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PALLADIUM CATALYZED C-ALLYLATION OF NITROALKANES

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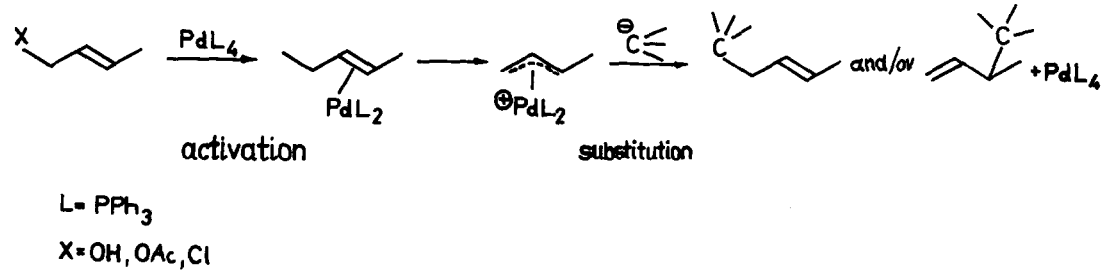
Abstract—A detailed study of palladium catalyzed C-allylation of aliphatic nitro compounds is described. Allylic alcohols and/or their acetates and allyl phenyl ethers were employed as allylating agents. The dependence of the reaction yield on nature and quantity of base and structure of the allylic unit is reported and explained. The lowest yield was obtained for allyl alcohol; however it could be considerably increased by addition of a stoichiometric amount of ethyl acetate. Order of reactivity of functional groups was OPh > OAc > OH. A novel method of synthesis of tetrakis (triphenylphosphine) palladium is also reported.

Palladium-catalyzed allylation of carboanions has proved its usefulness in organic synthesis.[1,2] The mechanism of this reaction has been proposed by Trost *et al.* (Scheme 1).[3]



Scheme 1.

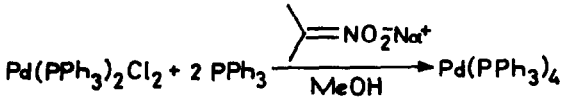
According to these authors the allylation process can be divided into two steps. The first step, formation of cationic π-allyl complex proceeding through π-olefin complex intermediate, has been called the activation step. The second step (substitution step) involves reaction of the π-allyl complex with the carboanion, formation of new C–C bond, and recovery of palladium catalyst.

Palladium (O) and palladium (II) compounds have been employed as catalysts; however in the last case *in situ* reduction of palladium (II) must occur.[11] A variety of allylic derivatives, e.g. acetates,[1-3] phenyl ethers,[4,5] alcohols[6,2e] etc, was reported as effective alkylating reagents. This reaction has been applied with success to alkylation of many carboanions,[1,2] e.g. methylphenylsulphonylacetate, malonates, acetylacetates and nitronates (nitroalkane anion).[2f,3,4] Among a variety of carboanions C-alkylation of alkylnitronates seems to be interesting because the typical alkylation of these species yields almost exclusively unstable O-alkylation products. This prompted us to undertake a detailed investigation of palladium-catalyzed allylation of nitroalkanes.

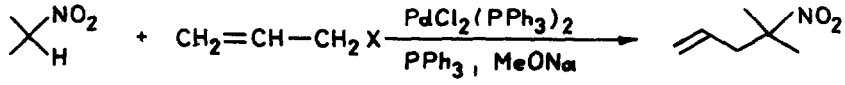
RESULTS

2-nitropropane was used as a model compound for establishing the optimal alkylation conditions using various O-substituted derivatives of allyl alcohol **1a–c** (Scheme 2). The results are collected in Table 1.

Dichlorobis(triphenylphosphine)palladium with two additional equivalents of triphenylphosphine were used as catalyst.[3,4] Smaller quantity of phosphine caused the separation of metallic palladium and the yield of **2** was lower. This suggested an *in situ* generation of tetrakis(triphenylphosphine)palladium. The formation of tetrakis(triphenylphosphine)palladium in reaction carried out according to eqn (1) confirmed this assumption.



(1)



1 2

a) X= OH ; b) X=OAc ; c) X= OPh

Scheme 2.

Table 1.

No	allylating agent	quantity of base %	temp. /°C/	time h	yield of 2 %
1	1a	100/0,05 M/	65	14	36[b]
2	1a[d]	100	65	14	68[b]
3	1b	100	65	14	54[b]
4	1b[d]	100	65	14	66[b]
5	1c	100	65	14	65[b]
6	1a	10	65	14	58[b]
7	1a[d]	25	65	14	62[b]
8	1b	25	65	14	6[c]
9	1c	10	65	17	65[c]
10	1a[d]	100	15	17	12[c]
11	1b	100	15	10	45[c]
12	1c	100	15	10	64[c]
13	1c	25	15	17	65[c]
14	1c	10	15	17	17[c]
15	ac	10	15	78	83[c]
16	1a[d,e,f]	100	65	14	37[b]
17	1a[d,e,g]	100	75	5	33[b]

a - all reactions were carried out using 0,00128 M $PdCl_2/PPh_3/_2$, 0,00256 M PPh_3, 0,05 M 2NP and 0,075 of allylating agent in 50 mL of MeOH with MeONa as a base. b - isolated yield. c - estimated by GLC. d - EtOAc 0,05. e - 2NP sodium salt. f - solvent THF. g - solvent DMF.

The reaction proceeded smoothly thus enabling to avoid the manipulation with rather unstable palladium (0) compounds.

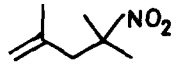
When a stoichiometric amount of sodium methoxide was used at 65° the highest yield of **2** was obtained for phenyl allyl ether, the lower for allyl acetate, and the lowest for allyl alcohol (Table 1, entries 1, 3, 5). However for **1a** and **1b** the yields were increased by *ca.* 32% and 12% respectively by addition of stoichiometric amount of ethyl acetate (Table 1, entries 2, 4). No effect was observed for **1c** allylation. **1a-c** Allylations were also performed at 15°. For this temperature the yield of **2** increased in order (Table 1, entry 10–13) **1a** < **1a**–EtOAc ≪ **1b** < **1c**. The elevated temperature was necessary for alkylation with allyl alcohol-ethyl acetate system.

The yield of allyl acetate alkylation (carried out at 65°) was dramatically reduced by decrease of sodium methoxide quantity to 25 mol% (entry 8). By contrast, for **1a**–EtOAc and **1c** systems the yields of **2** were not affected by the same lowering of methoxide quantity or replacement of this base by sodium acetate (only for **1a**-EtOAc, entries 7, 9). For **1a** itself the yield of **2** was increased to 60% by applying only 10 mol% of sodium methoxide (entry 6).

Alkylations accomplished in methanol gave better results than those performed in THF or DMSO (entries 17, 18), probably owing to low solubility of 2-nitropropane salt in aprotic solvents.

Further allylation experiments were carried out using allylic alcohol–ethyl acetate system and allylic acetates which seem to be easier accessible than the corresponding allyl phenyl ethers.

2-nitropropane was next subjected to alkylation by methallyl alcohol **3**, crotyl alcohol **4**, 2-butenol-3 **5**, *E*-2-pentenol-4 **6**, cinnamyl alcohol **7** and/or their acetates giving the corresponding allyl derivatives of 2-nitropropane **8–11**. Alkylation of 2-NP by 3-methyl-2-butenol-1 failed.



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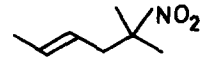

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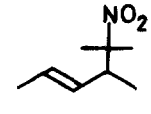

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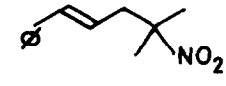


11

Introduction of alkyl or phenyl groups into the allylic part of compound **1a–b** consistently slowed the alkylation rate. The optimal conditions found for **1a–b** generally appeared to be too mild for **3–7**, and yields of **8–11** under these conditions never exceeded 12%. To obtain higher yields it was necessary to increase the temperature above 65° and/or to prolong the reaction time. The results are given in Table 2.

The structure of compounds **8–11** was established on the basis of elemental analyses (except **9**), IR and PMR spectra. The regio- and stereoselectivity observed for

Table 2.

No	allylating agent	solvent	time /h/	temp. /°C/	isolated yield	product	b.p. or m.p.
1	1a[b]	MeOH	14	65	65	2	73/30
2	5a[b]	MeOH	93	60	24		
3	5b	MeOH	66	65	21		
4	4a[b]	SecBuOH	22	85	46	9	88-89/27
5	4b	IsoPrOH	8	75	29		
6	3a[b]	MeOH	48	61	56	8	84-85/29
7	7a[b]	MeOH	27	64	45		
8	7b	MeOH	38	65	35	11	120-128/0,3
9	6a[b]	SecBuOH	38	84	10		
10	6b	MeOH	69	65	31	10	100-102/26

a - All reactions were carried out using 0,00128 M $PdCl_2/PPh_3/_2$, 0,00256 M PPh_3, 0,05 M 2NP and 0,075 M of allylating afent.

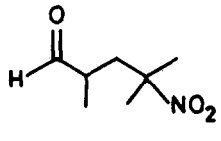
b - 0,05 M EtOAc. C^- main product 85%, E-configuration.

alkylation of 2-NP is similar to that found for other carboanions, i.e. C-reaction centre of ambident 2-NP anion attacks exclusively or almost exclusively the primary carbon of π-allyl unit and double bond has E configuration.[1, 2f, 5, 7]

The lowest selectivity was observed for reactions of 2-NP with **4** and **5** which both gave the same mixture of three alkylation products. The content of the main component **9** was 85% (on GLC). We were not able to separate this mixture and get the correct elemental analyses.

Compounds **8–11** showed in IR spectra weak bands at 16300–1649 cm^{-1} and strong ones at 960–970 cm^{-1}, characteristic for *E* configuration. PMR spectra were helpful in determination of configuration only in the case of compound **11** for which the signals of alkenic protons could be distinguished. The coupling constant between these protons had value of 16 Hz supporting former conclusion.

In reaction of 2-NP with alcohols **3–6** and/or their acetates the formation of side products, nitro-carbonyl compounds **12–14** respectively, was observed.



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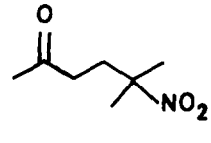

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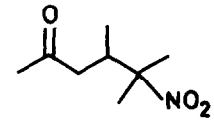

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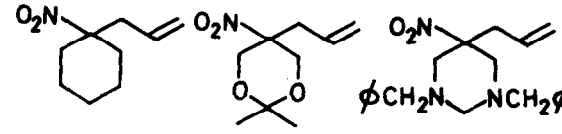
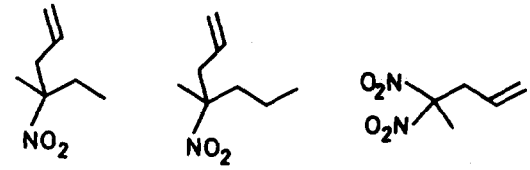
Using the optimal conditions found for reaction of 2-NP with **1a–b** following nitro compounds: nitrocyclohexane **15**, 2,2-dimethyl-5-nitro-1,3-dioxane **16**, 1,3-dibenzyl-5-nitrohexahydropyrimidine **17**, 2-nitrobutane **18**, 2-nitropentane **19**, 1,1-dinitroethane **20**, nitroethane NE and nitromethane NM were treated by **1a**-EtOAc, **1b** or **1c**. The results are collected in Table 3.

The alkylation of **15–17** by **1a**-EtOAc proceeded smoothly giving the corresponding allyl derivatives **21–23** with yields comparable to those obtained for 2-NP.



21 22 23



24 25 26

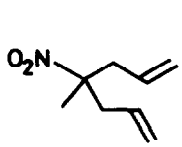
For **18** and **19** the rate of allylation was consistently slowed down and yields of **24** and **25** were low even under more vigorous conditions than for 2-NP. The yield of **24** could be improved by doubling the amount of palladium catalyst. 1,1-Dinitroethane did not react with **1a**-EtOAc system, however the use of **1b** gave **26** with 50% yield.

27 was obtained in 78% yield when an excess of **1a**-EtOAc was used. To obtain **28** it was necessary to employ an excess of allyl phenyl ether. When nitroethane and nitromethane were treated with stoichiometric amount of **1a**-EtOAc or **1c** products of mono- and polyallylation were obtained with low yield. These results were not placed in Table 3, and the problem of mono- and polyallylation will be reported in future.

Table 3.

No	nitro-comp.	allylating agent	temp. /°C/	time /h/	base	solvent	isolated yield	product	b.p.or m.p
1	15	1a-EtOAc	65	14	MeONa	MeOH	68,6%	21	$129\text{-}30/_{25}$
2	16	1a-EtOAc	65	14	MeONa	MeOH	49,0%	22	45
3	17	1a-EtOAc	65	14	MeONa	MeOH	53,4%	23	105-6
4	18	1a-EtOAc	85	5	MeONa	secBuOH	29,2%	24	$84\text{-}85/_{26}$
5	19	1a-EtOAc	65	17	MeONa	MeOH	32,0%	25	90/20
6	20	1b	75	5	MeOK	isoPrOH	50,0%	26	$97\text{-}100/_{22}$
7	NE	1a-EtOAc[d]	65	14	MeONa	MeOH	78,5%	27	$98\text{-}100/_{23}$
8	NM	1c[e]	81	4	NM-sodium salt	isoPrOH	75,0%	28	$100\text{-}2/_{12}$

a - all reactions were carried out using 0,00128 M $PdCl_2/PPh_3/_2$, 0,00256 M PPh_3, 0,05 M of base, 0,075 M of allylating agent and 0,05 M of nitrocompound. b - using double amount of catalyst afforded 24 with the yield of 47% /MeOH, MeONa, 14h, 65°/. c -not optymalizde. d - fivefold excess of 1a.e - threefold excess of 1c.



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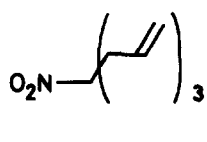


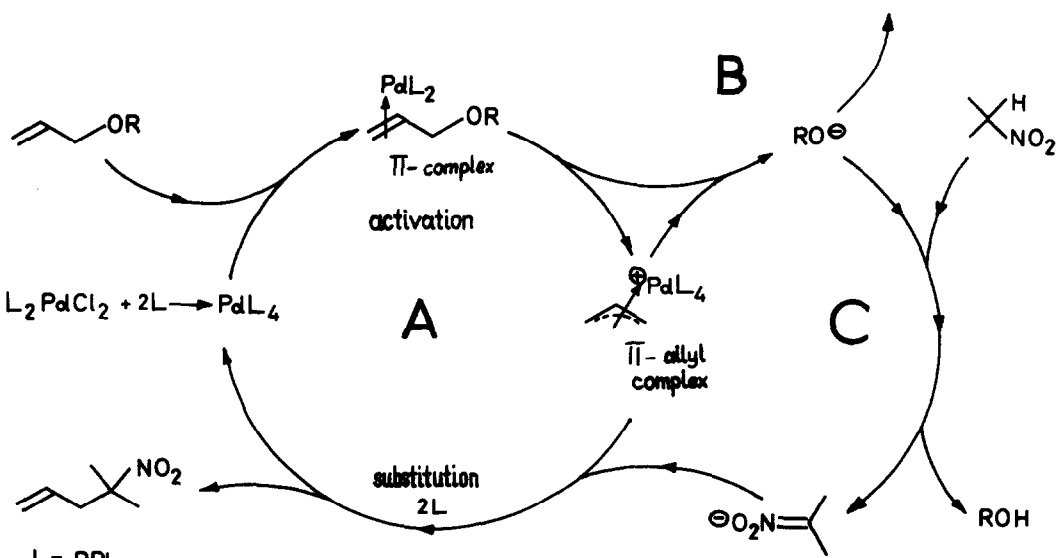
28

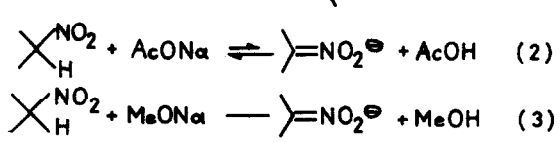
DISCUSSION

The mechanism of palladium-catalysed allylation of nitro-alkanes is presented in Scheme 3.

The loop A shows the contribution of palladium (O) complex in the reaction[1] described at the beginning of this paper.

Our experiments indicate that the results of alkylation depend on the leaving group, the character and amount of the base. This dependence is most sharply exhibited for allyl alcohol alkylations. The reaction products are then the allyl derivative of nitroalkane and hydroxide anion. This anion is a strong nucleophile, so π-allyl complex can competitively react both with OH^- (loop B) and with nitroalkane anion (substitution step). This competition explains the low yield in reaction of **1a** and 2-NP anion. The concept of competitive reactions explains the





Scheme 3.

role of ethyl acetate. The ester acts as hydroxy anion scavenger replacing the strong nucleophile OH^- by the weak one- acetate anion.

Basicity of the leaving anion determines the amount and strength of the base to be applied (loop C and eqns 1 and 2). Two extreme cases should be thus distinguished. Case A in which RO^- anion is a strong base (e.g. OH^-, PhO^-) able to abstract proton from nitroalkane. Case B involves formation of an anion of low basicity (e.g. AcO^-) which is able to abstract a proton from nitroalkane only to a very limited extent (compare Scheme 3, eqn 2). In case A a catalytic quantity of strong base (sodium methoxide) or stoichiometric amount of weak base (sodium acetate) can be used. For **1a** itself it is necessary to use only catalytic quantity of sodium methoxide. In this instance 2-NP plays the role of hydroxyl anion scavenger. By contrast, in case B stoichiometric amount of sodium methoxide must be used. Acetate anion is able to generate some quantity of 2-NP anion (Scheme 3, eqn 2) but formation of acetic acid shifts the equilibrium to the left side, and the alkylation is stopped due to the absence of the anion.

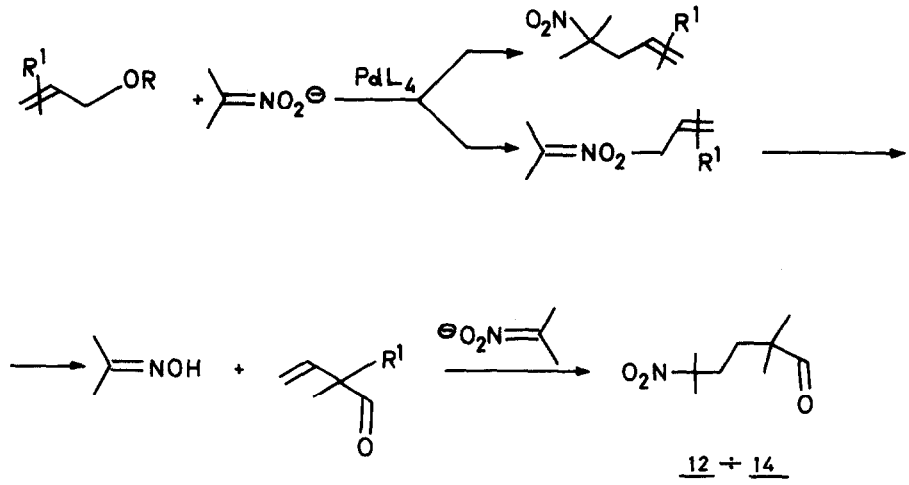
Palladium–catalyzed allylation is a complicated process, and the yield of the product sometimes might not be a good criterion of reactivity (readiness of alkylating reagent to form the π-allyl complex). Chauvin *et al.*[28] found that in the presence of catalytic amounts of sodium phenoxide the yield of allylation of (acylamido) malonate was higher for allyl alcohol than for allyl acetate and chloride, and suggested that the alcohol is more reactive. In the light of present investigations the low yield for allyl acetate and chloride could be due to stopping the substitution step due to the absence of carboanion.

According to our results alcohol **1a** is less reactive than the acetate **1b**. Lowering the temperature from 65° to 15° caused the reduction of yield of **2** only for **1a**-EtOAc system although at 65° all reagents gave **2** with comparable yields. In this case the yield of reaction reflects the reactivity of allylating reagents because only

Table 4.

Compound	R^1	R^7	R^2	R^3	R^4	R^5	R^6	J constant Hz
2	H	H	H	H	H	Me	Me	H_2-$H_{3,4}$= 7,2
	5,22 - 4,99 /m/		5,47 - 5,87 /m/	2,60/d/			1,52 /s/	
8	H	H	Me	H	H	Me	Me	
	4,85 /s/	4,67 /s/	1,69 /s/	2,65/s/			1,57 /s/	
9	CH_3	H	H	H	H	Me	Me	H_2-$H_{3,4}$= 6,7
	1,67 /d/	5,74 - 5,00 /m/		2,50 /d/			1,48 /s/	H_2- H_1 = 5,7
24	H	H	H	H	H[b]	Me	Et	CH_2-CH_3= 7,2
	5,22 - 4,96 /m/		5,87-5,42 /m/	2,68-2,48 /m/		1,51 /s/	2,13-1,59 /CH_2, m/ 0,88 /CH_3, t/	
21	H	H	H	H	H	CH_2-/CH_2/$_3$- CH_2		H_2- $H_{3,4}$= 7,1
	5,16 - 4,92 /m/		5,82-5,37 /m/	2,50 /d/		1,22 - 2,44 /m/		
10[c]	CH_3	H	H	H	Me	Me	Me	H_1 - H_7 = 5,8
	1,66 /d/	5,75 - 5,07 /m/		2,73 /q/	0,95 /d/		1,46 /s/	H_3 - H_4 = 7,0
27	H	H	H	H	H[b]	C_3H_5	CH_3	
	5,23 - 4,99 /m/		5,87-5,45 /m/	2,44-3,02 /m/			1,55 /d/	
22[d]	H	H	H	H	H	-CH_2-O-C-OCH_2		H_2-$H_{3,4}$ = 7,1
	5,27 - 5,03 /m/		5,77-5,39 /m/	2,57 /d/		4,47/H_c, d/ 3,96/H_e, d/		$H_{3e}$$H_{3a}$ = 12,7
28	H	H	H	H	H	C_3H_5	C_3H_5	H_{3-4}-H_7 = 7,2
	4,93 - 5,27 /m/		5,88-5,37 /m/	2,60 /d/				
11	Ph	H	H	H	H	Me	Me	H_2-H_7/E/ = 16,2
	7,37-7,19 /m/	6,51/d/	6,01 /dt/	2,76 /d/		1,59 /s/		H_2- $H_{3,4}$ = 7,1
23[e]	H	H	H	H	H	-CH_2-N-CH_2-N-CH_2-		
	5,54 - 4,86 /m/			2,56 /d/		2,60 - 3,26 /m/		
25	H	H	H	H	H	CH_3	-C-CH_2 NO_2 1,96 - 1,69 /m/ -CH_2-CH_3 1,02 - 0,82 /m/	
	5,17 - 4,94 /m/		5,88-5,38 /m/	2,65-2,48 /m/		1-46 /s/		

a - CCl_4 . b - C-pseudoassimetrical . c- 14 PMR: 2,75-2,46 /-CH m/; 2,34-2,15 /-CH_2-,m/; 2,06 /CH_3-C-, s/; 1,49 /CH_3-C-CH_3,s/; 0,9 /CH_3-C-,d, I = 6,7 Hz/ . d - CH_3 in dioxane 1,42 /s/, 1,38 /s/. e - 3,48/CH_2 benzylic, s/, 09/CH_3-C-,d, I = 6,7 Hz/



Scheme 4.

the rate of the activation step depends on the character of the leaving group, and therefore the reactivity increases along the series **1a** < **1b** < **1c**. At present stage of investigation we are not able to offer any explanation of this phenomenon.

The enlargement of carbon skeleton of allyl unit involves a decrease of the alkylation rate and formation of nitrocarbonyl compounds (**12-14**) takes place.

Introduction of alkyl or aryl substituent into allyl core increases the steric crowding[7c] and electron-donating properties of the double bond (see Ref. 2*c* and Refs. therein). Both these effects make the coordination of palladium (0) complex to double bond difficult slowing down the rate of the activation step and hence the alkylation.

Formation of **12–14** might be interpreted taking into account the competition between C- and O-alkylation (Scheme 4).

O-alkylation produces nitronic ester which is very unstable and decomposes to oxime and α,β-unsaturated ketone and/or aldehyde. These compounds undergo subsequent Michael reaction yielding **12–14**. For **1**, **4**, **5**, **7**, beside of C-allyl derivative of 2-NP and nitro-ketone **13** (for **4** and **5**), the corresponding nitro-aldehyde should be also formed. We did not isolate these compounds but this does not mean that O-alkylation did not occur at primary carbon of π-allyl unit. Nitro-aldehydes seem to be rather unstable, and might undergo to further transformation and/or decomposition in basic medium. Compound **12** which we isolated seems to be more stable to basic medium due to the presence of methyl group in the α position to the carbonyl.

EXPERIMENTAL

General

PMR spectra were taken on Jeol MH 100 as CCl_4 solutions with TMS as internal standard, IR spectra were measured on Perkin–Elmer 577 spectrophotometer. Glc chromatography was performed on Chrom 4 apparatus using 3.5 m × 3 mm SE 52 column at 120–170°.

Allyl, crotyl, cinnamyl and methallyl alcohol, buten-1-ol-3, allyl acetate, triphenylphosphine, nitroethane, nitromethane, 2-nitropropane, 2-nitrobutane, nitrocyclohexane were commercial samples.

Dichlorobis(triphenylphosphine)palladium,[9] tetrakis(triphenlyphosphine)palladium,[10] penten-2-ol-4,[11] phenyl allyl ether,[12] allyl acetates,[13] 1,3-dibenzyl-5-nitrohexahydropyrimidine[14] and 2,2-dimethyl-5-nitrodioxane-1,3[15] were prepared according to the literature methods.

Solvents, allyl alcohols or acetates and nitro compounds were purified using standard methods.[16]

General procedure for allylation of nitro compounds

To 50 ml of methanol and appropriate quantity of base were added 0.05 M of nitro compound, 0.00256 M of triphenylphosphine, 0.00128 M of dichlorobis(triphenylphosphine)palladium. The yellow suspension was heated with stirring to 65°. After short time the reaction mixture turned orange and again yellow. The yellow precipitate was successfully compared with authentic sample of tetrakis(triphenylphosphine)palladium. Then the alkylating agent (0.075M) was added. If the reaction was carried out at 15° the reaction mixture was first cooled to this temperature. The reaction was terminated by pouring the mixture onto 250 ml of water. When phenyl allyl ether was used as allylating agent the mixture was poured onto 10% sodium hydroxide solution. The product was extracted three times with hexane, combined organic layers were washed with water, diluted hydrochloric acid and water, and dried over anhydrous magnesium sulfate. The solvent was removed under reduced pressure, and the residue vacuum distilled or in the case of compounds **16** and **17** crystallized from ethyl ether–hexane.

All compounds, except **9**, gave satisfactory elemental analyses.

Tetrakis(triphenylphosphine)palladium

0.001M of dichlorobis(triphenylphosphine)palladium and 0.002M of triphenylphosphine were suspended in 50 ml of methanol containing 0.002M of 2-nitropropane sodium salt employed as reducing agent. The mixture was heated at 65° for 10 min, cooled, the precipitate was filtered off and washed with methanol. The yield of the product was 80%, m.p. 100–102° with decomposition.

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REFERENCES

[1]For reviews see: B. M. Trost, *Tetrahedron* **33**, 2615 (1977); *Pure Appl. Chem.* **51**, 787 (1979).

[2]For most recent work see [a]B. M. Trost and T. R. Verhouven, *J. Am. Chem. Soc.* **101**, 1595 (1979); [b]B. M. Trost and T. P. Klun, *Ibid.* **101**, 6756 (1979); [c]B. M. Trost and F. W. Gowland, *J. Org. Chem.* **44**, 3448 (1979); [d]B. M. Trost, S. Godleski and J. J. Belletire, *Ibid.* **44**, 2052 (1979); [e]J.-P. Haudegond, Y. Chauvin, D. Commerene, *Ibid.* **44**, 3063 (1979); [f]P. A. Wade, S. D. Morrow, S. A. Hardinger, M. S. Saft and H. R. Hiney, *J. Chem. Soc., Chem. Commun.* 287 (1980).

[3]M. Mitsuyasu and J. Tsuji, *Japan* 7211.408 *Chem. Abstr* **77**, P19163s (1972).
[4]T. Mitsuyasu, J. Tsuji and K. Ohno, *Japan* 7211.201 *Chem. Abstr.* **77**, P19165u (1972).
[5]K. Takahashi, A. Miyake and G. Hata, *Bull. Soc. Chim. Japan* **45**, 230 (1972).
[6]K. E. Atkins, W. E. Walker and R. M. Manyik, *Tetrahedron Letters* 3821 (1970).
[7a]B. M. Trost and T. R. Verhoeven, *J. Am. Chem. Soc.* **98**, 630 (1976); [b]B. M. Trost and T. R. Verhoeven, *J. Org. Chem.* **41**, 3215 (1976); [c]B. M. Trost and T. R. Verhoeven, *J. Am. Chem. Soc.* **100**, 3435 (1978); [d]B. M. Trost and T. R. Verhoeven, *Ibid.* **100**, 7779 (1978).
[8]*The Chemistry of Nitro and Nitroso Groups* (Edited by M. Feuer), Vol. 1, Chap. 7. Wiley, New York (1969).
[9]P. Hartley, *Organic Chemistry of Pt and Pd.* Wiley, New York (1971).
[10]L. Malatesta and N. Angoletta, *J. Chem. Soc.* 1186 (1957).
[11]*Org. Synth., Coll. Vol. III*, p. 696. Wiley, New York (1955).
[12]D. I. Smith, H. H. Hoehn and A. G. Whitney, *J. Am. Chem. Soc.* **62**, 1863 (1940).
[13]Usual method of acetylation with acetyl chloride and pyridine in ethyl ether was employed.
[14]H. Piotrowska, W. Sas, T. Urbański, *Roczniki Chem.* **47**, 1233 (1973).
[15]B. Kędzierski, Ph.D. Thesis, Technical University, Warsaw, 1972.
[16]A. Weissberger, E. S. Proskauer, J. A. Riddick, and E. E. Togs Jr., *Organic Solvents, Physical Properties and Methods of Purification.* Interscience, New York (1955).