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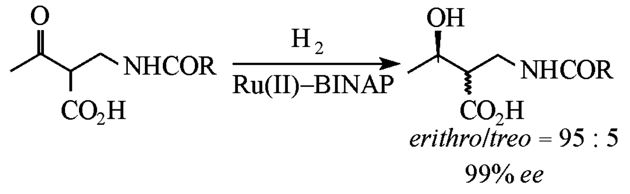
13th International Conference on Organic Synthesis–ICOS-13

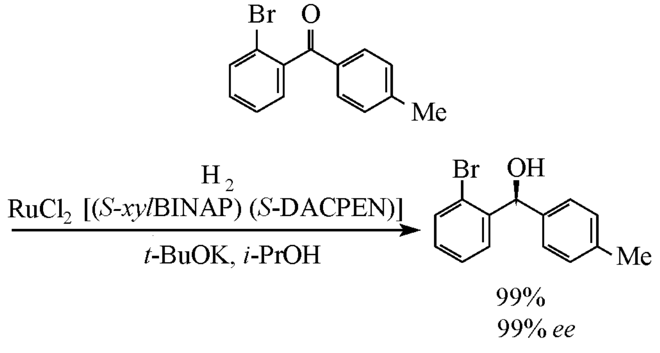
R. R. Kostikov

From July 1 to 5, 2000 in Warsaw took place the regular 13th Conference on Organic Synthesis under auspices of IUPAC and Polish Academy of Sciences (Chairman of the Organizing Committee Prof. M. Makosza). The conference was attended by over 600 chemist from 46 countries of the world. 8 scientists gave plenary lectures. The main work of the conference occurred in 4 sections (new synthetic methods, stereoselective synthesis, catalysis with metallocomplexes, and directed organic synthesis). In the sections were held 26 invited and 64 short oral communications, and also 175 posters. Besides within a framework of the conference was carried out a mini-symposium “Green Organic Synthesis” where the environmental problems of the industrial organic synthesis were discussed. During the Conference Professor A. Furstner (Max-Plank Institute, Mulheim, Germany) was awarded with IUPAC-Thieme Prize of 2000 for developments of new methods in organic synthesis. Besides the Organizing Committee bestowed two prizes for advances in organic synthesis on two young chemists from Poland and England who presented posters.

The modern state of the organic synthesis is characterized by development of highly selective catalysts, especially metal complexes, that generate chiral centers in molecules.

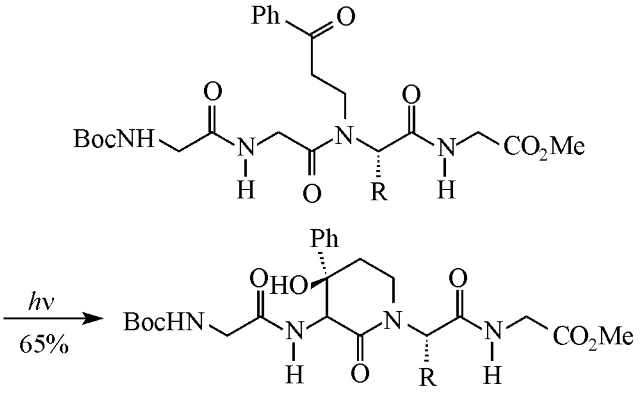
R. Noyori (Japan) reported on homogeneous asymmetrical hydrogenation of ketones in the presence of new complexes $RuCl_2(phosphine)_2(1,2\text{-diamine})$. The ruthenium complexes in the presence of a base in 2-propanol provide selective reduction of C=O function of various types into alcohols. The use of chiral diphosphines and diamines resulted in highly efficient asymmetrical hydrogenation.





The new ruthenium catalysts are both highly stereoselective and very active: the TON value (turnover number, the ratio of moles of product per 1 mole of catalyst) attains 2.4×10^6, and TOF value (turnover frequency, the number of catalysis acts per 1 molecule of catalyst) is 2.3×10^5.

In the lecture of B.Giese (Switzerland) was shown that biradicals formed by photolysis might demonstrate high selectivity, and the stereochemical result depended on the multiplicity: In the triplet systems could arise asymmetric induction, and in the singlet ones “memory effect” was observed. These specific features of radical reactions were applied to the following highly selective peptide cyclization.



H. Davies (USA) described the high regio-, diastereo-, and enantioselectivity of intramolecular insertion into a C–H bond of chiral rhodium carbenoids generated from aryl diazoacetates.

Stereocontrolled asymmetrical synthesis was performed in the Diels–Alder reaction of chiral acrylamides with cyclopentadiene or in preparation of pinacols from chiral α-ketoamides in the presence of SmI_2 (Y. H. Kim, Korea), and in [2+3]-cycloaddition of chiral oxazoline-*N*-oxides with various dipolarophiles (Y. Langlois, France).

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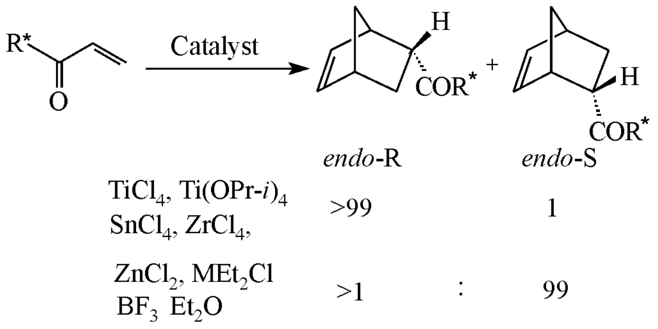

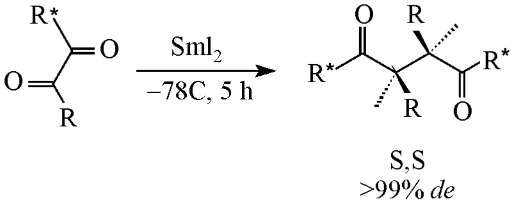

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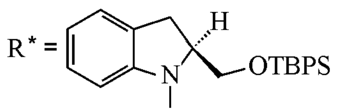
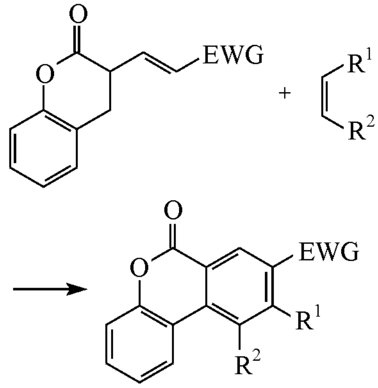
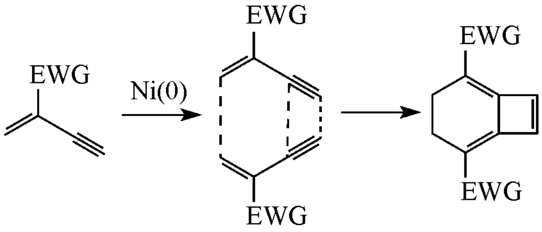


The reversed Diels–Alder reaction with participation of electron-deficient dienes of coumarin series with enamines furnished functionalized benzocoumarins (G. J. Bodwell, Canada). It was established that [4+2] benzoannelation of the conjugated enynes with electron-withdrawing groups (EWG) catalyzed with Pd also successfully proceeded in the presence of Ni(0) catalysts.

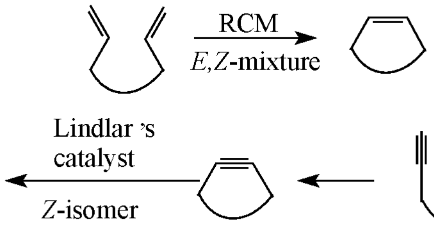


Dimerization of electron-deficient allenes afforded dimethylenecyclobutanes containing EWG at the methylene atoms (S. Saito, Japan).

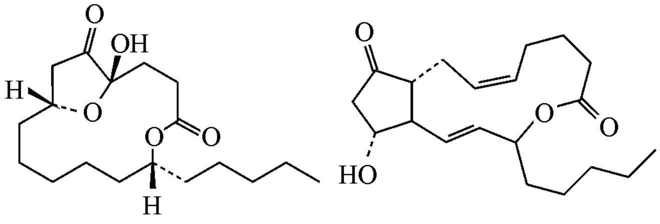


M. T. Reetz (Germany) reported on the way of creating genes mutations in order to obtain biological systems producing mutant enzymes (e.g.lipases) carrying out the biochemical processes with high enantioselectivity. An important trend in the development of organic synthesis is creating new synthetic methods, and also new building blocks for synthesis.

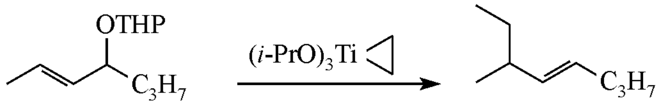
In the lecture of A.Furstner (Germany) were revealed the modern views on the mechanism of catalytic olefin metathesis that had underwent considerable alterations within the last decade. A. Furstner developed methods of syntheses of macrocycloalkenes and cycloalkynes from terminal diolefins and diacetylenes.



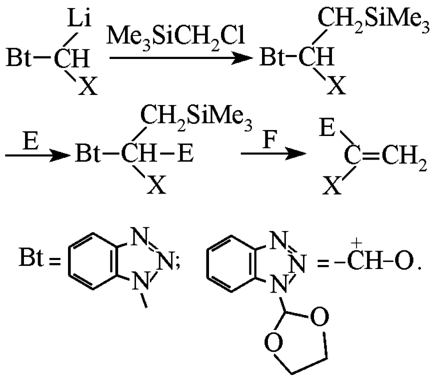
The efficiency of this technique was confirmed by preparation of a series of bioactive natural systems, for instance, those shown below.



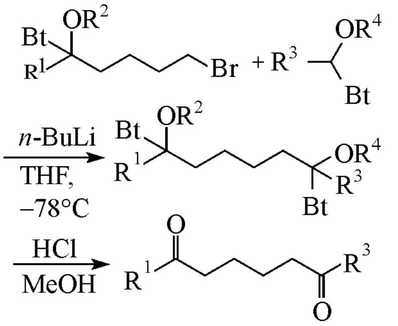
O. G. Kulinkovich (Belarus) presented a review of new modifications and practical applications of a new synthetic procedure for preparation of cyclopropanols and cyclopropylamines. This procedure recently developed by the author allowed to obtain the latter compounds in one stage from esters or amides of carboxylic acids, a Grignard reagent, and titanium(IV) isopropoxide. In the report was described the presumed mechanism of the reaction involving an intermediate formation of titanacyclopropane and its bis-alkylated derivative. The mechanism explains all the features of the reaction. New examples of reactions between dialkoxytitanacyclopropane and protected allyl alcohols resulting in 3-ethyl or 3-vinyl propenes were also mentioned.



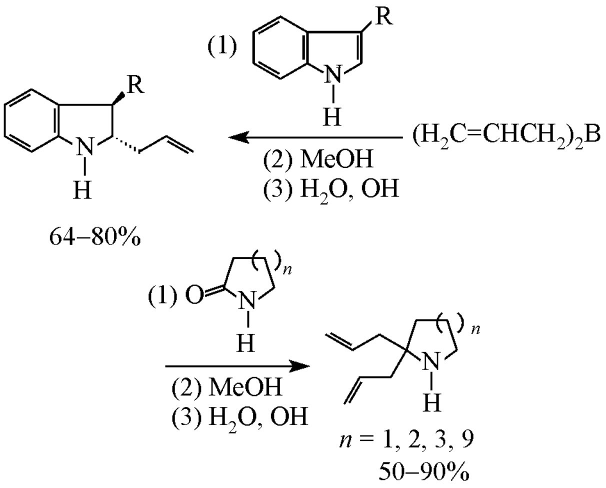
A. R. Katritzky (USA) discussed the strategy of synthesis of various classes of organic compounds using benzotriazole as a controlling protective group. This method permitted the author generation of a new synthetic analog of formyl cationic synthon.



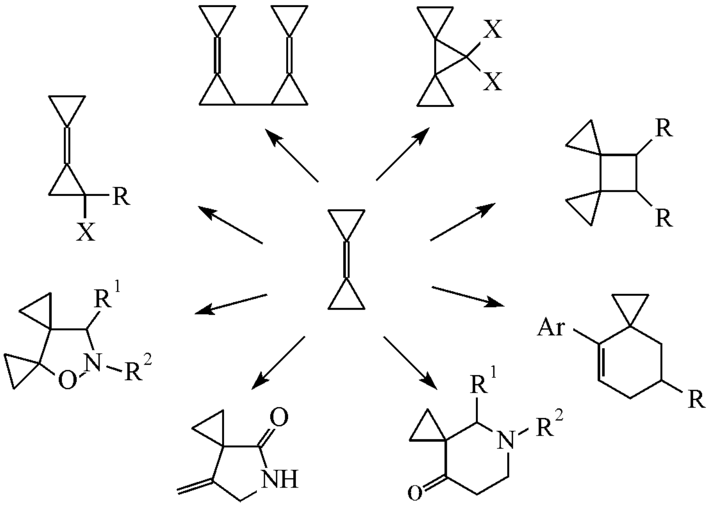
This technique can be illustrated by the synthesis of 1,6-diketones.



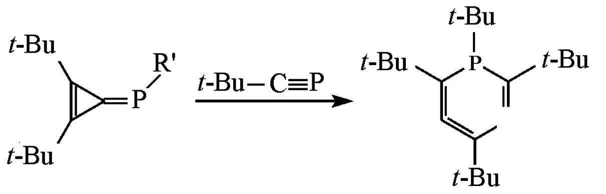
Yu. N. Bubnov (Russia) reported on application of allyl-substituted boron and zinc derivatives in the synthesis and transformation of nitrogen-containing heterocycles. Triallylborane turned out to be efficient allylating reducing agent. In reaction with substituted indoles it afforded 2-allylindoles in high yield. Cyclic lactams of various ring size were converted into 2,2-diallylazacyclanes when treated with triallylborane.



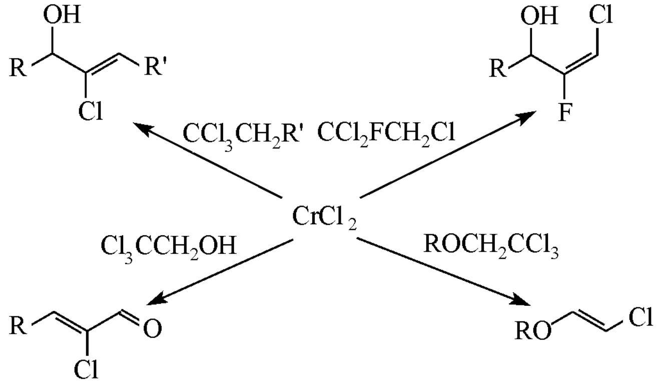
A. de Meijere (Germany) communicated numerous instances of application of bicyclopropylidene that was uncommon by properties and at the same time available and useful C_6 building block in the organic synthesis.



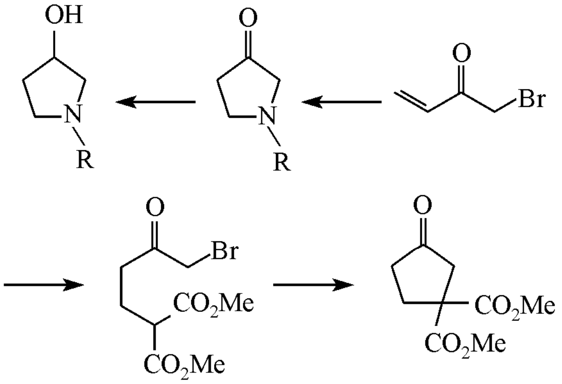
Another example of molecules with unusual characteristics is phosphatrifulvenes that have an opposite to phosphaalkenes electron density distribution. Their reaction with *tert*-butylphosphaacetylenes provided the first stable six-membered phosphaallenes.



C. Mioskowski (France) told of wide synthetic prospects of the new chromium vinylidene carbenoids prepared from $CrCl_2$ as shown below.

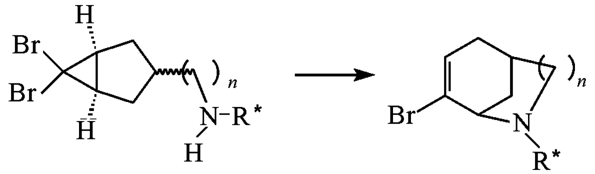


A. Westerland (Norway) reported on application of 1-bromo-3-buten-2-one as a convenient synthetic equivalent in preparation of cyclopentanone and 3-pyrazolidone systems.



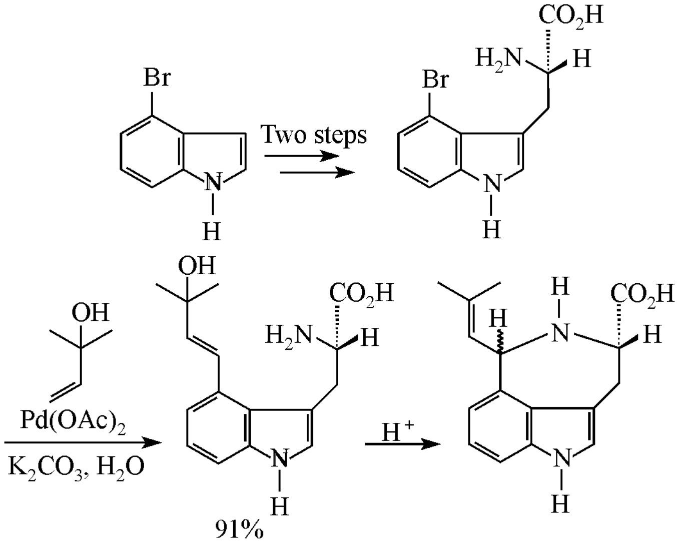
R = Ph, CH_2Ph, t-Bu.

Allyl cations (Banwell, Australia) generated by Ag^+-catalyzed electrocyclic cleavage of a three-membered ring in the gem-dihalocyclopropanes undergo intramolecular cyclization with nucleophile participation to form bicyclic systems. Therewith a chiral center (R^*) notably affects the stereoisomeric composition.

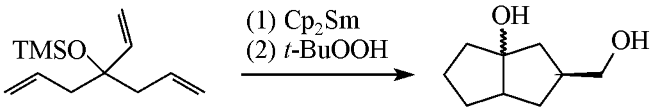


R. Dembinski (USA) communicated preparation, structural study, and reactions of a new group of bimetallic compounds of the type $L_nM(C{\equiv}C)_xM'L'_n$ (M = Re, W, L_n = ν-5-C_5Me_5, PPh_3 etc, x = 5–11) obtained by Kadio–Hotkevich reaction.

In the presentation of Y. Yokoyama (Japan) was demonstrated that the direction of the Pd-catalyzed reaction of 3-methyl-1-propenol with m-bromoaniline in water medium depended on the process conditions: in the presence of potassium carbonate occurred Heck reaction, and with no base proceeded alkylation. This result was utilized in the synthesis of clavopicitic acid from 4-bromotryptophan.

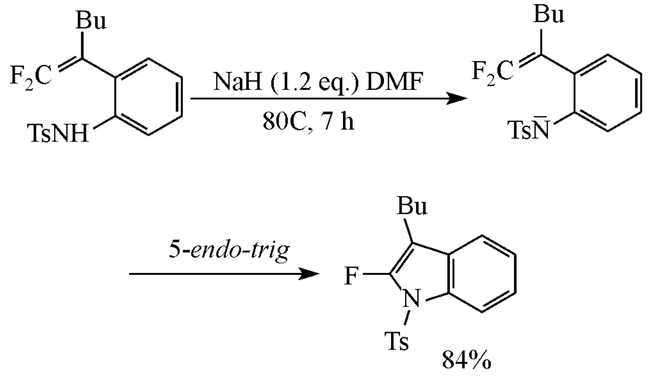


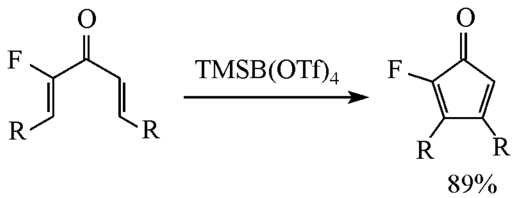
In the lecture of G. A. Molander (USA) were given examples of metallocene catalysis of high activity and selectivity for cyclization, allylation of dienes, trienes, enynes, and dienynes.



In the lecture of M. Malacria (France) were presented interesting examples of using vinyl radicals for initiating synthetically valuable radical cascade processes. The key stage here is 5-endo-trig-radical cyclization of allyl- or propargyl-substituted bromomethylsiloxanes. An example was also given of a one-pot construction of linear triquinane structures from acyclic molecules.

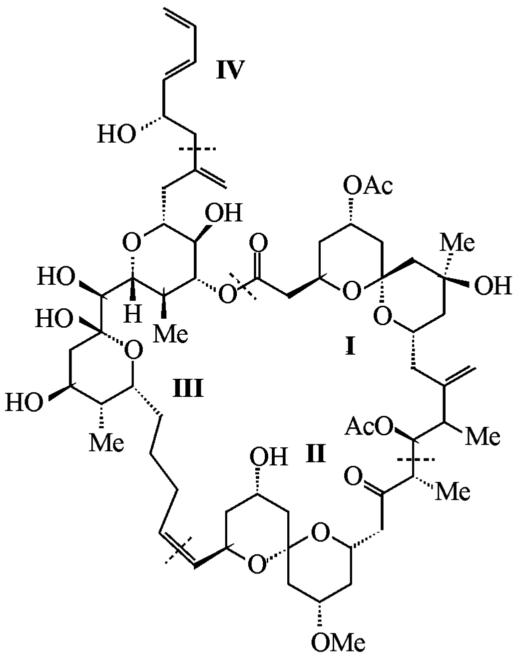
In the paper of J. Ichkawa (Japan) was shown that a fluorine atom at a double bond facilitated the intramolecular cyclization of fluoro- and difluoroolefins in the presence both of acidic and basic reagents.



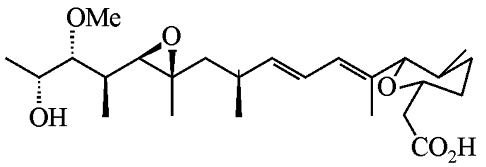


A major achievement in the modern organic synthesis is a complete synthesis of a number of complex natural molecules. Nowadays virtually any organic structure is accessible however complicated.

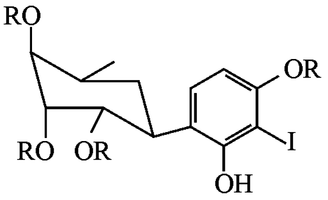
C. H. Heathcock (USA) reported on the planned synthesis of spongistatin **I** (Altohytrin A) that was considered as the most active and promising drug for anti-cancer chemotherapy since it by 50% suppressed the tumor growth in 10^{-11} to 10^{-12} mol l^{-1} concentration. In order to develop a multigram synthesis of this exceedingly active sea product a retrosynthetic analysis of its molecular structure was carried out, were determined the four fragments of the molecule (**I**–**IV**), and selected functionality thereof. The synthesis of these parts of the molecule required the following number of stages respectively: **I**, 57; **II**, 43; **III**, 21; **IV**, 33. The target product was built up from the fragment along a convergence scheme: (**I** + **II**) + (**III** + **IV**).



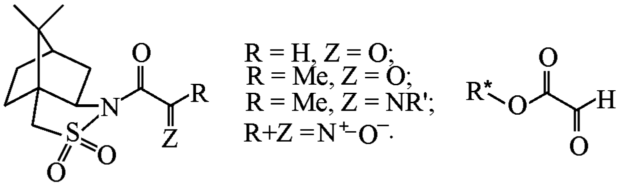
M. G. Banwell (Australia) informed of a total synthesis of enantiomerically pure Herboxidiene that was a metabolite of Streptomyces A7847.



The strategy and tactics of a total synthesis of Ravidomycin was mentioned in the lecture of K. Suzuki (Japan).

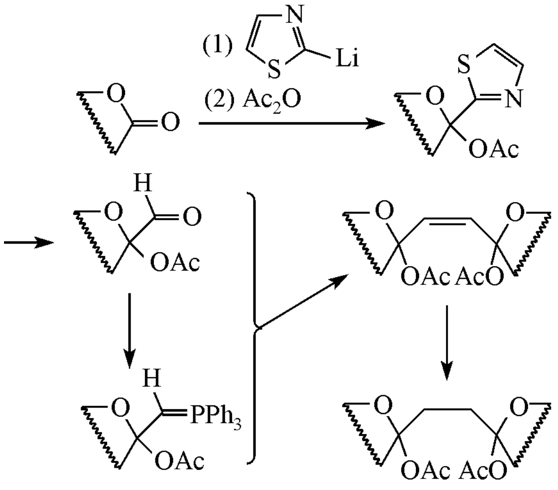


J. Jurczak (Poland) proposed a strategy of total synthesis for various natural compounds (*Purpurosamine C*, *Compactin* etc.) based on the activity of the carbonyl group in *N*-glyoxyl-(2R)-bornane-10,2-sultam in highly diastereoselective reactions of [4+2]-cycloaddition, cyclocondensation, 1,3-dipolar cycloaddition, enic reaction etc. The reactions of the other glyoxal derivatives were also considered.



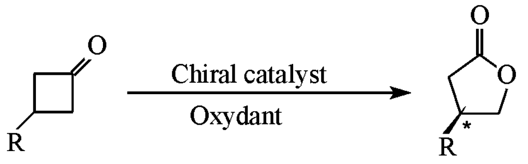
As already mentioned, within the framework of the Conference ICOS-13 was carried out a minisymposium on “green” organic synthesis. Its target was discussion on the environmental problems arising from the extensive development of industrial organic synthesis.

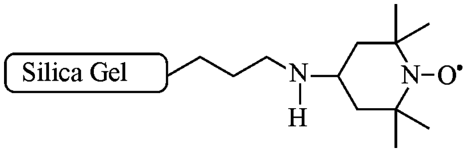
A. Dondoni (Italy) presented a procedure for preparation of oligosaccharides and glyconjugates (glycoproteins and glycolipides). The vinylidene bridge is formed in reaction of formyl-containing sugar with Wittig reagent prepared in its turn from a formyl-substituted sugar. The introduction of a formyl group to the anomeric C-atom of a monosaccharide is carried out with 2-lithiothiazole or 2-lithiobenzothiazole.



M. Anpo (Japan) reported on the application of photocatalytic titanium oxide films that under irradiation with sunlight (λ > 450 nm) oxidize in air various organic substances (e.g., 2-propanol or phenol) to CO_2 and H_2O.

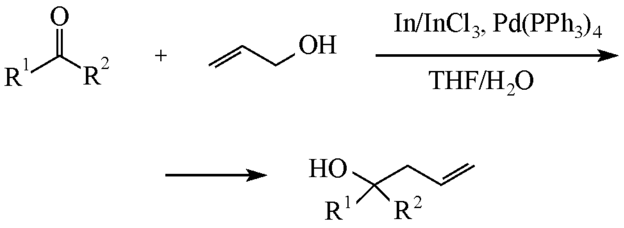
In a report of C. Bolm (Germany) were considered some trends in development catalytic processes used in the synthesis of valuable products. The application of chiral metal complexes in catalysis provided a possibility to prepare optically active lactones from racemic and prochiral cycloalkanes with enantioselectivity over 99% *ee*. Catalyzed with metal complex asymmetric oxidation of sulfides by hydroperoxides and hydrogen peroxide afforded enantiomerically enriched sulfoxides (up to 85% *ee*). A very efficient oxidation of alcohols into carbonyl compounds was performed with sodium hypochlorite in the presence of catalyst linked to "TEMPO" silica gel. In a number of reports was proposed a replacement of environmentally harmful dimethyl sulfate and methyl halides with dimethyl carbonate or methyl alkyl carbonates as "green" reagents.





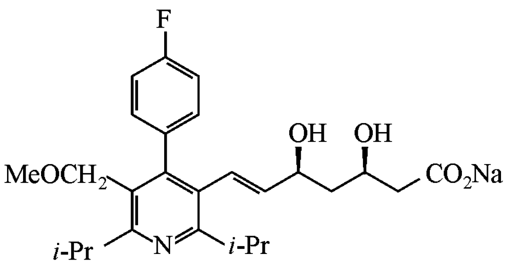
$$RCH_2OH \xrightarrow[\text{NaOCl}]{\text{TEMPO-silica gel, catalyst}} RCH{=}O$$

Indium metal is used in reactions of one-electron transfer in the neutral water medium for reduction of fused heterocycles containing one or two nitrogens into tetrahydro derivatives or for reduction of the substituted nitrobenzenes into anilines. The treatment of various carbonyl compounds with allyl alcohol and $In/InCl_2$ in the presence of catalytic amounts of $Pd(PPh_3)_4$ afforded homoallyl alcohols in high yields.



Proceeding from oxidative polymerization of tetrafluoroethylene in the presence of oxygen was developed a synthesis of a new class of fluorinated solvents, hydrofluoropolyethers $CHF_2–O(CF_2O)_n(CF_2CF_2O)_m$ (HEPE). HEPE possess low freezing point, high boiling point, and are well miscible with polar solvents.

R. Angerbauer (Germany) considered the prospects of extension in the new century of new drugs production, in particular, of synthetic and enantiomerically pure cerivastatin (commercial name Lipobary) that is



an inhibitor of HMMG-CoA reductase 300 times more efficient than the known flurolstatin.

The Conference ICOS-13 provided a certain summing-up of the advances in the organic synthesis within the last two years. It demonstrated virtually unlimited possibilities of the organic synthesis whose main directions are now as follows: (1) directed synthesis of various natural substances, especially with several stereocenters; (2) developments of new techniques and procedures of organic synthesis, in particular stereoselective with the use of metal complex catalysts and biochemical catalysts (enzymes etc.); (3) development of environmentally friendly industrial synthetic methods and creating new organic compounds useful for humans.

The next Conference ICOS-14 will take place in July 2002 in New Zealand.