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STUDIES ON THE OXIDATION OF HYDRAZONES WITH IODINE AND WITH PHENYL-SELENENYL BROMIDE IN THE PRESENCE OF STRONG ORGANIC BASES; AN IMPROVED PROCEDURE FOR THE SYNTHESIS OF VINYL IODIDES AND PHENYL-VINYL SELENIDES

Derek H.R. Barton†, George Bashiardes and Jean-Louis Fourrey

Institut de Chimie des Substances Naturelles, C.N.R.S.
91190 Gif-sur-Yvette, France

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Abstract - *The oxidation of hydrazones by iodine in the presence of strong organic bases (guanidines) has been studied. Improved yields of vinyl iodides can be obtained by inverse addition using dry solvents and with a final heating period where appropriate. The reaction has been extended to various dihydrazones with interesting results.*
In complementary studies hydrazones have been oxidized by phenyl-selenenyl bromide in the presence of strong organic bases to give the corresponding phenyl vinyl selenides in good yield.

Synthesis of Vinyl Iodides

Vinyl iodides are important intermediates in organic synthesis. They are often obtained from acetylenes via hydro- or carbo- metallation and subsequent treatment with iodine of the resulting organometallic compound. This second step occurs in most cases with retention of configuration.

The metal complexes which are the most commonly added to acetylenes are the alanes[1,2,3] (DIBAL, LAH, R_3Al) or boranes[4,5] (e.g. catechol borane), which under the right conditions react with the triple bond stereo- and regio- selectively to give a vinylic derivative of known configuration. Other effective preparations along this line include hydrosilylation[6,7] and hydrostannylation.[8,9,10] The elegant work of J.F. Normant on the 1,2-addition of organo cuprates is particularly noteworthy.[11,12]

As vinyl organometallics obtained by these routes are of little use as vinylic carbanions, they must be transformed into iodoalkenes which are subsequently converted into reactive metallic derivatives. Vinylic complexes of such metals as magnesium, copper, zinc or palladium, which may not be obtained conveniently by direct reduction or reductive alkylation of acetylenes, are used commonly.

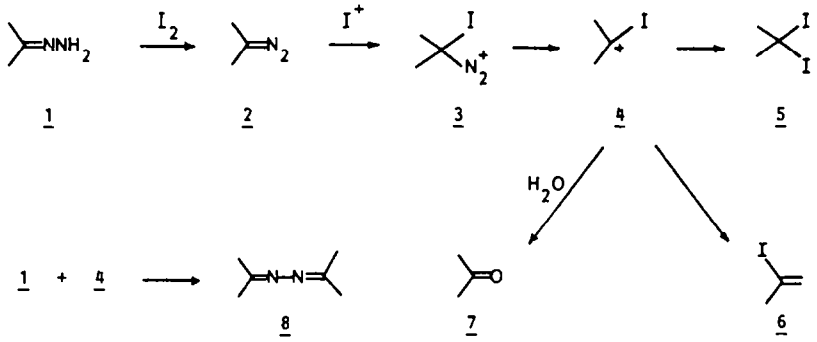
Alternatively, addition of hydrogen iodide to acetylenes as well as iodine addition-elimination to acetylenes have been used to obtain vinyl iodides. In this paper we describe another method of preparation of iodoalkenes starting from simple ketohydrazones which are oxidized at room temperature by iodine in the presence of a hindered guanidine base.[13]

† *Present address: Department of Chemistry, Texas A&M University, College Station, Texas 77843, U.S.A.*

During the determination of the structure of limonin[14] we had need to design a reaction for the conversion of an aldehyde into a methyl under mild conditions. We showed that the hydrazones of aldehydes on oxidation with iodine in the presence of triethylamine gave good yields of gem.-diiodides easily reduced to hydrocarbons.[15] The same reaction when applied to hindered ketone hydrazone afforded vinyl iodides in useful yields, but unhindered ketone hydrazones afforded mixtures of vinyl iodides and geminal diiodides. The scope of this reaction was more extensively studied by Sternhell et al.[16]

In view of the interest given to vinyl iodides in synthesis, we wished to reinvestigate this reaction and optimize the conditions for the preferential or exclusive formation of vinyl iodides.

This study was based on the mechanism originally postulated for this reaction[15] indicated in Scheme 1. It proposes that the hydrazone 1 is oxidized by iodine to the diazo compound 2 which reacts further to give the iodo derivative 3. The latter by loss of nitrogen affords the key iodocarbonium ion 4. Addition of iodide ion gives gem.-diiodides 5 whilst loss of a proton in the case of a hindered substrate 4 gives vinyl iodide 6. The side products, such as ketone 7 and azine 8 are formed as indicated. In order to favour the formation of vinyl iodide 6 we undertook a systematic study of the factors which might determine the outcome of this reaction, notably the nature of the organic base, the type of solvent, the presence of water and/or oxygen, and the type of ketone used.

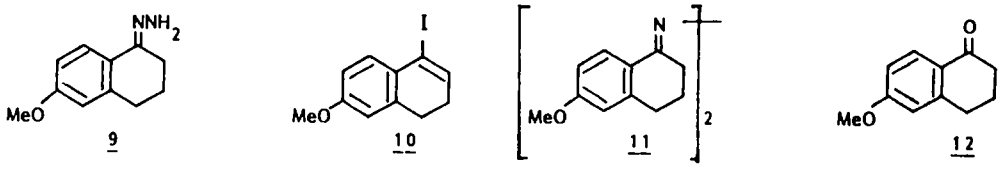


Scheme 1

Role of the Base.

According to the mechanism (Scheme 1) three equivalents of base and two equivalents of iodine are required with respect to hydrazone.

A typical experiment was performed by adding a tetrahydrofuran (THF) solution of iodine (3.2 eq.) to a stirred THF solution of hydrazone (1.5 eq.) and base (5.3 eq.). For this study we used 6-methoxy-α-tetralone hydrazone 9 as a model compound.* It was transformed into 3,4-dihydro-1-iodo-6-methoxynaphtalene 10, the azine 11 and 6-methoxy-α-tetralone 12.



* We thank Professor M.E. Jung (U.C.L.A.) who kindly drewn our attention to two ketone hydrazones 9 and 15 which gave moderate yields of vinyl iodide under standard conditions.

All three compounds are relatively stable and are easily separated by silica gel chromatography. The results obtained[17,18] (Table 1) with different types of base show that strong, hindered guanidine bases, as well as DBN favour the formation of vinyl iodide 10. In the presence of weaker bases the yields in vinyl iodide are lower, while that of azine 11 are considerably increased. These observations support the proposed mechanism (Scheme 1) which involves the reactive iodonium intermediate 4, the β-proton of which being efficiently removed by strong non-nucleophilic bases to give vinyl iodide 6 thus avoiding undesired side reactions.

Table 1. Variation of the Base used in Oxidation of the Hydrazone 9.

Base	Products : Yields (%)[a]	
	Iodoalkene 10	Azine 11
DBN[b]	55	8
Piperidine	35	18
N-methylmorpholine	30	25
n-Butylamine	35	20
Triethylamine	38	20
BTMG[c]	70	15
PPG[d]	78	8

a) The original ketone 12 is also formed.
b) DBN = diaza-1,5-bicyclo[4,3,0]non-5-ene.
c) BTMG = N-t-butyl-N',N',N'',N''-tetramethylguanidine.
d) PPG = Pentaisopropylguanidine.

Choice of the Solvent.

The same reaction in the presence of t-butyltetramethylguanidine (BTMG) was performed using six different solvents. As shown in Table 2 the best yields of vinyl iodide 10 are obtained when toluene, THF or ether are used. However the two side products 11 and 12 are still produced. In the case of DMF and DMSO, ketone 12 is the major reaction product. According to the mechanism (Scheme 1), ketone 7 arises from the hydrolysis of the cationic intermediate 4. It could also arise in the case of DMF and DMSO by nucleophilic oxygen attack of the solvent on 4. When the reaction was performed in THF solution in the presence of increased proportions of water, the yield of ketone reached 21% in a solution of THF: water (9:1) (Table 3). The reaction should, therefore, be carried out in a dry, non-nucleophilic solvent.

Table 2. Variation of the Solvent Used.

Solvent	Products : Yields (%)		
	Iodoalkene 10	Azine 11	Ketone 12
Ether	78	8	10
THF[a]	70	15	10
Toluene	68	15	12
Acetonitrile	42	28	15
DMF[b]	45	8	40
DMSO[c]	12	15	65

a) : THF = tetrahydrofuran; b) : DMF = N,N-dimethylformamide;
c) : DMSO = dimethylsulfoxide.
Conditions : BTMG (3.5 eq.) ; I_2 (2.5 eq.) ; 20°C ; 0.5 h.

The formation of ketone was not enhanced when oxygen was bubbled through the reaction medium. Hence it is not necessary to run the reaction under an inert atmosphere.

Inverse Addition.

Azine 8 is another unwanted product in this reaction. It is formed by reaction between an intermediate such as 4 and excess unreacted hydrazone 1, still present in the medium. To avoid its formation, a solution of hydrazone was added slowly to a solution of base and iodine. By using this procedure in the case of 6-methoxy-α-tetralone hydrazone 9 we obtained the corresponding iodoalkene 10 almost exclusively.

Scope of the Reaction.

Since we had now optimized the conditions for the preparation of vinyl iodides, we proceeded to apply the reaction to hydrazones of various types of carbonyl compounds (Table 4).

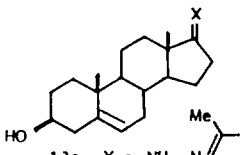
Table 3. Effect of Water

H_2O in THF (%)	Products : Yield (%) Iodoalkene 10	Ketone 12
1	87	traces
2.3	86	7.4
6	80.4	11
10.5	70	21

Conditions : BTMG (3.5 eq.) ; THF ; I_2 (2.5 eq.) ; 20°C ; 0.5 h.

As indicated above, the less hindered hydrazones led to inseparable mixtures of vinyl iodides and gem.-diiodides. In the case of isobutyraldehyde hydrazone 16 the latter is formed exclusively (70%).

Increasing the concentration of guanidine leads to a slight increase in the yield of iodoalkene indicating that the gem.-diiodides are stable under the conditions of the reaction. However, by simply removing the solvent at the end of the reaction and heating the residue at 80-90°C hydrogen iodide elimination does occur. In this manner vinyl iodides are obtained in yields ranging from 70 to 90% (Table 4).

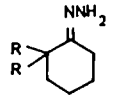


13a X = NH_2-N , H

13b X = β-C I=CH_2, H

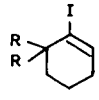
13c X = NNH_2

13d X = O



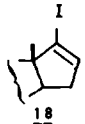
14 R = H

15 R = CH_3



19 R = H

20 R = CH_3



18

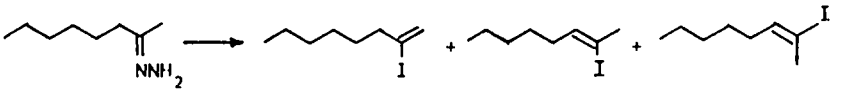
16

Table 4.

Hydrazone		Time (h)	Products (%)
Androstenone	13c	2	18 (95)
Cyclohexanone	14	0.5	19 (91)
Dimethylcyclohexanone	15	0.5	20 (88)
Octan-2-one	17	5	21 (27) ; 22 (8) ; 23 (27)
Pregnenolone[a)]	13a	0.25	13b (81)

a) This experiment was carried out in toluene using normal addition.

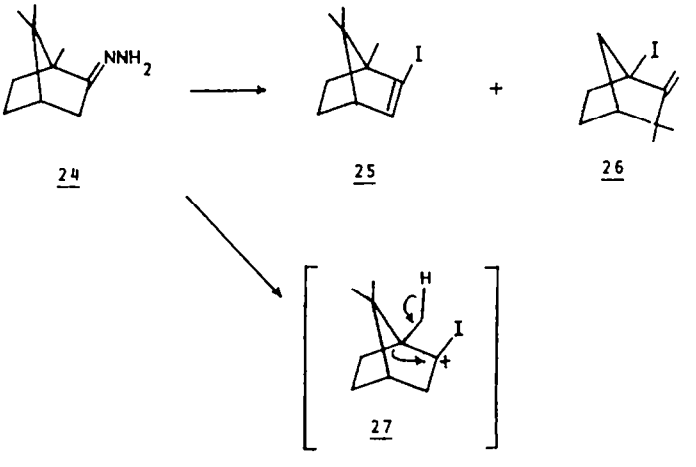
In some cases, such as octane-2-one hydrazone 17 where the three vinyl iodides 21, 22 and 23 are obtained, the regio- and stereoselectivity of the reaction is poor (Scheme 2).



17 21 22 23

Scheme 2

One interesting example is that of camphor hydrazone 24 (Scheme 3) which leads to a mixture of unrearranged 2-iodobornene 25 and of 1-iodocamphene 26, the latter being formed in small amount via Wagner-Merwein rearrangement of the proposed iodocarbonium intermediate 27. In the presence of a strong guanidine base, the lifetime of this intermediate is considerably shortened. This contrasts with triethylamine[16] in the presence of which the rearranged compound 26 is the major product. Such iodocarbonium rearrangements have also been reported by others.[18]

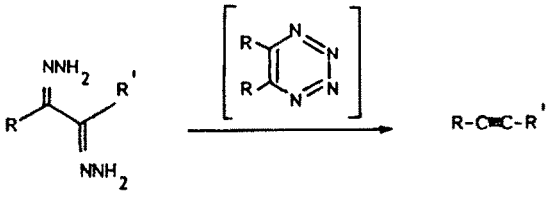


24 25 26 27

Scheme 3

Hydrazones of Dicarbonyl Compounds (and Derivatives) :
1,2-Dihydrazones.

The oxidation of 1,2-dihydrazones have been often reported in the literature to give alkynes.[19,20]. We wished to apply our mild procedure as an alternative way to obtain such compounds in good yield. The intermediate in this reaction is probably a bis-diazoalkane which may undergo cyclization with subsequent loss of two molecules of nitrogen (Scheme 4).

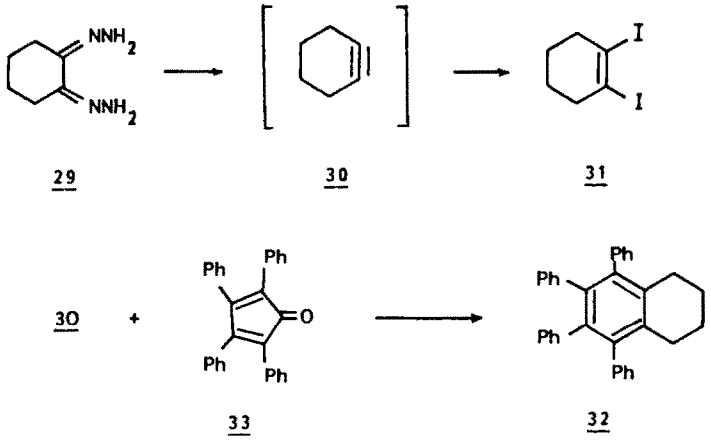


28a R = R' = C_6H_5

28b R = C_6H_5, R' = CH_3

Scheme 4

An interesting case is that of cyclohexane-1,2-dione dihydrazone 29 (Scheme 5) which gave 1,2-diiodocyclohexene 31. We suggest that the oxidation of the α-dihydrazone leads to cyclohexyne 30 which adds iodine which is present in excess in the medium.



Scheme 5

To confirm this hypothesis, we prepared 5,6,7,8-tetrahydro-1,2,3,4-tetraphenylnaphtalene 32 in 80% isolated yield by performing the reaction in the presence of 2,3,4,5-tetraphenylcyclopentadienone 33.[21] The Diels-Alder adduct 34 formed between 33 and cyclohexyne 30 eliminates carbon monoxide to afford 32.[22]

Other Hydrazones of Various Diketone Derivatives.

Benzil monohydrazone 35, which does not possess β-hydrogen, and 1,3-indanedione dihydrazone 36, which has only one α-methylene group, were oxidized to diazo compounds 37[23]

and 38, respectively. The diazo-functions in 37 and 38 are stabilized by charge distribution and do not react further. These observations support the mechanism proposed in Scheme 1.

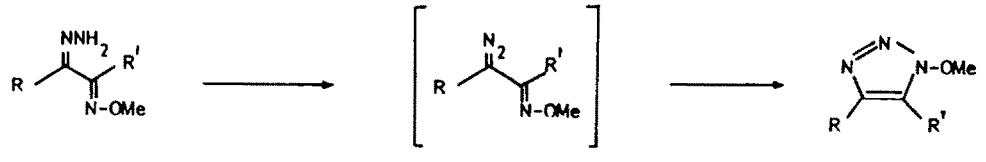
35 37

36 38

Oxidation of α-methyloximinohydrazones 39a and 39b gave the 4,5-dialkyl-N-1-methoxy-1,2,3-triazoles 41a and 41b, respectively in excellent yield. Such a preparation of these compounds compares favourably with previous methods.[24] The most probable intermediate is a α-diazomethyloxime 40 which cyclizes spontaneously to the N-1-methoxy-1,2,3-triazole 41.

The dihydrazone of 5,5-dimethyl-1,3-cyclohexanedione (dimedone) 42 is oxidized to 1,3-diiodo-5,5-dimethyl-1,3-cyclohexadiene 43. The corresponding 1,4-diene isomer was not observed suggesting that conjugation in 43 stabilizes the molecule.

Finally, using the conditions we have recommended throughout this work, 1,4-cyclohexadione dihydrazone 44 gave a mixture of the two 1,4-diiododienes 45 and 46 in a ratio which depends on the reaction conditions. In a previous report a complex mixture of saturated and unsaturated polyiodides had been obtained.[25]

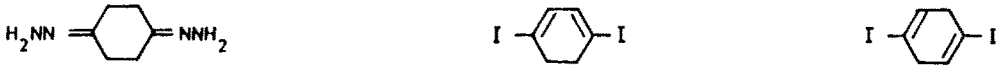


39a R = C_6H_5, R' = CH_3

39b R = CH_3, R' = C_5H_{11}

40 41a,b

42 43

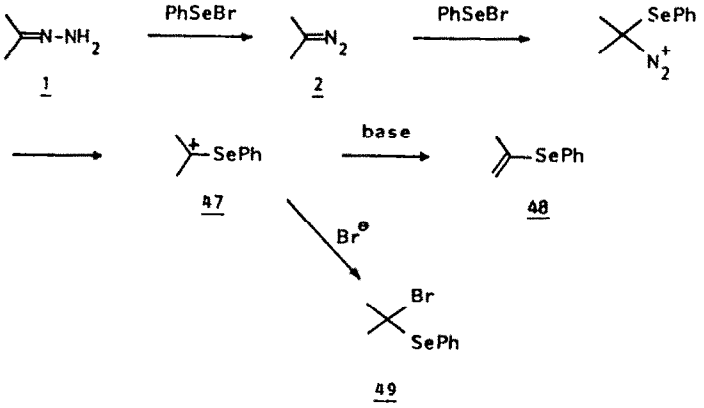


44 45 46

Synthesis of Phenyl Vinyl Selenides

Vinyl selenides and their derived selenoxides and selenones can undergo a wide variety of reactions.[26] In view of their synthetic utility it is still necessary to develop new useful methods for the preparation of vinyl selenides.

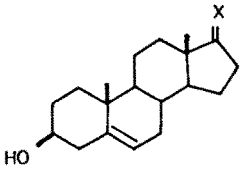
It occurred to us that the chemistry which led to vinyl iodides in high yield from ketones via their hydrazones could be extended to the preparation of vinyl selenides.[27] Here again the mechanism (Scheme 6) involves the in situ formation of a diazoalkane 2 by the oxidation of a ketohydrazone using phenylselenenyl bromide (PhSeBr) and a strong guanidine base N-t-butyl-N',N',N",N"-tetramethylguanidine (BTMG). The unstable diazo compound 2 leads to the cationic intermediate 47 which eliminates a proton in the presence of the base to give the vinyl selenide 48.



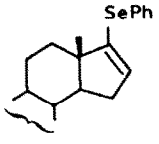
1 2 47 48 49

Scheme 6

The experimental procedure consists in the simple addition of a solution of hydrazone and BTMG to a solution of PhSeBr. In this manner we were able to synthesize a number of phenyl vinyl selenides in excellent overall yields from the corresponding ketones after the usual work up of the reaction mixture (Table 5).



13c (X = NNH_2)



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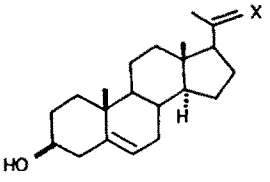
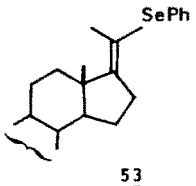


13a (X = NNH_2)



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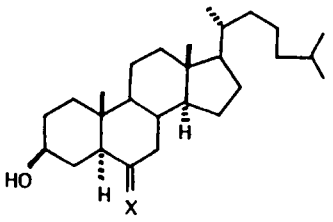
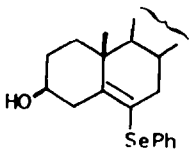


52 (X = NNH_2)



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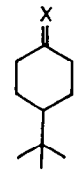

56 (X = NNH_2)

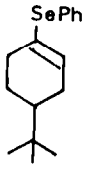

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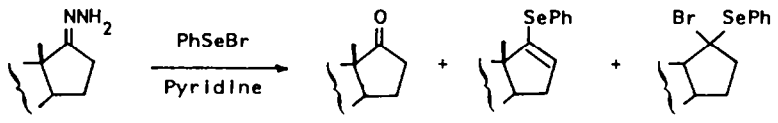
Table 5. Preparation of Phenylvinylselenides

Hydrazone (eq.)	BTMG (eq.)	PhSeBr (eq.)	Product Yield (%)
13c	5	9	50 (90)
13a	5	10	53 (83)
52	5	12	54 (87)
56	6	10	57 (71)

Although, according to the mechanism, only two equivalents of PhSeBr are required, we found that it was necessary to use at least nine equivalents and to prepare PhSeBr in situ from diphenyldiselenide and bromine. Use of less than nine equivalents in a reaction performed on hydrazone 13c led to a mixture of vinylselenide 50 and starting ketone 13d (Table 6). The use of pyridine as base, even in a very large excess resulted in the formation of three products ketone 13d, vinyl selenide 50 and the gem-disubstituted product 51 (Scheme 7).



13c 13d 50 51

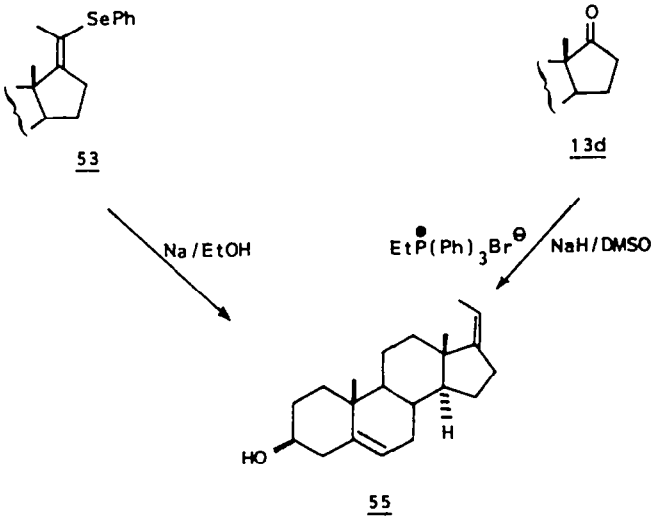
Scheme 7

Table 6.

Hydrazone	Base (eq.)	PhSeBr (eq.)	Products (Yield %)
13c	BTMG (6)	6	50 (56), 13d (20)
13c	Pyridine (100)	12	50 (20), 13d (45), 51 (8)

The mechanism (Scheme 6) indicates that the kev cationic intermediate 47 can lead to vinyl selenide by proton abstraction or to the gem-disubstituted compound 49 by the nucleophilic attack of bromide ions. The use of a guanidine base strongly favours proton abstraction (rendered acidic by the α-selenium function)[28] to the exclusion of other side reactions. In the presence of a weaker base, abstraction and nucleophilic attack become competitive reactions and so both products 48 and 49 are formed. The importance of a strong hindered guanidine base in this reaction must therefore be underlined here. It is not very likely that the gem-disubstituted product 51 leads to vinyl selenide 50 by elimination of HBr under our experimental conditions. The formation of ketone 13d is probably due to the hydrolysis of 51 on acidic work up of the reaction.

Pregnelonone hydrazone 13a and cholestan-6-one hydrazone 52 were transformed selectively to the vinyl compounds 53 and 54, respectively. Compound 53 was formed as a single isomer with the configuration probably as indicated. The structure was confirmed by reduction with sodium and ethanol to a mixture of stereoisomeric olefins, one component of which 55 was compared with an authentic sample, prepared by the Wittig condensation of ethyltriphenylphosphonium ylide on androstenone 13d[29] (Scheme 8).



53 13d 55

Scheme 8

The formation of the $\Delta^{17,18}$ double bond in 53 contrasts with the result obtained above during the analogous reaction which provided vinyl iodide 13b where the $\Delta^{20,21}$ derivative was formed exclusively. The smaller steric repulsion to the hindered base (BTMG) created by the selenium atom (in the key intermediate 47) on the approach towards the acidic proton could account for the differences in these two cases.

In conclusion, we have described an efficient method for the preparation of vinyl iodides and phenyl vinyl selenides from ketones. Thus, oxidation of ketohydrazones with iodine or phenylselenenyl bromide in the presence of guanidine bases leads to the desired compounds in high yield under mild reaction conditions.

In the case of iodine oxidation, application of the method to various hydrazones of dicarbonyl derivatives provides different types of product, depending on the starting compound, such as alkynes, diazoketones, 1-methoxy-1,2,3-triazoles and diiododienes. The formation of these derivatives is illustrative of the reaction mechanism which proposed a diazoakane subsequently transformed into a reactive iodo-carbonium ion as key intermediates in this oxidation reaction.

Experimental

Melting points were determined with a Reichert hot-block microscope and are uncorrected. Optical rotations were recorded in chloroform solution on a Perkin Elmer 241 polarimeter. U.v. spectra were obtained in ethanolic solution on a Perkin-Elmer Lambda 5 spectrophotometer. I.r. spectra were recorded in nujol mulls, when solid or neat, when liquid, on a Perkin Elmer 297 spectrometer. ^{1}H n.m.r. spectra were measured on Brucker WP80 (80 MHz) and WP 200 SY (200 MHz) spectrometers using tetramethylsilane as internal standard. ^{13}C n.m.r. spectra were recorded on the WP200 SY instrument operating at 50.30 MHz in the pulsed F.T. mode. Electron impact mass spectra were determined on a AEI MS 50 instrument. Elementary analyses were performed at the Laboratoire de Microanalyses, I.C.S.N. Tetrahydrofuran and ether were distilled prior to use from sodium benzophenone. T.l.c. was performed on Schleicher-Schüll plastic backed silica gel plates (F 1500/LS 254). Column chromatography was effected using Merck Kieselgel (Type 60).

Hydrazone preparations

Hydrazones were prepared by treating ketones with hydrazine hydrate, usually in ethanol, in the presence of triethylamine. After completion of the reaction the solvent was evaporated, the residue was dissolved in ether or dichloromethane and the solution was washed with water to neutrality. Then the organic phase was dried over sodium sulphate, and evaporated to give the desired hydrazone. Solid compounds were crystallized to complete purity.

Oxidation of Hydrazones

Normal addition refers to the procedure whereby a solution of iodine is added dropwise to a stirred solution of a hydrazone and an organic base. Inverse addition corresponds, in the case of a ketohydrazone, to the addition of a solution of the latter to a solution of an organic base and iodine. In the case of hydrazones derived from diketones, a solution of a hydrazone and base is added to a solution of iodine in the appropriate solvent. For mono- and diketohydrazones 2.2 and 4.4 mole equivalents of iodine are used, respectively, using either ether, toluene or dichloromethane as solvent.

The standard work-up procedure consisted in diluting the reaction mixture by adding more solvent and washing successively with aqueous 2N HCl, water (or brine) to neutrality, saturated aqueous sodium sulfite, water (or brine), saturated aqueous bicarbonate and water (or brine). The organic phase was then dried over sodium sulphate, evaporated to give the reaction product which was purified by crystallisation or flash chromatography. In the case of reactions which were run in THF or any water mixible solvent the latter was removed by evaporation and the residue taken up in ether. Then the etheral solution was treated as above.

Pregnenolone Hydrazone 13a

1) Triethylamine.- Oxidation of pregnenolone hydrazone 13a by normal addition of iodine is known[15,30] to give in the presence of triethylamine (60 eq.) 3β-hydroxy-20-iodopregna-5,20-diene 13b in 79% yield, a result which we have confirmed.

2) N-t-Butyl-N',N',N'',N''-tetramethylguanidine (BTMG).- When the known procedure was repeated by replacing triethylamine with BTMG (5 eq.) product 13b was obtained in 81% yield. M.p. 142-144°C (lit.[15], 142-144°C) (EtOH:H_2O); m/z: 422 ($M^{+\cdot}$), 407; $\nu_{max.}$: 3340, 1610 and 1600 cm^{-1}; δ_H: 6.15 (1H, s, H-21), 5.35 (1H, s, H-6), 3.52 (2H, m, H-3, OH), 1.02 (3H, s, Me-19), 0.79 (3H, s, Me-18); δ_C: 140.92, 126.21, 121.31, 111.40, 71.60, 62.49, 56.44, 50.18, 44.00, 42.22, 38.42, 37.26, 36.55, 32.14, 31.75, 31.58, 28.84, 24.03, 20.98, 19.45, 12.88.

6-Methoxy-α-tetralone Hydrazone 9

A toluene solution of 6-methoxy-α-tetralone hydrazone 9 (0.2 g, 1.05 mmole) and BTMG (0.63 g, 3.7 mmole) was treated with iodine by normal addition. Work-up of the reaction mixture and chromatography on a silica gel column using a gradient of ethyl acetate in hexane gave successively 3,4-dihydro-1-iodo-6-methoxynaphthalene 10 (0.205 g, 68%), azine 11 (0.055 g, 15%) and 6-methoxy-α-tetralone 12 (0.022 g, 12%).

After in situ formation of hydrazone.- A solution of 6-methoxy-α-tetralone 12 (0.36 g, 2 mmole) and hydrazine hydrate (5 ml) in ethanol (15 ml) was refluxed for 2.5 hr. After disappearance of the ketone (monitored by t.l.c.) ethanol and hydrazine were removed by azeotropic distillation with toluene (30 ml). To the resulting toluene solution were added BTMG (1.70 g, 10 mmole) and a toluene (10 ml) solution of iodine (1.6 g, 6 mmole). Usual work-up and chromatography provided the iodide 10 (0.370 g, 65%), azine 11 (0.076, 11%) and starting ketone 12 (0.035 g, 10%); 10 m/z: 286 ($M^{+\cdot}$), 159 ; δ_H: 7.20 (1H, d, J = 8 Hz, H-8), 6.42 (3H, m, H-2, H-5, H-7), 5.5 (3H, s, OCH_3), 2.72 (2H, t, 2xH-4), 2.27 (2H, m, 2xH-3).

Oxidation of Hydrazones. Inverse Addition

In this series of experiments 3.5 eq. of guanidine base and 2.2 eq. of iodine were used. The reaction products were isolated as previously indicated.

1-iodo-6-methoxy-3,4-dihydronaphthalene 10

When hydrazone 9 (0.38 g, 2 mmoles) was treated by inverse addition using BTMG, only vinyliodide 10 (0.51 g, 89%) was isolated. By using tetramethylguanidine (TMG) the yield was 87%.

1-Iodocyclohexene

(1) Treatment of cyclohexanone hydrazone 14 (0.15 g, 104 mmole) in ether with an etheral solution of iodine and TMG gave an inseparable mixture of 1-iodocyclohexene 19 and 1,1-diiodocyclohexane. The respective yields determined by ^1H n.m.r. were 45.2 and 27.8%.

(2) In the presence of BTMG 19 and 1,1-diiodocyclohexane were obtained in a ratio of 3.4:1 in a total yield of 75%. Similar results were observed after using 7 eq. of base.

(3) The mixture obtained according to (1) above, and 1.3 g of BTMG (7.5 eq.) was heated at 90°C with stirring for 1 hr. under an inert atmosphere. After the usual work-up 1-iodocyclohexene 19 was isolated in 93% yield.

(4) Direct transformation of 14 into 19.- Hydrazone 14 (0.34 g, 3 mmole) was treated with an etheral solution of BTMG (4.6 g, 27 mmole) and iodine (1.6 g, 6.2 mmole). After 30 min. the solvent was removed by evaporation and the residue heated at 90°C for 1 hr. under an inert atmosphere to give 0.5 g of 1-iodocyclohexene 19 (91%); m/z: 208 ($M^{+\cdot}$), 127; $\nu_{max.}$: 2930, 1620 cm^{-1}; δ_H: 5.91 (1H, m, H-2), 2.14 (2H, m, 2xH-3), 1.73 (2H, m, 2xH-6), 1.31 (4H, m, 2xH-4 + 2xH-5).

6,6-Dimethyl-1-iodocyclohexene 20

(1) Treatment of 2,2-dimethylcyclohexanone hydrazone 15 (0.21 g, 1.5 mmole) with 3.5 eq. of BTMG and iodine gave a mixture (0.32 g) of 6,6-dimethyl-1-iodocyclohexene 20 and 1,1-diiodo-6,6-dimethylcyclohexene in 49 and 29% yields respectively, as determined by ^1H n.m.r.

(2) By repeating this experiment with 11 eq. of BTMG the yields were 54 and 33% respectively.

(3) The mixture obtained in (1) was heated at 90°C for 1 hr. under an inert atmosphere in BTMG (1.3 g, 7.5 mmole, 8 eq.) to give 0.31 g of 6,6-dimethyl-1-iodocyclohexene 20 in 88% overall yield starting from 2,2-dimethylcyclohexanone hydrazone 15.

(4) Direct transformation of 15 into 20.- 2,2-dimethylcyclohexanone hydrazone 15 (0.49 g, 2.8 mmole) was treated under the same conditions as cyclohexanone hydrazone 14 (see above) to give 6,6-dimethyl-1-iodocyclohexene 20 (0.6 g) in 91% yield; m/z: 236 ($M^{+\cdot}$), 221, 127; $\nu_{max.}$: 3010, 1620 cm^{-1}; δ_H: 5.98 (1H, t, $J_{2,3}$ = 4 Hz, H-2), 1.64 (2H, m, 2xH-3), 1.36 (4H, m, 2xH-4 + 2xH-5), 0.70 (6H, s, $2xCH_3$).

2-Iodooctenes

(1) Treatment of 2-octanone hydrazone 17 (0.21 g; 1.5 mmole) in the presence of TMG (0.9 g, 7.5 mmole) under inverse addition conditions as above gave an inseparable mixture of vinyl iodides 23, 22 and 21 in 15:35:50 ratio as indicated by n.m.r. (total yield 53%) and 2,2-diodooctane in 32% yield.

(2) In the presence of BTMG (0.9 g, 5.25 mmole) the same reaction gave the vinyl iodides 23, 22 and 21 (12:30:58) and 2,2-diiodooctane in 67 and 22% respective yields. Using BTMG (3.8 g; 22.5 mmole) these respective yields were 74 and 9%.

3β-Hydroxy-17-iodo-5,16-androstadiene 18

(1) Treatment of the androstenone hydrazone 13c (0.08 g, 0.26 mmole) under inverse addition conditions with tetramethylguanidine and iodine in THF led to a mixture (0.101 g) of 3β-hydroxy-17-iodo-5,16-androstadiene 18 and 17,17-diiodo-3β-hydroxy-5-androstene in 4.6:1 ratio.

(2) The above experiment was repeated twice using BTMG (3.5 and 6 eq.) to give a 3:1 mixture of the above compounds in 91% overall yield.

(3) In the presence of an excess of BTMG (30 eq.) the ratio was 7.1:1 (overall yield 90%).

(4) Direct transformation of 13c into 18.- The androstenone hydrazone 13c (0.1 g, 0.33 mmole) was first treated as above with BTMG (0.39 g, 2.3 mmole) and iodine (0.18 g, 0.7 mmole). After 15 min. the solvent was evaporated and the resulting residue heated at 80°C under an inert atmosphere for 5 hr. Work-up gave 18 (0.13 g) in 95% yield which crystallised in aqueous ethanol; m.p. 173-174°C (lit.[15] 172-174°C) (EtOH/H_2O); m/z: 398 ($M^{+\cdot}$), 383, 365, 127; ν_{max}: 3260, 2910, 1650 cm^{-1}; δ_H: 6.08 (1H, m, H-16), 5.29 (1H, m, H-6), 3.52 (2H, m, H-3 + OH), 1.02 (3H, s, Me-19), 0.73 (3H, s, Me-18).

Diketones Derivatives

(1) Diphenylacetylene.- A solution of benzil dihydrazone 28a (0.24 g, 1 mmole)and BTMG (1.2 g, 7 mmole) in THF (8 ml) was added dropwise to a 0.5 M solution of iodine in THF (10 ml) at room temperature. The usual work-up gave diphenylacetylene (0.175 g) in nearly quantitative yield.

(2) 3-Phenylpropyne.- Similar treatment of the propanedione dihydrazone 28b (0.18 g, 1 mmole) led to 0.11 g of 3-phenylpropyne (95% yield).

(3) 1,2-Diiodo-1-cyclohexene.- A solution of 1,2-cyclohexanedione dihydrazone 29 (0.21 g, 1.5 mmole) and BTMG (1.8 g, 10.5 mmole) in dichloromethane (10 ml) was added to a 7.5 M solution of iodine in dichloromethane (10 ml). Then the solvent was evaporated. To the residue was added BTMG (2.3 ml). The resulting mixture was heated at 90°C for 4 hrs. Usual work-up and silica gel chromatography (elution: hexane/ethyl acetate 95:5) gave 1,2-diiodo-1-cyclohexene 31 (0.175 g) in 35% yield as a colourless liquid; m/z: 334 ($M^{+\cdot}$), 127; ν_{max}: 2900, 1580 cm^{-1}; δ_H: 2.76 (4H, m, 2xH-3 + 2xH-6), 1.74 (4H, m, 2xH-4 + 2xH-5); δ_C: 110 (C-1; C-2). 42.69 (C-3, C-6), 25.17 (C-4, C-5).

(4) 1,2,3,4-Tetraphenyltetralin.- A solution of 1,2-cyclohexanedione dihydrazone 29 (0.14 g, 1 mmole) and BTMG (1.2 g, 7 mmole) in ether (15 ml) was added dropwise to a stirred solution of iodine (1.27 g, 5 mmole) and 2,3,4,5-tetraphenyl-2,4-pentadien-1-one ("cyclone") 33 (0.5 g, 1.3 mmole) in ether (20 ml). Usual work-up and chromatography (hexane:ethyl acetate gradient) gave 1,2,3,4-tetraphenyltetralin 32 (0.36 g) in 82% yield; m.p. 271-273°C (lit.[22] 271-272°C); m/z: 436 ($M^{+\cdot}$), 359 (M - Ph); ν_{max}: 3000, 1580 cm^{-1}; δ_H: 7.34 (s, 10H, aromatic), 6.97 (s, 10H, aromatic), 2.55 (m, 4H, $2xCH_2$), 1.71 (m, 4H, $2xCH_2$).

(5) 1-Diazo-1-phenylacetophenone 37.- A solution of benzil monohydrazone 35 (0.23 g, 1 mmole) and BTMG (1.5 ml, 7 mmole) in THF (8 ml) was added dropwise to a solution of iodine (0.65 g, 2.5 mmole) in THF (15 ml). The usual work-up and chromatography (hexane:ethyl acetate 85:15) gave 1-diazo-1-phenylacetophenone 35 (0.14 g) in 80% yield as a yellow oil[23]; ν_{max}: 2050, 1660, 1590, 1200 cm^{-1}; m/z: 222 ($M^{+\cdot}$), 194 (M - N_2), 77; δ_H: 8.18 and 7.23 (10H, m, 2xPh). Found: C, 75.52; H, 4.67. $C_{14}H_{10}N_2O$ requires: C, 75.68; H, 4.50.

(6) N-1-Methoxy-5-methyl-4-phenyl-1,2,3-triazole 41a.- A solution of the hydrazone of 1-phenyl-1,2-propanedione-2-O-methyloxime 39a (0.19 g, 1 mmole) and BTMG (1.5 ml, 7 mmole) in ether (10 ml) was added dropwise to a 0.25 M iodine solution in ether (10 ml) to give, after work-up, N-1-methoxy-5-methyl-4-phenyl-1,2,3-triazole 41a (0.17 g) in 88% yield as a pale yellow liquid, ν_{max}: 2930, 1600, 1580, 1010 cm^{-1}; m/z: 190 ($M^{+\cdot}$ + 1), 130, 77; δ_H: 7.74 (5H, m, Ph), 4.31 (3H, s, OCH_3); 2.42 (3H, s, CH_3). Found: C, 63.40; H, 5.98. $C_{10}H_{11}N_3$ requires: C, 63.49; H, 5.82.

(7) N-1-Methoxy-5-methyl-4-pentyl-1,2,3-triazole 41b.- The above reaction was performed on the hydrazone of 2,3-octanedione-3-O-methyloxime 39b (0.18 g, 1 mmole) to give N-1-methoxy-5-methyl-4-pentyl-1,2,3-triazole (0.15 g) in 79% yield as an oil, ν_{max} 2950, 1610, 1580 and 1050 cm^{-1}, m/z: 184 ($M^{+\cdot}$ + 1), 124; δ_H: 4.08 (3H, s, OCH_3), 2.87 (2H, m, CH_2), 2.19 (3H, s, CH_3), 1.31 (6H, m, $3xCH_2$), 0.78 (3H, t, CH_3). Found: C, 58.81; H, 9.47. $C_9H_{17}N_3O$ requires C, 59.02; H, 9.29.

(8) 1,3-Diiodo-5,5-dimethyl-1,3-cyclohexadiene 43.- The usual procedure was carried out on dimedone dihydrazone 42 (0.085 g, 0.5 mmole) to give after column chromatography (hexane/ethyl acetate 95:5) 1,3-diiodo-5,5-dimethyl-1,3-cyclohexadiene 43 (0.071 g) in 39% yield as a colourless liquid; ν_{max} 3030, 1460 cm^{-1}; m/z: 360 ($M^{+\cdot}$), 345 ($M-CH_3$); δ_H: 6.83 (m, 1H, H-2), 6.32 (m, 1H, H-4), 2.59 (m, 2H, CH_2), 1.09 (s, 6H, $2xCH_3$).

(9) 3-Diazo-1-iodoindene 38 and 3-iodo-2-indenone.- A solution of 1,3-indanedione dihydrazone 36 (0.17 g, 1 mmole) and BTMG (1.5 ml, 7 mmole) in THF was added to a solution of iodine (1.3 g, 5 mmole) in THF to give after column chromatography (hexane/ethyl acetate 90:10) 3-diazo-1-iodoindene 38 (0.17 g) in 63% yield as an oil; ν_{max} : 3000, 2050, 1590 cm^{-1}; m/z: 268 ($M^{+\cdot}$), 129 ($M-N_2$); δ_H: 6.51 (m, 4H, aromatic), 6.34 (s, 1H, H-2) and 3-iodo-2-indenone (0.025 g) in 10% yield as an oil; ν_{max} : 1700, 1600 cm^{-1}; m/z: 256 ($M^{+\cdot}$), 129 (M-I); δ_H: 6.51 (m, 5H, aromatic + H-2).

1,4-Diiodo-1,3-cyclohexadiene 45 and 1,4-Diiodo-1,4-cyclohexadiene 46

(1) A solution of 1,4-cyclohexanedione dihydrazone 42 (0.14 g, 1 mmole) and TMG (0.88 ml, 7 mmole) in dichloromethane (10 ml) was added dropwise to a stirred solution of iodine (1.3 g, 5 mmole) in the same solvent (15 ml). Normal work-up and column chromatography (hexane/ethyl acetate 95:5) gave 0.23 g of an inseparable mixture (2:1) of 1,4-diiodo-1,3-cyclohexadiene 45 and 1,4-diiodo-1,4-cyclohexadiene 46 (69% total yield).

(2) In the presence of BTMG the 45 to 46 ratio was 3:1 and the total yield 75%.

(3) As above after a reaction in the presence of BTMG (7 eq.) the solvent was evaporated then BTMG was added to the residue and the mixture heated at 80°C under a nitrogen atmosphere for two hours. Normal work-up provided a mixture of 45 and 46 in 4:1 ratio (60% total yield).

General Procedure for Vinylselenides

For all the reactions, phenylselenenyl bromide (PhSeBr) was prepared *in situ* by adding slowly a solution of bromine in THF to a stirred solution of diphenyldiselenide (PhSeSePh) at 10°C. The reaction mixture was then allowed to reach room temperature; after 30 min., a solution of hydrazone and BTMG in THF was then added dropwise. After addition, the solvent was removed *in vacuo*, the residue was taken up in ether and washed successively with aqueous HCl(2N), water, to neutrality, aqueous sodium sulphite (sat.), water, and finally, brine. The organic phase was dried over sodium sulphate, filtered and the solvent removed *in vacuo*. Excess diphenyl diselenide was separated from the products by rapid chromatography on silica (hexane).

3β-Hydroxy-17-phenylselenoandrosta-5,16-diene 50

(1) To a stirred solution of PhSeBr (10 eq., 0.12 ml bromine and 1 g diphenyldiselenide) in THF (20 ml) was added a solution of 3β-hydroxyandrost-5-en-17-one hydrazone 13c (0.15 g, 0.5 mmole) and BTMG (0.43 g, 2.5 mmol) in the same solvent (8 ml). After normal work-up and flash chromatography (hexane/ethyl acetate 75:25) 50 was obtained as white cubic crystals (0.19 g, 90% yield), m.p. 171-173°C; $[\alpha]_D^{24}$ ($CHCl_3$, c 0.1) -86°; ν_{max} : 3350, 1580, 1430 and 1370 cm^{-1}; m/z: 428 ($M^{+\cdot}$), 271 (M - PhSe); λ_{max} (ε): 257 nm (6340). δ_H: 7.35 (5H, m, Ph), 5.60 (1H, m, H-16), 5.25 (1H, t, J = 6 Hz, H-6), 3.45 (1H, m, H-3), 1.00 (3H, s, Me-19), 0.86 (3H, s, Me-18). Found: C, 70.02, H, 7.70. $C_{25}H_{32}OSe$ requires C, 70.26; H, 7.49.

(2) The above reaction was performed in the presence of 6 eq. of PhSeBr (0.70 ml bromine and 0.6 g diphenyldiselenide). After flash chromatography, vinylselenide 50 (0.108 g, 56% yield) and starting ketone 13d (0.08 g, 20% yield) were obtained.

(3) To a stirred solution of PhSeBr (12 eq., 0.03 ml bromine and 0.25 g diphenyldiselenide) in THF (30 ml) was added a solution (10 ml THF) of hydrazone 7 (0.03 g, 0.1 mmole) and pyridine (0.79 g, 10 mmole). Normal treatment gave ketone 13d (13 mg, 45% yield), vinylselenide 50 (8 mg, 20% yield) and 17-bromo-3β-hydroxy-17-selenophenylandrost-5-ene 51 (4 mg, 8% yield), m/z: 508 ($M^{+\cdot}$), 428 (M - Br).

3β-Hydroxy-20-phenylselenopregna-5,17-diene 53

A solution of 3β-hydroxypregn-5-en-20-one hydrazone 13a (0.15 g, 0.45 mmole) and BTMG (0.88 g, 2.3 mmole) in THF (5 ml) was added dropwise to a stirred solution of PhSeBr (9 eq., 0.1 ml bromine and 0.85 g diphenyldiselenide) in the same solvent (20 ml). After normal treatment and chromatography (hexane/ethyl acetate 80:20) pure vinylselenide 53 was obtained as white needles (0.172 g, 83% yield), m.p. 148-150°C; $[\alpha]_D^{24}$ ($CHCl_3$, c 0.1) - 60°; ν_{max} : 3330, 2920, 1580, 1430 cm^{-1}; m/z: 456 ($M^{+\cdot}$), 441 (M - Me), 299 (M - PhSe), 77; λ_{max} (ε): 260 nm (8440); δ_H: 7.31 (5H, m, Ph), 5.35 (1H, m, H-6), 3.45 (1H, m, H-3), 2.05 (3H, s, Me-21), 1.00 and 0.98 (2x3H, 2s, Me-18 and Me-19). Found: C, 71.07, H, 7.74. $C_{27}H_{36}OSe$ requires C, 71.05; H, 7.89.

3β-Hydroxy-6-selenophenylcholest-5-ene 54

A solution of 3β-hydroxycholestan-6-one hydrazone 52 (0.1 g, 0.24 mmole) and BTMG (0.2 g, 1.2 mmole) in THF (10 ml) was added to a stirred solution of PhSeBr (12 eq., 0.075 ml bromine and 0.56 g diphenyldiselenide) in the same solvent (15 ml). Normal work-up and flash chromatography (hexane/ethyl acetate 85:15) gave pure vinylselenide 54 as white needles (0.114 g, 87% yield), m.p. 126-128°C; $[\alpha]_D^{24}$ ($CHCl_3$, c 0.1) -26°; ν_{max}: 3350, 1575, 1470, 1435 cm^{-1}; m/z: 542 ($M^{+\cdot}$), 527 ($M-CH_3$), 77; λ_{max} (ε): 259 nm (8070); δ_H: 7.15 (5H, m, Ph), 3.32 (2H, m, H-3, OH), 0.92 (3H, s, Me-19). Found: C, 72.85; H, 9.18. $C_{33}H_{50}OSe$ requires C, 73.06; H, 9.23.

4-t-Butyl-1-selenophenylcyclohex-1-ene 47

A solution of 4-t-butylcyclohexanone hydrazone 56 (0.08 g, 0.47 mmole) and BTMG (0.41 g, 2.4 mmole) in tetrahydrofuran (10 ml) was added slowly to a stirred solution of PhSeBr (10 eq., 0.13 ml bromine and 1.0 g diphenyldiselenide) in the same solvent (25 ml). Normal work-up and chromatography gave pure vinylselenide 57 as a white liquid (0.095 g, 70% yield); ν_{max}: 1580, 1475, 1440, 1360 cm^{-1}; m/z: 294 ($M^{+\cdot}$); λ_{max} (ε): 255 nm (9250); δ_H: 7.31 (5H, m, Ph), 6.13 (1H, m, H-2), 1.1-2.56 (7H, m, $3xCH_2$-3,5,6 + H-4), 0.81 (9H, s, t-Bu-4). Found: C, 65.52; H, 7.51. $C_{16}H_{22}Se$ requires C, 65.30; H, 7.48.

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