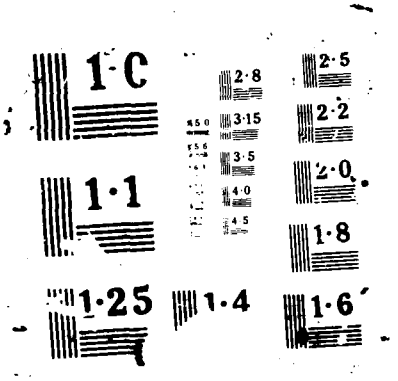
AD-A194 586 NEW SYNTHETIC APPROACHES TO TAT(U) BONN UNIV (GERMANY F R) H WAMHOFF 24 FEB 87 DAJA45-85-C-0016 1/1

UNCLASSIFIED F/G 7/3 NL


1·C
1·1
1·25
1·4
2·8
3·15
3·5
4·0
4·5
2·5
2·2
2·0
1·8
1·6

INSTITUT FÜR ORGANISCHE CHEMIE
UND BIOCHEMIE
DER UNIVERSITÄT BONN

Prof. Dr. H. Wamhoff

Gerhard-Domagk-Straße 1
D-5300 Bonn 1, 24.2.1987
☎ (0228) 731
Bei Durchwahl 73 26 51, 73 26 71
Telex 886 657 unibo d

(2)

European Research Office
USARDSG(UK) - Chemistry Branch
Attn.: Fiscal Officer
Edison House
223 Old Marylebone Road
GB - London NW1 5TH ENGLAND

Ref.: Contract No. DAJA 45-85-C-0016
"New Synthetic Approaches to TAT"

FIFTH INTERIM REPORT (Item 0005)

At present we are continuing our synthetic strategy on three different pathways:

(a) ring synthetic methods from easily accessible small molecules without template effect

(b) half-synthetic methods starting from partially destructed hexamethylenetetramine, such as DAPT

(c) template-catalyzed approaches: phenyl- and tert.butyl substituted methyleneimines and their tetramerizations in the presence of suitable ions

Regarding the pathways (a) and (b) we can report now on two promising approaches to TAT:

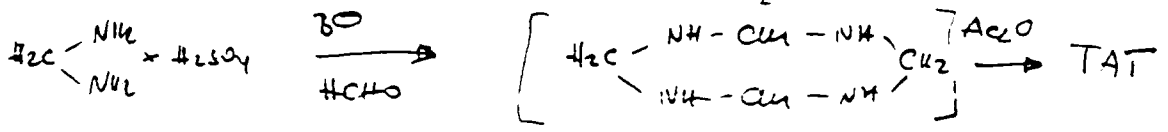
(a) (Work of Mr. Bongen): Considering the observations made by B.S. Thyagarayan and K.C. Majumdar, J.Heterocycl.Chem. 11, 937 (1974) in their synthesis of 1,3,5,7-tetracarbalkoxy-tetrazocanes, and with the knowledge of US-pat. 3.978.046 by C.L. Coon (United States Dept. of the Army) on TAT synthesis by treating methylene-bisacetamide with paraformaldehyde in the presence of H_2SO_4, we have reacted acetamide first with 37% aq formaldehyde, 3g of acetic acid for 4h, then we added more equivalents of paraformaldehyde (8g) and 3 g of acetic acid. - Working up the reaction mixture, we were able to detect TAT by TLC, besides methylenebisacetamide. At present we are trying intensively to alterate the reaction conditions and to imorove the yield of TAT. It is the aim of these investigations to furnish a simple one-step, one-pot procedure starting from easily accessible starting materials and to obtain TAT under mild conditions, according to the following equation:

$$Me\,CONH_2 + HCHO \longrightarrow Ac\,NH-CH_2-NH-Ac \xrightarrow[<Cat.>]{\text{paraformald.}\ (24CH_2O)} TAT$$

(b) (work of Mr. Bongen): Starting from DAPT prepared easily by the direct and elaborate method of V.I. Siele, M. Warman, E.E. Gilbert, J.Heterocycl.Chem. 11, 237 (1974), we have treated 5.3g DAPT in Acetanhydride with a mixture of Ac_2O (150 ml), 1.5 ml of H_2O, 3g $SOCl_2$ and 2 g NH_4OAc. The temperature is maintained at 5°C. After 1 h stirring at room temp. the Ac_2O and all volatile material is evaporated. We obtained TAT in a yield of 3.66g (25.8%).

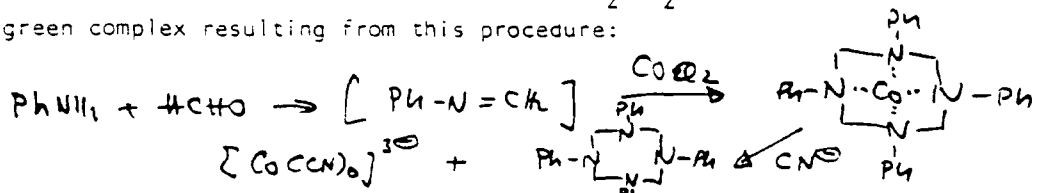
Besides this successful approach, many other experiments involving controlled decomposition of DAPT turned out to be not successful:, e.g. with TsCl (autoclav), $TsCl/AlCl_3$, $ClSO_2Cl$, with TsCl in a melt, $t\text{-butCl}/AlCl_3$, $CH_2Cl_2/AlCl_3$, $COCl_2$ etc.

Furthermore, the work published originally by H.H. Richmond, G.S.Myers, and G.F. Wright (J.Am.Chem.Soc. 70, 3659 (1948)) is continued. The aim is to react methylenediamine-sufate in a controlled way with HCHO, $COCl_2$, etc.:



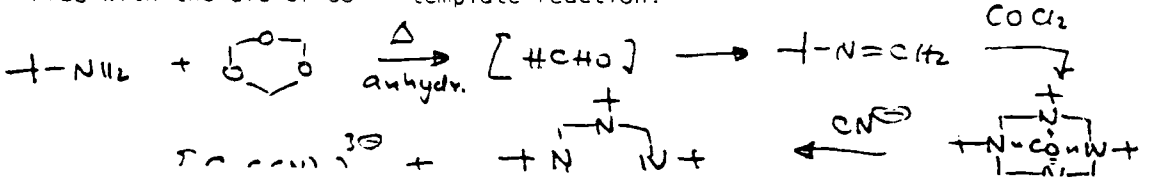
Furthermore, controlled degradation of DAPT is planned with the aid of the systems $POCl_3/CHCl_3$ or PCl_5/CH_2Cl_2, $POCl_3/Ac_2O$.

(c) (Work of Mr. Nagelschmitz): The template tetramerization reactions on the basis of the formentioned Roumanian publication are continued. It has been found that the reaction conditions published are in part irreproducible. Nevertheless, the published reaction aniline + HCHO + $CoCl_2 \cdot 6H_2O$ will be followed up, and the green complex resulting from this procedure:



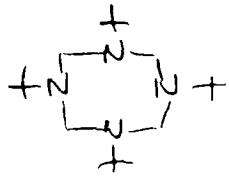
is tried to remove the central atom Co^{++} by ligand displacement, e.g. with CN^-, upon this reaction an oxidation process is expected to generate Co^{+++}, which is well known to form very stable complexes, especially with cyanide ions. This template approach is presently also investigated employing t-but-amine and HCHO to get intermediary t-but-methyleneimine, which should react then accordingly.

In an anhydrous reaction course, t-but-methyleneimine is planned to generate by treating t-butamine with paraformaldehyde, which should give alternatively during thermolysis (HCHO) and also t-but-methyleneimine, which we will try to tetramerize with the aid of Co^{++} -template reaction:



At present Mr. Nagelschmitz tries hard to remove the templating central atom by ligand exchange in the way described above, to treat the complex with much more potent ligands, like CN^-; easy oxidation, just by air, is expected to lead then to the veyr stable $[Co(CN)_6]^{3-}$ complex.

After working on the phenyl substituted tetrazocane, these decomplexation reactions are planned to be transferred to the tetra-tert.-butyl-tetrazocanes, in order to isolate free:

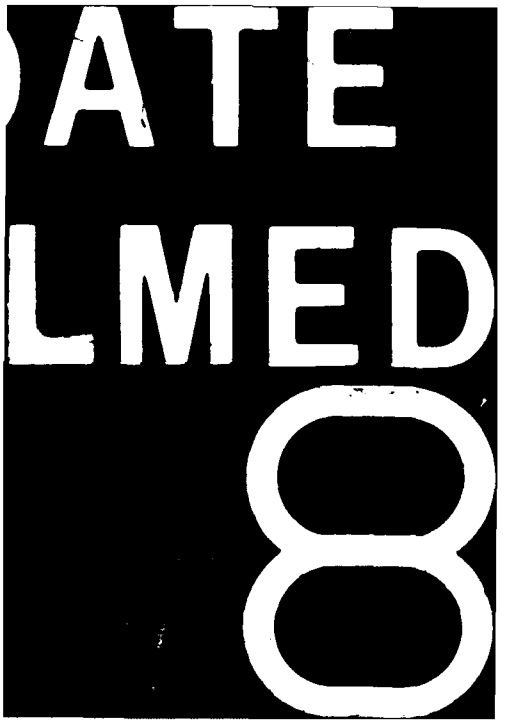


which is a promising intermediate for further substituent exchanges and developments.

Mid of July, I am planning another visit and conference with Dr.E.E. Gilbert and his group at Picatinny areal in Dover, NJ, and at present I am arranging a suitable schedule for this meeting, where our recent results in the synthesis of TAT should be discussed in detail.

(Professor Dr.Heinrich Wamhoff)

Contractor


ATE
LMED
8