Generation and Trapping of *N*-Acyliminium Ions Derived from Isomünchnone Cycloadducts. A Versatile Route to Functionalized Heterocycles†

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A series of 2-diazo-*N*-hept-6-enoylmalonamides were prepared and treated with a catalytic amount of rhodium(II) perfluorobutyrate. The resultant carbenoids underwent facile cyclization onto the neighboring amide carbonyl oxygen atom to generate isomünchnone-type intermediates. Subsequent 1,3-dipolar cycloaddition across the pendant olefin afforded intramolecular cycloadducts in high yield. The cascade sequence is simple, direct, and extremely tolerant of structural diversity. Exposure of these cycloadducts to Lewis acids resulted in oxabicyclic ring opening. *N*-Acyliminium ions of wide structural variety can be easily generated by this sequence of reactions. Different cyclization pathways become available depending on the nature of the substituent group attached to the amide nitrogen. When the tethered group is electrophilic in nature, proton loss from the initially formed *N*-acyliminium ion occurs rapidly to give an acyl enamide which undergoes a subsequent cyclization at the electrophilic center.

N-Acyliminium ions can be considered to be one of the more versatile carbon electrophiles for use in carbon−carbon bond forming reactions.[1−3] They have been extensively utilized as intermediates to produce a large variety of structurally diverse nitrogen heterocycles.[4−14] Of the great variety of precursors used to create *N*-acyliminium ions,[15−18] the most widely employed are the α-alkoxy amides and carbamates.[19] These materials are often stable compounds that readily undergo conversion to *N*-acyliminium ions under a variety of acidic conditions. Typically, these versatile systems are prepared from the partial reduction of the corresponding carbonyl group[20] or oxidation of an amine under electrochemical[21] or transition metal mediated conditions.[22] Subsequent *N*-acyliminium ion formation by Lewis or protic acids followed by trapping with weak carbon nucleophiles provides an exceptionally useful method for carbon−carbon bond formation, in both intermolecular[23] and intramolecular[24] cases.

Our earlier studies of the 1,3-dipolar cycloaddition reactions of isomünchnones derived from α-diazo imides

† This paper is dedicated to my good friend, George R. Newkome, on the occasion of his 60th birthday.

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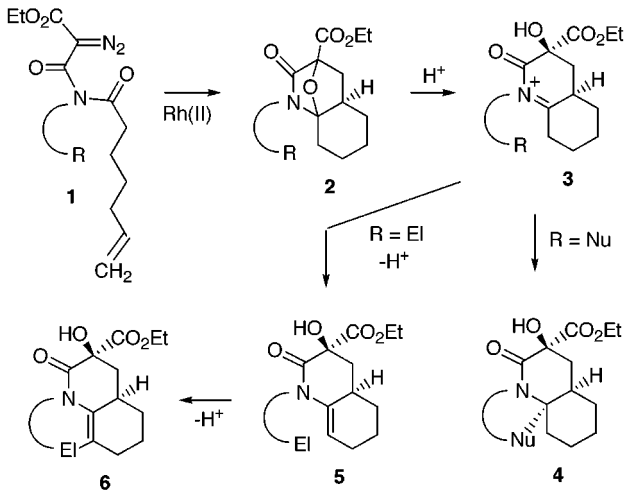
Scheme 1

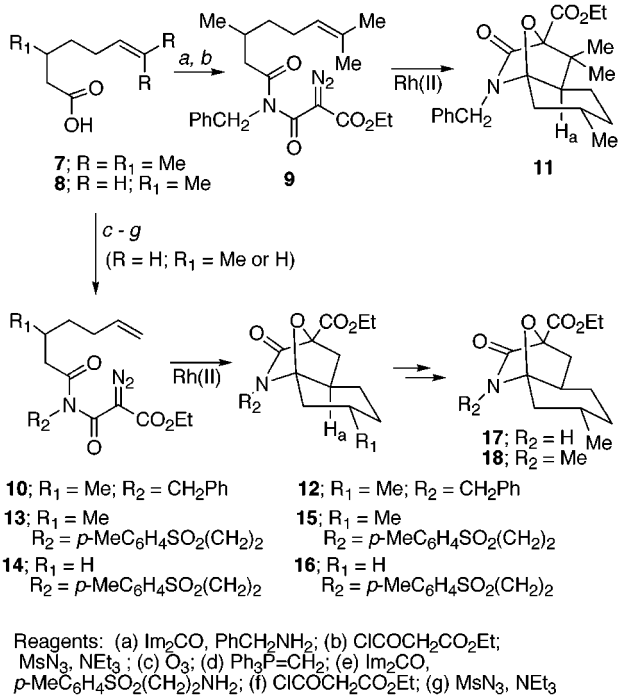


(e.g., **1**) has provided us with a uniquely functionalized cycloadduct **2** containing a "masked" *N*-acyliminium ion.[25−26] Because we were interested in applying the methodology toward the synthesis of nitrogen-containing natural products,[27] we embarked on a more systematic investigation of the cycloaddition/N-acyliminium ion cyclization process. In particular, we were intrigued with the notion of changing the reaction profile of the isomünchnone cycloadduct whereby the initially formed *N*-acyliminium ion could be channeled into a different product distribution, as this would significantly expand the synthetic flexibility of this cascade sequence. We reasoned that the electronic character of the group tethered to the amido nitrogen should dictate the course of the reaction. When a nucleophilic center is available (R = Nu), cyclization onto the initially generated *N*-acyliminium ion **3** will be rapid thereby leading to lactam **4**. On the other hand, if the tethered group possesses a terminal site which is electrophilic in nature (i.e., R = El), deprotonation of **3** should occur first and this will favor formation of product **6**, arising from attack of the nucleophilic enamide present in **5** on the electrophilic center of the tethered amide (Scheme 1).[28] This report presents the experimental details of the conversion of isomünchnone cycloadducts to *N*-acyliminium ions and the internal trapping of these intermediates as a method to prepare complex heterocyclic systems.

Results and Discussion

We began our investigations of the sequential cycloaddition−Mannich cyclization protocol by examining the

Scheme 2



Rh(II)-catalyzed reaction of several unsaturated diazo imides to first establish the propensity of these systems to undergo the intramolecular cycloaddition reaction. Construction of the prerequisite diazo imides necessary for dipole generation started with commercially available citronellic acid (**7**) (Scheme 2). By means of a modified literature procedure, **7** was converted into 3-methyl-6-hexenoic acid (**8**) by ozonolysis followed by a Wittig olefination reaction.[29] Treating citronellic or 3-methyl-6-hexenoic acid with 1,1-carbonyldiimidazole and then quenching with benzylamine afforded the corresponding *N*-benzylamides in excellent yield.[26] The amides were subjected to *N*-malonylation,[30] and the resulting imido esters were treated with mesyl azide in the presence of triethylamine[31] to provide diazo imides **9** and **10**. A related set of reactions was used to prepare the *N*-β-tosylethylamine (TSE)[32] derivatives **13** and **14** from **8** and hexenoic acid, respectively. The advantage of the TSE group is that it can be readily deprotected upon treatment with base.

Formation of the isomünchnone dipole proceeded smoothly when diazo imides **9**, **10**, **13**, and **14** were treated with rhodium(II) perfluorobutyrate in CH_2Cl_2 at 25 °C. After initial generation of the rhodium carbenoid species, intramolecular cyclization occurs on the neighboring carbonyl oxygen to form the mesoionic oxazolium ylide. This dipole is the cyclic equivalent of a carbonyl ylide and readily undergoes 1,3-dipolar cycloaddition across the pendant olefinic π-bond. In all four cases, the reaction provided the internal cycloadduct **11** (90%), **12** (90%), **15** (85%), and **16** (85%) as single diastereomers resulting from *endo* cycloaddition with respect to the dipole (Scheme 2). Assignment of the stereochemistry of

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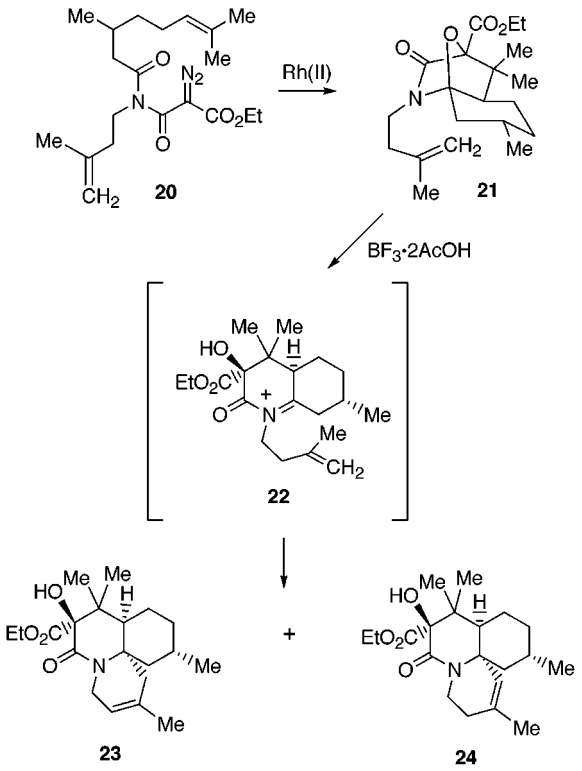
Scheme 3



the cycloadducts was based on a comparison of NMR signals of related substrates synthesized in this laboratory whose structures had been confirmed by X-ray crystallography. In all cases, the *anti* stereochemistry exists between the oxa-bridge and the angular proton (H_a), whereas the methyl group is in the syn relationship to this proton. The formation of the *endo* cycloadduct is in full accord with molecular mechanics calculations which show a large ground-state energy difference between the two diastereomers.

With the intramolecular isomünchnone cycloadducts on hand, we attempted to deprotect them and then attach an appropriate olefinic tether on the amide nitrogen to probe the facility of the Mannich cyclization reaction. The *N*-benzyl protected cycloadducts **11** and **12** proved unsuitable for our purposes because the reductive dealkylation conditions led to a complex of products. By means of Weinreb's conditions for amide deprotection,[32] cycloadduct **15** was easily converted to the unsubstituted amide **17**. Quenching the initially formed anion derived from **15** with iodomethane did produce the *N*-methylated amide **18**, but the yields were 50% or less. Unfortunately, all of our attempts to alkylate the anion with a variety of alkenyl halides proved unsuccessful, and consequently we abandoned this approach.

We decided that the simplest adjustment to our model would be to first prepare the *N*-alkenyl substituted amide and then introduce the diazo imido ester functionality. To this end, we synthesized *N*-3-methyl-3-butenylamide, starting from citronellic acid. Conversion to diazo imide **20** was accomplished by *N*-malonation followed by standard diazo transfer. Addition of rhodium(II) perfluorobutyrate (Rh_2pfb_4) to a solution of **20** in CH_2Cl_2 at 25 °C effected loss of nitrogen and cyclization to the isomünchnone dipole, which underwent an intramolecular cycloaddition with the tethered alkene to give cycloadduct **21** in 94% isolated yield (Scheme 3). Subsequent treatment of **21** with BF_3•2AcOH afforded a 4:1 mixture of the tetracyclic lactams **23** and **24**. Formation of the observed products is perfectly consistent with the sequence of events proposed in Scheme 1. The critical step in this transformation involves the Lewis acid assisted generation of *N*-acyliminium ion **22**, which then undergoes intramolecular cationic π-cyclization from the less sterically congested face. Under the reaction conditions, cationic cyclization results in the formation of a thermodynamically equilibrated mixture of lactams **23** and **24**. The same ratio of products (4:1) was obtained by subjecting either product to the acidic conditions used to effect cyclization. When TMSOTf was used as the Lewis acid, the major product formed corresponded to lactam **24**. The fact that there was no interconversion of the two lactams under these conditions suggests that the Mannich cyclization step is kinetically controlled. The *cis* stereochemistry about the A/B ring junction is consistent with related cationic π-cyclizations carried out by Mondon[33] and Ishibashi[34] in their synthetic approach toward the erythrinane class of alkaloids.

In a further investigation of the sequential cycloaddition π-cyclization process for the construction of nitrogen heterocycles, we decided to examine what effect an electrophilic carbonyl group anchored on the tether would have on the cyclization reaction. Toward this end, cycloadduct **21** was treated with ozone at −78 °C, and this was followed by reductive workup with dimethyl sulfide to furnish the expected methyl ketone **25** in 89% yield. When **25** was treated with a catalytic quantity of *p*-TsOH in acetonitrile, dienyl enamide **29** was obtained in 70% yield. No detectable quantities of the Mannich cyclized product **27** were present in the crude reaction mixture. In this case, proton loss from *N*-acyliminium ion **26** occurs in preference to Mannich cyclization. The initially formed enamide **28** undergoes subsequent condensation on the tethered carbonyl group to ultimately give **29** (Scheme 4).

Two additional systems involving tethered carbonyl groups on the amide nitrogen, which further illustrate the scope of the cascade sequence, are outlined below. Ozonolysis of the *N*-butenyl cycloadduct **30** afforded aldehyde **31**, which on heating with *p*-TsOH in CH_3CN for 24 h gave the aromatic tricyclic lactam **34** in 64% yield. When the reaction was carried out for a shorter period of time (i.e., 6 h), dienyl enamide **32** was formed in 60% yield in addition to lactam **34** (20%). Opening of the oxabicyclic ring with acid followed by proton loss furnishes an enamide that undergoes condensation with the adjacent aldehyde carbonyl to give **32** in a manner similar to that depicted in Scheme 4. Heating a pure sample of **32** under the acidic reaction conditions cleanly afforded the aromatic lactam **34**. We suspect that **32** is first isomerized to cyclohexadiene **33**, which undergoes subsequent oxidative aromatization to produce **34** (Scheme 5).

In the second example (Scheme 6), the acid-catalyzed behavior of the homologous aldehyde **35** was studied. When **35** was heated at reflux in dry acetonitrile in the presence of *p*-TsOH for 12 h, no trace of the Mannich cyclization product was observed. We isolated instead a

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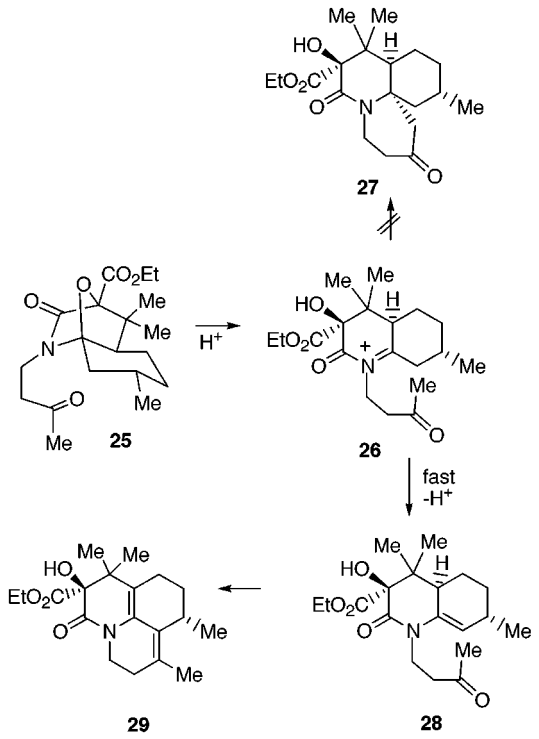
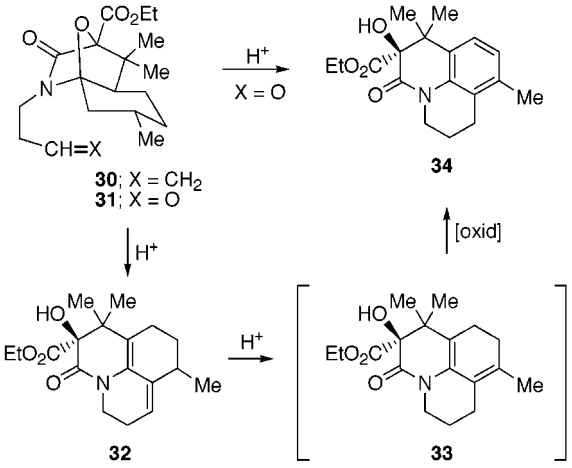
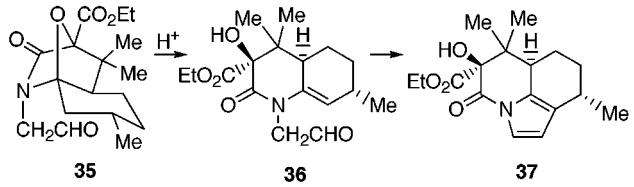
Scheme 4



Scheme 5



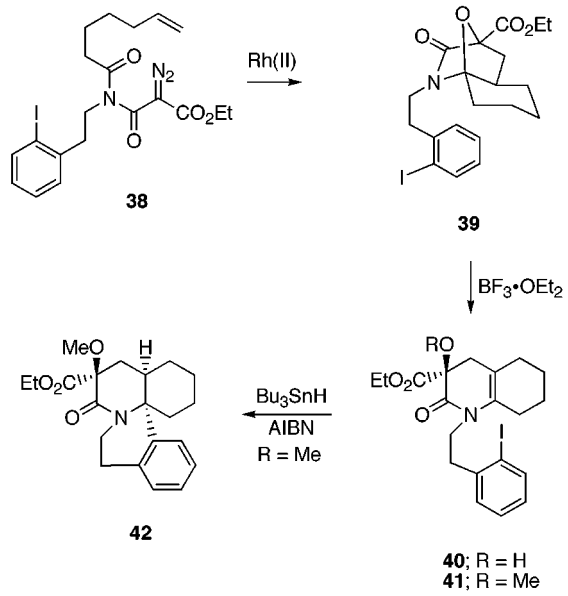
Scheme 6



70% yield of pyrrole **37**. Once again we assume that the intermediate *N*-acyliminium ion formed from the acid-assisted ring opening undergoes rapid proton loss to produce an equilibrating mixture of enamides. Eventual cyclization of the trisubstituted enamide **36** on the aldehyde center followed by dehydration affords pyrrole **37**.

Several examples of radical cyclization to the enamide double bond have been reported over the past few years.[35,36] Aryl radical cyclizations onto cyclic enamides generally produce heterocycles in which the nitrogen atom is present in the newly formed ring.[37] Rigby[38] and

Scheme 7



Schultz[39] have conducted selective 6-*endo* and 7-*endo* cyclizations of aryl radicals onto hydroindole and hydroquinoline enamide systems and have used this reaction as the key step for several alkaloid syntheses. Because radical cyclizations to the enamide double bond have excellent potential for heterocyclic synthesis, we became interested in the possibility of using isomünchnone cycloadducts as precursors for radical cyclizations. We are unaware of any previous examples where dipolar cycloaddition of a mesoionic betaine has been coupled with a subsequent radical cyclization reaction.

o-Iodophenyl diazoimide **38** was prepared starting from hept-6-enoic acid and 2-(2-iodophenyl)ethylamine, and this was followed by *N*-malonylation and diazo transfer of the resulting amide. Rhodium(II)-catalyzed cyclization of **38** furnished the expected isomünchnone cycloadduct **39**. Subsequent Lewis acid induced ring opening with $BF_3{\cdot}OEt_2$ afforded enamide **40**, which was converted to the corresponding methyl ether **41** by treatment with NaH/CH_3I. Treatment of enamide **41** with AIBN and Bu_3SnH in refluxing benzene solution gave lactam **42** in 45% yield (Scheme 7). Attempts to minimize the dehydrohalogenation by slow addition of tributyltin hydride and AIBN to the solution resulted in only minor improvement of the yield. Further efforts to improve the yield by either employing a smaller amount of AIBN or by adding tris(trimethylsilyl)silane and AIBN slowly with a syringe pump met with no success. Even though the yield is modest, this transformation does reveal that the intramolecular radical arylation of enamides derived

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from isomünchnone cycloadducts can be used to prepare complex azapolyheterocyclic systems. Further studies to improve the yield of the 6-*exo*-aryl radical cyclization reaction are now in progress.

In conclusion, the results presented herein demonstrate the potential of the carbenoid cyclization/dipolar cycloaddition/N-acyliminium ion sequence for the construction of functionalized piperidines. This three-step protocol begins with the Rh(II)-catalyzed cyclization of an α-diazo imide to give rise to an isomünchnone dipole. This is followed by an intramolecular 1,3-dipolar cycloaddition. *N*-Acyliminium ion formation is triggered by exposure of the cycloadduct to a Lewis acid. Different cyclization pathways become available depending on the nature of the substituent group attached to the amide nitrogen. We are currently investigating application of the methodology outlined here toward the synthesis of several alkaloid natural products.

Experimental Section

Melting points are uncorrected. Mass spectra were determined at an ionizing voltage of 70 eV. Unless otherwise noted, all reactions were performed in oven-dried glassware under an atmosphere of dry argon. Solutions were evaporated under reduced pressure with a rotary evaporator, and the residue was chromatographed on a silica gel column using an ethyl acetate−hexane mixture as the eluent unless specified otherwise.

General Procedure for the Synthesis of Diazo Imides. A solution containing 5.0 mmol of the appropriate amide and 10.0 mmol of ethyl malonyl chloride in 15 mL of anhydrous benzene was heated at reflux for 1 h. After cooling to room temperature, the reaction was diluted with ether and washed with 10% aqueous NaOH and brine. The organic layer was dried over $MgSO_4$ and concentrated under reduced pressure. The residue was purified by flash chromatography on a silica gel column. A variation of the procedure described by Taber and co-workers[31] was used to prepare the diazo imide system. To a solution containing 2 mmol of the appropriate ketolactam and 2.2 mmol of mesyl azide in 5 mL of CH_2Cl_2 was added 4.0 mmol of Et_3N under N_2 at room temperature. After 3 hr of stirring, the solvent was removed under reduced pressure, and the residue was subjected to flash chromatography on a silica gel column.

2-Diazo-*N*-benzyl-*N*-(3,7-dimethyl-oct-6-enoyl)-malonamic Acid Ethyl Ester (9). To a solution containing 3.0 g (18 mmol) of citronellic acid (**7**) in 100 mL of CH_2Cl_2 was added 4.3 g (26 mmol) of 1,1′-carbonyldiimidazole, and the solution was stirred at room temperature for 2 h. To this mixture was added 4.7 g (44 mmol) of benzylamine at 0 °C, and the solution was allowed to warm to room temperature, stirred for 12 h, and concentrated under reduced pressure. The residue was subjected to flash silica gel chromatography to give 3.9 g (70%) of 3,7-dimethyl-oct-6-enoic acid benzylamide as a white solid: mp 43−44 °C; IR (neat) 3288, 1559, 1455, and 1018 cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz) δ 0.97 (d, 3H, J = 6.3 Hz), 1.05−1.20 (m, 1H), 1.25−1.40 (m, 1H), 1.59 (s, 3H), 1.67 (s, 3H), 1.95 (m, 3H), 2.24 (m, 2H), 4.45 (dd, 2H, J = 5.7 and 1.2 Hz), 5.09 (t, 1H, J = 7.1 Hz), 5.72 (brs, 1H), and 7.26−7.35 (m, 5H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 17.6, 19.5, 25.4, 25.6, 30.4, 36.9, 43.5, 44.4, 124.3, 127.4, 127.7, 128.6, 131.4, 138.4, and 172.3.

N-Malonylacylation was carried out on the above amide in the normal manner to give 3.5 g (93%) of *N*-benzyl-*N*-(3,7-dimethyl-oct-6-enoyl)malonamic acid ethyl ester as a colorless oil: IR (neat) 3060, 1701, and 1154 cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz) δ 0.85 (d, 3H, J = 6.8 Hz), 1.05−1.20 (m, 1H), 1.25−1.40 (m, 1H), 1.29 (t, 3H, J = 7.2 Hz), 1.55 (s, 3H), 1.66 (s, 3H), 1.85−1.95 (m, 2H), 1.95−2.05 (m, 1H), 2.30 (dd, 1H, J = 15.8 and 7.9 Hz), 2.49 (dd, 1H, J = 15.8 and 5.6 Hz), 3.92 (s, 2H), 4.21 (q, 2H, J = 6.9 Hz), 5.03 (m, 3H), and 7.19−7.45 (m, 5H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 13.9, 17.4, 19.4, 25.2, 25.5, 29.0, 36.5, 40.4, 46.4, 46.7, 61.1, 123.9, 125.8, 127.2, 128.6, 131.3, 136.5, 167.2, 168.7, and 175.5; HRMS calcd for $C_{22}H_{31}NO_4$ 373.2253, found 373.2258.

The above imide was subjected to the standard diazo transfer conditions to give 3.2 g (91%) of **9** as a yellow oil: IR (neat) 2128, 1723, 1645, and 1111 cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz) δ 0.85 (d, 3H, J = 6.6 Hz), 1.05−1.20 (m, 1H), 1.25−1.40 (m, 1H), 1.30 (t, 3H, J = 7.1 Hz), 1.56 (s, 3H), 1.66 (s, 3H), 1.95 (m, 3H), 2.31 (dd, 1H, J = 15.8 and 7.9 Hz), 2.50 (dd, 1H, J = 15.8 and 5.6 Hz), 4.27 (q, 2H, J = 7.1 Hz), 4.90 (s, 2H), 5.03 (t, 1H, J = 7.4 Hz), 7.31 (s, 3H), and 7.38 (s, 2H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 14.2, 17.6, 19.5, 25.4, 25.7, 29.8, 36.7, 43.3, 49.1, 61.8, 73.0, 124.2, 127.2, 127.4, 128.6, 131.4, 137.1, 160.5, 166.5, and 174.9.

10-Benzyl-3,7,7-trimethyl-9-oxo-11-oxa-10-aza-tricyclo-[6.2.1.0^{1,6}]-undecane-8-carboxylic Acid Ethyl Ester (11). A solution containing 2.5 g (6.3 mmol) of diazoimide **9** in 60 mL of CH_2Cl_2 at room temperature was treated with 5 mg of rhodium(II) perfluorobutyrate. The reaction mixture was stirred for 24 h at room temperature and was concentrated under reduced pressure. The resulting residue was purified by flash silica gel chromatography to give 2.1 g (90%) of **11** as a white solid: mp 119−120 °C; IR (neat) 1744, 1452, and 1118 cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz) δ 0.72−0.85 (m, 2H), 0.88 (d, 3H, J = 6.3 Hz), 1.04 (s, 3H), 1.18 (s, 3H), 1.37 (t, 3H, J = 7.1 Hz), 1.31−1.41 (m, 1H), 1.48 (t, 2H, J = 14.1 Hz), 1.63−1.70 (m, 2H), 2.06 (dd, 1H, J = 7.3 and 1.1 Hz), 4.33 (d, 1H, J = 15.6 Hz), 4.40 (q, 2H, J = 7.1 Hz), 4.52 (d, 1H, J = 15.6 Hz), and 7.20−7.42 (m, 5H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 14.4, 21.1, 22.1, 26.0, 26.1, 28.3, 33.0, 36.9, 43.4, 44.9, 51.0, 61.7, 92.1, 96.3, 127.7, 128.0, 128.7, 137.0, 165.4, and 169.6. Anal. Calcd for $C_{22}H_{29}NO_4$: C, 71.13; H, 7.87; N, 3.77. Found: C, 70.88; H, 7.80; N, 3.67.

2-Diazo-*N*-benzyl-*N*-(3-methyl-hept-6-enoyl)-malonamic Acid Ethyl Ester (10). To a solution containing 3.0 g (18 mmol) of 3-methyl-hept-6-enoic acid in 100 mL of CH_2Cl_2 was added 5.1 g (32 mmol) of 1,1′-carbonyldiimidazole, and the solution was stirred at room temperature for 2 h. The reaction mixture was charged with 5.6 g (53 mmol) of benzylamine at 0 °C, and the solution was allowed to warm to room temperature, stirred for 12 h, and concentrated under reduced pressure. The residue was subjected to flash silica gel chromatography to give 3.7 g (75%) of 3-methyl-hept-6-enoic acid benzylamide as a colorless oil: IR (neat) 3395, 3068, 1737, 1367, and 1146 cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz) δ 0.96 (d, 3H, J = 6.3 Hz), 1.25−1.35 (m, 1H), 1.42−1.52 (m, 1H), 1.95−2.13 (m, 4H), 2.19−2.26 (m, 1H), 4.45 (d, 2H, J = 5.7 Hz), 4.90−5.03 (m, 2H), 5.71 (brs, 1H), 5.72−5.86 (m, 1H), and 7.26−7.35 (m, 5H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 19.4, 30.2, 31.1, 35.8, 43.3, 44.1, 114.3, 127.2, 127.6, 128.5, 138.4, 138.5, and 172.3.

N-Malonylacylation was carried out on the above amide in the normal manner to give 1.6 g (90%) of *N*-benzyl-*N*-(3-methyl-hept-6-enoyl)-malonamic acid ethyl ester as a colorless oil: IR (neat) 3068, 2968, 1737, 1694, 1630, and 1026 cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz) δ 0.85 (d, 3H, J = 6.8 Hz), 1.10−1.15 (m, 1H), 1.25−1.40 (m, 1H), 1.29 (t, 3H, J = 7.2 Hz), 1.94−2.06 (m, 3H), 2.32 (dd, 1H, J = 16.4 and 7.5 Hz), 2.49 (dd, 1H, J = 16.4 and 5.4 Hz), 3.92 (s, 2H), 4.21 (q, 2H, J = 7.2 Hz), 4.89−5.02 (m, 2H), 5.02 (s, 2H), 5.69−5.78 (m, 1H), and 7.19−7.45 (m, 5H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 14.0, 19.4, 29.0, 31.0, 35.5, 43.7, 46.4, 46.8, 61.2, 114.4, 125.9, 127.3, 128.8, 136.5, 138.3, 167.2, 168.8, and 175.4; HRMS calcd for $C_{20}H_{27}NO_4$ 345.1940, found 345.1945.

The above imide was subjected to the standard diazo transfer conditions to give 1.1 g (88%) of **10** as a yellow oil: IR (neat) 2128, 1709, 1645, and 1452 cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz) δ 0.86 (d, 3H, J = 6.6 Hz), 1.10−1.30 (m, 1H), 1.30−1.41 (m, 1H), 1.30 (t, 3H, J = 6.9 Hz), 1.94−2.04 (m, 3H), 2.31 (dd, 1H, J = 15.8 and 7.9 Hz), 2.50 (dd, 1H, J = 15.8 and 5.6 Hz), 4.27 (q, 2H, J = 7.1 Hz), 4.90 (s, 2H), 4.93−5.00 (m, 2H), 5.67−5.81 (m, 1H), 7.31 (s, 3H), and 7.38 (s, 2H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 14.2, 19.4, 29.5, 31.0, 35.6, 43.1, 49.1, 61.7, 73.0, 114.3, 127.1, 127.4, 128.5, 137.0, 138.4, 160.3, 166.4, and 174.7.

10-Benzyl-9-oxo-11-oxa-10-aza-tricyclo[6.2.1.0^{1,6}]-undecane-8-carboxylic Acid Ethyl Ester (12). A solution of 0.9 g (2.3 mmol) of diazoimide **10** in 30 mL of CH_2Cl_2 at room temperature was treated with 3 mg of rhodium(II) perfluorobutyrate. The reaction mixture was stirred for 12 h at room temperature and was concentrated under reduced pressure. The resulting residue was purified by flash silica gel chromatography to give 0.70 g (90%) of **12** as a white solid: mp 96−97 °C; IR (neat) 1745, 1716, 1403, and 1239 cm^{-1}; ^{1}H NMR ($CDCl_3$, 300 MHz) δ 0.71−0.85 (m, 1H), 0.91 (d, 3H, J = 6.6 Hz), 1.14−1.28 (m, 1H), 1.38 (t, 3H, J = 7.2 Hz), 1.43−1.51 (m, 2H), 1.54−1.64 (m, 2H), 1.72−1.86 (m, 2H), 2.12−2.26 (m, 2H), 4.33 (d, 1H, J = 15.6 Hz), 4.40 (m, 2H), 4.50 (d, 1H, J = 15.6 Hz), and 7.25−7.40 (m, 5H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 14.4, 22.2, 28.3, 32.3, 33.4, 36.1, 36.9, 41.5, 43.3, 62.2, 86.3, 97.6, 127.8, 127.9, 128.9, 136.9, 166.2, and 171.2. Anal. Calcd for $C_{20}H_{25}NO_4$: C, 69.95; H, 7.34; N, 4.08. Found: C, 69.75; H, 7.32; N, 4.05.

2-Diazo-*N*-(3-methyl-hept-6-enoyl)-*N*-[2-(toluene-4-sulfonyl)ethyl]-malonamic Acid Ethyl Ester (13). To a solution containing 1.9 g (13 mmol) of 3-methyl-hept-6-enoic acid in 100 mL of CH_2Cl_2 was added 2.6 g (16 mmol) of 1,1′-carbonyldiimidazole, and the solution was stirred at room temperature for 2 h. To this mixture was added 4.0 g (20.0 mmol) of β-tosylethylamine[32] at 0 °C, and the solution was allowed to warm to room temperature, stirred for 12 h, and concentrated under reduced pressure. The residue was subjected to flash silica gel chromatography to give 3.0 g (70%) of 3-methyl-hept-6-enoic acid [2-(toluene-4-sulfonyl)ethyl]amide as a yellow oil: IR (neat) 2910, 1730, and 1630 cm^{-1}; ^{1}H NMR ($CDCl_3$, 300 MHz) δ 0.93 (d, 3H, J = 6.0 Hz), 1.22−1.30 (m, 1H), 1.37−1.48 (m, 1H), 1.91−2.19 (m, 5H), 2.46 (s, 3H), 3.23−3.27 (m, 2H), 3.65−3.71 (m, 2H), 4.93−5.05 (m, 2H), 5.73−5.87 (m, 1H), 6.23 (brs, 1H), 7.38 (d, 2H, J = 8.3 Hz), and 7.77 (d, 2H, J = 8.3 Hz); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 19.5, 29.8, 30.2, 31.2, 33.4, 35.8, 44.0, 55.5, 114.5, 127.9, 130.2, 136.0, 138.6, 145.2, and 173.1.

N-Malonylacylation was carried out on the above amide in the normal manner to give 0.89 g (88%) of *N*-(3-methyl-hept-6-enoyl)-*N*-[2-(toluene-4-sulfonyl)-ethyl]malonamic acid ethyl ester as a white solid: mp 79−80 °C; IR (neat) 1735, 1708, 1697, and 1139 cm^{-1}; ^{1}H NMR ($CDCl_3$, 300 MHz) δ 0.94 (d, 3H, J = 6.6 Hz), 1.21−1.33 (m, 1H), 1.25 (t, 3H, J = 7.2 Hz), 1.37−1.49 (m, 1H), 1.99−2.15 (m, 3H), 2.32 (dd, 1H, J = 16.9 and 7.8 Hz), 2.46 (s, 3H), 2.59 (dd, 1H, J = 16.4 and 5.7 Hz), 3.39 (dd, 2H, J = 7.8 and 6.6 Hz), 3.79 (s, 2H), 4.07 (dd, 2H, J = 9.0 and 6.0 Hz), 4.16 (q, 2H, J = 7.2 Hz), 4.95−5.05 (m, 2H), 5.73−5.86 (m, 1H), 7.39 (d, 2H, J = 8.2 Hz), and 7.79 (d, 2H, J = 8.2 Hz); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 14.0, 19.5, 21.6, 29.1, 31.1, 35.7, 38.6, 43.7, 46.1, 53.9, 61.3, 114.7, 127.9, 130.1, 135.8, 138.3, 145.3, 167.1, 168.7, and 174.5; HRMS calcd for $C_{22}H_{31}NSO_6$ 437.1872, found 437.1872.

The above compound was subjected to the standard diazo transfer conditions to give 0.6 g (85%) of **13** as a yellow oil: IR (neat) 2143, 1716, 1645, and 1445 cm^{-1}; ^{1}H NMR ($CDCl_3$, 300 MHz) δ 0.88 (d, 3H, J = 6.6 Hz), 1.19−1.27 (m, 1H), 1.31 (t, 3H, J = 7.2 Hz), 1.35−1.41 (m, 1H), 1.99−2.08 (m, 3H), 2.30 (dd, 1H, J = 15.5 and 7.8 Hz), 2.45 (s, 3H), 2.50 (dd, 1H, J = 15.5 and 6.1 Hz), 3.45 (t, 2H, J = 6.6 Hz), 3.96 (t, 2H, J = 6.6 Hz), 4.27 (q, 2H, J = 7.2 Hz), 4.91−5.02 (m, 2H), 5.70−5.83 (m, 1H), 7.39 (d, 2H, J = 8.2 Hz), and 7.79 (d, 2H, J = 8.2 Hz); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 14.3, 19.6, 21.7, 30.0, 31.2, 35.8, 40.7, 43.2, 54.7, 62.2, 114.6, 128.0, 130.1, 136.1, 138.5, 145.1, 160.1, 166.6, and 174.2.

3-Methyl-9-oxo-10-[2-(toluene-4-sulfonyl)ethyl]-11-oxa-10-aza-tricyclo-[6.2.1.0^{1,6}]undecane-8-carboxylic Acid Ethyl Ester (15). A solution of 0.5 g (1.1 mmol) of diazo imide **13** in 20 mL of CH_2Cl_2 at room temperature was treated with 3 mg of rhodium(II) perfluorobutyrate. The reaction mixture was stirred for 6 h at room temperature and was then concentrated under reduced pressure. The resulting residue was purified by flash silica gel chromatography to give 0.4 g (85%) of **15** as a white solid: mp 154−155 °C; IR (neat) 1752, 1724, 1452, and 1139 cm^{-1}; ^{1}H NMR ($CDCl_3$, 300 MHz) δ 0.99 (d, 3H, J = 6.3 Hz), 0.90−1.08 (m, 1H), 1.21−1.31 (m, 1H), 1.32 (t, 3H, J = 7.2 Hz), 1.45−1.56 (m, 2H), 1.63−1.76 (m, 2H), 1.89−1.99 (m, 2H), 2.20 (dd, 2H, J = 12.8 and 7.1 Hz), 2.45 (s, 3H), 3.23−3.61 (m, 4H), 4.33 (dq, 2H, J = 7.2 and 2.1 Hz), 7.39 (d, 2H, J = 8.2 Hz), and 7.79 (d, 2H, J = 8.2 Hz); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 14.1, 21.6, 22.0, 28.1, 32.1, 33.0, 33.8, 35.5, 36.6, 41.3, 54.3, 62.1, 85.8, 97.6, 127.9, 130.1, 135.5, 145.3, 165.4, and 171.2. Anal. Calcd for $C_{22}H_{29}NO_6$: C, 60.67; H, 6.71; N, 3.22. Found: C, 60.75; H, 6.69; N, 3.22.

3-Methyl-9-oxo-11-oxa-10-aza-tricyclo[6.2.1.0^{1,6}]undecane-8-carboxylic Acid Ethyl Ester (17). To a solution containing 0.2 g (0.5 mmol) of cycloadduct **15** in 20 mL of THF at −78 °C was added 0.08 g (0.7 mmol) of potassium *tert*-butoxide. The reaction mixture was stirred for 2 h, poured into 2 mL of water, extracted with ether, and dried over Na_2SO_4. The resulting residue was concentrated under reduced pressure and purified by flash silica gel chromatography to give 0.06 g (50%) of **17** as a white solid: mp 154−155 °C; IR (neat) 1750, 1721, and 1110 cm^{-1}; ^{1}H NMR ($CDCl_3$, 300 MHz) δ 0.96 (d, 3H, J = 6.6 Hz), 1.01−1.09 (m, 1H), 1.24−1.29 (m, 1H), 1.36 (t, 3H, J = 7.2 Hz), 1.24−1.29 (m, 1H), 1.40−1.45 (m, 1H), 1.65−1.81 (m, 2H), 1.89−2.11 (m, 2H), 2.32−2.39 (m, 2H), 4.33 (m, 2H), and 6.29 (brs, 1H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 14.4, 22.1, 28.5, 32.3, 33.4, 36.1, 36.8, 43.5, 62.3, 86.7, 94.6, 166.1, and 173.9. Anal. Calcd for $C_{13}H_{19}NO_4$: C, 61.64; H, 7.56; N, 5.54. Found: C, 61.56; H, 7.50; N, 5.54.

3,10-Dimethyl-9-oxo-11-oxa-10-aza-tricyclo[6.2.1.0^{1,6}]-undecane-8-carboxylic Acid Ethyl Ester (18). To a solution of 0.5 g (1.2 mmol) of cycloadduct **15** in 50 mL of THF at −78 °C was added 0.19 g (1.7 mmol) of potassium *tert*-butoxide. The reaction mixture was stirred for 2 h at −45 °C, and then 0.7 g (5 mmol) of methyl iodide was added. After 15 min of stirring at −45 °C, the reaction was allowed to warm to room temperature and was stirred for an additional 6 h. The solution was poured into 20 mL of H_2O, extracted with ether, washed with brine, and dried over Na_2SO_4. The resulting residue was concentrated under reduced pressure and purified by flash silica gel chromatography to give 0.12 g (40%) of **18** as a white solid: mp 87−88 °C; IR (neat) 1751, 1726, 1241, and 1111 cm^{-1}; ^{1}H NMR ($CDCl_3$, 300 MHz) δ 0.99 (d, 3H, J = 6.6 Hz), 0.95−1.09 (m, 1H), 1.26−1.31 (m, 1H), 1.35 (t, 3H, J = 7.2 Hz), 1.24−1.29 (m, 1H), 1.44−1.53 (m, 1H), 1.65−1.77 (m, 2H), 1.84−1.99 (m, 2H), 2.18−2.27 (m, 2H), 2.75 (s, 3H), and 4.30−4.43 (m, 2H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 14.4, 22.3, 25.2, 28.3, 32.2, 33.5, 35.6, 37.1, 40.1, 62.2, 86.4, 97.1, 166.2, and 171.2. Anal. Calcd for $C_{14}H_{21}NO_4$: C, 62.90; H, 7.92; N, 5.24. Found: C, 62.97; H, 7.87; N, 5.27.

2-Diazo-*N*-hept-6-enoyl-*N*-[2-(toluene-4-sulfonyl)ethyl]-malonamic Acid Ethyl Ester (14). To a solution containing 7.5 g (59 mmol) of hept-6-enoic acid in 250 mL of CH_2Cl_2 was added 12 g (70 mmol) of 1,1′-carbonyldiimidazole, and the solution was stirred at room temperature for 2 h. The reaction mixture was charged with 15.0 g (74.9 mmol) of β-tosylethylamine at 0 °C. The solution was allowed to warm to room temperature, stirred for 12 h, and concentrated under reduced pressure. The residue was subjected to flash silica gel chromatography to give 8.6 g (60%) of hept-6-enoic acid [2-(toluene-4-sulfonyl)ethyl] amide as a white solid: mp 63−64 °C; IR (neat) 2926, 1651, and 1536 cm^{-1}; ^{1}H NMR ($CDCl_3$, 300 MHz) δ 1.40 (quint, 2H, J = 7.8 Hz), 1.62 (quint, 2H, J = 7.2 Hz), 2.03−2.10 (m, 2H), 2.16 (t, 2H, J = 7.8 Hz), 2.46 (s, 3H), 3.26 (m, 2H), 3.67 (dd, 2H, J = 11.4 and 5.7 Hz), 4.93−5.04 (m, 2H), 5.72−5.86 (m, 1H), 7.38 (d, 2H, J = 8.2 Hz), and 7.77 (d, 2H, J = 8.2 Hz); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 21.7, 25.0, 28.5, 36.3, 55.5, 114.8, 128.0, 130.2, 136.1, 138.5, 145.2, and 173.3.

N-Malonylacylation was carried out on the above amide in the normal manner to give 5.9 g (87%) of *N*-hept-6-enoyl-*N*-[2-(toluene-4-sulfonyl)ethyl]-malonamic acid ethyl ester as a white solid: mp 68−69 °C; IR (neat) 2940, 1737, 1712, and 1026 cm^{-1}; ^{1}H NMR ($CDCl_3$, 300 MHz) δ 1.25 (t, 3H, J = 7.1 Hz), 1.41 (quint, 2H, J = 7.8 Hz), 1.64 (quint, 2H, J = 7.2 Hz), 2.08 (dt, 2H, J = 7.2 and 6.9 Hz), 2.45 (s, 3H), 2.60 (t, 2H, J = 6.9 Hz), 3.39 (dd, 2H, J = 8.1 and 6.9 Hz), 3.78 (s, 2H), 4.08 (t, 2H, J = 7.5 Hz), 4.16 (q, 2H, J = 7.1 Hz), 4.95−5.05 (m, 2H), 5.72−5.85 (m, 2H), 7.38 (d, 2H, J = 8.4 Hz), and 7.78 (d, 2H, J = 8.4 Hz); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 14.2, 21.8, 24.0,

28.2, 33.5, 36.6, 38.7, 46.2, 54.1, 61.5, 115.0, 128.0, 130.3, 136.0, 138.3, 145.5, 167.3, 168.9, and 175.2; HRMS calcd for $C_{21}H_{29}NSO_6$ 423.1715, found 423.1715.

The above compound was subjected to the standard diazo transfer conditions to give 4.9 g (85%) of **14** as a yellow oil: IR (neat) 2140, 1717, 1653, and 780 cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz) δ 0.88 (d, 3H, J = 6.6 Hz), 1.19−1.27 (m, 1H), 1.31 (t, 3H, J = 7.2 Hz), 1.35−1.41 (m, 1H), 1.99−2.08 (m, 3H), 2.30 (dd, 1H, J = 15.5 and 7.8 Hz), 2.45 (s, 3H), 2.50 (dd, 1H, J = 15.5 and 6.1 Hz), 3.45 (t, 2H, J = 6.6 Hz), 3.96 (t, 2H, J = 6.6 Hz), 4.27 (q, 2H, J = 7.2 Hz), 4.91−5.02 (m, 2H), 5.70−5.84 (m, 1H), 7.39 (d, 2H, J = 8.2 Hz), and 7.79 (d, 2H, J = 8.2 Hz); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 14.1, 21.5, 24.4, 28.1, 33.2, 35.6, 40.3, 54.4, 62.0, 72.7, 114.6, 127.8, 129.9, 135.8, 138.3, 145.1, 160.0, 166.2, and 174.6.

9-Oxo-10-[2-(toluene-4-sulfonyl)ethyl]-11-oxa-10-aza-tricyclo[6.2.1. $0^{1,6}$]undecane-8-carboxylic Acid Ethyl Ester (16). A solution of 5.0 g (11 mmol) of diazo imide **14** in 120 mL of CH_2Cl_2 at room temperature was treated with 5 mg of rhodium(II) perfluorobutyrate. The reaction mixture was stirred for 20 h at room temperature and was then concentrated under reduced pressure. The resulting residue was purified by flash silica gel chromatography to give 4.0 g (85%) of **16** as a white solid: mp 144−145 °C; IR (neat) 1749, 1722, and 1145 cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz) δ 0.99 (d, 3H, J = 6.3 Hz), 0.90−1.08 (m, 1H), 1.21−1.31 (m, 1H), 1.32 (t, 3H, J = 7.2 Hz), 1.45−1.56 (m, 2H), 1.63−1.76 (m, 2H), 1.89−1.99 (m, 2H), 2.20 (dd, 2H, J = 12.8 and 7.1 Hz), 2.45 (s, 3H), 3.20−3.61 (m, 4H), 4.33 (dq, 2H, J = 7.2 and 2.1 Hz), 7.38 (d, 2H, J = 8.4 Hz), and 7.79 (d, 2H, J = 8.4 Hz); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 14.3, 21.5, 21.8, 24.5, 27.5, 32.7, 34.0, 36.9, 42.0, 54.6, 62.3, 85.9, 97.3, 128.2, 130.3, 135.7, 145.5, 165.7, and 171.5. Anal. Calcd for $C_{21}H_{27}NO_6$: C, 59.84; H, 6.46; N, 3.32, found C, 59.81; H, 6.42; N, 3.25.

2-Diazo-*N*-(3,7-dimethyl-oct-6-enoyl)-*N*-(3-methyl-but-3-enyl)-malonamic Acid Ethyl Ester (20). To a solution containing 5.0 g (35 mmol) of citronellic acid (**7**) in 125 mL of benzene was added 15.6 g (123 mmol) of oxalyl chloride and 0.14 mL (1.8 mmol) of DMF. The solution was stirred at room temperature for 2 h and concentrated under reduced pressure. The resulting oil was taken up in 20 mL of CH_2Cl_2 and was added to a solution of 3.6 g (42 mmol) of 3-methyl-but-3-enylamine[40] in 150 mL of CH_2Cl_2 at 0 °C. The solution was allowed to warm to room temperature, stirred for 12 h, and concentrated under reduced pressure. The residue was subjected to flash silica gel chromatography to give 3.6 g (44%) of 3,7-dimethyl-oct-6-enoic acid-*N*-(3-methyl-but-3-enyl)-amide as a clear oil: IR (neat) 2927, 1645, and 1551 cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz) δ 0.93 (d, 3H, J = 6.3 Hz), 1.17−1.24 (m, 1H), 1.30−1.41 (m, 1H), 1.59 (s, 3H), 1.68 (s, 3H), 1.74 (s, 3H), 1.86−2.03 (m, 4H), 2.15−2.20 (m, 1H), 2.21 (t, 2H, J = 6.8 Hz), 3.39 (t, 2H, J = 6.6 Hz), 4.74 (s, 1H), 4.82 (s, 1H), 5.06−5.11 (m, 1H), and 5.39 (brs, 1H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 17.7, 19.6, 22.1, 25.6, 30.5, 37.0, 37.1, 37.6, 44.6, 112.2, 124.5, 131.4, 142.7, and 172.7.

N-Malonylacylation was carried out on the above amide in the normal manner to give 2.2 g (73%) of *N*-(3,7-dimethyl-oct-6-enoyl)-*N*-(3-methyl-but-3-enyl)-malonamic acid ethyl ester as a colorless oil: IR (neat) 1743, 1699, and 1140 cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz) δ 0.95 (d, 3H, J = 6.6 Hz), 1.18−1.28 (m, 1H), 1.27 (t, 3H, J = 7.2 Hz), 1.32−1.39 (m, 1H), 1.60 (s, 3H), 1.68 (s, 3H), 1.79 (s, 3H), 1.97−2.10 (m, 3H), 2.27 (t, 2H, J = 7.7 Hz), 2.36 (dd, 1H, J = 16.2 and 8.1 Hz), 2.57 (dd, 1H, J = 16.2 and 5.4 Hz), 3.79 (t, 2H, J = 7.7 Hz), 3.81 (s, 2H), 4.18 (q, 2H, J = 7.2 Hz), 4.74 (s, 1H), 4.82 (s, 1H), and 5.06−5.11 (m, 1H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 14.2, 17.7, 19.8, 22.6, 25.5, 25.7, 29.5, 36.9, 36.9, 43.2, 43.9, 46.5, 61.2, 112.5, 124.2, 131.6, 142.1, 167.4, 168.7, and 175.3; HRMS calcd for $C_{20}H_{33}NO_4$ 351.2409, found 351.2415.

The above compound was subjected to the standard diazo transfer conditions to give 1.8 g (94%) of **20** as a yellow oil; IR (neat) 2140, 1726, 1700, and 1654 cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz) δ 0.92 (d, 3H, J = 6.6 Hz), 1.16−1.24 (m, 1H), 1.24−1.36 (m, 1H), 1.28 (t, 3H, J = 7.2 Hz), 1.57 (s, 3H), 1.65 (s, 3H), 1.73 (s, 3H), 1.94−2.04 (m, 3H), 2.31 (dd, 1H, J = 15.7 and 8.1 Hz), 2.30 (t, 2H, J = 8.0 Hz), 2.51 (dd, 1H, J = 15.7 and 5.4 Hz), 3.75 (t, 2H, J = 8.0 Hz), 4.24 (q, 2H, J = 7.2 Hz), 4.69 (s, 1H), 4.77 (s, 1H), and 5.06 (t, 1H, J = 6.9 Hz); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 14.4, 17.8, 19.8, 22.5, 25.6, 25.8, 30.2, 37.0, 37.5, 43.4, 45.2, 61.9, 112.6, 124.4, 131.6, 142.4, 160.5, 166.7, and 174.6.

3,7,7-Trimethyl-10-(3-methyl-but-3-enyl)-9-oxo-11-oxa-10-aza-tricyclo-[6.2.1.$0^{1,6}$]undecane-8-carboxylic Acid Ethyl Ester (21). A solution containing 1.7 g (4.5 mmol) of diazoimide **20** in 100 mL of CH_2Cl_2 at room temperature was treated with 5 mg of rhodium(II) perfluorobutyrate. The reaction mixture was stirred for 6 h at room temperature and was then concentrated under reduced pressure. The resulting residue was purified by flash silica gel chromatography to give 1.5 g (94%) of **21** as a white solid: mp 90−91 °C; IR (neat) 1751, 1728, and 1113 cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz) δ 0.89−0.92 (m, 1H), 0.97 (d, 3H, J = 6.6 Hz), 1.04 (s, 3H), 1.20 (s, 3H), 1.34 (t, 3H, J = 7.1 Hz), 1.30−1.38 (m, 1H), 1.43−1.47 (m, 1H), 1.51−1.57 (m, 1H), 1.68−1.74 (m, 3H), 1.77 (s, 3H), 2.17−2.26 (m, 3H), 3.23−3.41 (m, 2H), 4.36 (q, 2H, J = 7.1 Hz), 4.80 (s, 1H), and 4.73 (s, 1H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 14.6, 21.1, 22.4, 22.6, 26.4, 26.6, 28.5, 33.2, 36.9, 37.8, 38.6, 44.8, 51.7, 61.8, 92.1, 96.0, 112.5, 142.5, 165.5, and 169.4. Anal. Calcd for $C_{20}H_{31}NO_4$: C, 68.74; H, 8.94; N, 4.01. Found: C, 68.64; H, 8.91; N, 3.98.

8-Hydroxy-3,9,9,13-tetramethyl-7-oxo-6-aza-tricyclo-[8.4.0.$0^{1,6}$]tetradec-3-ene-8-carboxylic Acid Ethyl Ester (23). To a solution of 0.3 g (0.9 mmol) of cycloadduct **21** in 20 mL of CH_2Cl_2 at room temperature was added 1.6 mL (8.6 mmol) of BF_3·2AcOH complex. The reaction mixture was stirred at 25 °C for 10 h and then quenched with 2 mL of ethanol. The solution was taken up in 50 mL of CH_2Cl_2 and extracted with water. The organic layer was dried over Na_2SO_4, filtered, and concentrated under reduced pressure. The resulting residue was analyzed by NMR spectroscopy and shown to consist of a 4:1 ratio of **23** and **24** (vide infra) by integration of the appropriate methyl signals. Flash silica gel chromatography afforded 0.24 g (75%) of **23** as a white solid: mp 110−111 °C; IR (neat) 1746, 1720, and 1234 cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz) δ 0.92 (s, 3H), 0.97 (s, 3H), 0.99−1.09 (m, 2H), 1.05 (s, 3H), 1.30 (t, 3H, J = 7.2 Hz), 1.34−1.44 (m, 1H), 1.68 (s, 3H), 1.87−1.91 (m, 1H), 2.16−2.22 (d, 1H, J = 16.8 Hz), 2.23 (dd, 1H, J = 12.1 and 2.1 Hz), 2.28 (dd, 1H, J = 12.1 and 4.5 Hz), 2.54 (d, 1H, J = 17.7 Hz), 3.46 (d, 1H, J = 18.2 Hz), 4.16−4.28 (m, 2H), 4.23 (q, 2H, J = 7.3 Hz), 4.27 (s, 1H), 4.98 (d, 1H, J = 18.2 Hz), and 5.38 (s, 1H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 14.4, 20.5, 21.0, 22.7, 23.8, 24.7, 29.2, 34.0, 35.6, 38.4, 39.2, 43.5, 46.3, 58.9, 62.2, 81.7, 117.6, 131.4, 168.1, and 172.1. Anal. Calcd. for $C_{20}H_{31}NO_4$: C, 68.74; H, 8.94; N, 4.01, found C, 68.74; H, 8.90; N, 4.02.

8-Hydroxy-3,9,9,13-tetramethyl-7-oxo-6-azatricyclo-[8.4.0.$0^{1,6}$]tetradec-2-ene-8-carboxylic Acid Ethyl Ester (24). When the above reaction was carried out using 0.3 g (0.9 mmol) of cycloadduct **21** in 20 mL of CH_2Cl_2 together with 2.1 g (10 mmol) of TMSOTf as the Lewis acid at 25 °C for 10 h, the major product (75%) obtained from silica gel chromatography of the reaction mixture corresponded to azatricyclic **24** which was obtained as a white solid: mp 113−114 °C; IR (neat) 1744, 1633, 1457, and 1243 cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz) δ 0.78 (s, 3H), 0.90−0.93 (m, 6H), 0.95−1.07 (m, 2H), 1.29 (t, 3H, J = 7.2 Hz), 1.61 (m, 5H), 1.86 (m, 2H), 2.13 (dd, 1H, J = 11.5 and 2.7 Hz), 2.30 (m, 1H), 2.46 (dd, 1H, J = 11.5 and 2.7 Hz), 3.32 (dt, 1H, J = 12.5 and 5.4 Hz), 4.21 (m, 2H), 4.35 (s, 1H), 4.50 (dd, 1H, J = 13.3 and 6.9 Hz), and 5.83 (s, 1H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 14.4, 18.9, 20.7, 22.8, 23.6, 23.8, 28.8, 29.1, 35.4, 36.5, 38.9, 46.0, 50.0, 60.3, 62.0, 81.7, 125.8, 132.0, 169.7, and 171.8. Anal. Calcd for $C_{20}H_{31}NO_4$: C, 68.74; H, 8.94; N, 4.01. Found: C, 68.70; H, 8.92; N, 3.99.

The minor component (18%) isolated from the above column chromatographic separation corresponded to compound **23**. Heating a sample of either **23** or **24** in the presence of

(40) Leonard, N. J.; Hecht, S. M.; Skoog, F.; Schmitz, R. Y. *Proc. Natl. Acad. Sci. U.S.A.* **1968**, *59*, 15.

BF_3·2AcOH in CH_2Cl_2 for 18 h afforded the same thermodynamic mixture of isomers (i.e., **23**:**24** = 4:1). The ratio was determined by NMR analysis of the appropriate methyl signals.

3,7,7-Trimethyl-9-oxo-10-(3-oxo-butyl)-11-oxa-10-aza-tricyclo[6.2.1. $0^{1,6}$]undecane-8-carboxylic Acid Ethyl Ester (25). A solution containing 0.25 g (0.7 mmol) of cycloadduct **21** in 30 mL of 1:1 CH_2Cl_2/MeOH mixture was cooled to −78 °C, and ozone was bubbled through the solution for 30 min. The solution was quenched with 0.3 mL (3.6 mmol) of dimethyl sulfide and warmed to room temperature. After 6 h of stirring at 25 °C, the solution was added to 10 mL of water, extracted with ethyl acetate, and dried over Na_2SO_4. The solution was concentrated under reduced pressure, and the resulting residue was purified by flash silica gel chromatography to give 0.23 g (89%) of ketone **25** as a white solid: mp 103−104 °C; IR (neat) 1751, 1718, and 1116 cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz) δ 0.91−0.95 (m, 1H), 0.97 (d, 3H, J = 6.9 Hz), 1.03 (s, 3H), 1.16 (s, 3H), 1.34 (t, 3H, J = 7.1 Hz), 1.47−1.61 (m, 3H), 1.66−1.74 (m, 3H), 2.12−2.20 (m, 1H), 2.16 (s, 3H), 2.64 (ddd, 1H, J = 18.1, 8.4, and 5.4 Hz), 2.91 (ddd, 1H, J = 18.1, 8.4, and 6.3 Hz), 3.30 (ddd, 1H, J = 14.6, 8.5, and 5.5 Hz), 3.5 (ddd, 1H, J = 14.6, 8.5, and 6.6 Hz), and 4.37 (q, 2H, J = 7.1 Hz); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 14.3, 20.8, 22.0, 26.1, 26.3, 28.2, 30.1, 32.8, 34.9, 36.3, 42.7, 44.6, 50.9, 61.6, 91.7, 96.3, 165.1, 169.8, and 206.6. Anal. Calcd for $C_{19}H_{29}NO_5$: C, 64.93; H, 8.32; N, 3.99, found C, 64.89; H, 8.30; N, 3.97.

2-Hydroxy-1,1,7,8-tetramethyl-3-oxo-2,3,6,8,9,10-hexahydro-1*H*,5*H*-pyrido[3,2,1-*ij*]quinoline-2-carboxylic Acid Ethyl Ester (29). A solution containing 0.1 g (0.3 mmol) of ketone **25** in 30 mL of acetonitrile was treated with 4 mg of *p*-toluenesulfonic acid. The mixture was heated at reflux for 10 h, and the solution was concentrated under reduced pressure. The crude residue was subjected to flash silica gel chromatography to give 0.7 g (78%) of **29** as a white solid: mp 93−94 °C; IR (neat) 3419, 1741, 1672, and 1232 cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz) δ 0.94 (s, 3H), 0.95 (d, 3H, J = 6.0 Hz), 1.16 (t, 3H, J = 6.9 Hz), 1.23 (s, 3H), 1.64−1.67 (m, 2H), 1.79 (s, 3H), 2.03−2.15 (m, 2H), 2.26−2.37 (m, 2H), 2.84−2.89 (m, 1H), 3.02 (dt, 1H, J = 12.3 and 4.5 Hz), 4.09 (q, 2H, J = 6.9 Hz), 4.47 (s, 1H), and 4.58 (ddd, 1H, J = 12.3, 6.0, and 1.5 Hz); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 14.1, 17.3, 18.4, 18.8, 20.4, 21.6, 28.1, 28.6, 30.6, 39.2, 39.9, 61.6, 78.8, 122.4, 125.5, 126.5, 127.3, 167.1, and 169.5. Anal. Calcd for $C_{19}H_{27}NO_4$: C, 68.44; H, 8.16; N, 4.20. Found: C, 68.32; H, 8.19; N, 4.14.

2-Diazo-*N*-but-3-enyl-*N*-(3,7-dimethyl-oct-6-enoyl)-malonamic Acid Ethyl Ester. To a solution containing 4.0 g (28 mmol) of citronellic acid (**7**) in 125 mL of CH_2Cl_2 was added 6.8 g (42 mmol) of 1,1′-carbonyldiimidazole, and the solution was stirred at room temperature for 1 h. To this reaction mixture was added 6.0 g (56 mmol) of but-3-enylamine[41] in 100 mL of CH_2Cl_2. The solution was allowed to warm to room temperature, stirred for 12 h, and concentrated under reduced pressure. The residue was subjected to flash silica gel chromatography to give 2.5 g (40%) of 3,7-dimethyl-oct-6-enoic acid but-3-enyl-amide as a clear oil: IR (neat) 3292, 1640, and 1552 cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz) δ 0.93 (d, 3H, J = 6.3 Hz), 1.15−1.26 (m, 1H), 1.30−1.42 (m, 1H), 1.60 (s, 3H), 1.68 (s, 3H), 1.86−2.06 (m, 4H), 2.18 (dd, 1H, J = 12.5 and 4.8 Hz), 2.26 (q, 2H, J = 6.6 Hz), 3.33 (m, 2H), 5.01−5.13 (m, 3H), 5.42 (brs, 1H), and 5.70−5.83 (m, 1H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 17.7, 19.6, 25.6, 25.8, 30.6, 34.0, 37.0, 38.5, 44.6, 117.1, 124.5, 131.5, 135.5 and 172.7.

N-Malonylacylation was carried out on the above amide in the normal manner gave 2.3 g (85%) of *N*-but-3-enyl-*N*-(3,7-dimethyl-oct-6-enoyl)-malonamic acid ethyl ester as a colorless oil: IR (neat) 3079, 1744, 1699, and 1029 cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz) δ 0.89 (d, 3H, J = 6.6 Hz), 1.14−1.26 (m, 1H), 1.20 (t, 3H, J = 7.2 Hz), 1.26−1.36 (m, 1H), 1.54 (s, 3H), 1.62 (s, 3H), 1.89−2.04 (m, 3H), 2.25−2.35 (m, 3H), 2.52 (dd, 1H, J = 16.2 and 5.4 Hz), 3.71 (q, 2H, J = 7.5 Hz), 3.75 (s, 2H), 4.12 (q, 2H, J = 7.2 Hz), 5.01−5.09 (m, 3H), and 5.69−5.78 (m, 1H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 14.2, 17.7, 19.8, 25.6, 25.8, 29.5, 33.3, 36.9, 43.8, 44.0, 46.6, 61.2, 117.8, 124.2, 131.7, 134.2, 167.4, 168.8, and 175.3; HRMS calcd for $C_{19}H_{31}NO_4$ 337.2253, found 337.2249.

The above compound was subjected to the standard diazo transfer conditions to give 1.8 g (90%) of 2-diazo-*N*-but-3-enyl-*N*-(3,7-dimethyl-oct-6-enoyl)-malonamic acid ethyl ester as a yellow oil: IR (neat) 2134, 1720, 1699, and 1121 cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz) δ 0.91 (d, 3H, J = 6.8 Hz), 1.14−1.23 (m, 1H), 1.27 (t, 3H, J = 6.0 Hz), 1.31−1.40 (m, 1H), 1.57 (s, 3H), 1.65 (s, 3H), 1.91−2.03 (m, 3H), 2.26−2.39 (m, 3H), 2.51 (dd, 1H, J = 15.5 and 5.4 Hz), 3.70 (t, 2H, J = 7.8 Hz), 4.23 (q, 2H, J = 6.8 Hz), 5.01−5.10 (m, 3H), and 5.67−5.81 (m, 1H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 14.5, 17.8, 19.6, 25.6, 25.9, 30.2, 34.9, 38.5, 42.9, 47.1, 62.4, 73.1, 118.5, 124.8, 132.1, 134.9, 161.0, 166.9, and 174.6.

10-Butenyl-3,7,7-trimethyl-9-oxo-11-oxa-10-aza-tricyclo-[6.2.1.$0^{1,6}$]-undecane-8-carboxylic Acid Ethyl Ester (30). A solution of 1.8 g (5.0 mmol) of the above diazo imide in 100 mL of CH_2Cl_2 at room temperature was treated with 5 mg of rhodium(II) perfluorobutyrate. The reaction mixture was stirred for 8 h at room temperature and was concentrated under reduced pressure. The resulting residue was purified by flash silica gel chromatography to give 1.48 g (90%) of **30** as a white solid: mp 77−78 °C; IR (neat) 1750, 1725, and 1112 cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz) δ 0.89−0.97 (m, 1H), 0.98 (d, 3H, J = 6.6 Hz), 1.04 (s, 3H), 1.20 (s, 3H), 1.35 (t, 3H, J = 7.2 Hz), 1.38−1.46 (m, 2H), 1.51−1.62 (m, 2H), 1.67−1.79 (m, 2H), 2.20−2.33 (m, 3H), 3.16−3.40 (m, 2H), 4.37 (q, 2H, J = 7.2 Hz), 5.06−5.14 (m, 2H), and 5.71−5.84 (m, 1H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 14.5, 21.0, 22.3, 26.3, 26.6, 28.4, 33.1, 34.1, 36.9, 39.4, 44.8, 51.5, 61.8, 92.0, 96.0, 117.5, 134.8, 165.4, and 169.4. Anal. Calcd for $C_{19}H_{29}NO_4$: C, 68.02; H, 8.73; N, 4.16. Found: C, 68.04; H, 8.65; N, 4.11.

3,7,7-Trimethyl-9-oxo-10-(3-oxo-propyl)-11-oxa-10-aza-tricyclo[6.2.1.0 ^{1,6}]-undecane-8-carboxylic Acid Ethyl Ester (31). A solution of 0.7 g (2.1 mmol) of cycloadduct **30** in 75 mL of CH_2Cl_2 was cooled to −78 °C, and ozone was bubbled through the solution for 30 min. The solution was quenched with 0.8 mL (10.4 mmol) of dimethyl sulfide, and the mixture was warmed to room temperature. After 4 h of stirring, the solution was added to 10 mL of H_2O, extracted with ethyl acetate, and dried over Na_2SO_4. The solution was concentrated under reduced pressure, and the resulting residue was purified by flash silica gel chromatography to give 0.6 g (85%) of **31** as an clear oil: IR (neat) 2955, 1749, 1726, and 1111 cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz) δ 0.89−0.93 (m, 1H), 0.97 (d, 3H, J = 6.6 Hz), 1.01 (s, 3H), 1.13 (s, 3H), 1.22 (t, 1H, J = 7.2 Hz), 1.32 (t, 3H, J = 7.2 Hz), 1.46−1.47 (m, 1H), 1.50−1.54 (m, 1H), 1.66−1.67 (m, 1H), 1.70−1.71 (m, 1H), 1.72−1.81 (m, 1H), 2.05−2.20 (m, 1H), 2.64 (t, 1H, J = 6.9 Hz), 2.70 (t, 1H, J = 6.3 Hz), 2.82 (t, 1H, J = 7.2 Hz), 2.88 (t, 1H, J = 7.2 Hz), 4.37 (q, 2H, J = 7.2 Hz), and 9.75 (s, 1H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 14.5, 21.0, 22.2, 26.3, 26.5, 28.4, 33.0, 33.6, 36.5, 43.6, 44.8, 51.1, 61.9, 91.9, 96.4, 165.2, 170.0, and 200.0; HRMS calcd for $C_{18}H_{27}NO_5$ 337.1889, found 337.1888.

2-Hydroxy-1,1,8-trimethyl-3-oxo-2,3,6,7-tetrahydro-1*H*,5*H*-pyrido[3,2,1-ij]quinoline-2-carboxylic Acid Ethyl Ester (34). A solution containing 0.1 g (0.3 mmol) of aldehyde **31** in 30 mL of acetonitrile was treated with 4 mg of *p*-toluenesulfonic acid. The reaction mixture was refluxed for 24 h, and the solution was concentrated under reduced pressure. The crude residue was then subjected to flash silica gel chromatography to afford 60 mg (64%) of **34** as a white solid: mp 88−89 °C; IR (neat) 1744, 1662, and 1457 cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz) δ 0.96 (t, 3H, J = 7.2 Hz), 1.14 (s, 3H), 1.46 (s, 3H), 1.91−1.97 (m, 1H), 2.05−2.11 (m, 1H), 2.23 (s, 3H), 2.71 (dt, 2H, J = 7.6 and 5.2 Hz), 3.31−3.40 (m, 1H), 3.92−4.02 (m, 2H), 4.45 (s, 1H), 4.55 (dt, 1H, J = 14.1 and 4.2 Hz), 6.90 (d, 1H, J = 7.6 Hz), and 7.00 (d, 1H, J = 7.0 Hz); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 14.0, 19.8, 21.5, 24.7, 25.0, 40.4, 41.4, 53.6, 61.9, 79.2, 122.1, 123.9, 125.5, 130.8, 134.1, 135.9, 167.7, and 169.4. Anal. Calcd for $C_{18}H_{23}NO_4$: C, 68.12; H, 7.30; N, 4.41. Found: C, 68.19; H, 7.34; N, 4.44.

(41) Tamaru, Y.; Hojo, M.; Higashimura, H.; Yoshida, Z. *J. Am. Chem. Soc.* **1988**, *110*, 3994.

2-Hydroxy-1,1,8-trimethyl-3-oxo-2,3,6,8,9,10-hexahydro-1*H*,5*H*-pyrido[3,2,1-ij]quinoline-2-carboxylic Acid Ethyl Ester (32). A solution containing 0.1 g (0.3 mmol) of aldehyde **31** in 30 mL of acetonitrile was treated with 5 mg of *p*-toluenesulfonic acid. The solution was heated at reflux for 6 h, and the solution was evaporated under reduced pressure. The crude residue was subjected to flash silica gel chromatography to afford 0.02 g (20%) of lactam **34** and 0.06 g (60%) of **32** as a white solid: mp 67−68 °C; IR (neat) 3419, 1739, 1670, and 1112 cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz) δ 0.97 (s, 3H), 1.04 (d, 3H, J = 7.2 Hz), 1.17 (t, 3H, J = 6.9 Hz), 1.21 (s, 3H), 1.45−1.55 (m, 1H), 1.65−1.75 (m, 1H), 2.11−2.24 (m, 2H), 2.27−2.32 (m, 2H), 2.34−2.46 (m, 1H), 2.96−3.06 (m, 1H), 4.10 (dq, 2H, J = 6.9 and 2.7 Hz), 4.44 (s, 1H), 4.57 (ddd, 1H, J = 12.5, 5.3, and 2.1 Hz), and 5.58 (d, 1H, J = 3.6 Hz); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 14.1, 18.8, 19.7, 21.8, 24.3, 29.2, 33.2, 39.4, 39.9, 61.7, 79.1, 105.6, 118.3, 124.1, 126.7, 134.4, 167.3, and 169.5. Anal. Calcd for $C_{18}H_{25}NO_4$: C, 67.69; H, 7.89; N, 4.39. Found: C, 67.42; H, 7.97; N, 4.24.

***N*-Allyl-2-diazo-*N*-(3,7-dimethyl-oct-6-enoyl)-malonamic Acid Ethyl Ester.** To a solution containing 4.0 g (28 mmol) of citronellic acid (**7**) in 125 mL of CH_2Cl_2 was added 6.8 g (42 mmol) of 1,1′-carbonyldiimidazole, and the solution was stirred at room temperature for 2 h. The reaction mixture was then charged with 3.2 g (56 mmol) of freshly distilled allylamine at 0 °C. The solution was allowed to warm to room temperature, stirred for 10 h, and concentrated under reduced pressure. The residue was subjected to flash silica gel chromatography to give 4.6 g (78%) of 3,7-dimethyl-oct-6-enoic acid allyl amide as a colorless oil: IR (neat) 3289, 1653, and 1110 cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz) δ 0.86 (d, 3H, J = 6.0 Hz), 1.08−1.18 (m, 1H), 1.24−1.35 (m, 1H), 1.52 (s, 3H), 1.59 (s, 3H), 1.86−1.96 (m, 4H), 2.10−2.20 (m, 1H), 3.79 (dt, 1H, J = 5.6 and 1.0 Hz), 4.99−5.13 (m, 2H), 5.67−5.82 (m, 1H), and 6.40 (brs, 1H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 17.7, 19.6, 25.5, 25.7, 30.5, 37.0, 41.9, 44.3, 116.0, 124.4, 131.4, 134.6, and 172.7.

N-Malonylacylation was carried out on the above amide in the normal manner to give 6.6 g (88%) of *N*-allyl-*N*-(3,7-dimethyl-oct-6-enoyl)-malonamic acid ethyl ester as a colorless oil: IR (neat) 1742, 1702, and 1190 cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz) δ 0.93 (d, 3H, J = 6.6 Hz), 1.17−1.26 (m, 1H), 1.27 (t, 3H, J = 7.1 Hz), 1.33−1.39 (m, 1H), 1.59 (s, 3H), 1.67 (s, 3H), 1.70−1.73 (m, 1H), 1.95−2.09 (m, 2H), 2.36 (dd, 1H, J = 16.4 and 8.4 Hz), 2.56 (dd, 1H, J = 16.4 and 2.3 Hz), 3.86 (s, 2H), 4.19 (q, 2H, J = 7.7 Hz), 4.35−4.45 (m, 2H), 5.05−5.10 (m, 1H), 5.17−5.23 (m, 2H), and 5.78−5.90 (m, 1H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 14.3, 17.9, 19.9, 25.7, 25.9, 29.5, 37.0, 43.9, 46.1, 46.6, 61.5, 116.6, 124.4, 131.9, 132.7, 167.6, 168.6 and 175.6; HRMS calcd for $C_{18}H_{29}NO_4$ 323.2096, found 323.2082.

The above compound was subjected to the standard diazo transfer conditions to give 4.5 g (70%) of *N*-allyl-2-diazo-*N*-(3,7-dimethyl-oct-6-enoyl)-malonamic acid ethyl ester as a yellow oil: IR (neat) 2128, 1720, 1695, and 1320 cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz) δ 0.87 (d, 3H, J = 6.9 Hz), 1.10−1.19 (m, 1H), 1.23 (t, 3H, J = 7.2 Hz), 1.28−1.36 (m, 1H), 1.52 (s, 3H), 1.60 (s, 3H), 1.57−1.63 (m, 1H), 1.86−1.99 (m, 1H), 2.27 (dd, 1H, J = 15.9 and 7.8 Hz), 2.47 (dd, 1H, J = 15.9 and 5.7 Hz), 4.19 (q, 2H, J = 7.2 Hz), 4.22−4.30 (m, 2H), 4.99−5.03 (m, 1H), 5.09−5.22 (m, 2H), and 5.73−5.84 (m, 1H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 14.5, 17.9, 19.9, 25.7, 25.9, 29.9, 37.1, 43.2, 48.2, 62.0, 72.9, 117.4, 124.5, 131.7, 133.4, 160.7, 166.4, and 175.0.

3,7,7-Trimethyl-9-oxo-10-(2-oxo-ethyl)-11-oxa-10-aza-tricyclo-[6.2.1. $0^{1,6}$]undecane-8-carboxylic Acid Ethyl Ester (35). A solution of 3.4 g (9.8 mmol) of the above diazo imide in 60 mL of CH_2Cl_2 at room temperature was treated with 5 mg of rhodium(II) perfluorobutyrate. The reaction mixture was stirred for 24 h at room temperature and was concentrated under reduced pressure. The resulting residue was purified by flash silica gel chromatography to give 2.8 g (87%) of 10-allyl-3,7,7-trimethyl-9-oxo-11-oxa-10-aza-tricyclo[6.2.1.$0^{1,6}$]-undecane-8-carboxylic acid ethyl ester as a colorless oil: IR (neat) 1754, 1722, 1403, and 1114 cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz) δ 0.82−0.89 (m, 1H), 0.95 (d, 3H, J = 6.3 Hz), 1.05 (s, 3H), 1.21 (s, 3H), 1.31−1.43 (m, 2H), 1.35 (t, 3H, J = 7.2 Hz), 1.47−1.60 (m, 2H), 1.68−1.76 (m, 2H), 2.17−2.22 (m, 1H), 3.86−3.89 (m, 2H), 4.38 (q, 2H, J = 7.2 Hz), 5.16−5.30 (m, 2H), and 5.69−5.82 (m, 1H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 14.4, 20.9, 22.2, 26.2, 26.4, 28.3, 32.9, 36.6, 42.2, 44.7, 51.3, 61.8, 92.1, 96.0, 118.1, 133.2, 165.4, and 169.1; HRMS calcd for $C_{18}H_{27}O_4N$ 321.1940, found 321.1941.

A solution of 0.5 g (1.6 mmol) of the above cycloadduct in 35 mL of CH_2Cl_2 was cooled to −78 °C, and ozone was bubbled through the solution for 20 min. The solution was quenched with 0.6 mL (7.8 mmol) of dimethyl sulfide and was warmed to room temperature. After 6 h of stirring at 25 °C, this solution was added to 10 mL of H_2O and extracted with ethyl acetate, and the extracts were dried over Na_2SO_4. The solution was concentrated under reduced pressure, and the resulting residue was purified by flash silica gel chromatography to give 0.4 g (83%) of **35** as a clear oil: IR (neat) 1748, 1732, and 1116 cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz) δ 0.94 (d, 3H, J = 6.6 Hz), 0.87−0.90 (m, 1H), 0.96−0.99 (m, 1H), 1.08 (s, 3H), 1.17−1.23 (m, 1H), 1.26 (s, 3H), 1.36 (t, 3H, J = 7.2 Hz), 1.37−1.42 (m, 1H), 1.69−1.80 (m, 2H), 1.89 (dd, 1H, J = 12.3 and 6.0 Hz), 2.13−2.19 (m, 1H), 4.10 (s, 2H), 4.39 (q, 2H, J = 7.2 Hz), and 9.57 (s, 1H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 14.5, 20.9, 22.1, 26.2, 26.4, 28.4, 32.9, 36.5, 44.8, 49.5, 50.9, 61.9, 92.1, 96.3, 165.0, 169.8, and 196.8; HRMS calcd for $C_{17}H_{25}NO_5$ 323.1733, found 323.1731.

5-Hydroxy-6,6,9-trimethyl-4-oxo-5,6,6a,7,8,9-hexahydro-4*H*-pyrrolo-[3,2,1-ij]quinoline-5-carboxylic Acid Ethyl Ester (37). A solution containing 0.1 g (0.3 mmol) of aldehyde **35** in 30 mL of acetonitrile was treated with 6 mg of *p*-toluenesulfonic acid. The mixture was heated at reflux for 12 h, and the solution was concentrated under reduced pressure. The crude residue was subjected to flash silica gel chromatography to give 0.07 g (70%) of **37** as a colorless oil: IR (neat) 1743, 1715, and 1251 cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz) δ 0.79 (t, 3H), 1.11 (s, 3H), 1.18 (d, 3H, J = 6.9 Hz), 1.25 (t, 3H, J = 7.2 Hz), 1.28−1.38 (m, 1H), 1.69−1.73 (m, 1H), 1.84−1.91 (m, 1H), 2.05−2.21 (m, 1H), 2.59−2.66 (m, 1H), 2.94−3.00 (m, 1H), 4.10 (bs, 1H), 4.20−4.31 (m, 2H), 6.23 (d, 1H, J = 3.3 Hz), and 7.20 (dd, 1H, J = 3.3 and 0.9 Hz); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 14.3, 17.4, 21.0, 21.1, 24.0, 29.1, 33.1, 39.2, 44.9, 62.8, 83.2, 113.6, 116.4, 127.1, 130.5, 167.4, and 169.9; HRMS calcd for $C_{17}H_{23}NO_4$ 305.1627, found 305.1625.

2-Diazo-*N*-hept-6-enoyl-*N*-[2-(2-iodophenyl)ethyl]-malonamic Acid Ethyl Ester (38). To a solution containing 1.9 g (14.4 mmol) of hept-6-enoic acid in 175 mL of CH_2Cl_2 was added 2.4 g (15 mmol) of 1,1′-carbonyldiimidazole, and the solution was stirred at room temperature for 2 h. The reaction mixture was charged with 3.6 g (15 mmol) of 2-(2-iodo-phenyl)-ethylamine. The solution was stirred for 8 h and concentrated under reduced pressure. The residue was subjected to flash silica gel chromatography to give 4.0 g (77%) of hept-6-enoic acid [2-(2-iodophenyl)ethyl] amide as a white solid: mp 38−39 °C; IR (neat) 3281, 1645, and 1552 cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz) δ 1.29−1.39 (m, 2H), 1.53−1.63 (m, 2H), 2.00 (q, 2H, J = 6.9 Hz), 2.10 (t, 2H, J = 7.5 Hz), 2.90 (t, 2H, J = 6.9 Hz), 3.46 (q, 2H, J = 6.6 Hz), 4.92 (m, 2H), 5.67 (bs, 1H), 5.69−5.80 (m, 1H), 6.84−6.89 (m, 1H), 7.15−7.24 (m, 2H), and 7.77 (d, 1H, J = 8.1 Hz); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 25.3, 28.7, 33.6, 36.7, 39.6, 40.4, 100.8, 114.9, 128.6, 128.7, 130.2, 138.6, 139.8, 141.8, and 173.2. Anal. Calcd for $C_{15}H_{20}NOI$: C, 50.43; H, 5.64; N, 3.92. Found: C, 50.56; H, 5.70; N, 3.91.

N-Malonylacylation was carried out on the above amide in the normal manner to give 4.9 g (97%) of *N*-hept-6-enoyl-*N*-[2-(2-iodo-phenyl)ethyl]-malonamic acid ethyl ester as a colorless oil: IR (neat) 1737, 1694, 1630, and 1190 cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz) δ 1.24 (t, 3H, J = 7.2 Hz), 1.30 (quint, 2H, J = 7.5 Hz), 1.52 (quint, 2H, J = 7.5 Hz), 1.99 (dd, 2H, J = 14.1 and 6.9 Hz), 2.44 (t, 2H, J = 7.2 Hz), 2.99 (t, 2H, J = 7.2 Hz), 3.79 (s, 2H), 3.86 (t, 2H, J = 7.5 Hz), 4.16 (q, 2H, J = 7.2 Hz), 4.89−4.98 (m, 2H), 5.66−5.79 (m, 1H), 6.89−6.92 (m, 1H), 7.25−7.26 (m, 2H), and 7.77 (d, 1H, J = 7.8 Hz); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 14.3, 24.1, 28.4, 33.6, 36.6, 39.7, 44.6, 46.7, 61.4, 100.5, 114.9, 128.9, 129.0, 131.0, 138.4, 139.7, 141.2, 167.5, 169.0, and 176.0; HRMS calcd for $C_{20}H_{26}NO_4I$ 471.0908, found 471.0899.

The above compound was subjected to the standard diazo transfer conditions to give 4.6 g (90%) of **38** as a yellow oil: IR (neat) 2135, 1737, 1652, and 1588 cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz) δ 1.25 (t, 3H, J = 7.2 Hz), 1.36 (quint, 2H, J = 7.5 Hz), 1.60 (quint, 2H, J = 7.5 Hz), 2.01 (dd, 2H, J = 14.2 and 7.5 Hz), 2.49 (t, 2H, J = 7.5 Hz), 3.02 (t, 2H, J = 7.5 Hz), 3.83 (t, 2H, J = 7.5 Hz), 4.21 (q, 2H, J = 7.2 Hz), 4.89−4.99 (m, 2H), 5.68−5.82 (m, 1H), 6.85−6.90 (m, 1H), 7.19−7.23 (m, 2H), and 7.77 (d, 1H, J = 7.8 Hz); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 14.5, 24.6, 28.6, 33.7, 36.1, 40.5, 46.3, 62.0, 77.5, 100.5, 114.8, 128.8, 128.9, 131.1, 138.6, 139.7, 141.1, 160.6, 166.5, and 175.7.

10-[2-(2-Iodophenyl)ethyl]-9-oxo-11-oxa-10-azatricyclo-[6.2.1.0^{1,6}]-undecane-8-carboxylic Acid Ethyl Ester (39). A solution containing 0.6 g (1.3 mmol) of diazoimide **38** in 50 mL of CH_2Cl_2 at room temperature was treated with 5 mg of rhodium(II) perfluorobutyrate. The reaction mixture was stirred for 12 h at room temperature and was then concentrated under reduced pressure. The resulting residue was purified by flash silica gel chromatography to give 0.51 g (86%) of **39** as a clear oil: IR (neat) 1740, 1695, 1644, and 1062 cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz) δ 1.19−1.28 (m, 2H), 1.37 (t, 3H, J = 6.9 Hz), 1.56−1.66 (m, 1H), 1.79−1.81 (m, 3H), 1.85−1.96 (m, 2H), 2.01−2.07 (m, 1H), 2.09−2.14 (m, 1H), 2.23 (dd, 1H, J = 12.6 and 7.2 Hz), 2.93−3.01 (m, 2H), 3.25−3.35 (m, 1H), 3.39−3.48 (m, 1H), 4.38 (dq, 2H, J = 7.1 and 2.7 Hz), 6.90−6.96 (m, 1H), 7.26−7.33 (m, 2H), and 7.81 (d, 1H, J = 7.5 Hz); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 14.4, 21.7, 24.8, 27.7, 32.8, 37.1, 40.2, 40.3, 42.4, 62.3, 86.1, 97.1, 100.4, 128.8, 128.9, 130.7, 139.7, 141.2, 166.2, and 171.6; HRMS calcd for $C_{20}H_{24}O_4NI$: 469.0752, found 469.0766.

3-Hydroxy-1-[2-(2-iodophenyl)ethyl]-2-oxo-1,2,3,4,5,6,7,8-octahydro-quinoline-3-carboxylic Acid Ethyl Ester (40). To a flask containing 2.0 g (4.3 mmol) of the cycloadduct **39** in 50 mL of CH_2Cl_2 at 0 °C was added 1.2 g (8.5 mmol) of BF_3·OEt_2, and the solution was stirred at 0 °C for 1 h. The reaction mixture was quenched with 4 mL of H_2O and extracted with CH_2Cl_2. The organic extracts were dried over Na_2SO_4, filtered, and concentrated under reduced pressure. The crude residue was subjected to flash silica gel chromatography to give 1.9 g (97%) of **40** as a colorless oil: IR (neat) 3416, 1730, 1666, and 1467 cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz) δ 1.24 (t, 3H, J = 7.2 Hz), 1.28−1.50 (m, 2H), 1.60−1.69 (m, 1H), 1.73−1.78 (m, 1H), 1.93−2.04 (m, 3H), 2.09−2.19 (m, 1H), 2.37 (d, 1H, J = 15.6 Hz), 2.61 (d, 1H, J = 15.9 Hz), 2.94−3.10 (m, 2H), 3.57−3.66 (m, 1H), 3.98−4.07 (m, 1H), 4.19 (dq, 2H, J = 7.1 and 2.4 Hz), 4.59 (s, 1H), 6.88−6.94 (m, 1H), 7.25−7.29 (m, 2H), and 7.80 (d, 1H, J = 8.1 Hz); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 14.3, 22.1, 22.8, 25.5, 29.3, 35.1, 39.6, 42.2, 61.9, 73.8, 100.6, 114.4, 128.6, 128.7, 130.7, 131.4, 139.6, 141.5, 168.8, and 170.1. Anal. Calcd for $C_{20}H_{24}NO_4I$: C, 51.18; H, 5.15; N, 2.98. Found: C, 51.19; H, 5.16; N, 2.95.

1-[2-(2-Iodophenyl)ethyl]-3-methoxy-2-oxo-1,2,3,4,5,6,7,8-octahydro-quinoline-3-carboxylic Acid Ethyl Ester (41). To a flask containing 0.3 g (0.6 mmol) of alcohol **40** in 25 mL of THF at 0 °C was added 0.02 g (0.8 mmol) of NaH, and the mixture was stirred for 45 min at 0 °C. To the reaction mixture was added 0.12 g (0.8 mmol) of iodomethane, and the mixture was stirred at room temperature for 3h. The mixture was quenched with 5 mL of H_2O and extracted with CH_2Cl_2. The organic extracts were dried over $MgSO_4$, filtered, and concentrated under reduced pressure. The crude residue was subjected to flash silica gel chromatography to give 0.16 g (60%) of **41** as a colorless oil: IR (neat) 1730, 1673, 1460, and 1253 cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz) δ 1.24 (t, 3H, J = 7.2 Hz), 1.46−1.64 (m, 3H), 1.96−1.99 (m, 3H), 2.04−2.09 (m, 1H), 2.36 (d, 1H J = 16.2 Hz), 2.61 (d, 1H, J = 16.2 Hz), 2.96 (t, 2H, J = 7.5 Hz), 3.47 (s, 3H), 3.61−3.71 (m, 1H), 3.75−3.87 (m, 1H), 3.99−4.13 (m, 1H), 4.17−4.31 (m, 2H), 6.83−6.88 (m, 1H), 7.18−7.27 (m, 2H), 7.75 (d, 1H, J = 7.8 Hz); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 14.4, 22.2, 22.9, 25.6, 29.3, 35.1, 39.7, 41.7, 54.9, 61.8, 80.6, 100.6, 112.3, 128.6, 128.5, 130.8, 131.1, 139.5, 142.0, 166.4, and 169.6; HRMS calcd for $C_{21}H_{26}NO_4I$ 483.0906, found 483.0898.

2-Methoxy-3-oxo-1,2,3,4,5,10,11,12,13,13a-decahydro-3*a*-aza-benzo[*d*]phenanthrene-2-carboxylic Acid Ethyl Ester (42). To a flask containing 0.09 g (0.2 mmol) of the above methyl ether **41** in 30 mL of benzene at room temperature was added 0.07 g (0.2 mmol) of Bu_3SnH and 10 mg of AIBN over a 2 h period, and the mixture was heated at reflux for 12 h. The reaction mixture was quenched with 2 mL of a saturated KF solution and extracted with ethyl acetate. The organic extracts were dried over Na_2SO_4, filtered, and concentrated under reduced pressure. The crude residue was subjected to flash silica gel chromatography to give 0.03 g (45%) of **42** as a white solid: mp 132−133 °C; IR (neat) 2935, 1730, and 1628 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz) δ 0.86 (t, 3H, J = 7.2 Hz), 1.35−1.43 (m, 1H), 1.47−1.54 (m, 1H), 1.61−1.68 (m, 2H), 1.80−1.86 (m, 2H), 1.94 (d, 1H, J = 11.1 Hz), 2.14 (dq, 1H, J = 13.6 and 4.6 Hz), 2.29−2.45 (m, 3H), 2.81 (dd, 1H, J = 17.2 and 6.0 Hz), 3.23 (dt, 1H, J = 17.2 and 9.6 Hz), 3.47−3.56 (m, 1H), 3.58 (s, 3H), 3.85−3.99 (m, 2H), 4.73 (ddd, 1H, J = 13.6, 9.2, and 2.0 Hz), 7.07−7.18 (m, 3H), and 7.52 (d, 1H), J = 8.0 Hz); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 13.7, 21.4, 25.2, 27.0, 30.1, 35.2, 36.6, 39.4, 39.5, 55.3, 61.1, 61.7, 81.5, 124.6, 126.2, 127.0, 130.7, 136.3, 140.5, 166.2, and 170.8; HRMS calcd for $C_{21}H_{27}NO_4$ 357.1939, found 357.1933.

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Supporting Information Available: ^1H NMR and ^{13}C NMR spectra for new compounds lacking analyses (15 pages). This material is contained in libraries on microfiche, immediately follows this article in the microfilm version of the journal, and can be ordered from the ACS; see any current masthead page for ordering information.

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