

ACHIEVEMENTS AND PROBLEMS IN YLID CHEMISTRY*

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Summary

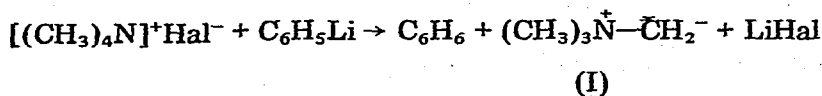
After a short historical review of ylid chemistry, questions concerning the structure and the Stevens and Sommelet rearrangements of nitrogen ylids are discussed.

Phosphorus ylids are described in more detail, and in particular the mechanism of their reaction with carbonyl compounds. Some specific examples from natural products syntheses are used to illustrate this carbonyl-olefination reaction.

The account is concluded with a description of sulphonium ylids and their characteristic behaviour towards aldehydes and ketones.

Nitrogen ylids

While attempting to prepare derivatives of pentavalent nitrogen Wittig and Wetterling [1] found, in 1947, that when tetramethylammonium halide is treated with phenyllithium a colourless lithium halide complex is formed, according to the following equation:

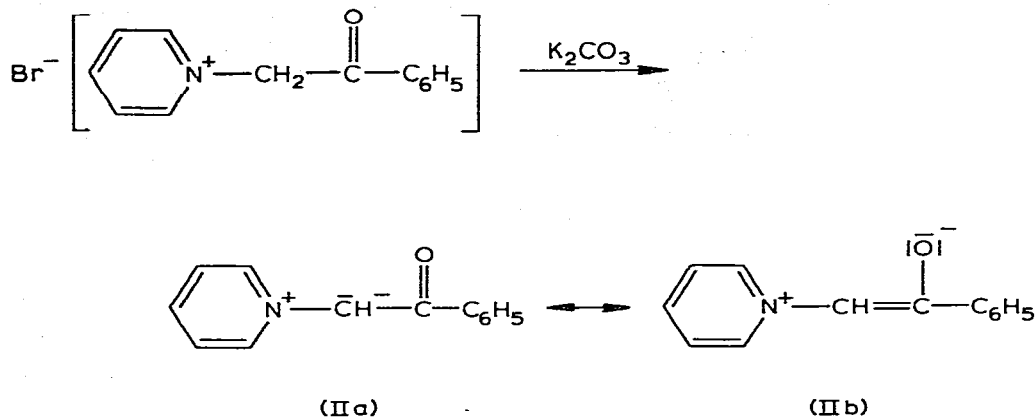


They named this complex trimethylammonium methyloid. To indicate that the two neighbouring atoms C and N are connected at the same time by a homopolar (yl) and an ionic bond (id) they designated these compounds as *ylids*.

Related to these ylids is a type of compound of the pyridine series, prepared by Kröhnke and coworkers [2] about ten years earlier, which they described

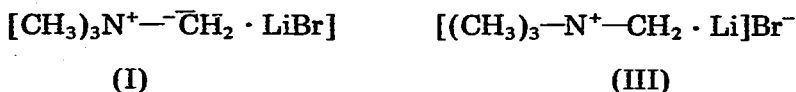
* A lecture delivered at the 25th IUPAC Congress in Jerusalem in July 1975.

correctly as "enolbetaines". Thus the pyridiniumbetain II was obtained by reaction of *N*-phenacylpyridinium bromide with potassium carbonate:



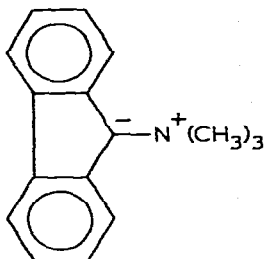
As far as the charge distribution is concerned the pyridinium ylid II cannot be compared with the ammonium ylid (I). Because of resonance in IIb the centre of gravity of the negative charge is at the carbonyl oxygen, and thus, in contrast to the situation with I, the charges are not localized at only two neighbouring atoms. This is also the reason why the resonance-stabilized pyridinium ylids may even be prepared by use of the weak base potassium carbonate, while for ammonium ylids only very strong bases such as organolithium compounds bring about the proton abstraction. The interesting work of Kröhnke therefore led to development along different lines than ammonium ylid chemistry [3].

The recent controversy about the structure of ammonium ylids does seem to me like a sham fight. Of the two alternatives, I and III, Daniel and Paetsch [4] prefer the latter formation of a metallated ammonium salt.



The fact that ylids react like organolithium compounds does not, however, exclude structure I, in which the ylid is complexed with lithium bromide via the metal [5]. Musker [6] correctly points out that organolithium compounds in ether solution are highly associated with themselves and with lithium halide, and that Grignard reagents, which undergo analogous reactions, are formulated not as a $[\text{RMg}]\text{X}$ salt but as being complexed with halogen. In order to bypass this currently unsolved problem the term crypto-ylid may be used, by analogy to the crypto-carbanions on which the effectiveness of organolithium reagents is based.

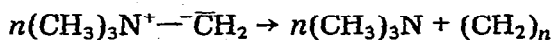
Furthermore, the ochre trimethylammonium fluorenylid (IV) has been obtained free of salt [7], but nevertheless shows the normal reactions of ammonium ylids. Its stability is connected with the effectiveness with which the free electron pair at C(9) can be delocalized by interaction with the π -electron system of the fluorene. The situation is very similar in the pyridiniumbetaines of Kröhnke mentioned above. In these the charge delocalization of the ylid is achieved by interaction with the pyridine ring. A combination of



(IV)

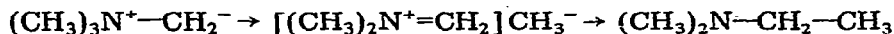
both of these delocalization possibilities exists in 9-fluorenylpyridinium-betaine [8], which is formed even by the action of sodium hydroxide on the corresponding pyridinium salt. It dissolves in chloroform to give a deep blue colour.

Since the tendency of the alkali metals to form complexes is most pronounced with lithium, it was expected that sodium halides stabilize the methylenid III to a lesser degree and this was indeed, found to be the case. Thus the reaction of phenyllithium/phenylsodium (1/5) with tetramethylammonium bromide [5] did not give the corresponding sodium bromide complex but instead trimethylamine and polymethylene:



This makes it seem very likely that the salt-free trimethylammonium ylid cannot exist.

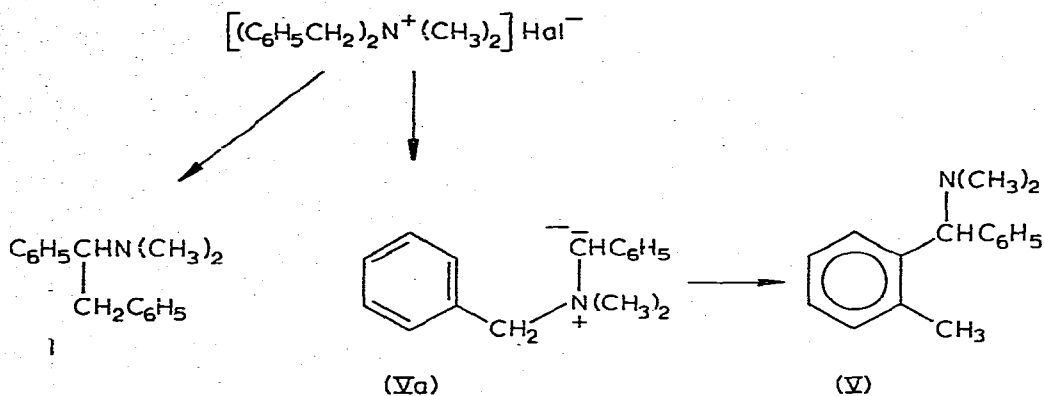
The reaction of tetramethylammonium bromide with phenyllithium/phenylsodium (1/5) in cyclohexene and ether did not give the methylene adduct of cyclohexene, but dimethylethylamine [9], which was isolated in about 50% yield. Hence, the ylid has rearranged in the sense of a Stevens isomerisation. The mechanism of this rearrangement has not been completely settled. The work of Jenny and Druey [10] and of others indicates that it involves an immonium ion pair isomerisation according to the scheme:



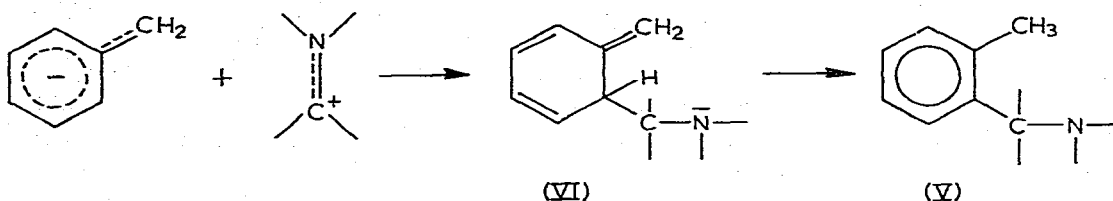
As an alternative, a radical dissociation-recombination mechanism postulated by Schöllkopf [11] is being considered.

A different type of rearrangement is observed when ammonium salts containing benzyl groups are treated with organolithium compounds. Thus, dibenzylidimethylammonium halides on reaction with phenyllithium give two amines, the 1,2-diphenylethyldimethylamine, the product of a Stevens isomerisation, and the *ortho*-methylbenzhydryldimethylamine (V) [12].

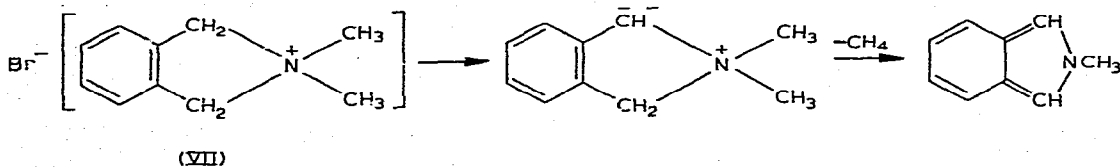
The product V originates from a dimethylaminobenzyl migration (intermediate Va) to the benzene ring, a reaction which we have classified as Sommelet rearrangement. According to more recent work [13], electrophilic attack of the immonium cation at the *ortho* position of the benzene ring leads to formation of the methylene derivative VI as an intermediate.



However, as long as the possibility of the intramolecular radical process is not excluded the mechanism must remain unclear [14].



The cyclic ammonium salt VII also represents a type of benzyl derivative. However, on treatment with phenyllithium, the salt VII does not undergo a benzyl shift to form the benzocyclobutadiene as the rearrangement product, as we had hoped, and instead the isoindol is formed by elimination of methane [15].

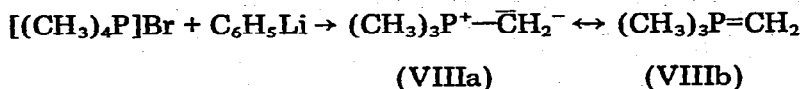


Nitrogen ylid chemistry is clearly not yet fully understood. But then even the chemistry of phosphonium ylids, which we now briefly discuss, is still full of problems.

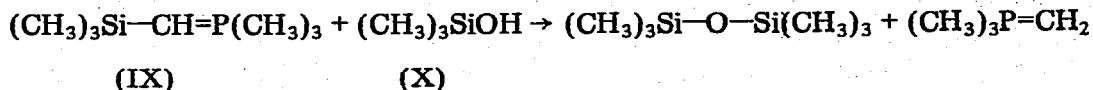
Phosphorus ylids

In connection with the ability of tetramethylammonium halide to undergo metallation by phenyllithium, the behaviour of tetramethylphosphonium halide towards this reagent was of interest. It was found that the phosphonium salt is metallated far faster than the analogous ammonium salt [16]. The pure homopolar character of pentaphenylphosphorane, prepared from tetraphenylphosphonium bromide and phenyllithium, proves that, in contrast to nitrogen, phosphorus, can form an electron decet. Therefore the ylid VIII may be represented by two mesomeric structures: VIIIa, the ylid, and VIIIb, the ylen, in

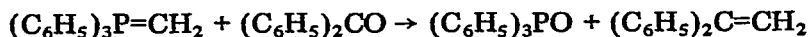
which the ylid represents the more reactive component:



In the light of more recent investigations [17] the metallated phosphonium salt is assumed to exist in the form of its adduct with lithium halide. The same work shows that the easily accessible compound IX reacts with trimethylsilanol X to give the salt-free trimethylphosphinemethylene according to the following scheme:

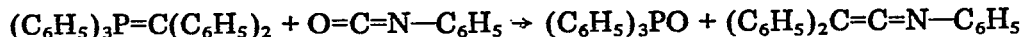


The methylene triphenylphosphorane is of special preparative interest, because it brings about olefination of carbonyl compounds [18].

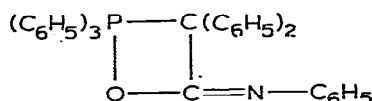


This carbonyl-olefination reaction has indeed, become of great importance, since it is widely applicable, and since the carbonyl function is replaced by a carbon double bond under very mild conditions [19].

In this connection it is noteworthy that even as long as 35 years ago Staudinger and Meyer [20] attempted carbonyl-olefination with the much less reactive triphenylphosphinediphenylmethylene, and succeeded in the case of the very reactive phenylisocyanate:



They suggested the participation as an intermediate in this reaction of the four-membered ring XI:

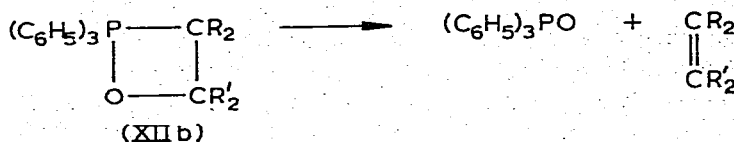


(XI)

The course of the carbonyl-olefination reaction is usually represented as follows [21]:



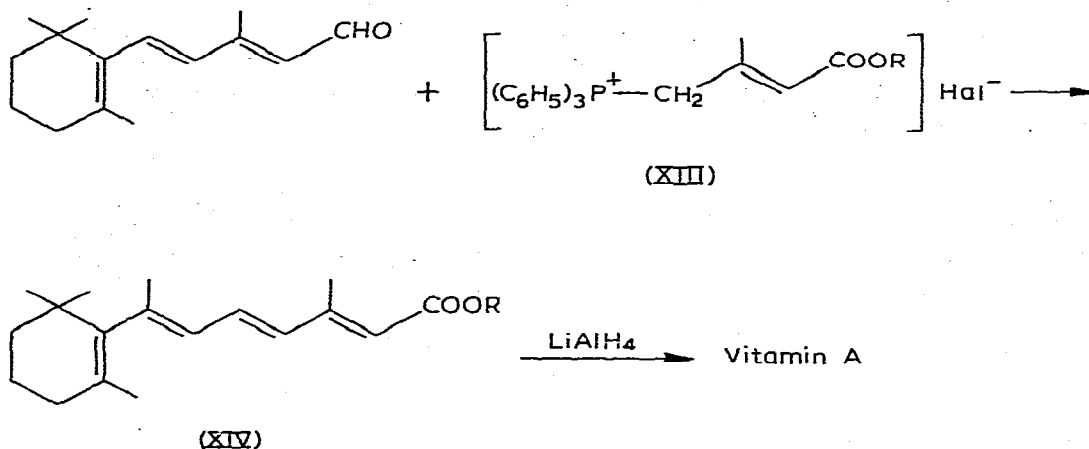
(XII a)



Thus, the olefin and triphenylphosphine oxide are formed via two intermediates, the betain adduct XIIIa and the oxophosphetane XIIIb. Which of these intermediates corresponds to a minimum in energy, and therefore is the more stable adduct, remains an open question [25].

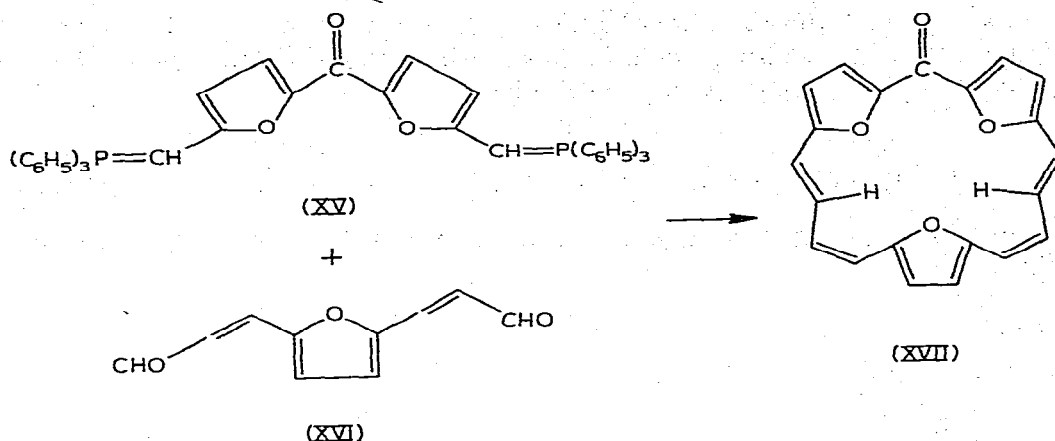
Recently, Vedejš and Snoble [22] have shown by ^{31}P NMR spectroscopy that in some reactions of ethylidinetriphenylphosphoranes with carbonyl compounds such as benzaldehyde or cyclohexanone, the oxophosphetane represents the low energy intermediate. Thus, a $\pi^{2s} + \pi^{2a}$ cycloaddition of both components occurs, and is followed by formation of the final products [23].

Since the discovery of the reaction, countless carbonyl-olefinations have been described in the literature and they cannot all be covered here. The new method was of special interest to natural product chemistry for the synthesis of unsaturated compounds. I may just mention its industrial application in the synthesis of vitamin A, which was carried out by the BASF in collaboration with Pommer [26]. β -Ionone combines with the phosphonium salt XIII to yield



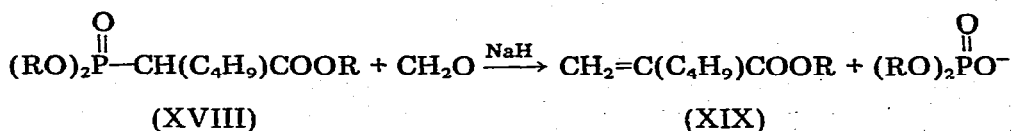
the vitamin A ester XIV, which then readily is reduced by lithium aluminium hydride.

Amongst the authors who have extended the carbonyl-olefination reaction in important respects I must mention Bestmann [27]. Furthermore I should point out that intramolecular carbonyl olefination can be used in the synthesis of heterocycles [28]. An olefination involving initially an intermolecular condensation pathway, which is followed by an intramolecular process is represented, e.g., by the reaction of XV and XVI to yield the annulenone XVII [24,29]:



The many variations of the carbonyl-olefination reaction, as developed especially by Corey [30], cannot be described in detail.

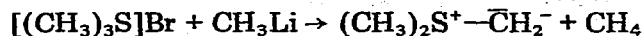
The PO-activated olefination described by Horner [31] five years after our first publication represents an important preparative extension of the carbonyl-olefination. Thus, the ester XIX is formed by the reaction of the phosphonate XVIII with formaldehyde in the presence of sodium hydride. Studies by Wadsworth and Emmons [32] show that glycol-dimethyl ether is an especially suitable solvent for this reaction.



It should be emphasized that this modified carbonyl-olefination usually leads to the formation of the *trans* compounds, while the original carbonyl-olefination leads predominantly to the *cis* isomer along with varying amounts of the *trans* compound.

Sulphur ylids

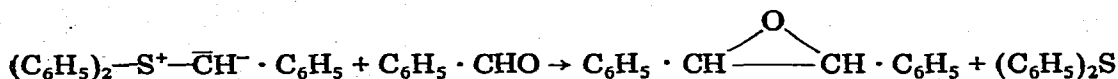
There has been little investigations of arsonium and stibonium ylids [33], but attention has been given to sulphonium ylids, which have novel implications for preparative chemistry. A comparison of these sulphonium ylids with phosphonium ylids is thus of special interest. According to Wittig and Fritz [34] the expected dimethylsulphonium methylid is formed from trimethylsulphonium bromide and methyllithium.



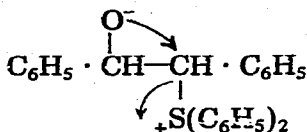
The stability of the sulphonium ylids is similar to that of the phosphonium ylids, and can be explained by overlap between the $2p$ orbital of the carbanion and the empty $3d$ orbital of sulphur.

The reaction of sulphonium ylids with carbonyl groups of aldehydes and ketones are especially notable, since they give epoxides, in contrast to the

reactions of phosphonium ylids which lead to olefination of the carbonyl group [35]. As one example amongst many, the reaction of benzylidenediphenylsulphane with benzaldehyde may be mentioned:



The initial adduct is thought to break down by the process represented in XX [34].



(XX)

This concludes the survey of the ylids of nitrogen, phosphorus, and sulphur. As we have seen, these ylids are capable of undergoing many types of reaction, and a great deal of work is still needed before the field is exhausted. Furthermore, many problems, especially those concerning mechanism, remain unsolved.

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