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PREPARATION OF α,β-UNSATURATED CARBOXYLIC ESTERS BY THE REACTION OF ACI-NITROESTERS WITH ETHOXYCARBONYLMETHYLENETRIPHENYLPHOSPHORANE

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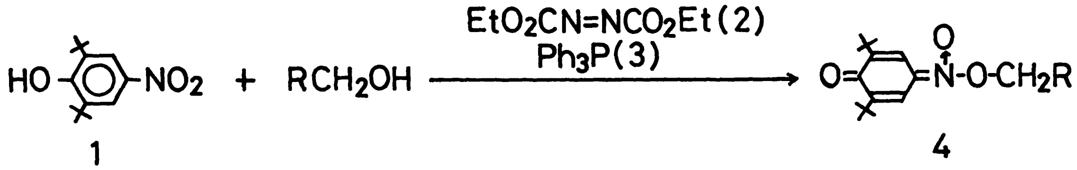
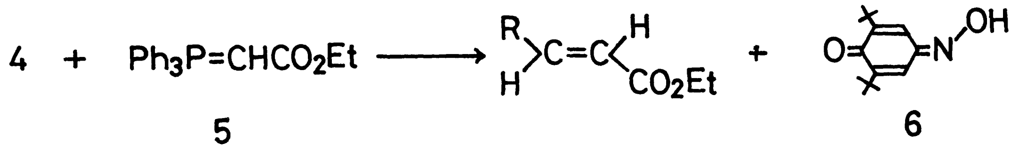
The reaction of ethoxycarbonylmethylenetriphenylphosphorane with *aci*-nitroesters derived from 2,6-di-t-butyl-4-nitrophenol and alcohols afforded α,β-unsaturated carboxylic esters. When mono-*aci*-nitroester of 1,3-butanediol or 1,6-hexanediol was used, (E)-ethyl 5-hydroxy-2-hexenoate or (E)-ethyl 8-hydroxy-2-octenoate was obtained.

The importance of the preparation of olefins has led to a continuing search for new and selective reactions which can be utilized in the synthesis of natural products.[1)] Of the various procedures developed so far, Wittig reaction is one of the most widely utilized methods.

In a preceding paper,[2)] we described the oxidation of alcohols to carbonyl compounds via *aci*-nitroesters. It would therefore be expected that olefins would be formed by combining this oxidation procedure with Wittig reaction. We wish to report in this paper the preparation of olefins from *aci*-nitroesters and ethoxycarbonylmethylenetriphenylphosphorane (**5**). The *aci*-nitroesters (**4**) used in these experiments were prepared by the reaction of alcohols with 2,6-di-t-butyl-4-nitrophenol (**1**), diethyl azodicarboxylate (**2**), and triphenylphosphine (**3**) as described previously.[2)] The yields of **4** are shown in Table 1.[3)]

When 2-phenylethyl *aci*-nitronate was heated in tetrahydrofuran (THF) at reflux in the presence of 2 molar equivalents of **5**, (E)-ethyl 4-phenyl-2-butenoate and 2,6-di-t-butyl-4-hydroxyimino-2,5-cyclohexadienone (**6**) were obtained in 72 and 92% yields, respectively. By the similar procedure, conjugated esters were prepared as summarized in Table 1. The products were separated by preparative layer chromatography.





Next, the effect of solvent and molar ratio of the reactants were examined. These studies were carried out in THF and benzene under reflux for 8 hr using 3-octynyl aci-nitronate. When the aci-nitronate was treated with 5 molar equivalents of 5 in THF, the yield of the olefin decreased to 35% (entry 4 and 5 in Table 1). A somewhat better result was obtained when the reaction was carried out in benzene for 8 hr (entry 4 and 7), while elongation of the reaction time led to the decrease of the yields of products (entry 7 and 8).

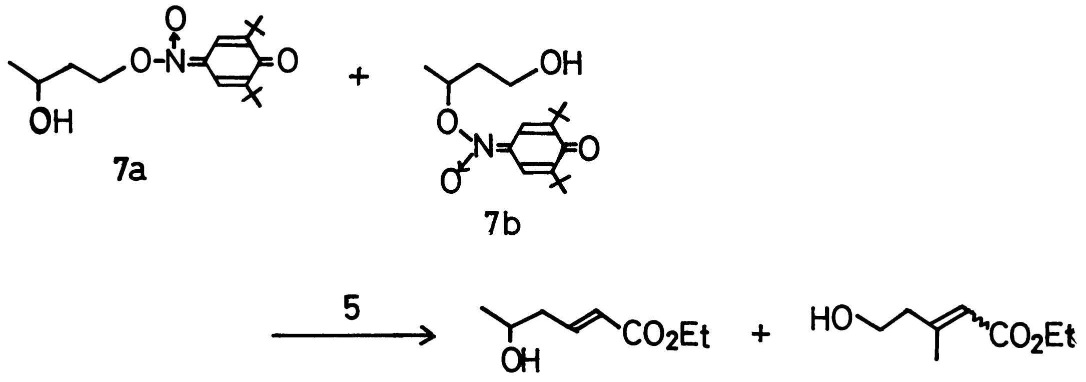
Table 1. Preparation of aci-nitroesters and olefins

Entry	RCH_2OH (R)	Yield of 4, %	5			Yield, %	
			equiv.	solv.*	hr**	Olefin	6
1	2-Phenylethanol ($PhCH_2$-)	92	2	T	10	72	92
2	1-Octanol ($CH_3(CH_2)_6$-)	92	2	T	16	50	75
3	(Z)-3-Hexen-1-ol ($CH_3CH_2CH=CHCH_2$-)	80	2	T	31	66	80
4	3-Octyn-1-ol ($CH_3(CH_2)_3C\equiv CCH_2$-)	70	2	T	8	50	75
5			5	T	8	35	46
6			1	B	8	43	77
7			2	B	8	61	87
8			2	B	16	50	-

* T = THF, B = benzene.

** The reaction of 4 with 5 was carried out until 4 had been consumed as indicated by tlc (entry 1-4).

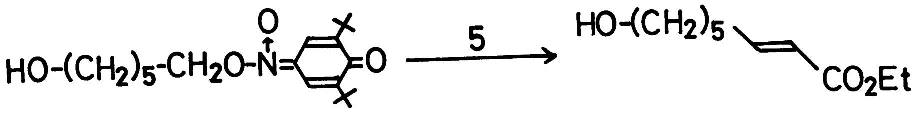
The reaction of 1,3-butanediol with 1, 2, and 3 resulted in the formation of monoesterified products containing secondary (7a) and primary (7b) hydroxyl groups in a ratio of 2.5 : 1.4) When the mixture was treated with 2 molar equivalents of 5 in benzene under reflux for 12 hr, (E)-ethyl 5-hydroxy-2-hexenoate and ethyl 5-hydroxy-3-methyl-2-pentenoate were obtained in a ratio of about 2.5 : 1 (total yield; 58%).



7a

7b

The reaction of 1,6-hexanediol with **1**, **2**, and **3** resulted in the formation of mono-aci-nitroester (**8a**) and di-aci-nitroester (**8b**) in 50 and 21% yields, respectively. Similar treatment of **8a** with **5** afforded (E)-ethyl 8-hydroxy-2-octenoate in an 85% yield.



8a

It is our tentative feeling that the reaction involves initial formation of carbonyl compounds. However, since there is no need to isolate the carbonyl compounds, the two-step route described in this paper makes it possible to utilize an unstable carbonyl compound such as aldol in Wittig reaction. By this procedure, a terminal carbon of diol can be elongated by two carbon unit without protection of another hydroxyl group.

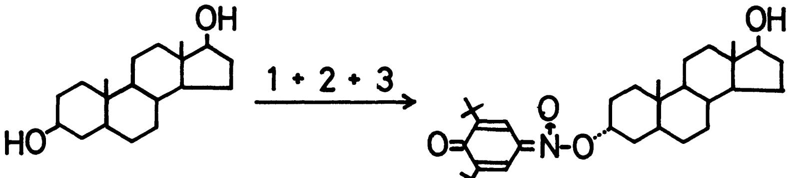
The experimental procedure which follows is illustrative.

(E)-Ethyl 8-hydroxy-2-octenoate. A solution of **2** (499 mg, 2.87 mmol) in THF (3 ml) was added dropwise at room temperature to a solution of 1,6-hexanediol (242 mg, 2 mmol), **1** (503 mg, 2 mmol), and **3** (788 mg, 3 mmol) in THF (10 ml). After the solution had been kept stirring overnight, the products were separated by preparative layer chromatography (plc) using benzene-ethyl acetate (10 : 1) giving mono-aci-nitroester (**8a**) and di-aci-nitroester (**8b**) in 50 and 21% yields, respectively. ^{1}H-NMR$^{5)}$ for **8a** ($CDCl_3$); δ 1.3 (s, t-Bu), 0.8-2.0 (m, CH_2-($\underline{CH_2}$)$_4$-CH_2), 2.95 (s, OH), 3.55 (br t, A_2B_2, $\underline{CH_2}$OH), 4.25 (br t, A_2B_2, $\underline{CH_2}$-O-N(O)=), 7.2 and 7.4 (both d, ring protons).

A solution of **8a** (308 mg, 0.876 mmol) and **5** (560 mg, 1.61 mmol) in benzene was refluxed for 9 hr and then (E)-ethyl 8-hydroxy-2-octenoate and **6** were isolated by plc using benzene-ethyl acetate (2 : 1) in 85 and 81% yields, respectively. ^{1}H-NMR for the 2-octenoate (CCl_4); δ 1.26 (t, $C\underline{H}_3CH_2O$), 0.85-1.80 (m, $-(C\underline{H}_2)_3CH_2OH$), 1.8-2.5 (br two lines, $CH_A=CH_B-CH_2$, J_{AB} = 7-8 Hz), 3.13 (br s, OH), 3.2-3.75 (br three lines, $C\underline{H}_2OH$), 4.05 (q, $CH_3C\underline{H}_2$), 5.6 (B of ABX_2, J_{AB} = 15-16 Hz), 6.75 (A of ABX_2, J_{AB} =15-16 Hz, J_{AX} = 7-8 Hz).

References and Notes

1) J. Reucroft and P. G. Sammes, Quat. Rev., **25**, 135 (1971); I. Kuwajima, Yuki Gosei Kagaku Kyokai Shi, 30th Aniversary Issue, 44 (1972); H. Nozaki, Kagaku, **30**, 508 (1975).
2) J. Kimura, A. Kawashima, M. Sugizaki, N. Nemoto, and O. Mitsunobu, J. Chem. Soc., Chem. Commun., **1979**, 303.
3) Satisfactory nmr data were obtained for all products. (Z)-3-Hexenyl *aci*-nitronate (CCl_4); δ 0.95 (t, $C\underline{H}_3CH_2$), 1.25 (s, t-Bu), 2 (br quintet, $CH_3C\underline{H}_2$), 2.35 (br q, $C\underline{H}_2CH_2O$), 4.2 (t, CH_2O), 4.9-5.65 (m, CH=CH), 7.15 and 7.4 (both d, ring protons). 3-Octynyl *aci*-nitronate (CCl_4); δ 1.25 (s, t-Bu; superimposed on m, 0.5-1.6, $CH_3CH_2CH_2$), 1.85-2.3 (m, $\equiv C-C\underline{H}_2-C_3H_7$), 2.3-2.8 (m, $OCH_2C\underline{H}_2-C\equiv$), 3.4 (t, CH_2O), 7.3 and 7.6 (both d, ring protons).
4) The lower regioselectivity of the present reaction compared to the formation of monobenzoate of 1,3-butanediol$^{6)}$ is due to the rearrangement of the *aci*-nitronate residue.$^{2)}$ The use of 5α-androstane-3β,17β-diol in the present reaction permitted selective esterification at less hindered 3β-hydroxyl group in preference to 17β-hydroxyl one affording mono-*aci*-nitronate (**9**) where 17β-hydroxyl group is located at an unfavorable position for rearrangement. Treatment of **9** with 1,8-bis(dimethylamino)naphthalene in THF under reflux afforded 5α-androstane-17β-ol-3-one in an 88% yield.



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5) Nuclear magnetic resonance spectra were measured on a Hitachi R-20 spectrometer (60 MHz) using tetramethylsilane as an internal standard.
6) O. Mitsunobu, J. Kimura, K. Iiizumi, and N. Yanagida, Bull. Chem. Soc. Jpn., **49**, 510 (1976).

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