HETEROCYCLIC SONOCHEMISTRY

Yu.Goldberg, R.Sturkovich, and E.Lukevics*

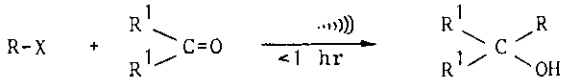
Institute of Organic Synthesis, Latvian SSR Academy of Sciences, Aizkraukles 21, 226006, Riga, USSR

Abstract - Sonochemical reactions involving heterocyclic compounds are surveyed. Major synthetic applications of sonolysis in the chemistry of heterocyclic compounds are described.

1. INTRODUCTION

A characteristic feature of organic synthesis in the past decade has been the use of various types of radiation (ultraviolet, microwave, laser, radioactive, ultrasonic, etc.) in chemical systems for induction, acceleration or modification of appropriate processes. A particular type of radiation used depends on the nature and agregate state of reactants, the type of reaction and its mechanism. One of the main reasons for the use of physical factors in a chemical system is the mutual insolubility of reacting substances. Among the different approaches employed those applicable to a wide range of reactions are particularly attractive. Such a versatile approach is, for example, the ultrasonic irradiation (sonolysis), which has been used to effec-

tuate a large number of reactions (mostly heterogeneous) involving various types of compounds. The chemical effects of ultrasonic waves* are commonly related with acoustic cavitation, i.e. the formation, growth and implosive collapse of vapour-gas bubbles accompanied by release of energy[1-5]. The process of cavitation occurring in a sonicated system is accompanied by the formation of short-lived ($\sim 10^{-9}$ s) local "hot spots" with a temperature of several thousand degrees and a pressure of several hundred atmospheres[1-4]. Effects of ultrasonic irradiation on chemical systems were first noted more than 50 years ago[2,3,5,6]. However, systematic application of sonochemistry in organic synthesis dates back to 1980, when Luche and Damiano[7] demonstrated that sonolysis (50 kHz) could lead to a faster and more efficient Barbier type reaction:



Over the past years, numerous sonochemical organic reactions have been conducted demonstrating the versatile applications of sonolysis for organic synthesis in heterogeneous (mostly liquid-solid) system[3,4,6,8-14].

The present survey examines sonochemical reactions involving heterocyclic compounds. Application of ultrasound in the case of heterocyclic compounds is highly beneficial due to the higher reaction rate and milder conditions used. Results obtained in the chemistry of heterocyclic compounds with sonolysis are compared, wherever possible, with those obtained under the same conditions without irradiation or with the use of other methods of activation (e.g., phase-transfer catalysis).

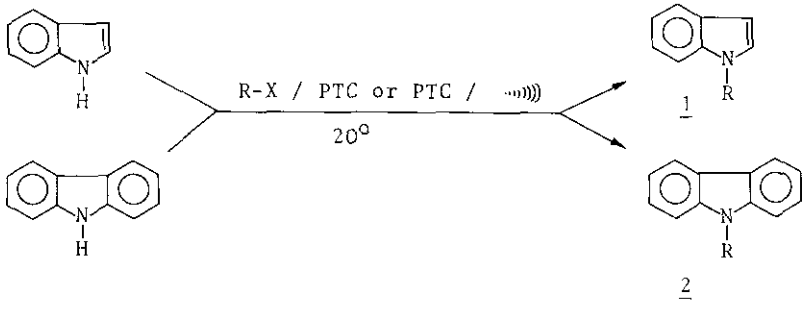
2. HETEROGENEOUS SONOCHEMICAL REACTIONS

2.1. Alkylation

Alkylation belongs to a common and very important reactions in the chemistry of heterocyclic compounds. The practical advantage of alkylation resides in the fact that it provides simple and convenient means for introduction of various substituents

*Ultrasonic waves have a frequency of above 16 kHz, the upper limit being 5 MHz for gases and 500 MHz for liquids and solids. Ultrasonic cleaners and ultrasonic disintegrators with the frequency 20-55 kHz are commonly used.

into the heterocycle or the side chain of these compounds. On the other hand, the use of heterocyclic derivatives as alkylating agents is a convenient method for the introduction of a heterocyclic moiety into various molecules. Phase-transfer catalysis (PTC) whose efficacy has been repeatedly demonstrated is extensively used for alkylation of heterocyclic compounds[15]. Nonetheless, attempts have been made recently to improve two-phase catalytic procedures by combining them with sonolysis. Alkylation of indole and carbazole with alkyl and benzyl halides under liquid-solid PTC conditions (toluene/solid KOH/catalyst (polyethylene glycol 350 methyl ether, tetrahexyl- or tetrabutylammonium salt)) proceeds at room temperature to give the corresponding N-substituted heterocycles (1 and 2) in satisfactory yield (Table 1)[16].



The rate of these reactions rises appreciably under sonolysis with concurrent increase in the yield of alkylated products.

Table 1

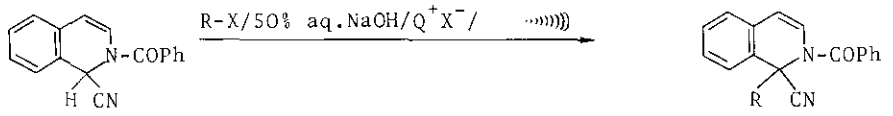
Alkylation of indole and carbazole under PTC conditions in the presence of polyethylene glycol 350 methyl ether with mechanical stirring and ultrasonic irradiation[16]

Heterocycle	Alkylating agent	Product	Mechanical stirring at 20°C		Ultrasonic irradiation	
			Time, hr	Yield, %	Time, hr	Yield, %
Indole	Methyl iodide	1	5	60	0.5	65
Indole	Benzyl bromide	1	8	80	2	95
Indole	1-Bromododecane	1	72	48	1.3	60
Indole	1-Bromododecane	1	3	19*	1.3	90*
Carbazole	Benzyl bromide	2	8	50	1	96
Carbazole	1-Bromodecane	2	-	-	3	84*

*Tetrabutylammonium nitrate used as the phase-transfer catalyst

The observed gain in the rate of alkylation is due to the specific effects of sonolysis but not to a rise in temperature during irradiation. It is noteworthy that in the absence of phase-transfer catalysts the alkylation of indole and carbazole occurred neither with vigorous stirring nor with ultrasonication[16].

Ultrasonic waves accelerate alkylation of the Reissert's isoquinoline compound 2-benzoyl-1,2-dihydroisoquinoline-1-carbonitrile (3) under PTC[17].

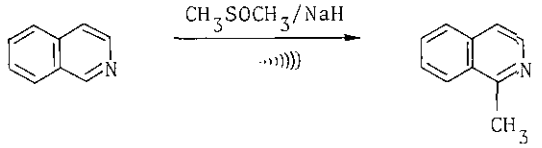


3 4

R = $PhCH_2$, o-$ClC_6H_4CH_2$, p-$ClC_6H_4CH_2$, p-$NO_2C_6H_4CH_2$, 2,4-$(NO_2)_2C_6H_3$, $EtOOCCH_2$;
X = Cl, Br; Q^+X^- = $Et_3\overset{+}{N}CH_2PhCl^-$ or $Me_3\overset{+}{N}(n\text{-}C_{16}H_{33})Br^-$

Alkylation with concomitant ultrasonication reduces the time of the reaction from 2 h to 20-25 min, the yield of alkylation products 4 being 50-88%, which is by 10-35% higher than that attained under PTC condition. In the case of compound 3 alkylated with ethyl chloroacetate, a combined use of ultrasound and PTC failed to increase the yield of 4 (R = CH_2COOEt); on the contrary, its yield declined from 45 to 24%. This may be possibly due to saponification of the ester group in these conditions (acceleration of ester bond hydrolysis by aqueous alkali in a two-phase system in response to ultrasonication is reported[18]). As in the case of N-alkylation of indole and carbazole in the absence of a phase-transfer agent, ultrasound does not initiate the reaction of dihydroisoquinoline 3 with benzyl halides in a two-phase (aqueous-organic) system.

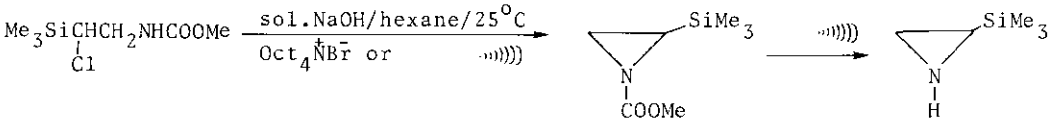
The well-known method[19] for the preparation of 1-methylisoquinoline (5) by reacting isoquinoline with methylsulphinylcarbanion generated by treating dimethyl sulphoxide with sodium hydride has been improved and facilitated by the use of ultrasound[20].



5

Under sonolysis, the reaction occurs in 2 h at room temperature to afford 5 in 72-76% yield. Without ultrasound a similar product yield (65-70%) is attainable only with vigorous stirring for 4 h at 70°C in nitrogen atmosphere[20].

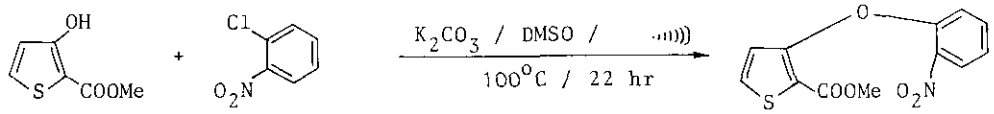
Intramolecular N-alkylation of ß-haloethylamines is one of the common synthetic routes to aziridines. Using this method, methyl N-(2-chloro-2-trimethylsilyl)ethylcarbamate in the two-phase system (hexane/solid NaOH) in the presence of tetraoctylammonium bromide as phase-transfer catalyst served to obtain 1-ethoxycarbonyl-2-trimethylsilylaziridine (6) in 75% yield[21,22]. The formation of 6 without catalyst occurs slowly, whereas upon ultrasonication (55 kHz, 100 W) the reaction rate is



6 7

close to that observed under PTC conditions. However, after reaching a 45% yield the amount of aziridine 6 begins to decline due to consecutive formation of 2-trimethylsilyl-1H-aziridine[22]. As this takes place only under sonolysis, it can be surmised that 1H-aziridine 7 results from ultrasound-induced saponification of the methoxycarbonyl group with subsequent decarboxylation.

Arylation of methyl 3-hydroxythiophene-2-carboxylate by o-chloronitrobenzene under ultrasonication doubles the yield of aryl thienyl ether 8, which without ultrasound amounts only to 17%[23].

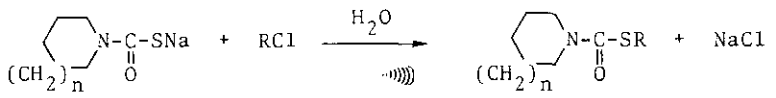


8

Alkylation of tricarbonyl(thiophene)chromium by ethyl bromide in the anhydrous alkali-18-crown-6 system leading to a mixture of 2-ethyl- and 2,5-diethylthiophene $Cr(CO)_3$- complexes can be accelerated by ultrasound[24].

The reaction of thiocarbamic acid salts (9) with halogenated hydrocarbons is one of the methods used for industrial synthesis of thiocarbamic acid esters (10) used in agriculture as herbicides. The reaction of these salts 9 with alkyl chlorides in a two-phase(aqueous-organic)system requires elevated temperature; however, as the salts 9 are thermally unstable, it is not feasible to gain esters 10 in greater than

60% yield. For process intensification, alkylation was performed under ultrasonication (22 kHz)[25,26]. The use of ultrasound allows one to obtain compounds 10 at room

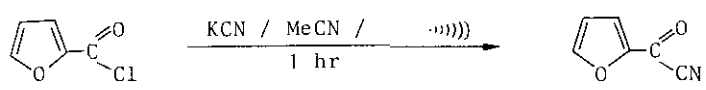


9 10

n = 1,2; R = Pr, Bu, Am, Hex

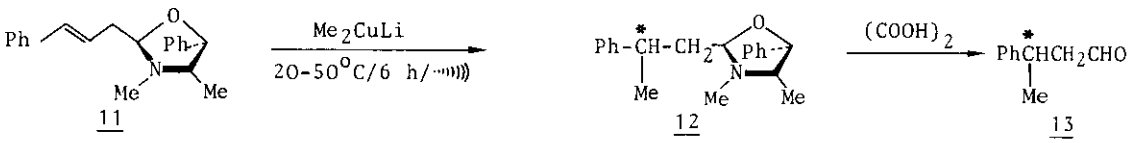
temperature during 10-20 min in 97-99% yield practically without side products. *Conversely*, S-*hexyl*-N-*pentamethylenethiocarbamate* (10, n = 1, R = Hex) obtained by mechanical stirring of the reaction mixture for 3 h at 70°C without ultrasonic irradiation contains 30-33% of products resulting from decomposition of the starting salt (piperidine, resins, etc.). According to kinetic data[25], the rate of reaction between sodium salt of pentamethylenethiocarbamic acid and propyl chloride under sonication is increased by 75-fold. The sodium salt of hexamethylenethiocarbamic acid (9, n = 2) reacts with ethyl chloride in homogeneous medium (ethanol) upon vigorous stirring (70-75°C) for 2.5 h to give S-ethyl-N-hexamethylenethiocarbamate (10, n = 2, R = Et) in 53.5% yield. Under sonolysis, this homogeneous reaction is considerably accelerated, the product yield reaching 98.4% in 20 min. Hence, the substantial gain in the rate of reaction between thiocarbamic acid salts and halogenated hydrocarbons cannot be explained merely by increased interphase area and enhanced mass transfer rate. The mechanism responsible for the accelerating effect of ultrasound under sonolysis remains obscure. It has been proposed that such process intensification may be due to acoustic cavitation. It should be noted that similar effects such as lower reaction temperature, shorter duration of reaction and higher product yield can be attained by synthesizing thiocarbamates 10 under liquid-liquid PTC conditions[27].

A convenient method was proposed for the preparation of aromatic and heterocyclic acyl cyanides by reacting appropriate carboxylic acid chlorides with solid potassium cyanide in acetonitrile accompanied by sonications (55 kHz, 100 W)[28]. 2-Furoyl chloride in such conditions can be rapidly converted to 2-furoyl cyanide in good yield (76%). A classical procedure for the preparation of acyl cyanides from acyl



halides involves the use of heavy metal (Cu, Ag, Tl) cyanides at high temperature, water in small amounts is known[29] to enchance reactions of acyl chlorides (furoyl chloride included) with KCN. However, this method is inconvenient, because one has to determine exactly the optimal amounts of water added, as its excess reduces the yield of acyl cyanides due to hydrolysis and dimerization. Sonochemical synthesis of acyl cyanides does not require the presence of water in the reaction mixture, a high yield of products being reached already at 40-50°C. It has been suggested that ultrasound in the reaction of acyl chlorides with solid KCN, like addition of water, acts by disrupting the crystalline lattice of the inorganic salt[28]. It should be noted that the use of liquid/liquid PTC for the preparation of aroyl cyanides[30] is much less effective than sonolysis.

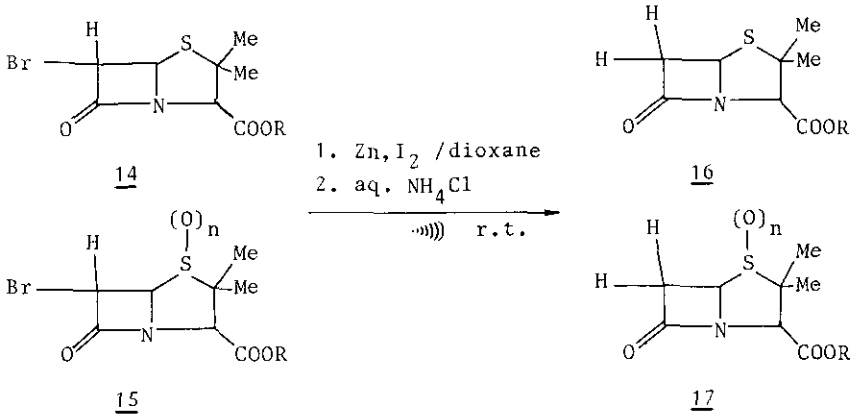
Application of ultrasound permits to perform heterogeneous asymmetric alkylation of chiral 2-alkenyl-1,3-oxazolidines (11) by reacting them with lithium dimethyl cuprate, the two reagents being in solid state. The adduct 12 thus obtained is a precursor of the chiral aldehyde 13 prepared in quantitative yield and having satisfactory optical purity (enantiomeric excess 22%)[31].



11 12 13

2.2. Reduction

The number of publications concerned with ultrasound application in reactions of reduction of heterocyclic compounds is limited, nonetheless the available evidence demonstrates convincingly the high effectiveness of sonolysis in these processes. Reductive debromination of 6-bromopenicillanic acid esters (14, 15) with zinc under ultrasonication affords the corresponding products (16, 17) in 44-71% yield[32]. The reaction proceeds *via* organozinc intermediates, which undergo decomposition in responce to aq.NH_4Cl also under ultrasonication. The method is particularly effective for the preparation of esters 17 containing SO and SO_2 groups. Cleavage of the C-Br bond in esters 15 is generally effected by means of hydrogenolysis in the presence of palladium catalyst or with the aid of Bu_3SnH. The former reaction requires fairly large amounts of the costly catalyst, while in the latter case large amounts of side products are formed. The ultrasonic approach is devoid of these shortcomings, it is convenient, easy to perform and gives esters 17 in 53-72% yield.

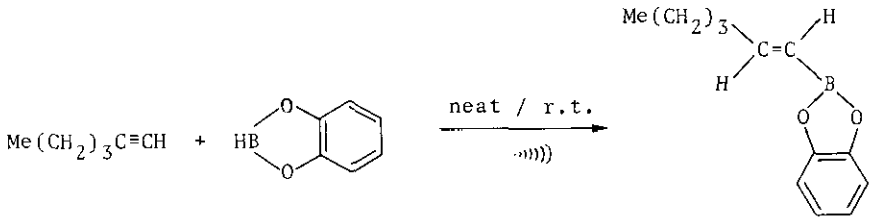


14 16

15 17

R = Me, CH_2Ph, CH_2-CH=CH_2; n = 1,2

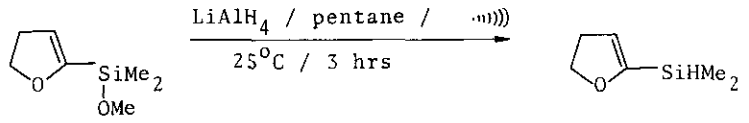
Ultrasonic waves (125 W) accelerate the slowly-occurring reactions of hydroboration[33]. Among the various hydroborating agents, boron-containing heterocycles have been employed for hydroboration under sonolysis conditions. For example, the reaction of hexyne-1 with catecholborane 18 under ultrasonication proceeds for 6 h (96%), while under usual conditions the reaction requires 24 h.



18

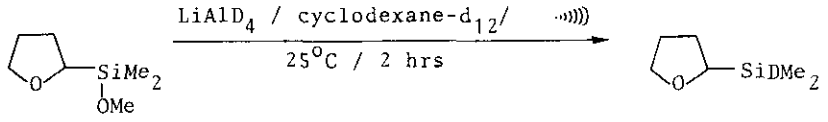
The hydroboration of (+)- or (-)-α-pinene with 9-borabicyclononane allows to obtain quantitatively alpineborane® - a chiral agent for asymmetric reduction of prochiral α,ß-acetylenic ketones and other carbonyl compounds. The reaction proceeds at room temperature and is complete within 1 h , whereas without ultrasound at 25°C it occurs slowly. For hydroboration to occur the reaction mixture must be heated to 65°C for 12 h (in THF) or for 5 h (without solvent)[33].

Ultrasound-induced reduction of halo, alkoxy and amino derivatives containing group IVB elements in nonpolar hydrocarbon solvents has been described[34]. The method can be efficiently used for the preparation of some heterylhydrosilanes. For example, 2-[dimethyl(methoxy)]silyl-4,5-dihydrofuran (19) in the presence of $LiAlH_4$ undergoes quantitative conversion to hydrosilane 20 under ultrasonication (55 kHz, 100 W).



19 20

By using $LiAlD_4$, deuterosilane 22 could be also obtained from silylated tetrahydrofuran 21 in quantitative yield. Reduction with $LiAlH_4$ in nonpolar medium fails to

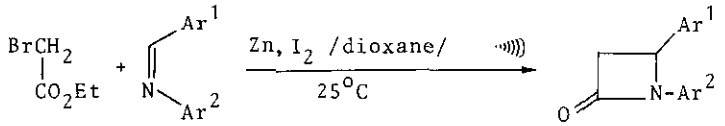


21 22

take place without ultrasound[34]. It is interesting to note, too, that the discovery of heterogeneous reduction in hydrocarbon solvents by lithium aluminium hydride promoted the application of liquid-solid PTC in reactions involving the reduction of various functions by $LiAlH_4$[35,36], which had been earlier believed principally impossible[15].

2.3. Cycloaddition

The common method for the preparation of ß-lactams 24 based on the Reformatsky type reaction involves ethyl bromoacetate reacting with Schiff's base 23 in the presence of zinc and an iodine crystal as catalyst in boiling toluene. The reaction is fairly simple and convenient to perform, but it takes a long time to proceed and the yield of ß-lactams does not exceed 40-50%[37]. Zinc foil used in these reactions instead of



23 24

powdered Zn increased the yield of ß-lactams to 54-70%[38]. By means of ultrasound the yield could be brought up to 70-95% (Table 2) at room temperature with activated zinc used instead of foil[39].

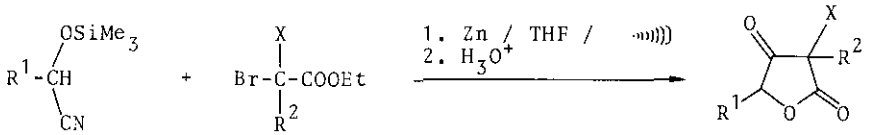
The Reformatsky type reaction serves, as a basis for the sonochemical synthesis (32 kHz) of fluorine containing ß-keto-γ-butyrolactones (27) developed by Kitazume[40].

Table 2

Synthesis of ß-lactams 24 under ultrasonication[39]

Ar^1	Ar^2	Reaction time, h	Yield, %
Ph	Ph	5	70
Ph	C_6H_4OMe-p	5	82
C_6H_4Me-p	C_6H_4OMe-p	4	95
C_6H_4Cl-p	C_6H_4OMe-p	6	77

The reaction has practical importance since compounds 27 are otherwise difficult to prepare.

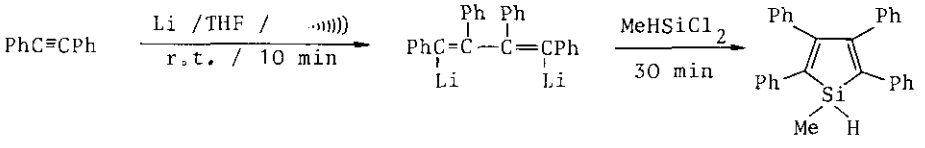


25 26 27

R^1 = Me, Ph; R^2 = H, Me; X = F, CF_3

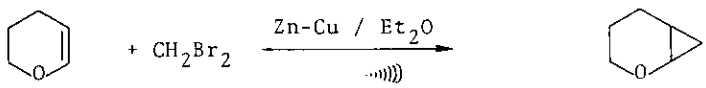
A mixture of O-trimethylsilylated cyanohydrin 25 with ethyl α-fluoro- or trifluoromethyl acetate 26 was sonicated in THF in the presence of zinc. Ketolactones 27 are not formed without ultrasound. Interestingly, the reaction under ultrasonication can be carried out with commercially available Zn powder without prior activation, whereas without ultrasound satisfactory yields can be attained in the Reformatsky reaction only with freshly prepared zinc powder gained by reducing anhydrous $ZnCl_2$ with active metal.

Ultrasound accelerates dramatically the synthesis of 1,4-dilithio-1,2,3,4-tetraphenylbutadiene (28) that reacts with methyldichlorosilane at room temperature to afford 1-methyl-2,3,4,5-tetraphenylsilacyclopentadiene (29)[41]. Organodilithium derivative 28 under ultrasonication is formed in 10 min, whereas without ultrasound stirring for 16 h is required[42].



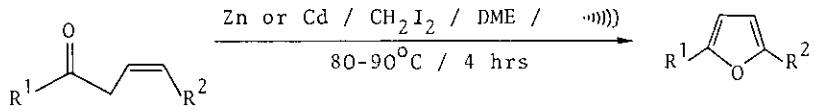
28 29

The effectiveness of sonolysis in the heterogeneous synthesis of heterocycles bearing a cyclopropane moiety can be illustrated by the following reactions. Cyclopropanes in the Simmons-Smith reaction can be synthesized by treating olefins with diiodomethane in the presence of zinc-copper pair (zinc blend and $CuCl_2$ are used for its generation)[43]. Dibromomethane, despite certain advantages as compared to its iodine-containing counterpart (it is cheaper, its purification and storage pose less problems), until recently had almost no practical application due to the low rate of cycloaddition and extremely low yields. By using CH_2Br_2 the Simmons-Smith reaction accompanied by sonication yielded satisfactory results comparable with those gained with CH_2I_2. For heterocycles it can be demonstrated by the synthesis of 2-oxabicyclo[4.1.0]heptane (30) from 5,6-dihydro-4H-pyran. By using ultrasound (125 W) adduct 30 is formed during 3.5 h in 41% yield[43].



30

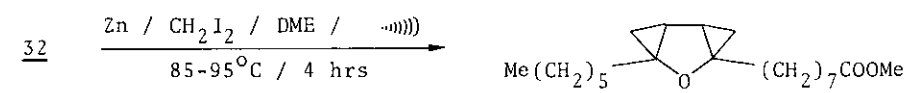
The ultrasound-assisted reaction of keto-ene ester 31 with Zn in the presence of CH_2I_2 and DME as a solvent gives a furan derivative (32) in 46% yield instead of the expected Simmons-Smith cyclopropanation product[44]. When zinc was replaced by cadmium the compound 31 also converted into 32 in *ca.* 10% yield. In the presence of copper the formation of 32 failed to occur.



31 32

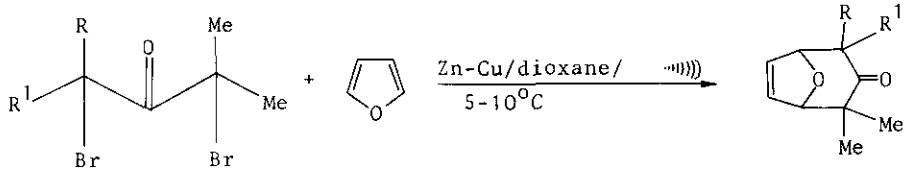
$R^1 = Me(CH_2)_5$; $R^2 = (CH_2)_7COOMe$

Concomitant ultrasonic irradiation during the Simmons-Smith reaction facilitated the cyclopropanation of ethylenic fatty esters and triglycerides[45]. When C_{18} furanoid fatty ester 32 was treated with zinc and diiodomethane in 1,2-dimethoxyethane (DME) under ultrasound (55 kHz, 150 W) a tricycloderivative (33) was obtained in 57% yield.



33

Reductive cycloaddition of α,α'-dibromoketones (34) to furan in the presence of zinc-copper couple under sonolysis lasts for 1-2 h to give 1,4-adducts 35 in ca. 90% yield[46]. Without sonication, continuous stirring (for 24 h) and the presence

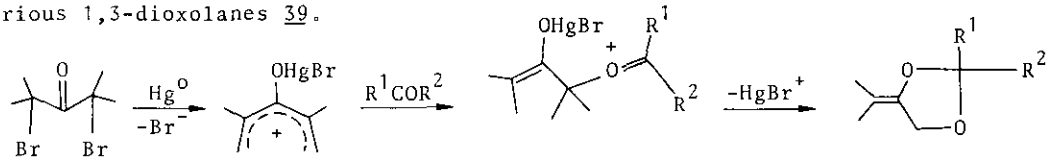


34a,b 35a,b

a) R = R^1 = Me; b) R+R^1 = -$(CH_2)_3$-

of equivalent amounts of Me_3SiCl (apart from Zn/Cu) used as mediator are required for the bicyclic adduct 35a to be formed (the yield is only 60%). Cycloaddition conducted in the presence of $Fe_2(CO)_9$ increased the yield of adduct 35a to 80%, though the reaction rate remained low (38 hrs)[47]. Hence, sonochemical cycloaddition is clearly advantageous.

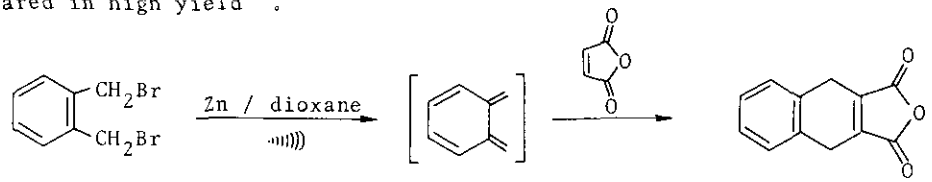
Reduction of 2,4-dibromo-2,4-dimethylpentan-3-one (36) with mercury dispersed in ketones by means of ultrasound (150 W) at 25°C leads to 4-isopropylidene-1,3-dioxolanes 39 [48]. The reaction allegedly involves the nucleophilic attack of the ketone oxygen on the 2-hydroxyallylic intermediate 37 with subsequent decomposition of adduct 38 to dioxolanes 39. Despite its long duration (1-2 days) and low yields of the cyclization products (25-59%) the process offers a simple and easy route to various 1,3-dioxolanes 39.



36 37 38 39

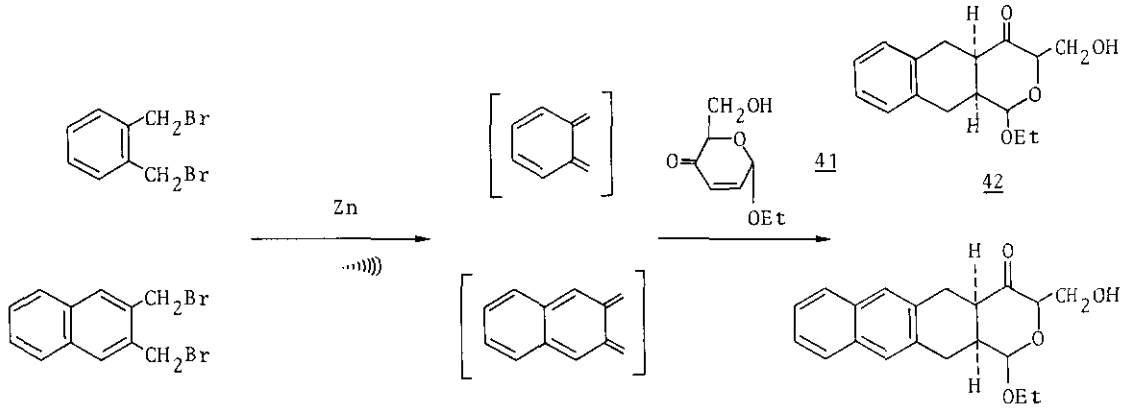
R^1 = Me, Et; R^2 = Me, Et, i-Pr

Ultrasonication of a mixture of zinc and o-bis(bromomethyl)benzene in dioxane yields *o*-xylylene which readily reacts with any dienophile to afford the corresponding adducts in high yields. Using maleic anhydride as dienophile, product 40 has been prepared in high yield[49].

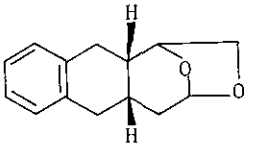


40

An interesting application of ultrasound is the annelation of unsaturated cyclic carbohydrate enone 41 by o-xylylenes[50]. These intermediates are generated from 1,2-bis(bromomethyl)benzene and 2,3-bis(bromomethyl)naphthalene, by treating them with zinc powder under ultrasound (50 kHz). In the presence of enone 41, crystalline tri- and tetracyclic adducts 42 and 43 were gained in 70 and 20-30% yield, respectively; the compounds 42 and 43 can be useful for the preparation of hexahydroanthracene *and -naphthacene derivatives* -analogues of naturally-occurring substances.

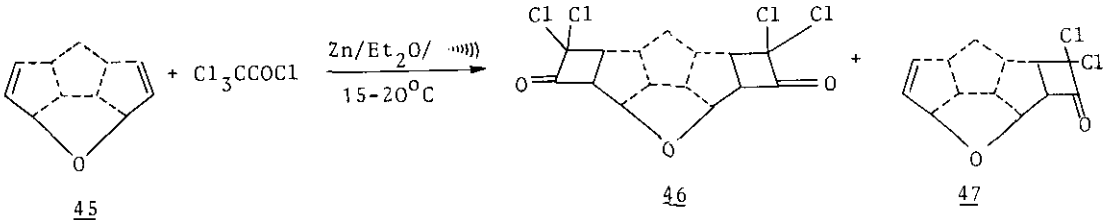


Similarly, the cyclization of o-xylylene with such dienophile as levoglucosenone affords 44 in 53% yield[50].



44

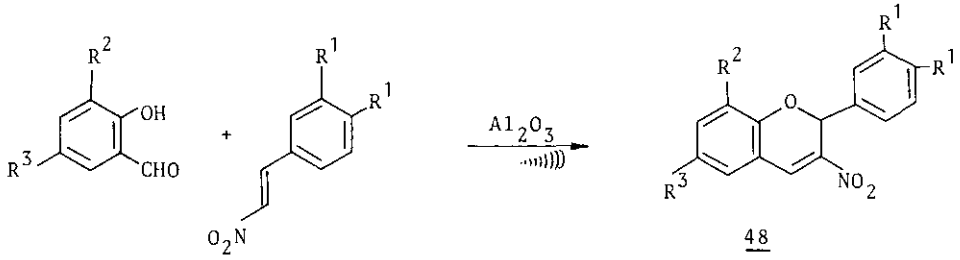
Ultrasonic waves (35 kHz, 100 W) substantially accelerate the [2+2]-cycloaddition of dichloroketene (generated by treating trichloroacetyl chloride with zinc) to olefins[51]. Heterocyclic alkene 45 under these conditions yields diadduct 46 (45%) and



45 46 47

monoadduct 47 (20%) in 0.5 h . The ultrasonic procedure is beneficial in that it makes use of commercially available zinc powder and suppresses the process of dichloroketene polymerization[51]. Without ultrasound the reaction lasts for 16 h and demands the use of activated zinc (Zn/Cu couple)[52].

3-Nitrochromenes (an important class of biologically active oxygen heterocycles) are usually obtained by the condensation of ß-nitrostyrene with o-hydroxybenzaldehydes in pyridine or triethylamine, the reactions being characterized by long duration, modest yields and tedions isolation procedures. Ultrasonication of a mixture of aldehyde and nitroalkene in the presence of basic Al_2O_3 provides rapid and simple preparation of 3-nitro-2H-chromenes 48[53].When the reactants are solid it is necessary to add a minimal amount of diethyl ether or dichloromethane. The products 48

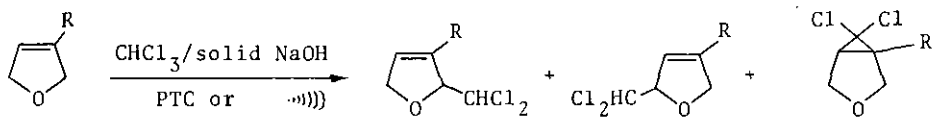


48

R^1 = H, OEt; R^2 = H, OMe; R^3 = H, Cl

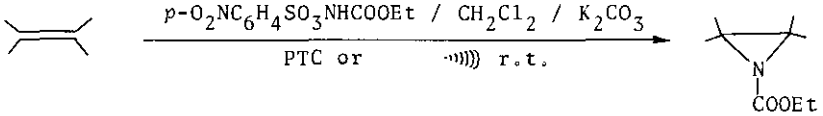
are easily isolated from the reaction mixture in 42-85% yield.

One of the various methods applied for the generation of dichlorocarbene consists in the reaction between solid alkali and chloroform in the presence of phase-transfer catalysts[54]. Without catalyst the dichlorocyclopropanation of alkenes practically fails to occur, however, sonolysis (45 kHz, 35 W) of a mixture of alkene, $CHCl_3$ and solid NaOH leads to dichlorocyclopropane adducts in high yield[55]. In most cases the use of ultrasound instead of phase-transfer agents decreases reaction time and increases the yield of products. This effect, though, can be only attained with small amounts of reagents (< 5 mmole), because of the low power of ultrasound source[54], as demonstrated by the reaction of a 3-substituted 2,5-dihydrofuran (49) with dichlorocarbene in the two-phase system $CHCl_3$/solid NaOH[56]. With 10 mmole of the substrate, sonolysis (55 kHz, 100 W, 40-45°C, 8 h) and PTC (25°C, 5 h) is comparable in efficiency.



49				
R = Me_3Si	PTC:	20%	23%	32%
	·))):	21%	31%	32%

A well-known method for ethoxycarbonylnitrene generation involving base induced α-elimination of p-nitrobenzenesulphonate anion from ethyl N-(p-nitrobenzenesulphonyl)-oxycarbamate treated in a two-phase (aqueous-organic) system[57,58] has been recently applied under liquid/solid PTC conditions for the synthesis of 1-ethoxycarbonyl-aziridines[59]. It was found that without phase-transfer catalyst, continuous ultrasonic irradiation (45 kHz, 200 W) of the system CH_2Cl_2/solid K_2CO_3 containing a nitrene precursor and alkene gives aziridines 50 in very low yield. More powerful irradiation (44 kHz, 2000 W) is nearly as effective as PTC, the reaction rate in the case of sonolysis being decreased from 2-3 h to 15 min.

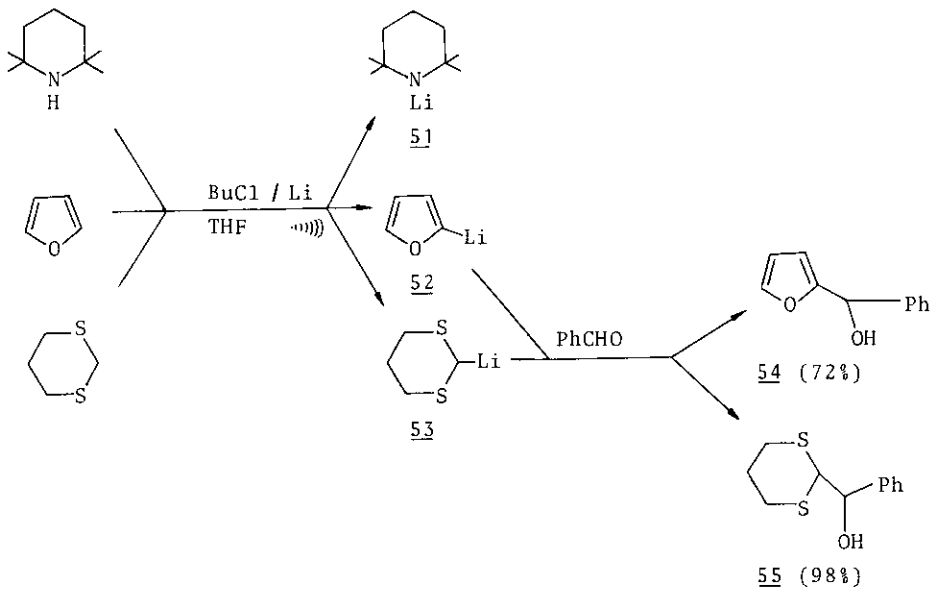


50

 : $Me_2C{=}CMe_2$, $PhCH{=}CH_2$, $Me_3CCH{=}CH_2$, $Me_3SiCH{=}CH_2$, $Et_3SiCH{=}CH_2$, cyclohexene

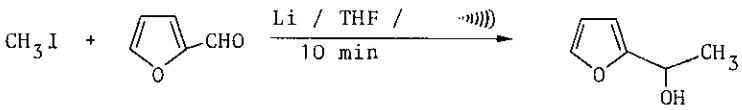
2.4. The Barbier and Bouveault type reactions

Organomagnesium and -lithium compounds have been extensively used in organic synthesis. Anhydrous solvents (ether or THF), inert atmosphere (especially in organolithium syntheses), activating additives (I_2, CH_3I) capable of decreasing the induction period are commonly employed for this purpose. Ultrasound essentially facilitates the preparation of organometallic compounds by increasing the rate of reaction and product yields[7,60]. For instance, lithium derivatives of 2,2,6,6-tetramethylpiperidine, furan and 1,3-dithiane (51-53) are formed in 15-30 min at room temperature under ultrasonication[60]. The synthetic procedure is very simple: a mixture of butyl chloride, lithium (wire or powder containing 2% Na) and a heterocyclic substrate in THF is subjected to ultrasonication until complete lithium dissolution. For comparison, the conventional method for the synthesis of 2-furyllithium involves



a prior preparation of butyllithium, furan addition at -20°C and subsequent boiling of the reaction mixture for 4 h[61]. An efficient approach to ultrasonic organometallic synthesis is to conduct the Barbier reaction under ultrasonication. Heterylithium derivatives 52 and 53 generated under sonolysis react with benzaldehyde to afford the corresponding heterylphenylcarbinols 54 and 55 after hydrolysis.

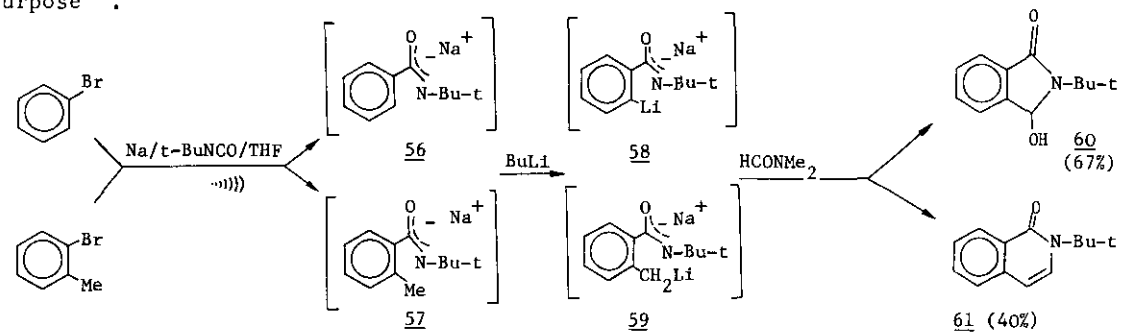
The one-pot Barbier reaction can be performed even in moist crude THF under ultrasonication (50 kHz, 60 W)[7]. Its duration in all cases is less than 1 h , the use of furfural as carbonyl component gives 1-(2-furyl)ethanol in 10 min in quantitative yield:



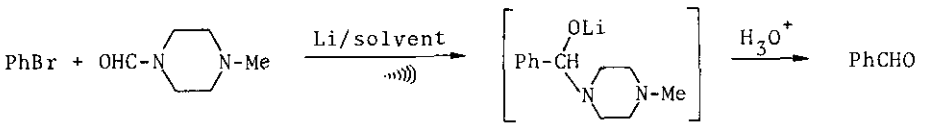
The commonly occurring side reactions such as reduction, enolization, Würtz's reaction are almost eliminated under ultrasonication. The sonochemical Barbier reaction because of its simplicity and effectiveness (it can be conducted with moist solvents at room temperature) holds much promise from the industrial standpoint. Organometallic intermediates 56, 57 are formed from corresponding aryl halides, t-butyl isocyanate and sodium in THF under ultrasonication at room temperature in 30-45 min (instead of 48 h without ultrasound)[62].

The resulting intermediates 56 and 57 can be further metallated with butyllithium to

give bimetallic intermediates 58 and 59, which can be easily trapped by electrophiles. Heterocyclic adducts 60 and 61 were synthesized by using dimethylformamide for this purpose[62].

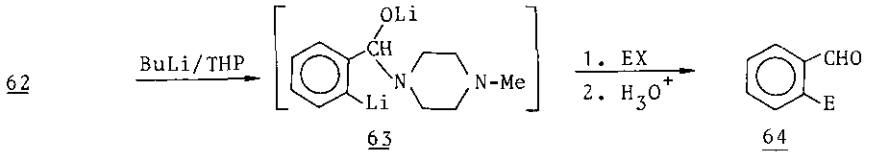


Under ultrasonication aryl halides rapidly and selectively react with lithium and N,N-disubstituted formamides to afford α-aminoalkoxide intermediates, whose acid hydrolysis yields aromatic aldehydes (the Bouveault reaction)[63,64]. Among the formamides used, N-formyl-N'-methylpiperazine was described for the preparation of benzaldehyde from bromobenzene. Ultrasonic waves accelerate the reaction both at the



62

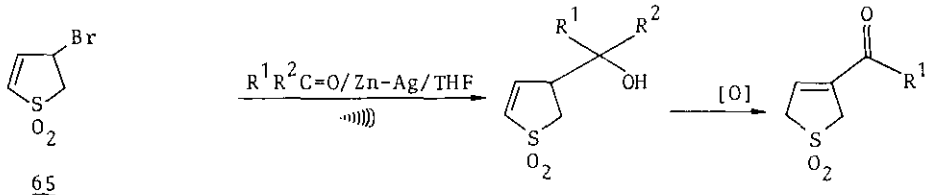
stage of organometallic synthesis and at the stage of intermediate 62 formation. Under ultrasonication (50 kHz) the reaction in tetrahydrofuran and tetrahydropyran proceeds in 10 min to give benzaldehyde in 80 and 75% yield, respectively. Diethyl ether is a less effective solvent for the sonochemical Bouveault reaction: at 50 kHz the reaction fails to occur but at 500 kHz a 77% yield of benzaldehyde is attained in 45 min[63]. Organometallic intermediates of the type 62 easily obtained in the sonochemical Bouveault reaction are extremely attractive from the synthetic standpoint. They undergo metallation readily in the *o*-position to afford bimetallic derivatives 63, which upon reacting with electrophils (methyl iodide, formamide) give aldehydes 64. To facilitate metallation and improve its efficiency an excess of lithium was



63 64

EX = MeI, $OHC-NMe_2$; THP = tetrahydropyran

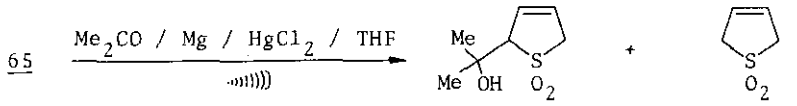
used at the stage of intermediate 63 formation[64] enabling one to apply butyl bromide instead of butyllithium for further metallation *in situ*; under sonolysis the reaction leads to dilithium intermediate 63 in 30 min at room temperature.
Recently, successful use of ultrasound for the regioselective synthesis of 3-acylated 2,5-dihydrothiophene S,S-dioxides (67) *via* ultrasound promoted allylzincation of 3-bromo-2,3-dihydrothiophene S,S-dioxide has been described[65]. The sonication of a mixture of 65, carbonyl compound and Zn-Ag in THF (room temperature, 5 h) gives products 66 *in almost quantitative yields. In the absence of ultrasound* a trace of γ-substituted product 66 was formed along with 2,5-dihydrothiophene S,S-dioxide as the main product.



65 66 67

R^1 = Me, Et, Ph, $[CH_2]_5CH$, $CH_2=CH[CH_2]_2$; R^2 = Me, Ph, H

When magnesium powder was used in place of Zn-Ag in the reaction of 65 and acetone with $HgCl_2$ as initiator, the regiochemistry was completely reversed. No 66 was formed; the α-substituted product 68 (31%), 2,5-dihydrothiophene S,S-oxide and the starting compound were obtained.

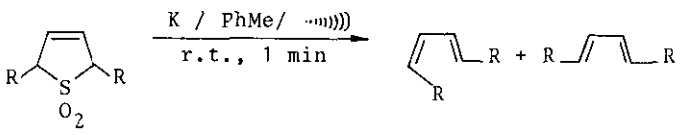


68

Oxidation of compounds 66 (R^2 = H) with pyridinium chlorochromate under mild conditions is accompanied by double bond migration and gives synthetically useful acetyl derivatives 67 in high yield[65].

2.5. Other reactions

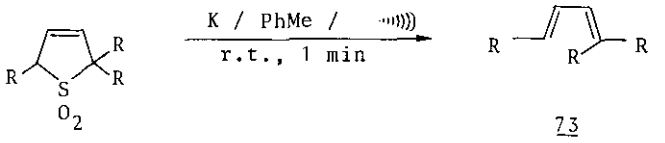
Ultrasonically-dispersed potassium (UDP) obtained by irradiation of metallic potassium in toluene has been successfully applied to accelerate cleavage of the S-C bond in cyclic sulphones[66,67]. In this case, 2,5-dialkyl-3-sulpholenes (69) immediately react with potassium (2.5 equiv.) to give the appropriate conjugated 1,3-dienes (70,71) in almost quantitative yield (92-97%). *Cis*-Dialkylsulpholenes 69 give exclusively



69 70 71

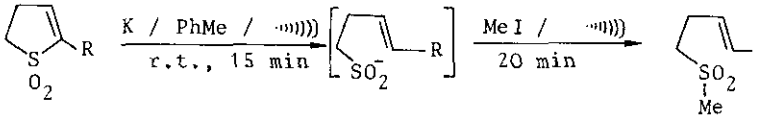
R = n-C_5H_{11}; n-C_6H_{13}, n-C_7H_{15}

(E,E)-dienes 71. In all cases, *trans*-dialkylsulpholenes form a mixture of (E,Z)-dienes 70 and (E,E)-dienes 71 in the ratio 8:1. When the reaction is carried out in nitrogen atmosphere its selectivity is increased and the isomer ratio (E,Z) : (E,E) amounts to 20:1, total yield falls to 80% and the time of reaction is somewhat increased (up to 30 min). Trisubstituted 3-sulpholenes 72 react with potassium to give exclusively *trans*-trisubstituted dienes 73 in 90% yield.



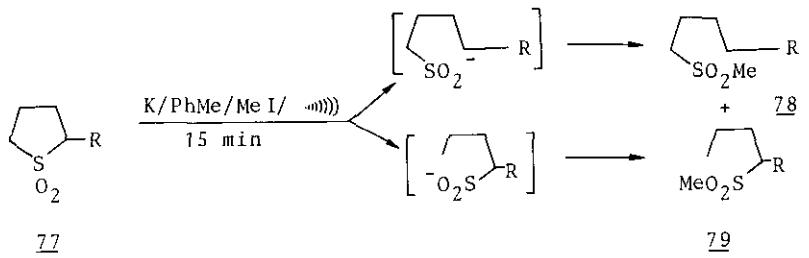
72 73

2,2,5,5-Tetrasubstituted 3-sulpholenes are not subject to cleavage by UDP even at 60°C during 4 h. Consequently, UDP can be used to effectuate SO_2 extrusion from 2,5-di- and 2,2,5-trisubstituted 3-sulpholenes in the presence of 2,2,5,5-tetrasubstituted derivatives. Substituted 2-sulpholenes 74 react in a different fashion. Under ultrasonication, only one S-C bond is cleaved (between the sulphur and the sp_2-hybridized carbon atom) leading to a reactive intermediate (75) characterized by sonochemical reaction with methyl iodide resulting in sulphone 76.



74 75 76

2-Substituted sulpholanes 77 react with potassium and MeI similarly[66]. Reductive cleavage of the C-S bond in sulpholane 77 affects predominantly the carbon atom with a larger number of substituents. For instance, in the case of 2-methylsulpholane 77 (R = Me), sulphone 78 and its isomer 79 are formed in the ratio 10:1. The selectivity of reaction increases for sulpholanes with bulkier substituents, viz. 2-isopro-

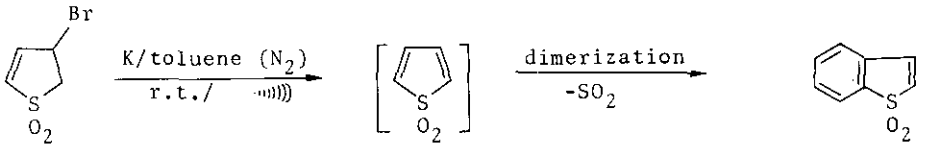


77 79

pyl-, *2-hexyl- and 2-benzylsulpholanes yield practically only one isomer* (stereoisomer purity > 95%).

Ultrasonic irradiation essentially contributes to successful completion of these reactions. The reaction of 2-sulpholene 74 with an excess of finely cut potassium upon mechanical stirring without ultrasound amounts to only 5% yield in 20 h. At the same time, ultrasound *per se* does not cause the extrusion of sulfur dioxide from substituted 3-sulpholenes[67].

The reactions of UDP with 4-bromo-2-sulpholenes resulted in chemoselective deprotonation at the C-5 position leading to the elimination-dimerization products 80 [68].



80

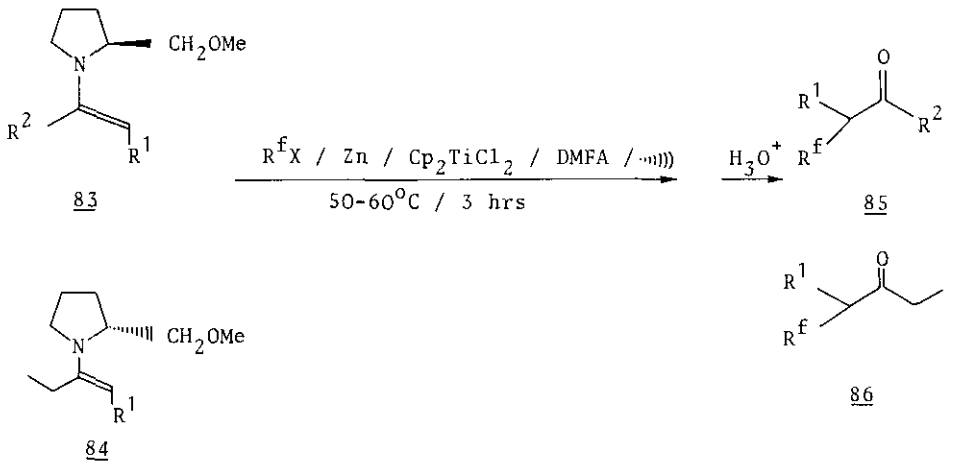
2,3-Dibromo-2-methylsulpholane (81) treated with UDP undergoes conversion exclusively into debrominated product 82 in 85% yield. Dehydrobromination is difficult to perform for 81, since there is no acidic proton adjacent to the bromine atom, and hence C-Br bond cleavage takes place instead of deprotonation[68].

81 82

It must be noted that the reactions of 4-bromo-2-sulpholenes with UDP are substantially accelerated when ultrasonic desintegrator is used instead of the common ultrasound cleaning bath[68].

Kitazume and Ishikawa[69] developed a method for the preparation of fluorine-containing optically active ketones (85,86), which are otherwise difficult to obtain, by

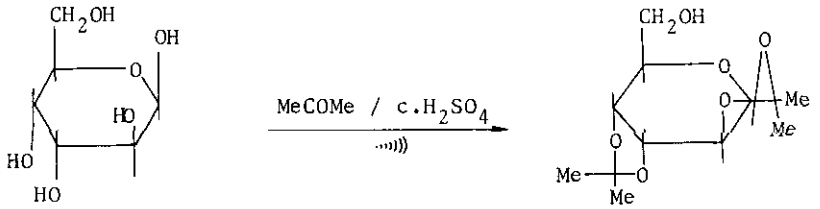
reacting chiral enamines (83,84) derived from (S)-proline with perfluoroalkyl halides in the presence of zinc powder and dichlorobis(π-cyclopentadienyl)titanium (IV) (Cp_2TiCl_2) under ultrasonication (45 kHz, 100 W).



R^1 = Et, cyclohexyl; R^2 = Me; R^fX = CF_3I, CF_3Br, C_2F_5I, C_3F_7I, C_4F_9Br, $C_6F_{13}I$, $C_8F_{17}I$

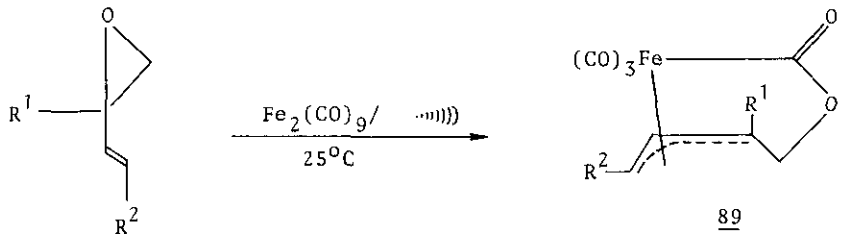
Sonolysis of a mixture of enamine 83 or 84, perfluorohalide R^fX, Cp_2TiCl_2 and Zn powder for 3h affords ketones 85 or 86 in 38-57% yield (optical purity 54-76%)[69]. Thus, ultrasound-promoted perfluoroalkylation enables one to introduce a perfluoroalkyl group with asymmetric induction. The virtual catalyst in the reaction is assumed to be the bis(π-cyclopentadienyl)titanium(II) formed from Cp_2TiCl_2 and Zn during ultrasonication.

Ultrasonic waves (50 kHz) considerably accelerate heterogeneous acetylation of sugars during their interaction with ketones (acetone, cyclohexanone) in the presence of concentrated H_2SO_4 resulting in higher yields of isopropylidene- or cyclohexylydene-protected products[70]. For example, upon mechanical stirring a 70% yield of 1,2,3,4-di-O-isopropylidene-α-D-galactopyranose (87) can be attained in 18 h[70], whereas with ultrasound the process requires 1.25 h[71].



87

New methods have been proposed for the preparation of π-allyltricarbonyliron lactone complexes 88 useful in the synthesis of β-lactones and -lactams serving as *structural constituents of major antibiotics*[72]. One of these methods includes ultra-



88 89

R^1 = H, Me, Ph; R^2 = H, C_6H_{13}, Ph, naphthyl

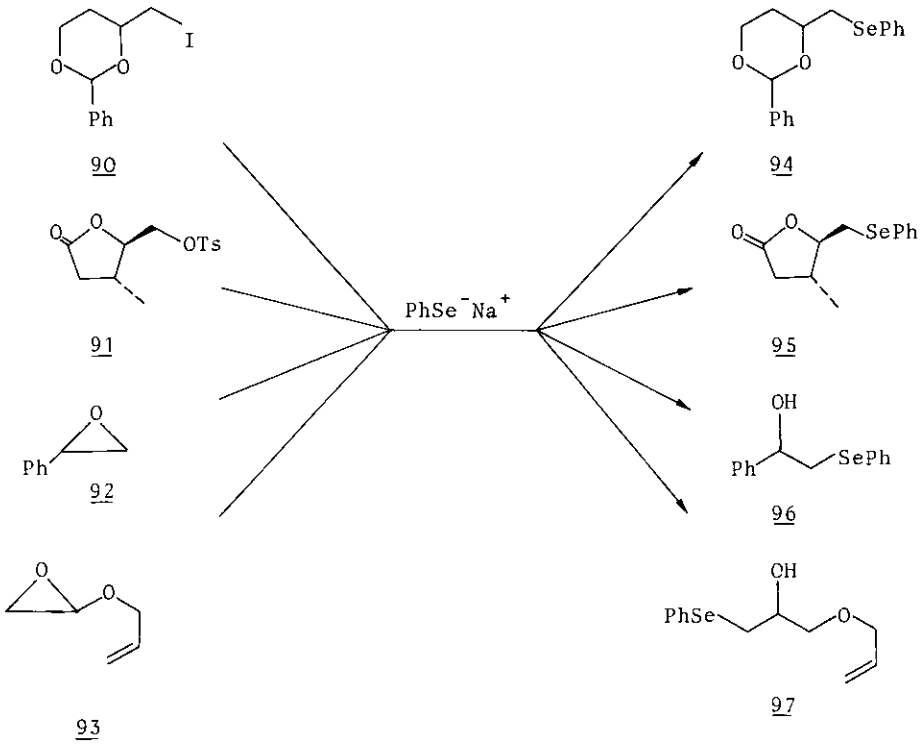
sonic irradiation (50 kHz, 80 W) of an alkylepoxide (88) solution in inert solvent (benzene, ether) in the presence of $Fe_2(CO)_9$. Under sonolysis, this reaction leads to various lactone complexes 89 at room temperature in fairly good yield (50-80%) during 1-5h; without ultrasound, epoxides 88 in these solvents fail to react with $Fe_2(CO)_9$. It should be noted, though, that these reactions occurring in homogeneous conditions (THF) lead to results similar to those gained with ultrasound in benzene (ether)[66]. The described approach to the synthesis of compounds 89 from alkenyloxiranes is more convenient, from the practical standpoint, than other known methods for the preparation of π-allyl(tricarbonyl)lactone complexes with iron (cf. ref . in[72]).

Ultrasound (50 kHz, 80 W) has been applied for acceleration of sodium phenylselenide formation in the reaction of diphenyldiselenide with sodium in THF[73]. Sodium phenyl-

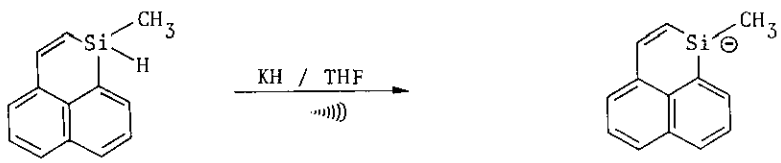
$$PhSeSePh + 2Na \xrightarrow[15\ min]{THF\ /\ \cdot))))} 2PhSe^{\ominus}\ Na^{\oplus}$$

selenide obtained under sonolysis further reacts *in situ* with electrophils including 1,3-dioxane 90, γ-butyrolactone 91, epoxides 92, 93 to give the corresponding phenylselenides 94-97 *in* 78-86% *yield*. The above method is superior to other synthetic pathways to PhSeNa due to the mild conditions used and to ease in operation.

Ultrasound (55 kHz, 150 W) can be successfully applied for the generation of silyl anion 98 from 1-methyl-1-silaphenalene by treating it with potassium hydride in THF[74].

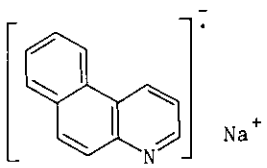


Silyl anion 98 is readily formed at room temperature during 1 h with ultrasound. Ultrasound facilitates the production of isobenzoquinoline radical anion salt of



98

sodium (99). The reaction of isobenzoquinoline with sodium in ether or dimethoxyethane under ultrasonication starts immediatly and is completed in 15 min as compared with 48 h without ultrasound[75].



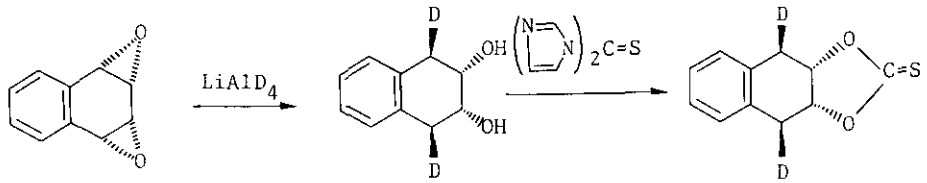
99

Ultrasonic irradiation has been also used to synthesize a stereoselectively deuterated *cis*-1,4-dideuteronaphthalene (101)[76]. Upon ultrasonication for 1 h , thiocar-

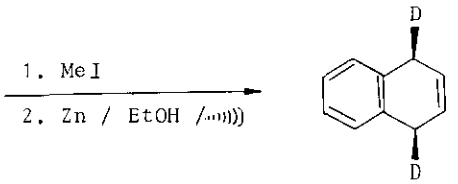
bonate 100 treated first with CH_3I and then *in situ* with activated zinc gives dideuteronaphthalene 101 in 59% yield.

Ultrasonication during the Raney nickel-catalysed hydrogen-deuterium exchange in galactosyl cerebroside and 1-O-methyl-ß-D-galactopyranoside in THF-D_2O permits to introduce the deuterium label under very mild conditions, which enhances the site selectivity of H-D exchange[77].

Ultrasonic irradiation increases the rates of intercalation of organic molecules into various layered solids to give (guest)$_x$host type compounds[78,79]. Sonolysis of a mixture of MoO_3 and pyridine (molar ratio 1:2) in toluene at 80°C for 3 days yields (pyridine)MoO_3. In order to prepare this compound in the absence of ultrasound, heating at 180°C for 30 days is required[79].



100

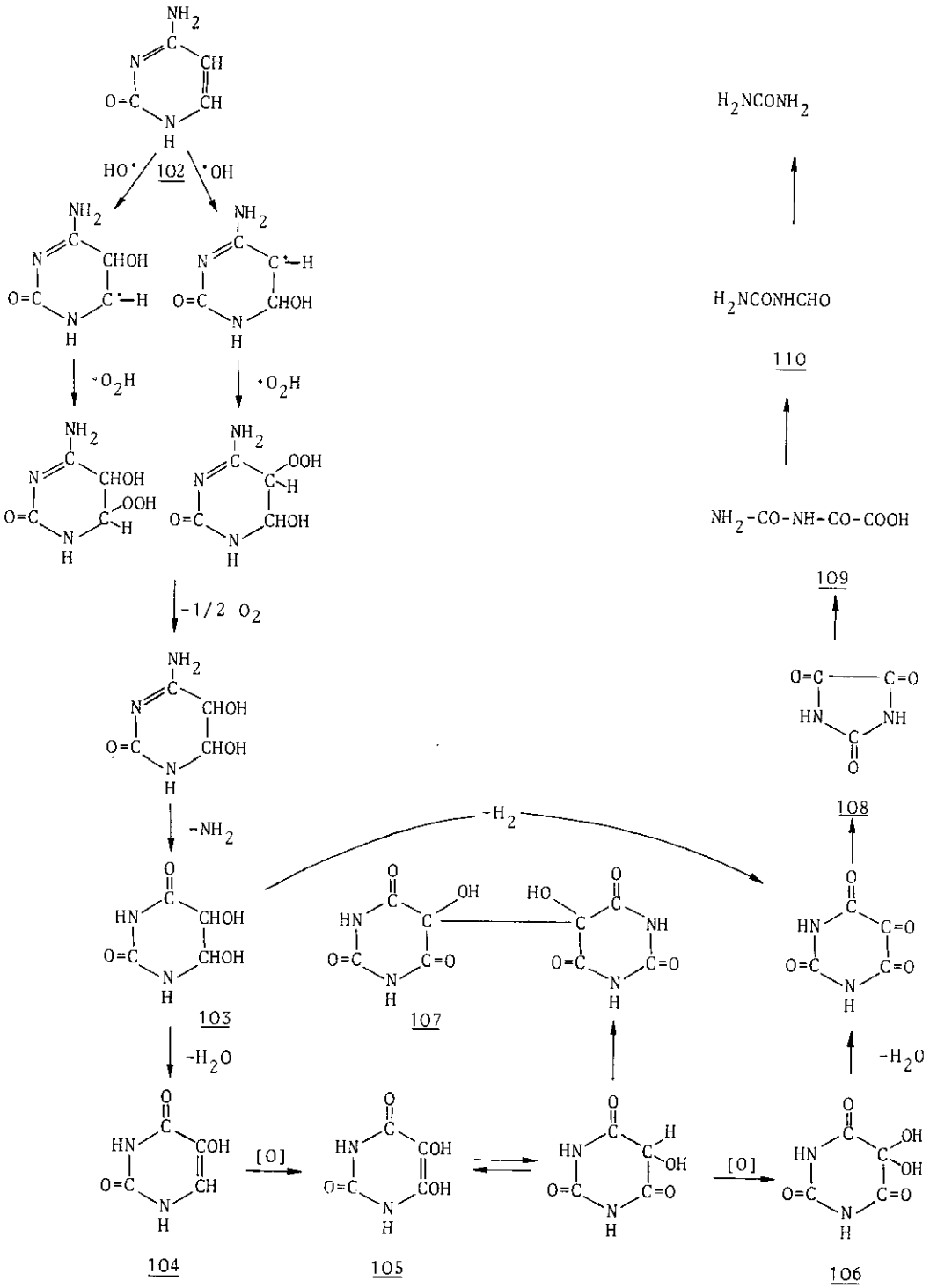


101

3. HOMOGENEOUS SONOCHEMICAL REACTIONS

Several studies deal with ultrasonic reactions of heterocyclic compounds including sonolysis of major naturally occurring pyrimidine and purine bases: uracil, thymine, cytosine, guanine, adenine in the form of nucleosides, nucleotides and nucleic acids[80-85]. As a result of ultrasonication, nucleic acid bases in aqueous solution undergo complex conversions by interacting with sonochemically generated species. Following ultrasonic irradiation (630 kHz) of cytosine (102) aqueous solution for 2 h in the air, 10 products were detected in the reaction mixture by GC-MS: 5,6-dihydroxy-5,6-dihydrouracil (103), isobarbituric acid (104), dialuric acid (105), alloxan monohydrate (106), alloxantin (107), parabanic acid (108), oxaluric acid (109), formylurea (110), urea, and unreacted cytosine (33%)[83]. The suggested mechanism of sonochemical decomposition of cytosine and other bases (Scheme 1) is

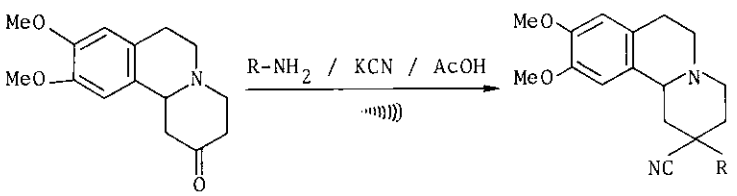
SCHEME 1


HO·
102
·OH
·O2H
·O2H
-1/2 O2
-NH2
-H2
-H2O
[O]
[O]
-H2O
H2NCONH2
H2NCONHCHO
110
NH2-CO-NH-CO-COOH
109
108
103
107
104
105
106

related to the fact that in the presence of air radical and ion species are formed in the course of cavitation: $H^{\cdot} + O_2 \longrightarrow HO_2^{\cdot}$; $\bar{e} + O_2 \longrightarrow O_2^{\cdot-}$. Sonolysis of cytosine solution in nitrogen atmosphere decreases the number of its conversion products to three (compounds 103, 104, 106), the amount of unreacted cytosine reaching 82%. In anaerobic conditions, hydroxyl radicals (the primary products of water decomposition during sonolysis) have been implicated in these processes.The pattern of conversions of uracil[82] and thymine[81,83,84] during sonication in the air is apparently similar to that observed for cytosine. For instance, six out of eight products registered in the reaction mixture during ultrasonic irradiation of aqueous uracil solution in the air are the same as those obtained in the case of cytosine (compounds 103, 104, 105, 106, 108, 109). N-Pyruvyl-N-formylurea, 5-hydroxymethyluracil, *cis*- and *trans*-5,6-dihydroxy-5,6-dihydrothymine and 5-hydroxy-5-methylbarbituric acid were detected following sonolysis of an aqueous solution of thymine[83]. Certain similarity was noted in the action of sonolysis and γ-radiolysis on nucleic acid bases in aqueous medium[83,84].

In order to examine the effects of ultrasound on biological systems its ability to destroy aqueous solutions of various nucleic acid bases was compared at 1 MHz frequency[85]. The reactivity of pyrimidine and purine bases was found to decline in the sequence: thymine > uracil > cytosine > guanine > adenine. The effectiveness of ultrasonic reactions for nucleic acid bases, depending on the medium, tends to increase in the sequence N_2O < He < N_2 < air < O_2 < Ar.

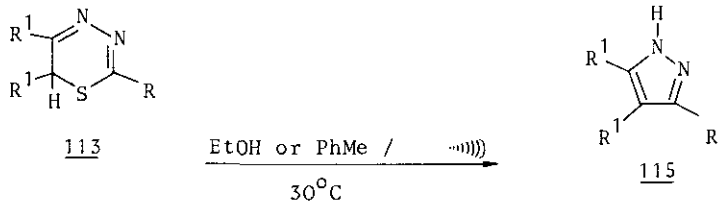
Ultrasound (50-55 kHz, 150 W) was successfully used in the Strecker synthesis of aminonitriles 112 from amino ketones 111. The duration of these homogeneous reactions in an ultrasonic field was reduced from 12-13 days to 20-35 h, the yields being increased by up to 87-100%, as compared with 60-80% for the mechanically stirred systems[86].



111 112

R = H, Bu, Ph, $PhCH_2$, *p*-MeC_6H_4

an interesting case of sonolysis applied for preparative purposes has been reported recently[87]. 6H-1,3,4-Thiadiazines 113 and 6H-1,3,4-selenadiazines 114 in acidic and alkaline media can be converted reasonably easily into pyrazoles, the process being accompanied by various side reactions. Sulphur or selenium elimination in neutral medium is only observed for very unstable 1,3,4-thia- or -selenadiazines upon continuous heating. Under ultrasonic irradiation (25 kHz) in mild conditions, heteradiazines 113, 114 are converted into the corresponding pyrazoles 115 in good yield (80-90%). Without ultrasound several days are required to attain good yields of



113 114 115

R = NH_2, NH-NH_2, NHMe, NHPr-i, NHBu-t, NHPh, NHAc, NMe_2, Ph, CH_2Ph, SMe;
R^1 = Ph

pyrazoles 115 under the same conditions. For example, 2-isopropylamino-5,6-diphenyl-6H-1,3,4-thiadiazine is converted to the corresponding pyrazole during 111 h at 30°C, whereas with ultrasonication the reaction was terminated in 15 h[87].

4. CONCLUSION

Applications of sonolysis in the chemistry of heterocyclic compounds mentioned in the present survey reveal that acceleration of heterogeneous reactions of various type under ultrasonication is a common occurrence. This is an indication that ultrasound may be put to use in a wide rage of processes. An intriguing possibility would be to use sonolysis in lieu of phase-transfer agents in a two-phase system. This would make unnecessary to the separation of products from the catalyst and to catalyst regeneration. However, it should be borne in mind that reaction direction can be altered in response to ultrasound[88,89]. It should be also added that the use of sonolysis sometimes leads to the destruction of both the reactants and the final product[90]. Finally, it can be concluded that heterocyclic sonochemistry, being part

of organic sonochemistry, is gaining popularity as one of routine approaches in organic synthesis.

5. REFERENCES

1. J.P.Lorimer and T.J.Mason, Chem.Soc.Rev., 1987, 16, 239.
2. M.A.Margulis, 'Fundamentals of Sonochemistry', Vysshaya Shkola, Moscow, 1984 (In Russian).
3. K.S.Suslick, Adv.Organomet.Chem., 1986, 25, 73.
4. K.S.Suslick (Ed.), 'Ultrasound: Its Chemical Physical and Biological Effects', VCH Publishers, New York, 1986.
5. M.A.Margulis, Ultrasonics, 1985, 23, 157.
6. M.A.Margulis, 'Sonochemical Reactions and Sonoluminescence', Khimiya, Moscow, 1986 (In Russian).
7. J.L.Luche and J.C.Damiano, J.Am.Chem.Soc., 1980, 102, 7926.
8. P.Boudjouk, Nachr.Chem.Tech.Lab., 1983, 31, 798.
9. Š.Toma and V.Kaliská, Chem.Listy, 1985, 79, 578.
10. P.Boudjouk, J.Chem.Educ., 1986, 63, 427.
11. K.S.Suslick, 'Modern Synthetic Methods', vol.4, Springer Verlag, New York, 1986, pp.1-60.
12. J.Lindley and T.J.Mason, Chem.Soc.Rev., 1987, 16, 275.
13. J.L.Luche, Ultrasonics, 1987, 25, 40.
14. Yu.Goldberg, R.Sturkovich, and E.Lukevics, Appl.Organomet.Chem., 1988 (In Press).
15. E.V.Dehmlow and S.S.Dehmlow, 'Phase Transfer Catalysis', 2nd ed., Verlag Chem., Weinheim, 1983.
16. R.S.Davidson, A.M.Patel, and A.Safdar, Tetrahedron Lett., 1983, 24, 5907.
17. J.Ezquerra and J.Alvarez-Builla, J.Chem.Soc.Chem.Commun., 1984, 54.
18. S.Moon, L.Duchin, and J.V.Cooney, Tetrahedron Lett., 1979, 3917.
19. G.A.Russell and S.A.Weiner, J.Org.Chem., 1966, 31, 248.
20. J.Ezquerra and J.Alvarez-Builla, Org.Prep.Proced.Intern., 1985, 17, 190.
21. E.Lukevics, V.Dirnens, Yu.Goldberg, E.Liepiņš, I.Kalviņš, and M.Shymanska, J.Organomet.Chem., 1984, 268, C29.
22. E.Lukevics, V.Dirnens, Yu.Goldberg, E.Liepiņš, M.Gavars, I.Kalviņš, and M.Shymanska, Organometallics, 1985, 4, 1648.

23. C.Corral, J.Lissavetzky, and A.M.Valdeolmillos, J.Heterocycl.Chem., 1985, 22, 1349.
24. M.N.Nefedova, Yu.I.Liakhovetsky, and Yu.S.Nekrasov, Izv.Akad.Nauk SSSR.Ser. khim., 1987, 1679.
25. R.B.Valitov, R.N.Galiakhmetov, A.K.Kurochkin, and M.A.Margulis, Zh.Fiz.Khim., 1985, 59, 2973.
26. R.N.Galiakhmetov, R.B.Valitov, A.K.Kurochkin, and M.A.Margulis, Zh.Fiz. Khim., 1986, 60, 1024.
27. Wang Chin-Hsien, Synthesis, 1981, 622.
28. T.Ando, T.Kawate, J.Yamawaki, and T.Hanafusa, Synthesis, 1983, 637.
29. M.Tanaka and M.Koyanagi, Synthesis, 1981, 973.
30. E.E.Koenig and W.P.Weber, Tetrahedron Lett., 1974, 2275.
31. J.Berlan, J.Besace, E.Stephen, and P.Cresson, Tetrahedron Lett., 1985, 26, 5765.
32. J.Brennan and F.H.S.Hussain, Synthesis, 1985, 749.
33. H.C.Brown and U.S.Racherla, Tetrahedron Lett., 1985, 26, 2187.
34. E.Lukevics, V.Gevorgyan, and Yu.Goldberg, Tetrahedron Lett., 1984, 25, 1415.
35. V.Gevorgyan and E.Lukevics, J.Chem.Soc.Chem.Commun., 1985, 1234.
36. V.N.Gevorgyan, L.M.Ignatovich, and E.Lukevics, J.Organomet.Chem., 1985, 284, C31.
37. H.Gilman and M.Specter, J.Amer.Chem.Soc., 1943, 65, 2255.
38. S.Mohan, P.S.Sethi, and A.L.Kapoor, J.Indian Chem.Soc., 1971, 48, 685.
39. A.K.Bose, K.Gupta, and M.S.Manhas, J.Chem.Soc.Chem.Commun., 1984, 86.
40. T.Kitazume, Synthesis, 1986, 855.
41. P.Boudjouk, R.Sooriyakumaran, and B.-H.Han, J.Org.Chem., 1986, 51, 2818.
42. F.C.Leavitt, T.A.Manuel, F.Johnson, L.U.Matternas, and D.S.Lehman, J.Am.Chem.Soc., 1960, 82, 5099.
43. E.C.Friedrich, J.M.Domek, and R.Y.Pong, J.Org.Chem., 1985, 50, 4640.
44. M.S.F.Kie Ken Tie and W.L.K.Lam, J.Chem.Soc.Chem.Commun., 1987, 1460.
45. M.S.F.Kie Ken Tie and W.L.K.Lam., J.Amer.Oil Chem.Soc., 1988, 65, 118.
46. N.N.Joshi and M.R.Hoffmann, Tetrahedron Lett., 1986, 27, 687.
47. H.Takaya, S.Makino, Y.Hayakawa, and R.Noyori, J.Am.Chem.Soc., 1978, 100, 1765.
48. A.J.Fry, G.S.Ginsburg, and R.A.Parente, J.Chem.Soc.Chem.Commun., 1978, 1040.
49. B.H.Han and P.Boudjouk, J.Org.Chem., 1982, 47, 751.
50. S.Chew and R.J.Ferrier, J.Chem.Soc.Chem.Commun., 1984, 911.

51. G.Mehta and H.S.P.Rao, Synth.Commun., 1985, 15, 991.
52. G.Mehta and N.S.Nair, J.Chem.Soc.Chem.Commun., 1983, 439.
53. R.S.Varma and G.W.Kabalka, Heterocycles, 1985, 23, 139.
54. S.Julia and A.Ginebreda, Synthesis, 1977, 682.
55. S.L.Regen and A.Singh, J.Org.Chem., 1982, 47, 1587.
56. E.Lukevics, V.Gevorgyan, Yu.Goldberg, A.Gaukhman, M.Gavars, J.Popelis, and M.Shimanska, J.Organomet.Chem., 1984, 265, 237.
57. M.Senō, T.Namba, and H.Kise, J.Org.Chem., 1978, 43, 3345.
58. E.Lukevics, V.Dirnens, Yu.Goldberg, and E.Liepiņš, J.Organomet.Chem., 1986, 316, 249.
59. V.Dirnens, Yu.Goldberg, and E.Lukevics, Dokl.Akad.Nauk SSSR, 1988, 298, 116.
60. J.Einhorn and J.L.Luche, J.Org.Chem., 1987, 52, 4124.
61. V.Ramanathan and R.Levine, J.Org.Chem., 1962, 27, 1216.
62. J.Einhorn and J.L.Luche, Tetrahedron Lett., 1986, 27, 501.
63. J.Einhorn and J.L.Luche, Tetrahedron Lett., 1986, 27, 1791.
64. J.Einhorn and J.L.Luche, Tetrahedron Lett., 1986, 27, 1793.
65. H.-H.Tso, T.Chou, and S.C.Hung, J.Chem.Soc.Chem.Commun., 1987, 1552.
66. T.-S.Chou and M.-L.You, Tetrahedron Lett., 1985, 26, 4495.
67. T.-S.Chou and M.-L.You, J.Org.Chem., 1987, 52, 2224.
68. T.-S.Chou and M.-M.Chen, Heterocycles, 1987, 26, 2829.
69. T.Kitazume and N.Ishikawa, J.Amer.Chem.Soc., 1985, 107, 5186.
70. C.Einhorn and J. L.Luche, Carbohydrate Research, 1986, 155, 258.
71. C.E.Ballow and H.O.L.Fisher, J.Amer.Chem.Soc., 1954, 76, 3188.
72. A.M.Horton, D.M.Hollinshead, and S.V.Ley, Tetrahedron, 1984, 40, 1737.
73. S.V.Ley, I.A.O'Neil, and C.M.R.Low, Tetrahedron, 1986, 42, 5363.
74. R.Sooriyakumaran and P.Boudjouk, J.Organomet.Chem., 1984, 271, 289.
75. W.Slough and A.R.Ubbelhode, J.Chem.Soc., 1957, 918.
76. M.Brock, H.Hintze, and A.Heesing, Chem.Ber., 1986, 119, 3718.
77. E.A.Cioffi and J.H.Prestegard, Tetrahedron Lett., 1986, 27, 415.
78. K.S.Suslick, D.J.Casadonte, M.L.H.Green, and M.E.Thompson, Ultrasonics, 1987, 25, 56.
79. K.Chatakondu, M.L.H.Green, M.E.Thompson, and K.S.Suslick, J.Chem.Soc. Chem.Commun., 1987, 900.
80. I.Ye.El'piner and A.V.Sokol'skaya, Dokl.Akad.Nauk SSSR, 1963, 153, 200.
81. E.L.Mead, R.G.Sutherland, and R.E.Verrall, Canad.J.Chem., 1975, 53, 2394.

82. T.-J.Yu., R.G.Sutherland, and R.E.Verrall, Canad.J.Chem., 1980, 58, 1909.

83. T.-J.Yu., R.G.Sutherland, and R.E.Verrall, Canad.J.Chem., 1987, 65, 1162.

84. K.Makino, H.Wada, T.Takeuchi, and H.Hatano, Nippon Kagaku Kaishi, 1984, 1739.

85. J.R.McKee, C.L.Christman, W.D.O'Brien, and S.Yi Wang, Biochemistry, 1977, 16, 4651.

86. J.C.Menedez, G.G.Trigo, and M.M.Söllhuber, Tetrahedron Lett., 1986, 27, 3285.

87. W.-D.Pfeiffer, E.Bulka, and R.Miethchen, Z.Chem., 1987, 27, 296.

88. T.Ando, S.Sumi, T.Kawate, J.Ichikawa, and T.Hanafusa, J.Chem.Soc. Chem.Commun., 1984, 439.

89. R.Neumann and Y.Sasson, J.Chem.Soc.Chem.Commun., 1985, 616.

90. J.Alvarez-Builla, M.T.Gandasegui, J.L.Novella, S.Otero, and M.G.Quintaniello, J.Chem.Res.(S), 1987, 63.

Received, 21st June, 1988