Ortho-Selective Side-Chain Nitration of Methyl-Substituted Alkenoylbenzenes and Its Application to Synthesis of 4-Nitro-1-tetralones

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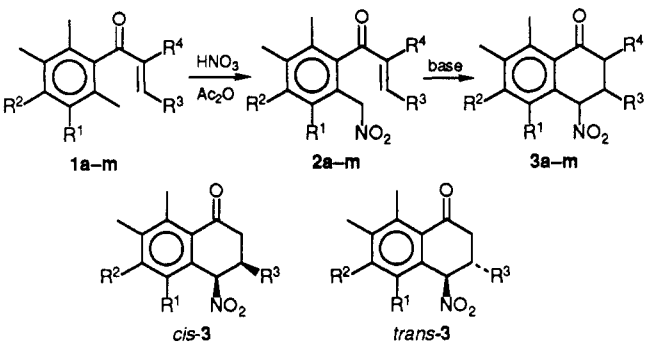
Methyl-substituted alkenoylbenzenes **1a–m** involving acryloyl, methacryloyl, β-(ethoxycarbonyl)acryloyl, crotonoyl, and cinnamoyl groups as alkenoyl functions reacted with fuming nitric acid in acetic anhydride to give 2-(nitromethyl)alkenoylbenzenes **2a–m** in satisfactory isolated yields, accompanied by the formation of some isomeric side chain nitrated or oxinitrated compounds. Compounds **2a–m** smoothly underwent an intramolecular Michael reaction in the presence of 1,8-diazabicyclo[5.4.0]undec-7-ene in boiling ethanol or with KF/alumina in tetrahydrofuran at room temperature to provide the corresponding polysubstituted 4-nitro-1-tetralones **3a–m** in good isolated yields. The Michael reactions of compounds **2** containing a substituent on the olefinic β-carbon gave a mixture of cis and trans adducts, whose relative ratios varied with the steric factor of the substituents at the olefinic β-carbon and the 3-position of the ring and on the nature of base used; the presence of bulky substituents such as ethoxycarbonyl and methyl groups and the use of a solid base such as KF/alumina gave adducts in a high trans/cis ratio.

Tetralones are key intermediates for the synthesis of various drugs and natural products. Their synthesis has attracted much attention.[1] 1-Tetralones have usually been synthesized by Friedel–Crafts reaction of aromatic hydrocarbons with succinic anhydride, followed by reduction and intramolecular cyclization.[2] This procedure is, however, unsuitable for the synthesis of polyfunctionalized tetralones because the reactions are carried out under quite severe reaction conditions.

Recently, we have shown that methyl-substituted acylbenzenes are regioselectively nitrated with a fuming nitric acid–acetic anhydride system at the methyl group ortho to an acyl group to give 2-(nitromethyl)acylbenzenes.[3] The reaction has been assumed to proceed via regioselective ipso attack by nitronium ion on the meta position of an acyl group, followed by side-chain nitration on the methyl group ortho to the acyl function. The regioselective side-chain nitration directed by an acyl function is useful for organic syntheses. The resulting nitromethyl group can be converted to various other useful functional groups.[4,5] We have applied the side chain nitration method to a convenient synthesis of polysubstituted phthalic acid derivatives from methyl-substituted benzoic acids.[3]

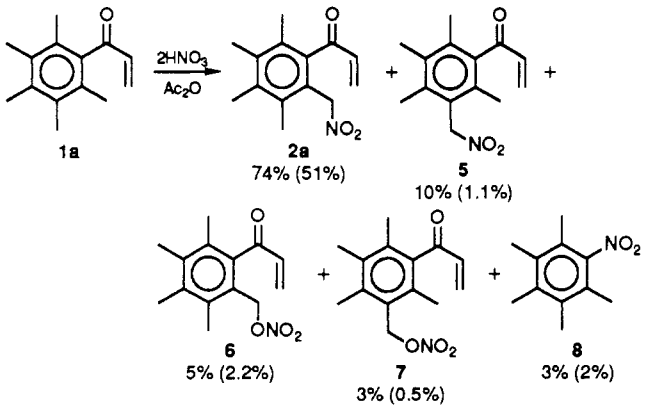
We now present extension of this regioselective side-chain nitration to the synthesis of polysubstituted 4-nitro-1-tetralones **3** from methyl-substituted alkenoylbenzenes **1**. According to our previous observations, the nitration of alkenoylbenzenes substituted with a methyl group at the 2-, 5-, and 6-positions will give the 2-(nitromethyl)alkenoylbenzenes **2**. Compounds **2** have a potential Michael donor, a nitromethyl grouup, ortho to the α,β-unsaturated carbonyl group, so an intramolecular Michael addition can occur on treatment of **2** with a base to provide the 4-nitro-1-tetralones **3**.

Scheme I[a]



[a] **a**, $R^1 = R^2 = CH_3$, $R^3 = R^4 = H$; **b**, $R^1 = R^2 = R^4 = CH_3$, $R^3 = H$; **c**, $R^1 = R^2 = CH_3$, $R^3 = COOCH_2CH_3$, $R^4 = H$; **d**, $R^1 = R^2 = CH_3$; $R^3 = Ph$, $R^4 = H$; **e**, $R^1 = R^2 = R^3 = CH_3$, $R^4 = H$; **f**, $R^1 = R^3 = R^4 = H$, $R^2 = CH_3$; **g**, $R^1 = R^4 = H$, $R^2 = CH_3$, $R^3 = Ph$; **h**, $R^1 = R^4 = H$, $R^2 = R^3 = CH_3$; **i**, $R^1 = CH_3$, $R^2 = OCH_3$, $R^3 = Ph$, $R^4 = H$; **j**, $R^1 = R^3 = CH_3$, $R^2 = OCH_3$, $R^4 = H$; **k**, $R^1 = R^3 = R^4 = H$, $R^2 = OCH_3$; **l**, $R^1 = R^4 = H$, $R^2 = OCH_3$, $R^3 = Ph$; **m**, $R^1 = R^4 = H$, $R^2 = OCH_3$, $R^3 = CH_3$.

Scheme II



The nitration of five types of (pentamethyl)alkenoylbenzenes involving the acryloyl, methacryloyl, β-(ethoxycarbonyl)acryloyl, crotonoyl, and cinnamoyl groups was undertaken to examine a directing effect of alkenoyl groups on the reaction. We have also carried out the nitration of a variety of alkenoylbenzenes substituted with a methyl

(1) (a) Swenton, J. S.; Raynolds, P. W. *J. Am. Chem. Soc.* **1978**, *100*, 6188. (b) Rathke, M. W.; Lindert, A. *Synth. Commun.* **1978**, 9. (c) Brawn, M. *Tetrahedron* **1984**, *40*, 4585. (d) Rizzi, J. P.; Kende, A. S. *Tetrahedron* **1984**, *40*, 4693. (e) Johansson, A. M.; Mellin, C.; Hacksell, U. *J. Org. Chem.* **1986**, *51*, 5252. (f) Tarnchompoo, B.; Thebtarabonth, C.; Thebtaranonth, Y. *Synthesis* **1986**, 785.

(2) (a) Somerville, L. F.; Allen, C. F. H. In *Organic Syntheses*; Blatt, A. H., D.; Wiley: New York, 1966; Collect. Vol. II, pp 81. Martin, E. L. *Ibid.* p 499. (b) Snyder, H. R.; Werber, F. X. *J. Am. Chem. Soc.* **1950**, *72*, 2962. (c) Truce, W. E.; Olson, C. E. *J. Am. Chem. Soc.* **1952**, *74*, 4721.

(3) Keumi, T.; Morita, T.; Teramoto, K.; Takahashi, H.; Yamamoto, H.; Ikeno, K.; Hanaki, M.; Inagaki, T.; Kitajima, H. *J. Org. Chem.* **1986**, *51*, 3439.

(4) (a) Olah, G. A.; Vankar, Y. D.; Gupta, B. G. B. *Synthesis* **1979**, 36. (b) Seebach, D.; Colvin, E. W.; Lehr, F.; Weller, T. *Chimia* **1979**, *33*, 1. (c) Ono, N.; Kamimura, A.; Hamamoto, I.; Kaji, A. *J. Org. Chem.* **1985**, *50*, 3692. (d) Ono, N.; Kaji, A. *Synthesis* **1986**, 695.

(5) Steliou, K.; Poupart, M. *J. Org. Chem.* **1985**, *50*, 4971.

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Scheme III

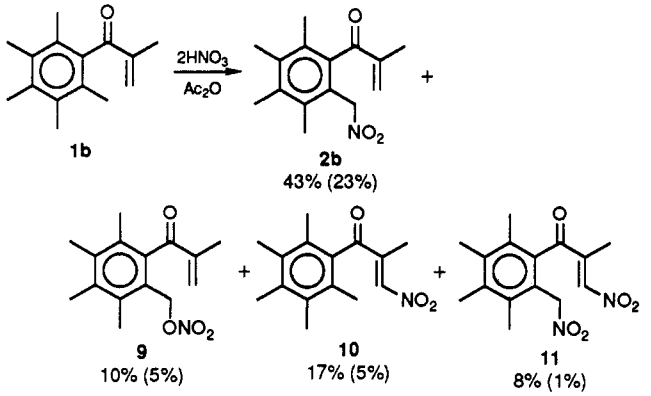


Table I. Nitration of Methyl-Substituted Alkenoylbenzenes 1 with Fuming Nitric Acid in Acetic Anhydride

entry	compd 1	product (isol yield, %; mp, °C)[a]
1	**1a**	**2a** (51; 105–106)
2	**1b**	**2b** (23; 102–103)
3	**1c**	**2c** (64; 92–93)
4	**1d**	**2d** (71; 146–147)
5	**1e**	**2e** (68; 123–124)
6	**1f**	**2f** (45; 58–59)
7	**1g**	**2g** (55; 83–84)
8	**1h**	**2h** (50; 64–65)
9	**1i**	**2i** (68; 111–112)
10	**1j**	**2j** (50; 98–99)
11	**1k**	**2k** (55; 110–111)
12	**1l**	**2l** (60; 124–125)
13	**1m**	**2m** (50; 90–91)

[a] The spectroscopic and analytical data are in good agreement with the structures.

group at the 2-, 5-, and 6-positions. The intramolecular Michael reactions of the resulting nitro compounds **2** were investigated in the presence of bases and shown to give 4-nitrotetralones. The entire reaction sequence is outlined in Scheme I.[6]

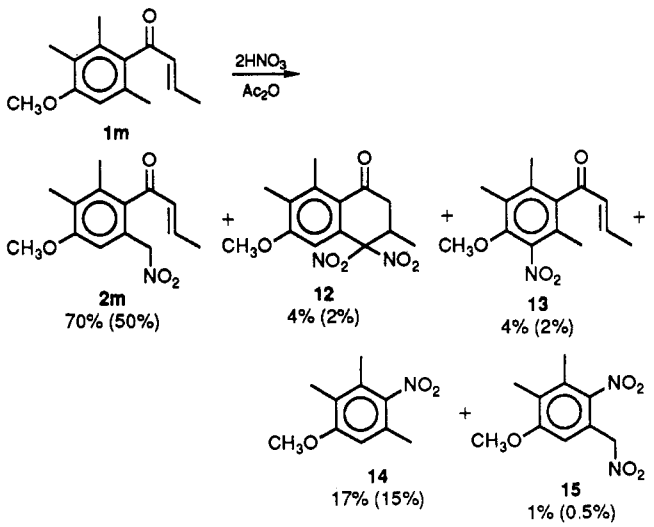
Results and Discussion

Nitration of Methyl-Substituted Alkenoylbenzenes. Nitration of five types of (pentamethyl)alkenoylbenzenes (**1a–e**) with fuming nitric acid was carried out in acetic anhydride. For example, 2,3,4,5,6-pentamethyl-1-acryloylbenzene (**1a**) was allowed to react with 2 equiv of fuming nitric acid in acetic anhydride at 0–5 °C. The product distribution is shown in Scheme II with isolated yields of products presented in parentheses. The nitration of **1a** gave 2-(nitromethyl)-3,4,5,6-tetramethyl-1-acryloylbenzene (**2a**) in 74% yield together with a small amount of compounds **5–8**.

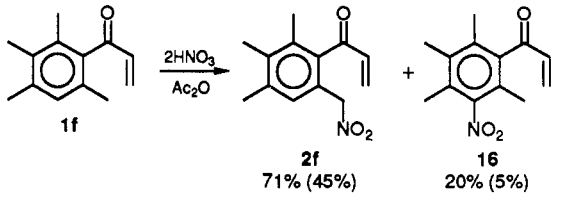
The nitrations of **1c**, **1d**, and **1e** also gave the side chain nitrated products **2c**, **2d**, and **2e** in good isolated yields, although accompanied by small amounts of isomeric nitromethyl or (nitrooxy)methyl compounds. From **1b**, the compounds **10** and **11** (nitrated at the olefinic β-carbon) were obtained in addition to **2b** as the major product (Scheme III).

The nitration of a variety of tri- and tetramethylalkenoylbenzenes (**1f–m**) involving acryloyl, cinnamoyl, and crotonoyl groups as the alkenoyl functions proceeded smoothly with the reagent system to afford the corresponding 2-(nitromethyl)alkenoylbenzenes (**2f–m**) in satisfactory isolated yields. The isolated yields and the melting points of compounds **2a–m** are shown in Table I. The sites of the side-chain nitration were easily determined by the change in intensity of methyl protons (at the 2- and 6-positions) in their ^{1}H NMR spectra, which appear at higher fields compared to the other methyl protons due to the anisotropic effect of the sterically twisted carbonyl function. The methylene protons of the 2-nitromethyl group are observed as a singlet in the region of 5.27–5.45 ppm.

Scheme IV



Scheme V



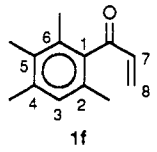
The nitration of alkenoylbenzenes containing a methoxy group at the 4-position resulted in the formation of a significant amount of nitrodeacylation products. For example, the nitration of 2,5,6-trimethyl-4-methoxy-1-crotonoylbenzene (**1m**) gave 2,5,6-trimethyl-4-methoxy-1-nitrobenzene (**14**), its side chain nitrated product **15**, and the ring-nitrated product **13**, along with compound **2m**. In addition to these compounds, the nitration of **1m** produced the 4,4-dinitro-1-tetralone **12** (Scheme IV). Compound **12** might be derived from the dinitrated compound of **1m** by the intramolecular Michael addition during workup by chromatography over silica gel. The formation of **12**, **14**, and **15** may be ascribed to the increased reactivity at the 1- and 5-positions by methoxyl group. The nitration of **1l** also gave a similar mixture.

It is worth noting that the nitration of **1** involving one unsubstituted meta position such as in **1f** and **1g** does not give conventional ring-nitrated compounds in high yields. The product side chain nitrated ortho to the alkenoyl group is obtained as the major product. The nitration of **1f** with a fuming nitric acid–acetic anhydride system gave a mixture of the side chain nitrated and ring-nitrated products, **2f** and **16**, in a ratio of 78/22, respectively (Scheme V).

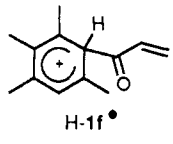
The predominant formation of **2f**, which appears to result from the initial electrophilic attack at the 5-position of **1f**, can be explained by an increased reactivity of this position owing to the additivity of substituent effects as described before.[3] We performed MNDO calculations to confirm the regioselective attack by electrophiles.[7] The

(6) A portion of this work has been reported in a short communication: Keumi, T.; Inagaki, T.; Nakayam, N.; Morita, T.; Kitajima, H. *J. Chem. Soc., Chem. Commun.* **1987**, 1091.

Table II. Positional Reactivities Estimated by MNDO Calculations of 1f and Its Protonated Species H-1f$^+$



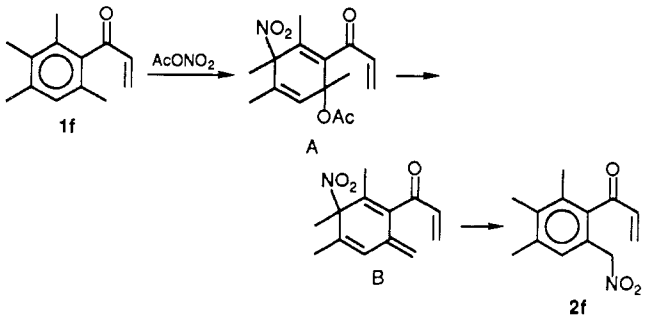
1f



H-1f$^+$

position	HOMO electron density of 1f	rel energy of H-1f$^+$, kcal/mol
1	0.0746	0
2	0.5464	7.66
3	0.2095	2.16
4	0.0956	8.82
5	0.6114	3.93
6	0.2494	3.51
7	0.0003	-
8	0.0003	-

Scheme VI

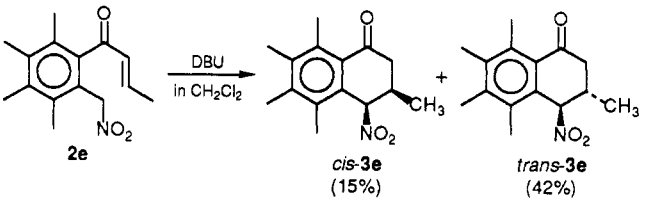


calculations with full geometry optimization were carried out on two reactivity indices: (i) HOMO electron density of free **1f** as a model for the early transition state and (ii) relative stability of the ring-protonated **1f** to simulate the Wheland intermediate as a model for the late transition state.[8,9] The results are listed in Table II.

The calculations indicate that the relative stability of the Wheland intermediate is increased in the order of position 1 > 3 > 6 > 5 > 2 > 4 in protonated **1f**, in contrast to the order of the HOMO electron density of the ring carbons, position 5 > 2 > 6 > 3 > 4 > 1. If the product distribution of the nitration of **1f** is controlled by the thermodynamic stability of the Wheland intermediates, then it should give conventional nitration products, 2,4,5,6-tetramethyl-1-nitrobenzene or **16**, which result from the stable intermediates estimated by the calculation. However, it is not consistent with the observed results wherein **2f** is obtained as the major product in the nitration of **1f**. Accordingly, the transition state controlling product formation of the reaction would be early on the reaction coodinate so that the 5-position with the highest HOMO electron density is prone to electrophilic attack by acetyl nitrate to give an adduct A. Subsequently, the adduct A would eliminate acetic acid to afford the intermediate B, leading to the side chain nitrated product **2f** as illustrated in Scheme VI.[10]

Intramolecular Michael Reactions of 2. This is in good agreement with the experimental data, and there is no evidence for the formation of compounds nitrated on the olefinic positions of **1a–m**, except for **1b**, which involves the olefinic carbons activated by a methyl group.

Scheme VII



Intramolecular Michael Reactions of 2. Compounds **2** involve a Michael acceptor and a nitromethyl group, which serves as a good Michael donor.[11] They were found to readily undergo an intramolecular cyclization reaction on treatment with 1,8-diazabicyclo[5.4.0]undec-7-ene (DBU) in boiling ethanol or dichloromethane, or by potassium fluoride adsorbed on basic alumina in tetrahydrofuran, to give the adducts **3** in good isolated yields. For example, 2-(nitromethyl)-3,4,5,6-tetramethyl-1-crotonoylbenzene (**2e**) reacted in the presence of 0.1 equiv of DBU in dichloromethane for 24 h to afford a mixture (70% yield) of diastereomeric adducts of 4-nitro-3,5,6,7,8-pentamethyl-1-tetralone (**3e**), which was separated into *cis*-**3e** and *trans*-**3e** in 15% and 42% yields, respectively (Scheme VII).

The isolated yields of the adducts **3** by the intramolecular Michael reaction of **2** are summarized in Table III. The structure of the adducts **3** was determined by their characteristic ^{1}H NMR chemical shifts for the methine (CHR^3) or the substituent (R^3) protons. The multiplet (2.65–2.67 ppm) assigned as the methine protons CH(CH$_3$) of *trans*-**3e** is shielded over that (3.07–3.13 ppm) in *cis*-**3e** as a consequence of the anisotropic effects by the nitro group on the same side of the ring. Similarly, the methyl protons of the CH(CH$_3$) of *cis*-**3e** were observed at high field (1.15 ppm) compared to those (1.25 ppm) of *trans*-**3e**.

Table III. Intramolecular Michael Reactions of 2-(Nitromethyl)alkenoylbenzenes 2

entry	compd 2	reactn condtns[a]	product (isol yield, %; mp, °C)[b]
1	**2a**	A	**3a** (73; 104–105)
2	**2b**	A	**3b** (74; 104–105)
3	**2c**	B	*trans*-**3c** (60; 116–117), *cis*-**3c** (0.3; 128–130)
4	**2d**	C	*trans*-**3d** (15; 179–180), *cis*-**3d** (23; 130–132)
5	**2e**	A	*trans*-**3e** (42; 143–144), *cis*-**3e** (15; 84–85)
6	**2f**	C	**3f** (72; 90–91)
7	**2g**	C	*trans*-**3g** (29; 140–141), *cis*-**3g** (56; 114–115)
8	**2h**	C	*trans*-**3h** (40; 99–100), *cis*-**3h** (36; 80–81)
9	**2i**	C	*trans*-**3i** (28; 174–175), *cis*-**3i** (10; 111–112)
10	**2j**	C	*trans*-**3j** (74; 162–164), *cis*-**3j** (3; 77–79)
11	**2k**	C	**3k** (60; 120–121)
12	**2l**	C	*trans*-**3l** (15; 166–167), *cis*-**3l** (36; 136–137)
13	**2m**	C	*trans*-**3m** (43; 97–98), *cis*-**3m** (34; 109–110)

[a] Reaction conditions: (A) DBU (0.1 equiv) in CH_2Cl_2 at room temperature for 24 h; (B) triethylamine (0.1 equiv) in CH_2Cl_2 at room temperature for 24 h; (C) DBU (0.1 equiv) in EtOH under reflux for 24 h. [b] The spectroscopic and analytical data are in good agreement with the structures.

(7) Dewar, M. J. S.; Thiel, W. *J. Am. Chem. Soc.* **1977**, *99*, 4899 and 4907.
(8) Olah, G. A. *Acc. Chem. Res.* **1971**, *4*, 240.
(9) Santiago, C.; Houk, K. N.; Perrin, C. L. *J. Am. Chem. Soc.* **1979**, *101*, 1336.
(10) (a) Hartshorn, S. R. *Chem. Soc. Rev.* **1974**, *3*, 169. (b) Reference 7b, pp 190.
(11) (a) Ono, N.; Miyake, H.; Kaji, A. *J. Chem. Soc., Chem. Commun.* **1983**, 875. (b) Colonna, S.; Hiemstra, H.; Wynberg, H. *J. Chem. Soc., Chem. Commun.* **1987**, 238.

Table IV. Diastereomeric Ratios of the Adducts 3 Formed in the Reaction of 2 with Base[a]

		substituents of 2			with DBU[b]		with KF/Al_2O_3[c]	
entry	compd 2	R^1	R^2	R^3	yield, %	trans/cis	yield, %	trans/cis
1	**2l**	H	OCH_3	Ph	92	28/72	84	43/57
2	**2m**	H	OCH_3	CH_3	95	58/42	86	64/36
3	**2g**	H	CH_3	Ph	89	33/67	88	60/40
4	**2h**	H	CH_3	CH_3	94	50/50	95	67/33
5	**2d**	CH_3	CH_3	Ph	73	60/40	97	79/21
6	**2e**	CH_3	CH_3	CH_3	76	64/36	95	96/4
7	**2i**	CH_3	OCH_3	Ph	90	67/33	77	79/21
8	**2j**	CH_3	OCH_3	CH_3	95	85/15	97	98/2
9	**2c**	CH_3	CH_3	COOEt	99	98/2	–	–

[a] Determined by HPLC using a silica gel column and *n*-hexane/ethyl acetate (8/2 v/v) as the eluent. [b] In boiling EtOH for 24 h. [c] In tetrahydrofuran at 20 °C for 2 h.

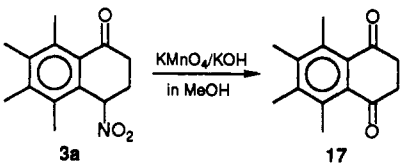
The methine protons due to the $CH(NO_2)$ of **3** are observed in the region of 5.55–6.21 ppm as multiplets with small coupling constants (J = 2–8 Hz). The singlets due to the 8-methyl protons appear at lower fields than those for the corresponding methyl protons of **2**, which indicates an increase in the coplanarity of the methyl group with the carbonyl group by the cycloaddition.

Table IV lists trans/cis ratios of the crude adducts obtained in the Michael reaction by DBU in ethanol. Recently, the use of a solid base for Michael reactions has come to our attention.[12] Potassium fluoride adsorbed on basic alumina has been shown to be an effective base in the Michael addition reaction between nitroparaffins and α,β-unsaturated carbonyl compounds.[12e] We also attempted to use the above solid base for our cycloadditions with an aim to enhance the stereoselectivity. These results are presented in Table IV. The ratios varied from 28/72 to 98/2 depending on the substituents R^1 and R^3 and the base used. The reactions of compounds **2** involving a methyl group as R^1 afforded more trans adducts than those of the unsubstituted **2** (R^1 = H). As the substituent R^3 on the β-olefinic carbon, a methyl group led to more trans adduct than a phenyl group. The cycloaddition of **2c** (R^1 = R^2 = CH_3, R^3 = COOEt) with DBU gave predominantly *trans*-**3c**. The use of the solid base KF/basic alumina showed a tendency to increase the ratio of trans adducts compared to the homogeneous base DBU. In particular, the remarkable trans selectivity was observed in the reaction for **2e** and **2j** with the solid base.

The substituent effects observed on the trans/cis ratios can be attributed to a steric hindrance between the substituents R^3 and the nitro group in the nitromethyl carbanion generated with base. Thus, a methyl group, which has a larger van der Waals radius than a phenyl group,[13] enhances steric interaction with the nitro group, resulting in enhanced trans selectivity. The presence of a methyl group at the 3-position of **2** may also cause an increase in the repulsion due to the compression effect by the ring substituents. Furthermore, the carbanion generated by the solid base would be tightly associated with the solid gegenion, so that the immobile gegenion may retard a free rotation leading to the cis configuration.

The nitro group of **3** can be converted into other functional groups and permit one to activate the 4-position of the 1-tetralones for further elaborations. As one application, we carried out the oxidation of the nitro group leading to the carbonyl group. For example, treatment of **3a** with methanolic potassium hydroxide followed by oxidation with an aqueous solution of potassium permanganate and magnesium sulfate at 0 °C gave 5,6,7,8-tetramethyldihydronaphthalene-1,4-dione (**17**) in 99% yield (Scheme VIII).

Scheme VIII



3a **17** (99%)

Conclusions

Alkenoylbenzenes **1a–m** having a methyl group at the 2-, 5-, and 6-positions were found to react with fuming nitric acid in acetic anhydride to give the corresponding 2-(nitromethyl)alkenoylbenzenes **2a–m** as the sole isolable product, suggesting that the alkenoyl groups could effectively direct the side-chain nitration at the ortho position. The exception was the reaction of **1b**, in which the formation of **2b** was accompanied by vinyl group nitration products. Treatment of **2a–m** with DBU in boiling ethanol or KF/basic alumina in tetrahydrofuran gave exclusively the corresponding 4-nitrotetralones **3a–m**, demonstrating that the intramolecular Michael reaction proceeds very smoothly. The yields for each step are excellent, and the nitro group of **3** can be easily converted into other functional groups. We believe that the two-step method consisting of side-chain nitration and subsequent intramolecular Michael reaction offers a convenient route to complex substituted 1-tetralones which are potentially valuable intermediates for natural products and drugs.

This work is an application of the ipso nitration directed by an acyl group to the ortho functionalization of methyl-substituted acylarenes. Further synthetic applications of the regioselective side-chain nitration are in progress.

Experimental Section

All melting points are uncorrected. IR spectra were recorded on a Hitachi Model EPI-S2 spectrophotometer as KBr pellets. ^{1}H NMR spectra were recorded on a JEOL-FX 270 FT-NMR (270 MHz) spectrometer in chloroform-*d* solution with tetramethylsilane internal standard. HPLC analysis was carried out on a JASCO-TRI ROTAR-IV high-performance liquid chromatograph using a Megapak SIL column (JASCO silica, 40 cm, 5 mm) as the column and *n*-hexane/ethyl acetate (8/2 v/v) as the eluent. Product distributions were calculated from the relative peak area with respect to the internal standard (naphthalene or dibenzofuran) on a System Instruments Chromatocorder 11 instrument after calibration for each authentic compound.

Preparation of Methyl-Substituted Alkenoylbenzenes. 2,3,4,5,6-Pentamethyl-1-acryloylbenzene (1a). A solution of pentamethylbenzene (34.17 g, 0.23 mol) in dichloromethane (70

(12) (a) Rosini, G.; Marotta, E. *Synthesis* **1986**, 237. (b) Ballini, R.; Petrini, M. *Synthesis* **1986**, 1024. (c) Ballini, R.; Petrin, M.; Rosini, G. *Synthesis* **1987**, 711. (d) Melot, J. M.; Boullet, F. T.; Foucaud, A. *Synthesis* **1987**, 364. (e) Bergbreiter, D. E.; Lalonde, J. J. *Org. Chem.* **1987**, *52*, 1601.

(13) Brown, H. C.; Marino, G.; Stock, L. M. *J. Am. Chem. Soc.* **1959**, *81*, 3310.

mL) was added dropwise to a solution of aluminum chloride (36.8 g, 0.28 mol) and acryloyl chloride (25 g, 0.28 mol) in dichloromethane (100 mL) with stirring at 0 °C over 30 min. After the reaction mixture was stirred for 2 h at the same temperature, it was poured into 500 mL of ice/water, extracted with dichloromethane, and washed with water. After evaporation of the solvent, the resulting residue was distilled under reduced pressure to obtain 2,3,4,5,6-pentamethyl-1-acryloylbenzene (**1a**) (26.4 g, 70%, bp 145–147 °C/3 mmHg). Recrystallization of the product from methanol gave the purified **1a** of mp 76–77 °C (40% yield).

In a similar manner, compounds **1b–m** were prepared from Friedel–Crafts reactions of corresponding polymethylbenzenes with alkenoyl chlorides.

Preparation of KF/Basic Alumina. The KF/alumina was prepared by the procedure described in the literature.[12e] The mixture of potassium fluoride (1.00 g), water (8 mL), and basic alumina (5.00 g, from ICN Biochemical GmbH) was placed on a rotary evaporator, and the water was removed under reduced pressure. The resulting powder was dried at 145 °C at 1 mmHg for 7 h before use.

General Procedure for the Nitration of 1. The Nitration of 2,3,4,5,6-Pentamethyl-1-acryloylbenzene (1a). A solution of 99% nitric acid (0.623 g, 9.9 mmol) in acetic anhydride (8 mL) was added to a solution of **1a** (1.00 g, 4.9 mmol) in acetic anhydride (8 mL) with stirring at 0 °C over 15 min. After the reaction mixture was stirred for 2 h at the same temperature, it was poured into 300 mL of ice/water and then stirred overnight. The resulting solid was extracted with ether, washed with water (3 × 100 mL), and dried over anhydrous sodium sulfate. Evaporation of the solvent gave a crude product (1.28 g). After measurement of the HPLC, the product was chromatographed on silica gel with benzene to isolate **2a** (0.63 g, 51%, mp 93–98 °C), **8** (0.019 g, 2%, mp 143–145 °C), **5** (0.013 g, 1.1%, mp 116–118 °C), and oily products (0.15 g). The above obtained oily products were again chromatographed by HPLC using a Finepack SIL column (JASCO silica gel) as the column and *n*-hexane/ethyl acetate (8/2 v/v) as the eluent to give **6** (0.028 g, 2.2%, mp 62–63 °C) and **7** (0.006 g, 0.5%, mp 128–131 °C). Recrystallization of the individual compounds from methanol gave the purified compounds **2a** (mp 105–106 °C), **5** (mp 117–118 °C), **6** (mp 63–64 °C), **7** (mp 129–131 °C), and **8** (mp 155–156 °C, lit.[14] mp 158–159 °C). The nitration of **1b–m** was also carried out under the same conditions described above.

General Procedure for the Intramolecular Michael Reaction. The Reaction of 2e with DBU. To a solution of **2e** (1.00 g, 3.83 mmol) in dichloromethane (20 mL) was added a solution of DBU (0.062 g, 0.38 mmol) in dichloromethane (5 mL) at room temperature, and the mixture was stirred for 24 h at the same temperature. The reaction was quenched by addition of 1 M hydrochloric acid (ca. 30 mL), and the reaction mixture was extracted with dichloromethane (50 mL), washed with water, and dried over anhydrous sodium sulfate. Removal of the solvent under reduced pressure gave a brown-colored residue. After measurement of the HPLC, the residue was passed on a short column of silica gel with *n*-hexane/ethyl acetate (8/2 v/v) to afford the adduct (0.70 g, 70%). The crude adduct was subjected to preparative column chromatography on silica gel. Elution with *n*-hexane/ethyl acetate (8/2 v/v) afforded the cis adduct (*cis*-**3e**) (0.15 g, 15% yield, mp 82–85 °C) and the trans adduct (*trans*-**3e**) (0.42 g, 42% yield, mp 142–144 °C). Recrystallization of the adducts from 80% MeOH and EtOH gave the compounds of mp 84–85 °C and 143–144 °C, respectively. In a similar manner, the Michael reactions of nitromethyl compounds **2b–m** were carried out to give the corresponding **3b–m**.

The Reaction of 2e with KF/Basic Alumina. The typical procedure for the Michael reactions is illustrated by the following procedure for **2e**. The KF/basic alumina (0.5 g) was added to a solution of **2e** (0.100 g, 0.38 mmol) in dry THF (7 mL), and the resulting suspension was stirred at room temperature for 2 h. After that, the reaction mixture was filtered, and the alumina was washed with ether (20 mL). The solvent of the combined filtrate was removed under reduced pressure to give the crude adduct of 0.095 g (95% yield). The product was subjected to HPLC measurement to determine the product distribution.

The Oxidation of 3f. The reaction was carried out according to the procedure described in the literature,[5] to give 5,6,7,8-tetramethyltetralin-1,4-dione (**77**): 99% yield; mp 125–126 °C (MeOH); ^{1}H NMR δ 2.33 (s, 6 H), 2.50 (s, 6 H), 3.00 (s, 4 H); IR ν 1685, 1671 cm^{-1}; MS *m/e* 216 (M$^+$, 95), 201 (17), 187 (23), 173 (100). Anal. Calcd for $C_{14}H_{16}O_2$: C, 77.75; H, 7.46. Found: C, 77.83; H, 7.66.

MNDO Calculations. The MNDO calculations of 2,3,4,6-tetramethyl-1-acryloylbenzene (**1f**) and its protonated benzenonium ions were made by using the MOPAC-MNDO program of Dewar and collaborators.[7] All geometric parameters (bond length, bond angles, and dihedral angles) were optimized without any specific assumptions.

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Supplementary Material Available: Physical and spectroscopic data of **1a–m**, **2a–m**, **3a–m**, **5–7**, and **9–16** (15 pages). Ordering information is given on any current masthead page.

(14) Suzuki, H.; Nakamura, K. *Bull. Chem. Soc. Jpn.* **1970**, *43*, 473.

Conjugate Addition of Acyloxy Groups to Alkynylphenyliodonium Tetrafluoroborates under Both Basic and Acidic Conditions. Synthesis of α-Acyloxy Ketones

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Reaction of alkynylphenyliodonium tetrafluoroborates **1** with sodium salts of carboxylic acids in the presence of water affords α-acyloxy ketones. The reaction also proceeds under acidic conditions. The fact that the reaction of (4-hydroxy-1-butynyl)phenyliodonium tetrafluoroborate (**11**) with 2 equiv of sodium acetate in THF–water (3:1) gives 1,4-diacetoxy-2-butanone (**12**) suggests a reaction mechanism involving an intervention of [2-(acyloxy)-1-alkenyl]phenyliodonium tetrafluoroborates, produced by Michael-type addition of acyloxy groups to **1**.

Alkynylphenyliodonium salts are highly electron-deficient species and react with a variety of nucleophiles. They are formally tetraphilic (α-, α′-, and β-carbons and iodine) toward the attack of nucleophiles.[1] Conjugate addition

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