Organic Chemistry

Neryl- and geranyltriethylammonium halides in the allylation of sodium diethyl malonate. The effect of the leaving group of the allylating reagent on the selectivity of the reaction

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In the absence of catalysts, *N*-neryl- and *N*-geranyltriethylammonium halides can allylate sodium diethyl malonate to give terpene malonate derivatives. Using the above-mentioned ammonium salts, geranyl and neryl acetates, geranyl ethyl carbonate, and geranyl diethyl phosphate as examples, it has been shown that with Pd^0 and Pd^{II} catalysts, the selectivity of the formation of neryl-, geranyl-, and linalylmalonates can be governed by varying the leaving group of the allylating agent.

Key words: palladium, complexes, catalysis, sodium diethyl malonate, allylation.

The use of palladium catalysts in the allylation of activated methylene compounds has been considered in review papers.[1—4] However, the effect of the leaving group of the reactant on the selectivity of the reaction has not received adequate attention. There are data on the possibility of Pd^0-catalyzed allylation of carbanions with various allyl derivatives of diethyl phosphates,[5] sulfonium and quaternary ammonium salts,[6] carbonates,[7—9] and tosylates.[10] In the catalytic allylation of sodium diethyl malonate with monoterpene derivatives to give linalyl- (**1**), neryl- (**2**), and geranylmalonic acid (**3**) esters, geranyl and neryl acetates and carbonates are usually employed.[1,2,8]

The present work is devoted to the study of the effect of the nature of leaving groups on the selectivity of the formation of malonates **1—3**. We compared the non-catalytic allylation of sodium diethyl malonate by neryl- and geranyltriethylammonium iodides (**4a** and **4b**) and neryltriethylammonium bromide (**4c**) with allylation catalyzed by Pd^0 and Pd^{II} complexes. Since allyl acetates and carbonates do not allylate carbanions in the absence of a catalyst,[4] we studied the effect of the leaving group on the regio- and stereoselectivity of the process using reactions with neryl acetate (**5a**), geranyl acetate (**5b**), geranyl ethyl carbonate (**6**), geranyl tosylate (**7**), and geranyl diethyl phosphate (**8**), and salts **4a** and **4b** catalyzed by Pd^0 and Pd^{II} complexes, as examples.

Neryl- and geranyldialkylamines are formed during anionic telomerization of isoprene with secondary amines[12,13] and in the reaction of myrcene with secondary amines in the presence of sodium, respectively.[14] They are smoothly quaternized with alkyl halides. The

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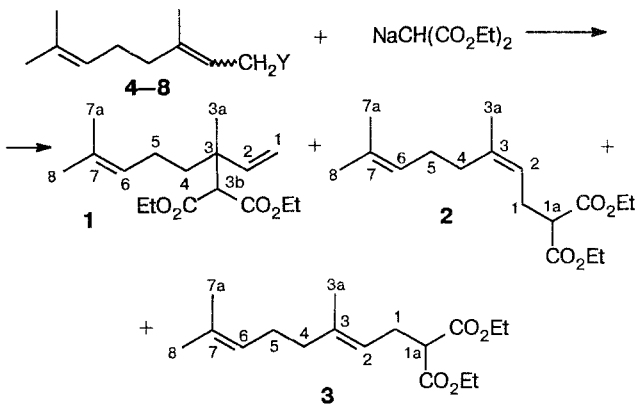

4a: Y = NEt_3X, X = I, *Z*-isomer
4b: Y = NEt_3X, X = I, *E*-isomer
4c: Y = NEt_3X, X = Br, *Z*-isomer
5a: Y = OAc, *Z*-isomer
5b: Y = OAc, *E*-isomer
6: Y = OC(O)OEt, *E*-isomer
7: Y = OTs, *E*-isomer
8: Y = $OP(O)(OEt)_2$, *E*-isomer

reaction of salt **4b** with sodium diethyl malonate in THF affords a mixture of malonates **1**—**3** in a high yield (91 %) only when the reaction mixture is boiled for a long time (up to 80 h at 70 °C); the purity of product **3** resulting from the normal allylic substitution without the change in the double bond geometry was as high as 79 %. The mixture contained 6 % of the product of the inversion of the double bond configuration (**2**) and 15 % of the product of allylic rearrangement (**1**). In the absence of a catalyst, in Bu_2O (6 h at 110—115 °C), salt **4a** affords malonate **2** of 97 % purity only in 46 % yield. At 20 °C, noncatalytic reactions of salts **4a** and **4b** do not occur (*cf.* Ref. 6).

We used the following Pd^{II} and Pd^0 complexes as the catalysts for this reaction, in some cases, in the presence of an excess of a phosphorus-containing ligand: $(Ph_3P)_2PdCl_2$ (**A**), $(Ph_3P)_4Pd$ (**B**), $(Ph_3P)_4Pd—Ph_3P$ (**C**), $PdCl_2—Ph_3P—PhONa$ (**D**), $Pd_2(dba)_3 \cdot CHCl_3—Ph_2P(CH_2)_2PPh_2$ (**E**), $Pd_2(dba)_3 \cdot CHCl_3—Ph_3P$ (**F**). Previously[15] Pd^{II} complexes were shown to promote reactions with allylic rearrangements. For example,[10] allylation of sodium diethyl malonate catalyzed by bis(π-allylpalladium chloride) gives 84—86 % of linalylmalonate from either neryl acetate **5a** or geranyl acetate **5b**. As can be seen from Table 1, boiling salts **4a** and **4b** in THF in the presence of complex **A** affords mixtures of malonates **1**—**3** in high yields, and the amount of the product of allylic rearrangement, **1**, practically does not depend on the geometry of the double bond in the allyl fragment of the starting salt (salt **4a**, unlike **4b**, affords a substantial amount of the product having the reversed geometry of the double bond; the **2** : **3** ratio is 2 : 1). Under the same conditions, neryl acetate **5a** yields 49 % of malonate **1**. Thus, with complex **A** as the catalyst, the leaving groups, $—NR_3^+$ and —OAc, do not substantially affect the ratio of the resulting isomers **1**—**3**. Under the same conditions, geranyl tosylate **7** affords predominantly the product of the normal allylic substitution **3** (66 %), *i.e.*, the leaving group has an effect on the selectivity of the formation of malonates **1**—**3** in the presence of Pd^{II} complexes. Allylation with acetate **5b** catalyzed by a Pd^{II} salt in the presence of PhONa, which promotes the conversion of Pd^{II} to Pd^0, (system **D**)[16] results in the predominant formation of the product of allylic rearrangement, **1**.

Lowering the reaction temperature to 20 °C in the case of salts **4a** and **4c** (complex **A** as the catalyst) results in a substantial increase in the proportion of the rearrangement product **1** (up to 62 %) and a decrease in the content of product **3** with reversed geometry at the double bond, as compared with the reaction carried out in boiling THF.

The use of Pd^0 complexes (systems **B** and **C**), rather than Pd^{II} complex (**A**) exerts a minor effect on the composition of malonates **1**—**3** obtained from salts **4a** and **4b**. In the case of salt **4a** having the Z-allylic bond, a larger amount of the allylic rearrangement product **1** is formed than in the case of salt **4b**. A different picture is observed when acetate **5b** or carbonate **6** is used in the

Table 1. Allylation of sodium diethyl malonate in a THF solution

Allylating reagent	Catalyst (mol. %)	τ/h	Composition of malonates (%)			Overall yield (%)
			1	**2**	**3**	
4b	—	80	15	6	79	91
4a	**A**(5)	16	48	35	17	81
4b	**A**(5)	16	42	4	54	85
4a*	**A**(5)	120	62	33	5	85
4c*	**A**(5)	120	61	33	6	40
4a	**B**(10)	16	53	36	11	90
4a	**C**(5-20)	16	58	36	6	85
4b	**B**(10)	16	37	4	59	75
4b	**C**(5-20)	16	39	4	57	67
4b**	**E**(2.5-20)	3	—	—	—	—
5a	**A**(5)	6	49	24	27	65
5b	**B**(10)	16	21	1	78	76
5b	**C**(5-20)	16	47	1	52	44
5b	**D**(5-20-85)	24	58	1	41	80
5b	**F**(5-20)	6	53	1	46	48
6	**B**(10)	16	28	2	70	74
6	**C**(5-20)	16	36	1	63	32
6**	**E**(2.5-20)	3	11	18	71	50
7	**A**(10)	24	32	2	66	70
8	**A**(10)	24	1	98	1	49
8	**A**(10)	120	1	98	1	82
8	**B**(10)	24	2	98	—	65

* The temperature of the reaction was 20 °C. In other cases, the reaction was carried out at the temperature of boiling of the mixture.

** The reaction was carried out with diethyl malonate at 50 °C.

reaction catalyzed by system **B**. These reactions afford the product of the normal allylic substitution **3** with high selectivity (78 % and 70 %, respectively), in contrast to the reactions with salts **4a** and **4b**. Thus, with the Pd^0 complex as the catalyst, we also found the effect of the leaving group on the reaction selectivity. The addition of an excess of the phosphorus-containing ligand to the catalytic system (system **C**), appreciably levels this effect. The selectivity of the reaction under study is essentially affected by the diethyl phosphate leaving group, the so-called «biogenic group». In the presence of either Pd^{II} or Pd^0 complexes (**A** and **B**, respectively), geranyl phosphate **8** exhibits high selectivity with respect to compound **2**, which has the changed geometry at the double bond, as was described[5] for reactions of allyl phosphates catalyzed by $(Ph_3P)_4Pd$.

To prepare malonates **1—3** we also used other systems, **E—F**, which catalyze allylation of carbanions and activated methylene compounds.[7] When we carried out allylation of diethyl malonate with carbonate **6** as described in Ref. 7 (catalytic system **E**), we observed high selectivity with respect to the formation of malonate **3**, identical to that observed in allylation of sodium diethyl malonate in the presence of system **B**. Allylation of sodium diethyl malonate with salt **4b** does not occur under these conditions. Allylation of sodium diethyl malonate with acetate **5b** catalyzed by system **F** affords predominantly the rearrangement product **1**.

By using various geranyl and neryl derivatives we were able to obtain isomers **1—3** with high selectivities: linalylmalonate **1** (up to 62 %) is formed when sodium diethyl malonate is allylated with salt **4a** in the presence of catalyst **A** at 20 °C; nerylmalonate **2** (up to 98 %) is produced by allylation with phosphate **8** catalyzed by **A**; geranylmalonate is obtained in noncatalyzed allylation with salt **4b**.

Experimental

GLC analysis was carried out on a LKhM-8MD(3) chromatograph on a 200×3 mm column packed with 15 % SKTFT (an analog of SE-30) on Chromaton N-AW at a thermostat temperature of 200 °C (an isotherm). Malonates were identified by GLC, by comparison with authentic samples obtained by the known procedure.[10]

***N*-(3,7-Dimethyl-2*Z*,6-octadienyl- and 3,7-dimethyl-2*E*,6-octadienyl)triethylammonium iodides (4a and 4b).** 11.9 g (76.4 mmol) of EtI was added at 20 °C to a solution of 8 g (38 mmol) of *N*-(neryl- or geranyl)diethylamine in 10 mL of benzene. The mixture was kept for 2 days at 20 °C. The precipitate was filtered off and washed with pentane to give 11.2 g (80 %) of salt **4a**, m.p. 86 °C, or of salt **4b**, m.p. 119 °C. **4b** — found (%): C, 52.62; H, 9.07; N, 3.87. $C_{16}H_{32}IN$. Calculated (%): C, 52.60; H, 8.82; N, 3.83.

***N*-(3,7-Dimethyl-2*Z*,6-octadienyl)triethylammonium bromide (4c).** 8.3 g (76.4 mmol) of EtBr was added to a solution of 8 g (38.2 mmol) of *N*-neryldiethylamine in 10 mL of abs. benzene. The mixture was boiled for 16 h. Benzene was evaporated and the residue was washed with pentane to give 11.5 g (94 %) of hygroscopic salt **4c**, m.p. 73 °C. Found (%): N, 4.29. $C_{16}H_{32}BrN$. Calculated (%): N, 4.40.

General procedure for allylation of sodium diethyl malonate. Sodium diethyl malonate was prepared by the dropwise addition of a calculated amount of diethyl malonate to EtONa in EtOH. The mixture was boiled for 0.5 h and EtOH was evaporated to leave a white powder. At 20 °C, a solution of 38.8 mmol of sodium diethyl malonate in 10 mL of THF was added dropwise to a suspension or a solution of 19.4 mmol of an allylating agent (**4a—8**) and a catalyst (see Table 1) in 20 mL of THF, and the mixture was stirred. Then it was diluted with ether, washed with brine, and dried with Na_2SO_4. The solvent was evaporated and the residue was distilled to afford a mixture of isomers, b.p. 138—144 °C (1 Torr), which was analyzed by GLC.

^1H NMR spectra were recorded on a Varian VXR-400 ($CDCl_3$, TMS), δ, **1**: 1.23 (t, J = 7.5 Hz, 6 H, Et—CH_3); 1.26 (s, 3 H, 3a-CH_3); 1.55 (s, 3 H, 7a-CH_3); 1.66 (s, 3 H, 8-CH_3); 1.90 (m, 4 H, 4-CH_2, 5-CH_2); 3.49 (s, 1 H, 3b-CH); 4.12 (q, 4 H, Et—CH_2); 4.97 (m, 1 H, 6-CH); 4.99 (d, J = 17 Hz, 1 H, 1a-CH); 5.35 (d, J = 10.6 Hz, 1 H, 1b-CH); 5.98 (d.d, J = 17 Hz, 10.6, 1 H, 2-CH).

2: 1.23 (t, J = 7.5 Hz, 6 H, Et—CH_3); 1.65 (s, 3 H, 3a-CH_3); 1.66 (s, 6 H, 7a-CH_3, 8-CH_3); 2.05 (m, 4 H, 4-CH_2, 5-CH_2); 2.57 (d.d, J = 7.5 Hz, 2 H, 1-CH_2); 3.29 (t, J = 7.5 Hz, 1 H, 1a-CH); 4.18 (q, J = 7.5 Hz, 4 H, Et—CH_2); 5.15 (m, 2 H, 2-CH, 6-CH).

3: 1.21 (t, J = 7.5 Hz, 6 H, Et—CH_3); 1.59 (s, 3 H, 3a-CH_3); 1.65 (s, 3 H, 7a-CH_3); 1.67 (s, 3 H, 8-CH_3); 2.05 (m, 4 H, 4-CH_2, 5-CH_2); 2.58 (d.d, J = 7.5 Hz, 2 H, 1-CH_2); 3.30 (t, J = 7.5 Hz, H, 1a-CH); 4.15 (q, J = 7.5 Hz, 2 H, Et—CH_2, 4 H); 5.15 (m, 2 H, 2-CH, 6-CH).

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