 15-20°, NMR: C_5H at 10.70δ in CD_3NO_2). On titration of VI with Et_3N in several solvents, N_2 was liberated and a solution of IV was obtained. The pure carbodiimide could be isolated from a solution of VI in sulfolane by vacuum distillation into a liquid N_2 trap as $(PhCH_2)_3N$ was dripped into the reaction mixture. At room temperature the product decomposed within a few hours but it was more stable in solutions in inert solvents; NMR: vinyl at 6.43 (q, J=7, 15 cps), 4.88 (d, J=15), and 4.58δ (d, J=7) and methyl at 3.03δ in $CDCl_3$.

It was usually not necessary to isolate IV in order to use it as a reactant. In fact the reaction of IV with benzoic acid was most conveniently performed by adding Et_3N to a mixture of VI and benzoic acid. In this experiment the product was not the hoped for acylacetaldehyde derivative (VII) but instead the two N-acylureas (IX: mp 57-60°, 10% and X: mp 93-95°, 71%[7,8]).



$$PhC(=O)CH{=}CHNHC(=O)NHMe \not\leftarrow \left[CH_2{=}CHN{=}C(NHMe)\text{-}O\text{-}C(=O)\text{-}Ph\right] \longrightarrow CH_2{=}CHNHC(=O)N(Me)C(=O)Ph + CH_2{=}CHN(C(=O)Ph)C(=O)NHMe$$

VII VIII IX X

It seems the initially formed iminoanhydride (VIII) prefers to rearrange to nitrogen via a 4-membered ring intermediate instead of to carbon by a 6-membered ring pathway.

We have also generated N-diethylamino-N'-methylcarbodiimide (XIII).[10] Alkylation of XI[11] afforded exclusively the 4-methyl salt (XII)[12] in 87% yield; mp 103°; NMR: C_5H at 10.04δ, Me

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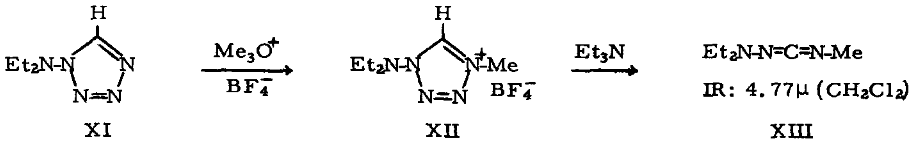
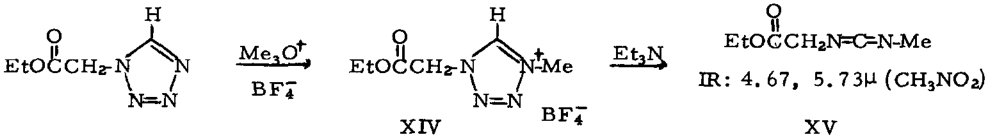
*Known examples include vinylisocyanates, acylisocyanates, acylketenes, imidoylisothiocyanates, acylisothiocyanates, thioacylketenes, thioacylisothiocyanates, imidoylketenes, iminoketenes, ketoketenimines, nitrosoketenimines, diazoketones, and acylazides. References are too numerous to list here but, for example, a monograph[9] is in large part devoted just to the cycloaddition reactions of some of these species.

at 4.31δ, Et at 3.33 and 0.95δ (J=7) in CD_3NO_2.

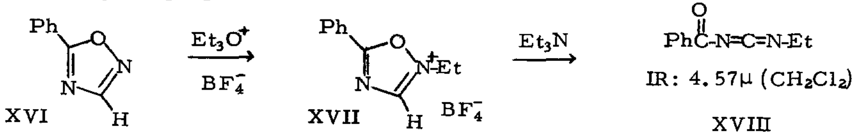


This on titration with Et_3N in CH_2Cl_2 yielded the aminocarbodiimide (XIII) which could be isolated as an unstable oil by precipitation of the by-product, $Et_3NH^+BF_4^-$, with ether followed by filtration and low temperature vacuum evaporation of the filtrate; NMR: NMe at 3.07δ, NEt_2 at 2.77 and 1.15δ (J=7) in $CDCl_3$. Even in 0.08 M solution in CH_2Cl_2, XIII was ca 20% decomposed after 24 hours at room temperature. As a further structure proof, XIII was converted to the anticipated semicarbazide (mp 65-67°) by reaction with dilute acid (comparison sample from Et_2NNH_2 and MeNCO).

Finally solutions of the unstable N-carbethoxymethyl-N'-methylcarbodiimide (XV), the first known prototype of the homoacylcarbodiimide series, have been prepared from the precursor tetrazole[6] via the tetrazolium salt (XIV, mp 55-60°, hygroscopic; NMR: C_5H at 10.41δ in CD_3NO_2).

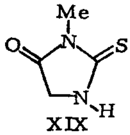


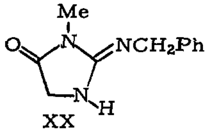
We have also attempted to form acylcarbodiimides[13] by the present procedure but have been unsuccessful because the alkylation of acyltetrazoles with trimethyloxonium fluoroborate was accompanied by the elimination of acyl fluoride. One very unstable example of this class of heteroatom substituted vinyl allenes (XVIII) has, however, been generated in these laboratories by a related ring scission process from the oxadiazolium cation (XVII, mp 115-117°, NMR: C_3H at 9.16δ in CH_3CN, prepared from XVI[14]).



The structure of XVIII was confirmed by immediate conversion to N-benzoyl-N'-ethylurea (compared with authentic sample[15]) on addition of water.

The utility of these new bifunctional carbodiimides as reagents and synthetic precursors will be the subject of future publications, but as a preview, the use of the simplest of these compounds, the carbethoxymethyl derivative (XV), as a source of some hydantoin derivatives is described here. When XV (or the precursor salt XIV plus base) was treated with H_2S, the product was XIX (mp 161°), with $PhCH_2NH_2$ either XX or XXI or a tautomer (mp of acetonyl derivative 153°) was isolated, and with $PhNHNH_2$ the very air sensitive XXII or a tautomer was obtained (mp 146-149°).


XIX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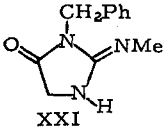
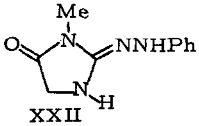

XXI


XXII

We wish to thank Dr. J. S. Michelman for performing some preliminary experiments and the U. S. Public Health Service for their support of this research (GM-13980).

REFERENCES

[1] F. Kurzer and K. Douraghi-Zadeh, Chem. Revs., 67, 107 (1967); H. G. Khorana, ibid., 53, 145 (1953).

[2] R.A. Olofson and J.M. Landesberg, J. Am. Chem. Soc., 88, 4263 (1966); R.A. Olofson, J.M. Landesberg, K.N. Houk, and J.S. Michelman, ibid., 88, 4265 (1966); R.A. Coburn, J.M. Landesberg, D.S. Kemp, and R.A. Olofson, Tetrahedron, 26, 685 (1970); R.A. Olofson, R.V. Kendall, A.C. Rochat, J.M. Landesberg, W.R. Thompson, and J.S. Michelman, Abs. of the 153rd Meeting of the ACS, Miami, Apr. 1967, p. Q34, and unpublished results.

[3] R.A. Olofson, W.R. Thompson, and J.S. Michelman, J. Am. Chem. Soc., 86, 1865 (1964); A.C. Rochat and R.A. Olofson, Tetrahedron Letters, 3377 (1969).

[4] H. Meerwein, Org. Syn., 46, 113, 120 (1966) and earlier references therein; see also R.B. Silverman and R.A. Olofson, Chem. Comm., footnote p. 1313 (1968).

[5] S. Kabuss, Angew. Chem. Internat. Edit., 5, 675 (1966); K. Dimroth and P. Heinrich, ibid., 5, 676 (1966); R.F. Borch, J. Org. Chem., 34, 627 (1969).

[6] D.M. Zimmerman and R.A. Olofson, Tetrahedron Letters, 5081 (1969).

[7] Satisfactory analytical data have been obtained for all stable new compounds.

[8] Structural assignments are based on NMR spectra (methyl split by NH in X while a similar coupling of NH with vinyl CH is seen in IX) and base hydrolysis of X to N-vinylbenzamide.

[9] H. Ulrich, Cycloaddition Reactions of Heterocumulenes, Academic Press, 1967.

[10] The very hindered but still unstable $Me_2NN{=}C{=}NCMe_2R$ (R=Me, n-Amyl) are already known; W.S. Wadsworth and W.D. Emmons, J. Org. Chem., 29, 2816 (1964).

[11] B. Föhlisch, H. Bredereck, and K. Walz, Angew. Chem. Internat. Edit., 3, 647 (1964).

[12] There was no evidence from NMR of the crude reaction mixture for any methylation on the diethylamino group or on any nitrogen in the tetrazole ring except the 4-position.

[13] Carbethoxycarbodiimides, $EtO_2CN{=}C{=}NR$ (R=iPr, Cyclohexyl, t-Bu), have been prepared and are unstable oils; R. Neidlein and E. Heukelbach, Tetrahedron Letters, 149 (1965).

[14] R. Lenaers, C. Moussebois, and F. Eloy, Helv. Chim. Acta, 45, 441 (1962).

[15] P.F. Wiley, J. Am. Chem. Soc., 71, 1310 (1949).