α-Nitro Ketones. 5.[1] Synthesis of 2-Nitrocyclopentanones[2]

Fadia E. Elfehail[3] and Walter W. Zajac, Jr.*

Department of Chemistry, Villanova University, Villanova, Pennsylvania 19085

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The synthesis of the *trans*-3-methyl, *trans-trans*- and *trans-cis*-3,4-dimethyl-, *trans*-3,5,5-trimethyl-, and *cis*- and *trans*-5-methyl-2-nitrocyclopentanones was accomplished by nitration of substituted cyclopentanone enol acetates with nitric acid at 15 °C and by nitration of potassium enolates of the substituted cyclopentanones with amyl nitrate in THF. The stereochemistry of the nitration reactions is discussed. The 2-nitrocyclopentanones undergo reactions with acid that make their isolation troublesome.

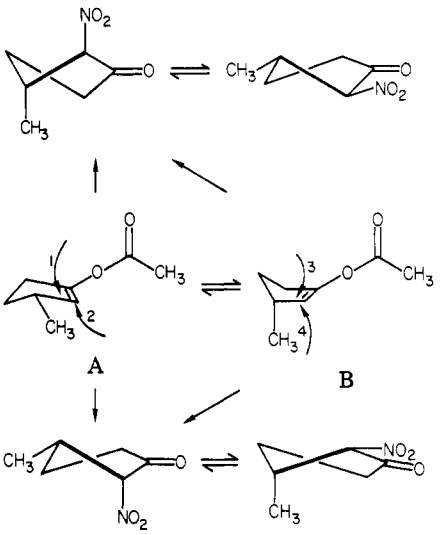
Previously we had demonstrated that the nitration of enol acetates is a synthetically useful reaction for the preparation of substituted 2-nitrocyclohexanones and that the reaction leads to products with the stereochemistry kinetically established.[4] Although the preparation of substituted 2-nitrocyclopentanones are scattered in the literature, no studies on the generality of these reactions for the synthesis of 2-nitrocyclopentanones has been carried out.[5] Futhermore, 2-nitrocyclopentanone was an unknown compound until our recent report on its synthesis.[1] As part of our ongoing study on the chemistry of α-nitro ketones we now report our results on the nitration of enol acetates of 3-substituted cyclopentanones with nitric acid and on the nitration of the potassium enolates with amyl nitrate, the latter method being developed because of the acid lability of 2-nitrocyclopentanones.

Results

The enol acetates **2** used in this investigation were prepared by the reaction of the cyclopentanones **1** with isopropenyl acetate in the presence of *p*-toluenesulfonic acid. In the case of 3-methylcyclopentanone, two isomeric enol acetates were formed in approximately equal amounts. In Table I are listed the ketones and enol acetates used in this work.

The 2-nitrocyclopentanones **4** prepared from the nitration of the enol acetates **2** or potassium enolates **3** are also listed in Table I. In the ^{1}H NMR spectra of α-nitro ketones,[6] the α-proton resonance appears several parts per million downfield from the rest of the ring protons. This spectral property was utilized to analyze the nitration reaction mixtures and ultimately to assign the configuration of the 3-substituted 2-nitrocyclopentanones. By X-ray crystallography we had previously unambiguously assigned the trans configuration to 2-nitro-3,5,5-trimethylcyclopentanone.[7] The conformation of this compound can be best described as a C_1 half-chair with the cyclopentanone ring severely puckered, with a dihedral angle of 157° between the vicinal protons on C-2 and C-3. The ^{1}H NMR of this compound has a doublet at δ 4.85 with a *J* value of 11.5 Hz for the α-proton. Since the other 3-substituted 2-nitrocyclopentanones had similar chemical shifts and coupling constants of 11.5 Hz, they were also assigned the trans configuration.

Scheme I. Pathways for the Approach of the Nitrating Species on 1-Acetoxy-3-methylcyclopentanone



Having established that the configurations of the 3-substituted 2-nitrocyclopentanones are trans, we can discuss the stereochemistry of the nitration reactions.

The nitration of enol acetates **2** is a regiospecific, electrophilic addition[4] of NO_2^+ (or its equivalent) to the β-carbon of the enol acetate followed by a hydrolytic conversion of the intermediate to the α-nitro ketone. The stereochemistry of the nitro group in the product is determined by the initial addition of the electrophile, and the factors that control the stereochemistry are the size and the position of substituents on the ring which affect the position of conformational equilibrium of the enol acetate and the direction of approach of the incoming electrophile.

1-Acetoxycyclopentenes would be expected to exist in two conformations, A and B, with conformer A being slightly favored when there is a substituent at the 3-position (pseudoequatorial). There are four possible pathways by which an electrophile can add to the enol acetate. Inspection of Scheme I shows that paths 1 and 3 lead to the trans isomer in the less stable conformation and that paths 2 and 4 lead to the cis isomer. Since the reaction is expected to be kinetically controlled, the exclusive formation of the *trans*-2-nitro-3-methylcyclopentanones rules out paths 2 and 4 which would necessitate the approach of the electrophile from the more hindered site. Also, significant is the fact that the enol acetate without a substituent at the 3-position, 4-methyl-1-acetoxycyclopentene, leads to approximately equal amounts of the *cis*- and *trans*-2-nitro-4-methylcyclopentanones. These results strongly suggest that the methyl group at the 3-position sterically hinders the approach of the electrophilic agent from the

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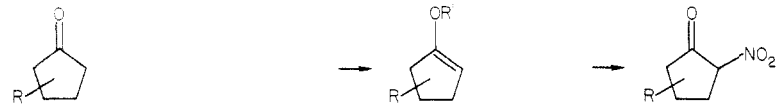
Table I. 2-Nitrocyclopentanones Synthesized from Cyclopentanone Enol Acetates and Potassium Enolates



1 2 or 3 4

R	compd	R	compd R' = Ac	compd R' = K	R	compd
3-methyl	1a	3-methyl	2a	3a	*trans*-2-nitro-3-methyl	4a
3-methyl	1b	4-methyl	2b	3b	*cis*- and *trans*-2-nitro-4-methyl	4b
trans-3,4-dimethyl	1c	*trans*-3,4-dimethyl	2c	3c	*trans*-2-nitro-*trans*-3,4-dimethyl	4c
cis-3,4-dimethyl	1d	*cis*-3,4-dimethyl	2d	3d	*trans*-2-nitro-*cis*-3,4-dimethyl	4d
2,2,4-trimethyl	1e	3,5,5-trimethyl	2e	3e	*trans*-2-nitro-3,5,5-trimethyl	4e

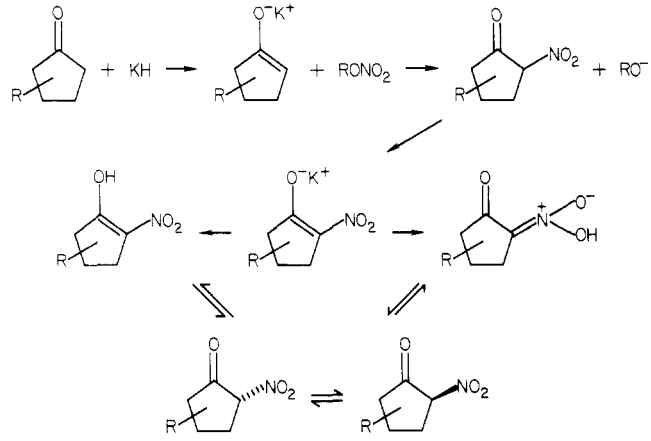
same side as the methyl group. Furthermore, the energy difference between conformers A and B is probably too small to be a major factor in determining if path 1 or 3 predominates, and, in fact, they are probably energetically very close.

Although the nitration of 1-acetoxycyclohexenes is a synthetically useful reaction for the preparation of 2-nitrocyclohexanones, we have found that although the crude yields of the 2-nitrocyclopentanones are very good, isolation of the 2-nitrocyclopentanones from the acidic reaction mixture proved to be difficult. Traces of acid present after the workup undoubtedly catalyze the ring-opening and rearrangement reactions of the 2-nitrocyclopentanones to the glutaric acids and glutarimides, respectively. These types of reactions have been previously observed[8] and on the basis of our experience seem to occur more readily with 2-nitrocyclopentanones than with 2-nitrocyclohexanones.

Because of the problem associated with the isolation of the 2-nitrocyclopentanones, we investigated the nitration of metal enolates with amyl nitrate. Previous workers[9] used bases such as sodium or potassium amide and metal alkoxides with limited or no success. If the nucleophilic displacement of the enolate on the alkyl nitrate is relatively slow and enolate formation is incomplete, then side reactions with unreacted ketone such as aldols are possible. The use of excess base has been previously demonstrated to lead to ring-cleavage products.[9] Brown[10] had demonstrated that kaliation with potassium hydride had proven to be a rapid and quantitative process for generating ketone enolates. Consequently, we chose potassium hydride as the base, and to our expectation the potassium enolates generated in this manner could be nitrated with amyl nitrate to the 2-nitrocyclopentanone potassium salts in good yields. The reaction mixture is worked up either by direct acidification of the reaction mixture or acidification of the potassium salt after its isolation from the reaction mixture by filtration. The latter method leads to better yields of the 2-nitrocyclopentanones.

The 2-nitrocyclopentanones prepared by the potassium hydride–amyl nitrate method are listed in Table I. Since the nitration of the enolate leads to the nitronate salt, the stereochemistry of the 2-nitrocyclopentanones is not governed by the mode of attack of the enolate on the alkyl nitrate but rather by the protonation of the keto nitronate. Protonation on oxygen leads to either the enol or the *aci*-nitronate of the α-nitro ketone which rapidly isomerizes to the more stable keto isomer. However, tautomeric forms could not be observed by NMR immediately after acidification of the salts. The pathway which accounts for the results of the nitration of the potassium enolates is shown in Scheme II.

Scheme II. Pathway for the Formation of 2-Nitrocyclopentanones via Nitration of Potassium Enolates



Examination of the results in Table I shows that the product obtained from the nitration of a given ketone through either its enol acetate or enolate are identical. Furthermore, in the case of 3-methylcyclopentanone, nitration by either method leads to the same ratio of isomeric ketones as well as the same ratio of epimeric nitro ketones. On the basis of these observations, it is tempting to suggest that the enol acetate nitration mechanism for the formation of the 2-nitrocyclopentanones also proceeds through a mechanism similar to that for the enolate nitration and involves an enol intermediate which ketonizes to the more stable form. However, we had previously demonstrated[4] that nitration of cyclohexanone enol acetates is a kinetically controlled process, and one could assume that the same holds true for nitrating cyclopentanone enol acetates. To account for the results, one can see that either the kinetic and thermodynamic products are fortuitously the same or the isomerization of the kinetic product is much more rapid for the 2-nitrocyclopentanones than for the 2-nitrocyclohexanones.

Attempts at nitrating a number of other ketones by using the enolate method were not as successful. *trans*-3,4-Diphenylcyclopentanone[11] led to a very poor yield of what appears to be *trans*-2-nitro-*trans*-3,4-diphenylcyclopentanone. Camphor leads to a 20% yield of a mixture of 3-nitrocamphor[12] and *N*-hydroxycamphorimide.[13] Nitration of norcamphor afforded a 32% yield

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of a mixture of compounds that appear to be the aldol condensation products of norcamphor and 3-nitronorcamphor. No 3-nitronorcamphor[14] could be isolated from the reaction mixture.

Some representative cyclohexanones were also nitrated under the enolate conditions to give 2-nitrocyclohexanone, 2-nitro-3,3,5,5-tetramethylcyclohexanone,[4] and *trans*-2-nitro-4-*tert*-butylcyclohexanone[4] in yields of 72%, 60%, and 85%, respectively. In order for the nitration of potassium enolates to be a successful method for the synthesis of α-nitro ketones, the enolates must be generated nearly quantitatively, and acidification of the potassium keto nitronates must be carried out very carefully. The exact conditions vary from compound to compound.

Unfortunately, generating the enolates by using potassium hydride leads to the thermodynamic mixture of enolates,[11] and therefore nitration of the potassium enolates does not allow for a regiospecific synthesis of α-nitro ketones. Nitration of lithium enolates which can be generating regioselectively by a variety of methods[15] would serve such a purpose. An attempt at nitrating a lithium ketone enolate of a steroid was unsuccessful,[16] but nitration of the dilithio anions of carboxylic acids has met with success.[17] We are currently studying the feasibility of nitrating lithium enolates. In connection with synthesizing α-nitro ketones regioselectively we will report in a subsequent publication the nitration of enol silyl ethers which can be generated regioselectively.[15]

Experimental Section

Infrared spectra were determined on a Perkin-Elmer 237 infrared spectrometer. The ^1H NMR spectra were determined on a Varian Associates A-60 spectrometer. The 100-MHz NMR spectra were determined on a Varian Associates HA-100 spectrometer through the courtesy of Dr. Kermit Ramey, ARCO Chemical Co. Chemical shifts were expressed as parts per million from Me_4Si. A Perkin-Elmer 202 ultraviolet-visible spectrophotometer was used for UV measurements. Melting points were determined on a Thomas-Hoover capillary melting point apparatus and were not corrected. Gas chromatographic analyses were carried out on a Hewlett-Packard, F&M Scientific Model 700 gas chromatography equipped with a thermal-conductivity detector. The elemental analyses were determined by Galbraith Laboratories.

1-Acetoxy-3-methyl- and 1-Acetoxy-4-methylcyclopentenes (2a,b; Enol Acetates of 3-Methylcyclopentanone). A mixture of 29.4 g (0.3 mol) of 3-methylcyclopentanone, 90.0 g (0.9 mol) of isopropenyl acetate, and 0.6 g of *p*-toluenesulfonic acid was placed in a 250-mL round-bottomed flask equipped with a magnetic stirrer, a thermometer, a Dean–Stark trap, and a condenser. The solution was refluxed for 16 h, during which time 32 mL of distillate containing acetone was collected. The solution was cooled to room temperature and partitioned between a 150-mL mixture of pentane and 5% K_2CO_3 solution. The organic layer was separated, washed with saturated salt solution, and dried over anhydrous $MgSO_4$, and the solvent was evaporated by means of rotary evaporator. The crude brown-yellow oily liquid was distilled under reduced pressure through a 6-ft Vigreaux column. Four fractions were collected and analyzed by GLC [$^1/_4$ in. × 6 ft, 15% Carbowax, 10% UC W98 (60–80-mesh) column]. Fractions one and two were isopropenyl acetate and unreacted ketone; fractions three and four were pure enol acetate. A yield of 36.2 g (84%) of a mixture of enol acetates was obtained: bp 56–57 °C (5.6 torr); NMR ($CDCl_3$) δ 5.32 (br s, olefinic protons), 2.6–1.9 (m, ring protons), 2.1 (s, $OCOCH_3$), 1.05 and 1.09 (2 overlapping d, $CHCH_3$); IR (film) 1760 (C=O), 1660 cm^{-1} (C=C). Gas chromatographic analysis on a $^1/_8$ in. × 8 ft, 15% silicon rubber SE-30, 60–80 WAW DMCS 700 column indicated a purity of >99% of the enol acetates. Anal. Calcd for $C_8H_{12}O_2$: C, 68.54; H, 8.63. Found: C, 67.67; H, 8.65.

1-Acetoxy-*trans*-3,4-dimethylcyclopentene (2c; Enol Acetate of *trans*-3,4-Dimethylcyclopentanone). By use of the same procedure as for the preparation of **2**, *trans*-3,4-dimethylcyclopentanone was converted into its enol acetate **2c**: yield 84%; bp 58–59.5 °C (4–4.5 torr); n^{20}_D 1.4416; NMR ($CDCl_3$) δ 5.25 (br s, 1, olefinic proton), 2.6–1.7 (m, 4, ring protons), 2.05 (s, 3, $OCOCH_3$), 1.08 (2 d, CH_3's); IR (film) 1770 (C=O), 1680 cm^{-1} (C=C). Gas chromatographic analysis with a $^1/_4$ in. × 6 ft 15%, Carbowax, 10% UC W98, 60–80-mesh column indicated a purity of 99% of the enol acetate. Anal. Calcd for $C_9H_{14}O_2$: C, 70.03; H, 9.08. Found: C, 69.71; H, 8.68.

1-Acetoxy-*cis*-3,4-dimethylcyclopentene (2d; Enol Acetate of *cis*-3,4-Dimethylcyclopentanone). By use of the same procedure as for the preparation of **2a**, *cis*-3,4-dimethylcyclopentanone was converted into its enol acetate **2d**: yield 81%; bp 50–51 °C (4.5 torr); NMR ($CDCl_3$) δ 5.41 (d, 1, olefinic proton, ^3J = 2 Hz), 2.13 (s, $3OCOCH_3$), 1.2 (d, 3, CH_3), 1.05 (d, 3, CH_3), 2.73 (m, 1, C_3H, CH_3), 1.3 (m, 2, C_5H_2). C_4 H_2). The purity of the enol acetate was >99%, as determined by GLC with a $^1/_4$ in. × 6 ft, silicon gum rubber GE SE-30 column. Anal. Calcd for $C_9H_{14}O_2$: C, 70.03; H, 9.08. Found: C, 70.30; H, 8.96.

1-Acetoxy-3,5,5-trimethylcyclopentene (2e; Enol Acetate of 2,2,4-Trimethylcyclopentanone). By use of the same procedure as for the preparation of **2a**, 2,2,4-trimethylcyclopentanone was converted into its enol acetate **2e**: yield 81%; bp 50–51 °C (4.5 mm); the purity of the enol acetate was >99% as determined by GLC with a $^1/_4$ in. × 6 ft silicon gum rubber GE SE-30 column; NMR ($CDCl_3$) δ 5.41 (d, 1, olefinic proton, ^3J = 2 Hz), 2.13 (s, 3, $OCOCH_3$), 1.2 (d, 3, CH_3), 1.05 (s, 6, $2CH_3$), 2.73 (s, 1, C_3HCH_3), 1.3 (m, 2, C_4H_2). Anal. Calcd for $C_{10}H_{16}O_2$: C, 71.42; H, 9.52. Found: C, 71.48; H, 9.37.

***trans*-2-Nitro-3-methylcyclopentanone and *cis*- and *trans*-2-Nitro-4-methylcyclopentanone (4a,b). (1) Nitration of 3-Methylcyclopentanone Enol Acetates (2a,b).** A mixture of 9.94 g (71 mmol) of a 1:1 isomeric mixture of 3-methylcyclopentanone enol acetates and 25.0 g (230 mmol) of acetic anhydride was placed in a three-necked, 100-mL, round-bottomed flask equipped with a magnetic stirrer, a pressure-equalizing addition funnel, and a thermometer. Concentrated nitric acid (70%, 5.0 mL, 71 mmol) was added dropwise to the stirred solution, and the temperature of the solution was kept between 18 and 20 °C. When all the nitric acid was added, the yellow-green solution was allowed to stir for 1 h at about 15–20 °C. The mixture was then transferred to a vacuum distillation apparatus, and the residual acetyl nitrate, acetic acid, and excess acetic anhydride were removed. During the distillation the flask was not heated above 35 °C. The crude product was purified by molecular distillation in which the pot temperature was not allowed to exceed 35 °C to give a clear yellow liquid, a mixture of nitro ketones. Purification and attempted separation of the isomeric nitro ketones by column chromatography with silica gel (Woelm, activity III/30 mm, contains 0.5% inorganic fluorescent indicator), and a hexane–methylene chloride mixture as the eluant was not successful. The NMR for all the fractions showed no identifiable α-$CHNO_2$ proton resonance and the IR showed no identifiable NO_2 absorption.

(2) Nitration of Potassium 3-Methylcyclopentanone Enolates (3a,b). Potassium hydride as a 50% mineral oil dispersion (2.24 g, 28.0 mmol) was weighed into an oven-dried, 100-mL three-necked, round-bottomed flask, and 30 mL of calcium hydride dried dimethoxyethane (DME) was added. The flask was equipped with a pressure-equalizing addition funnel, a magnetic stirrer, and a thermometer. The suspension of KH in DME was allowed to stir at room temperature for 10–15 min. The flask was then cooled in an ice–water bath and flushed with nitrogen. 3-Methylcyclopentanone (2.45 g, 25 mmol) in 15 mL of dry DME was added dropwise at 0–20 °C, (addition took about 10 min), and the reaction mixture was allowed to stir for 10 min. The mixture was cooled to −70 °C by means of a dry ice–acetone external bath, and then 3.6 g (27.5 mmol) of amyl nitrate in 10 mL of dry DME was added dropwise over 15 min. The mixture was stirred at −70 °C for 15 min, was allowed to come to room temperature, and was then stirred for 2 h. Dilute hydrochloric

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acid (2.5%) was added at 0 °C until the solution was acidic to litmus. The organic layer was separated and the aqueous layer extracted several times with ether. The combined organic ether extracts were washed with water and dried over anhydrous $MgSO_4$. The solvent was evaporated on a rotary evaporator. Distillation of the remaining brown oil by using a molecular distillation apparatus, in which the pot temperature was kept between 45 and 50 °C (0.5–0.6 torr), gave 2.0 g (56%) of a clear yellow liquid, a mixture of the nitro ketones. An NMR spectrum shows both positional isomers in an almost equal ratio: IR (film) 1760 (C=O), 1555 cm^{-1} (NO_2); NMR ($CDCl_3$) δ 4.85 (d, 1, $CHNO_2$, *trans*-2-nitro-3-methyl, ^3J = 11.5 Hz), 5.18 (m, 1, $CHNO_2$ both *cis*- and *trans*-2-nitro-4-methyl), 2.8–1.9 (m, ring protons), 1.25 (2 d, CH_3's). Anal. Calcd for $C_6H_9NO_3$: C, 50.34; H, 6.34; N, 9.79. Found: C, 50.02; H, 6.19; N, 9.67.

The same nitration was repeated, and the potassium nitronate salt was separated prior to acidification by vacuum distillation of the solvent and then filtration of the yellow precipitate. The potassium salt was purified by washing several times with pentane and then recrystallizing from a 1:1 mixture of ethanol and 2-propanol. The salt was vacuum dried overnight to give 3.0 g (67%) of pure potassium nitronate salt, mp 225–226 °C dec. The potassium salt was dissolved in 10 mL of water and acidified with dilute hydrochloric acid to yield a yellow oil, which was extracted into ether and then dried over anhydrous $MgSO_4$. The solvent was removed by rotary evaporation, and 2.1 g (90%) of nitro ketones, purified by molecular distillation, was obtained. An NMR spectrum was obtained immediately after acidification as well as after purification of the nitro ketone, and the spectra were identical. Thin-layer chromatography was carried out by using silica plates (5 × 20 cm, Quantum Industry) and indicated three spots in the ratio of 1:0.5:0.5 by using a 1:1 CH_2Cl_2/hexane solvent mixture as an eluant. Gas chromatographic analysis with a $^1/_3$ in. × 6 ft, 10% Se-30, 60-80 WAW HMDS or a $^1/_4$ in. × 8 ft, 15% silicon rubber SE-30, 60-80 WAW DMCS 700 column showed only two peaks with very close retention times.

***trans*-2-Nitro-*trans*-3,4-dimethylcyclopentanone (4c). (1) Nitration of *trans*-3,4-Dimethylcyclopentanone Enol Acetate (2c).** A mixture of 5.5 g (35 mmol) of 1-acetoxy-*trans*-3,4-dimethylcyclopentene and 12.5 g (115 mmol) of acetic anhydride was placed in a 50-mL round-bottom flask equipped with a magnetic stirrer, a pressure-equalizing funnel, and a thermometer. Concentrated nitric acid (70%, 2.5 mL, 35 mmol) was added dropwise to the stirred solution, during which time the temperature was maintained between 18 and 20 °C. After the addition was completed, the solution was allowed to stir for an additional hour at approximately the same temperature. Vacuum distillation was carried out to remove residual acetyl nitrate, acetic acid, and excess acetic anhydride with a maximum pot temperature of 40 °C. A clear reddish brown oil remained which was then distilled under reduced pressure by using a molecular distillation apparatus. The pure nitro ketone was collected as a yellow liquid between 35 and 36 °C (0.2 torr).

(2) Nitration of Potassium *trans*-3,4-Dimethylcyclopentanone Enolate (3c). Potassium hydride (2.24 g, 28.0 mmol, as a 50% mineral oil dispersion) was weighed in an oven-dried, 100-mL, round-bottomed flask equipped with an addition funnel, a thermometer, and a magnetic stirrer. Calcium hydride dried DME was added and the suspension allowed to stir at room temperature for 15 min. *trans*-3,4-Dimethylcyclopentanone (2.8 g, 25 mmol) in 15 mL of dry DME was added dropwise at 0–20 °C over a period of 20 min. Amyl nitrate (3.6 g, 27.5 mmol) in 10 mL of DME was added dropwise at −70 °C over a period of 30 min, and the reaction mixture was allowed to warm to room temperature. The solvent was removed from the potassium nitronate salt by means of vacuum distillation, and the salt was purified by crystallization from a 1:1 mixture of ethanol and 2-propanol. The yellow crystals were dried under vacuum to give 3.0 g (63%) of the potassium 2-oxo-*trans*-4,5-dimethylcyclopentane nitronate: mp 110–112 °C; NMR (D_2O) δ 2.75 (m, CHCO), 2.1–1.85 (m, 2, ring protons), 1.05 and 1.23 (2 d, CH_3's); IR (Nujol) 1610 (C=C), 1510 cm^{-1} (NO_2, conjugated). The pure salt (1.0 g) was dissolved in water and acidified with glacial acetic acid. A yellow oil separated which darkened on standing. It was extracted into ether, and then the solvent was removed to yield the crude nitro ketone.

Another 1.8 g of the potassium nitronate salt was dissolved in 10 mL of water and then acidified with 2% hydrochloric acid. The aqueous solution was extracted with diethyl ether and dried over $MgSO_4$, and the solvent was removed. A pale yellow liquid remained which was distilled by using a molecular still at 45–48 °C (0.7–0.5 torr) to give 0.995 g (63%) of pure *trans*-2-nitro-*trans*-3,4-dimethylcyclopentanone: IR (film) 1765 (C=O), 1560 cm^{-1} (NO_2); NMR ($CDCl_3$) δ 4.81 (d, 1, $CHNO_2$, ^3J = 11.5 Hz), 2.85–2.2 (m, ring protons), 1.2 (d, CH_3 on C_4), 1.29 (d, CH_3 on C_3). Anal. Calcd for $C_7H_{11}NO_3$: C, 53.49; H, 7.065; N, 8.91. Found: C, 53.80; H, 7.13; N, 9.10.

***trans*-2-Nitro-*cis*-3,4-dimethylcyclopentanone (4d). (1) Nitration of *cis*-3,4-Dimethylcyclopentanone Enol Acetate (2d).** A mixture of 4.31 g (28 mmol) of 1-acetoxy-*cis*-3,4-dimethylcyclopentene and 10.0 g (98 mmol) of acetic anhydride was placed in a 50-mL, three-necked, round-bottomed flask equipped with a magnetic stirrer, an addition funnel, and a thermometer. Concentrated nitric acid (70%, 2.0 mL, 32 mmol) was added dropwise to the stirred solution, and the flask was cooled with an ice–water bath to keep the reaction temperature between 18 and 20 °C. After the addition of nitric acid was completed, the clear, yellow solution was allowed to stir for 1 h at approximately the same temperature. The mixture was then transferred to a vacuum distillation apparatus, and the residual acetyl nitrate, acetic acid, and excess acetic anhydride were removed under reduced pressure. The maximum pot temperature was 35 °C. For purification of the liquid a molecular distillation was carried out at 35–40 °C (0.1 torr), and *trans*-2-nitro-*cis*-3,4-dimethylcyclopentanone was obtained as a clear yellow oil.

(2) Nitration of Potassium *cis*-3,4-Dimethylcyclopentanone Enolate (3d). Potassium hydride (2.24 g, 28.0 mmol, as a 50% mineral oil dispersion) was weighed in an oven-dried, 100-mL, three-necked, round-bottomed flask, and 30 mL of dry DME was added. The flask was equipped with a thermometer, a magnetic stirrer, and an addition funnel. The suspension of KH in DME was stirred at room temperature for 15 min, and *cis*-3,4-dimethylcyclopentanone (2.8 g, 25 mmol) in 15 mL of dry DME was added dropwise over 15 min at 0–20 °C. The reaction mixture was cooled to −70 °C, and then amyl nitrate (3.6 g, 27.5 mmol) in 10 mL of DME was added dropwise. The reaction mixture was stirred at this temperature for 30 min, was allowed to warm to room temperature, and was stirred for an additional hour. The orange-brown nitronate salt was separated by filtration and was crystallized several times from a 1:1 mixture of ethanol and 2-propanol to give 3.7 g (75%) of pure nitronate salt, mp 125–128 °C. The salt was dissolved in water, acidified with dilute hydrochloric acid, extracted with ether, and dried over anhydrous $MgSO_4$. The solvent was removed, and the remaining yellow oil was subjected to a molecular distillation at 45–50 °C (0.6–0.7 torr) to give pure *trans*-2-nitro-*cis*-3,4-dimethylcyclopentanone as a pale yellow oil: IR (film) 1760 (C=O), 1555 cm^{-1} (NO_2); NMR ($CDCl_3$) δ 4.85 (d, 1, $CHNO_2$, ^3J = 11.0 Hz), 3.18–2.32 (m, ring protons), 1.25 (d, CH_3 at C_3), 1.05 (d, CH_3 at C_4). Anal. Calcd for $C_7H_{11}NO_3$: C, 53.49; H, 7.055; N, 8.91. Found: C, 53.63; H, 7.12; N, 9.11.

***trans*-2-Nitro-3,5,5-trimethylcyclopentanone (4e). (1) Nitration of 2,2,4-Trimethylcyclopentanone Enol Acetate (2e).** A mixture of 10.8 g (64 mmol) of 1-acetoxy 3,5,5-trimethylcyclopentene and 22.6 g (220 mmol) of acetic anhydride was placed in a three-necked, 100-mL, round-bottomed flask equipped with an addition funnel, a magnetic stirrer, and a thermometer. Concentrated nitric acid (70%, 4.5 mL, 64 mmol) was added dropwise to the stirred solution, and the temperature was maintained between 15 and 20 °C. After the addition of nitric acid was completed, the green solution was allowed to stir for 1 h at 15–20 °C. The residual acetyl nitrate, acetic acid, and excess acetic anhydride were removed under reduced pressure. The flask was heated to a maximum of 40 °C. An NMR of the crude product showed formation of only the trans isomer. The reddish brown oil was purified by a molecular distillation [55–56 °C (0.2 torr)] to give a pale yellow liquid.

(2) Nitration of Potassium 2,2,4-Trimethylcyclopentanone Enolate (3e). Potassium hydride (2.24 g, 28.0 mmol as a 50% mineral oil dispersion) was weighed in an oven-dried, 100-mL, three-necked, round-bottomed flask. The flask was then equipped with a magnetic stirrer, a thermometer, and an addition funnel,

30 mL of dry DME was added, and the KH and DME suspension was stirred for 15–20 min at room temperature. 2,2,4-Trimethylcyclopentanone (3.15 g, 25.0 mmol) in 15 mL of DME was added dropwise over 10–15 min at 0–20 °C. Amyl nitrate (3.6 g, 27.5 mmol) in 8 mL of dry DME was added dropwise at −70 °C over 15 min. The reaction mixture was allowed to warm to 0 °C and allowed to stir for 2 h at 0–10 °C. The reaction mixture was transferred to a vacuum distillation apparatus from which the solvent was removed, the temperature being kept below 45 °C. The yellow potassium salt was purified by crystallization from a 1:1 propanol–ethanol mixture and dried under vacuum to give 4.3 g (82%) of the potassium nitronate salt: mp 238 °C dec; NMR (D_2O) δ 2.95 (m, 1, $CHCH_3$), 1.9–1.4 (m, CH_2), 1.25 (d, $CHCH_3$), 1.0 and 1.05 (2 s, $2CH_3$). The potassium salt was dissolved in water and acidified with dilute hydrochloric acid, and the white crystals were separated and recrystallized from *n*-hexane to give white needles of *trans*-2-nitro-3,5,5-trimethylcyclopentanone: mp 54.5–55.5 °C (Lit.[9] mp 54–55 °C); NMR ($CDCl_3$) δ 4.85 (d, 1, $CHNO_2$, ^3J = 11.5 Hz), 3.0 (m, 1, $CHCH_3$), 2.1–1.55 (m, CH_2), 1.3 (d, $CHCH_3$), 1.2 (2 s, $2CH_3$).

Nitration of Cyclohexanone Potassium Enolates. (1) Cyclohexanone. Potassium hydride (12.83 g, 112 mmol, as a 35% oil dispersion) was weighed into a 250-mL round-bottomed flask equipped with a magnetic stirrer, a thermometer, and an addition funnel. The KH was suspended in 100 mL of dry DME. Cyclohexanone (9.82 g, 100 mmol) in 50 mL of DME was added dropwise over 30 min. Amyl nitrate (14.4 g, 110 mmol) in 30 mL of DME was added over a period of 30 min at −78 °C. Then the reaction mixture was allowed to come to room temperature and was stirred for 4 h. The potassium nitronate salt was precipitated as a yellow amorophorous crystals which were purified after separation by crystallization several times from a mixture of 1:1 ethanol/2-propanol to give 13.0 g (72%) of the nitronate salt. Acidification of the salt by dilute hydrochloric acid gave the corresponding 2-nitrocyclohexanone.[6]

(2) 4-*tert*-Butylcyclohexanone. Potassium hydride (12.83 g, 112 mmol, as a 35% oil dispersion) was weighed in an oven-dried, 250-mL, round-bottomed flask, and then 100 mL of dry DME was added. The flask was then equipped with a magnetic stirrer, an addition funnel, and a thermometer. 4-*tert*-Butylcyclohexanone (15.43 g, 100 mmol) in 50 mL of DME was added at room temperature over 1 h followed by the addition of amyl nitrate (14.4 g, 110 mmol) in 30 mL of DME at −78 °C over 30 min. The reaction mixture was stirred for 2 h at −78 °C and then allowed to come to room temperature. A yellow precipitate of the potassium nitronate salt was formed which was separated from the reaction mixture and purified to give 19.5 g (82%) of the salt. Acidification of the salt gave *cis*-2-nitro-4-*tert*-butylcyclohexanone.[6]

(3) 3,3,5,5-Tetramethylcyclohexanone. Potassium hydride (12.83 g, 112 mmol, as a 35% oil dispersion) was weighed into a 250-mL round-bottomed flask and suspended in 100 mL of dry DME. The flask was then equipped with a magnetic stirrer, a thermometer, and an addition funnel. 3,3,5,5-Tetramethylcyclohexanone (15.43 g, 100 mmol) in 50 mL of DME was added dropwise at room temperature over a period of 1 h. Amyl nitrate (14.4 g, 110 mmol) in 30 mL of DME was added at −78 °C over a 45-min period. The reaction mixture was allowed to warm to room temperature. The potassium nitronate salt was separated from the clear yellow solution by vacuum distillation of the solvent with a pot temperature not higher than 30 °C (1.0 mm). Yellow crystals of the salt begun to form which were separated and purified by crystallization from a 1:1 mixture of ethyl alcohol and isopropyl alcohol to give 13.0 g (60%) of the salt, mp 260 °C. Acidification of the salt gave white crystals of 2-nitro-3,3,5,5-tetramethylcyclohexanone which was crystallized from hexane.[6]

Nitration of Camphor Potassium Enolate. Potassium hydride (8.96 g, 0.112 mol, as a 50% oil dispersion) was weighed into an oven-dried, 250-mL, three-necked, round-bottomed flask, 100 mL of dry DME was added, and then the suspension was stirred at room temperature. The flask was equipped with a magnetic stirrer, a dry nitrogen inlet tube, a thermometer, and an addition funnel. Camphor (15.22 g, 0.1 mol) in 50 mL of DME was added dropwise at room temperature over a 10-min period. The mixture was allowed to stir for 6 h. The reaction mixture was cooled to −78 °C, amyl nitrate (14.11 g, 0.11 mol) in 30 mL of DME was added dropwise over 30 min, and the mixture was stirred at this temperature for 12 h, at −50 °C for 4 h, and at 20 °C for 20 h. The bright orange solution was acidified with 5% hydrochloric acid and turned green. Extraction with ether, followed by drying the ether layer over anhydrous $MgSO_4$ and removal of the solvent, gave 5.0 g (20%) of a yellow oil. Attempts to crystallize the oil were not successful; however, an NMR spectrum indicated the formation of 3-nitrocamphor[12] along with a small amount of rearranged compound which is believed to be *N*-hydroxycamphormide[13] on the basis of its spectral properties.

Nitration of Norcamphor Potassium Enolate. Potassium hydride (9.0, 112 mmol, as a 50% oil dispersion) was suspended in a 100 mL of dry THF, and the mixture was stirred at room temperature for 15–20 min in a 250-mL round-bottomed flask equipped with a magnetic stirrer, a thermometer, and an addition funnel. Norcamphor (11.0 g, 100 mmol) in 50 mL of THF was added dropwise over 1 h. The formation of the enolate anion was very slow, as indicated by the color of the reaction mixture. The reaction mixture was allowed to stir at room temperature for 24 h, and the color changed to a bright orange. It was then cooled to −78 °C, and amyl nitrate (14.4 g, 110 mmol) in 30 mL of THF was added dropwise over 90 min. The mixture was allowed to come to room temperature and was stirred for 20 h more at room temperature, at 50 °C for 2 h, and then at room temperature again for 1 h. The color changed to a dark red, and workup of the reaction mixture by acidification with 5% hydrochloric acid gave a green oily liquid. The reaction mixture was extracted four times with ether and dried over $MgSO_4$, and the solvent was evaporated on a rotary evaporator to give 5.7 g (32%) of an oily product. The crude product was purified by microscale evaporative distillation in vacuo at 60 °C (0.1 mm) to give a yellow oily liquid which is believed to be a mixture of 3-nitro-3-(2-hydroxynorbornyl)norcamphor and 3-(2-hydroxy-3-nitronorbornyl)norcamphor: NMR ($CDCl_3$) δ 5.9 (br, OH, exchangeable with D_2O), 5.42 (t, 1, $CHNO_2$), 4.45 (d, C_4 H), 4.0 (br s), 2.9, 2.2–1.4 (m, ring protons); IR (film) 3200 (OH), 1725 (C=O), 1535 cm^{-1} (NO_2). Anal. Calcd for $C_{14}H_{19}NO_4$: C, 63.38; H, 7.22; N, 5.28; mol wt 265.31. Found: C, 63.30; H, 7.10; N, 5.45; mol wt 266. Attempts to purify this oil by crystallization were not successful; however, TLC analysis on silica plates (Quanta-gram) and alumina plates (Woelm alumina, neutral) showed at least three compounds to be present.

Caution: All nitronate salts are to be considered potentially hazardous and toxic and should be handled accordingly.

Registry No. 1a, 1120-72-5; **1c**, 19550-73-3; **1d**, 19550-72-2; **1e**, 28056-54-4; **2a**, 79449-31-3; **2b**, 79449-32-4; **2c**, 79449-33-5; **2d**, 79449-34-6; **2e**, 79449-35-7; **3a**, 79449-36-8; **3b**, 79449-37-9; **3c**, 79449-38-0; **3d**, 79449-39-1; **3e**, 79449-40-4; **4a**, 79449-41-5; *cis*-**4b**, 79449-42-6; *trans*-**4b**, 79449-43-7; **4c**, 79449-44-8; **4d**, 79449-45-9; **4e**, 63296-76-4; potassium 2-oxo-5-methylcyclopentane nitronate, 79449-46-0; potassium 2-oxo-*trans*-4,5-dimethylcyclopentane nitronate, 79449-47-1; potassium 2-oxo-*cis*-4,5-dimethylcyclopentane nitronate, 79449-48-2; potassium 2-oxo-3,3,5-trimethylcyclopentane nitronate, 13154-56-8; cyclohexanone, 108-94-1; potassium 2-oxocyclohexane nitronate, 51483-27-3; 2-nitrocyclohexanone, 4883-67-4; 4-*tert*-butylcyclohexanone, 98-53-3; potassium 5-*tert*-butyl-2-oxocyclohexane nitronate, 77507-10-9; *cis*-2-nitro-4-*tert*-butylcyclohexanone, 74609-73-7; 3,3,5,5-tetramethylcyclohexanone, 14376-79-5; potassium 2-oxo-4,4,6,6-tetramethylcyclohexane nitronate, 79449-49-3; 2-nitro-3,3,5,5-tetramethylcyclohexanone, 74609-83-9; camphor, 464-49-3; 3-nitrocamphor, 2243-88-1; norcamphor, 497-38-1.