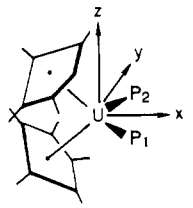
$\{Th[\eta^5\text{-}(CH_3)_5C_5]_2[\mu\text{-}CO(CH_2C(CH_3)_3)CO]Cl\}_2$, (2).[14]

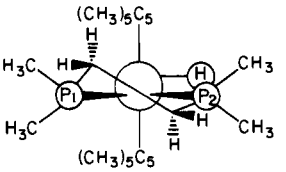
Although it was not possible to locate the hydride ligand with the X-ray diffraction data, a reasonable position, which is in agreement with the low-temperature NMR data (vide infra), can be inferred from the positions of the other ligands in 1. We define a Cartesian coordinate system which is centered on the U(III) ion (A) and has the x axis at the intersection of the "equatorial



girdle" (the plane containing U which bisects the dihedral angle between the two C_5-ring mean planes) and the plane defined by U and the two C_5-ring centers-of-gravity (C_{ga} and C_{gb}). The y axis lies in the equatorial girdle parallel to both C_5-ring mean planes. Since steric factors in mononuclear bis(pentamethylcyclopentadienyl)methyl complexes are known to preclude any substantial displacements of coordinated noncyclopentadienyl atoms from the equatorial girdle,[2,14,15] the hydride ligand must lie in or very near the girdle. The orientation of the dmpe ligand in the equatorial girdle strongly argues that the hydride is in the vicinity of the positive y axis: P_1 is displaced from the C_{ga}-U-C_{gb} plane by 2.26 Å in the direction of the negative y axis while P_2 is displaced by 1.01 Å in the direction of the positive y axis. In contrast, the X ligands in $M[\eta^5\text{-}(CH_3)_5C_5]_2X_2$ actinide complexes[2,14,15] are usually symmetrically disposed about the x axis in the equatorial girdle. Therefore the most likely diffraction-derived position for the hydride ligand in 1 is in the equatorial girdle between the U-P_2 vector and the positive y axis—a position similar to that occupied by Cl in 2.[14]

The C_{ga}-U-C_{gb} plane in 1 intersects the C_5-ring mean planes in angles of 89.1 and 90.0°, respecitvely, and the P_1-U-P_2 plane in a dihedral angle of 87.8°. Bond lengths and angles for selected chemically distinct groupings of atoms in 1 are U-C, 2.79 (3, 4, 7, 10) Å;[16] U-P_1, 3.211 (8) Å; U-P_2, 3.092 (8) Å; (cyclopentadienyl ring) C-C, 1.39 (4, 3, 6, 10) Å; (Cp ring to methyl) C-C, 1.55 (5, 3, 13, 10) Å; P-C, 1.78 (5, 11, 31, 6) Å; C_{ga}-U-C_{gb}, 136.2°; C_g-U-P_1, 105.4 (-, 3, 3, 2)°; C_g-U-P_2, 110.7 (-, 24, 24, 2°); P_1-U-P_2, 63.8 (2); U-P-C, 119 (2, 3, 9, 6)°;[16] C-P-C, 99 (2, 2, 4, 6)°.

As the temperature of 1 in $C_6D_5CD_3$ is lowered, the ^1H NMR methylene and methyl signals of coordinated dmpe broaden and collapse; the η^5-$(CH_3)_5C_5$ resonance also broadens. At -50 °C, the methylene resonances appear as two singlets, δ -35.8 (1w = 79 Hz, 2 H) and -26.4 (1w = 78 Hz, 2 H), and the methyl resonance as three singlets, δ -20.6 (1w = 47 Hz, 6 H), -15.8 (1w = 45 Hz, 3 H), -15.65 (1w = 45 Hz, 3 H); two pentamethylcyclopentadienyl resonances are observed at δ -8.65 (1w ~ 25 Hz, 15 H) and -8.57 (1w ~ 25 Hz, 15 H). That the splitting of the low field methyl and η^5-$(CH_3)_5C_5$ resonances is field and temperature dependent indicates that it is not scalar coupling[17] in origin. Rather, the slow exchange limit spectrum reflects the low symmetry (C_1) of the dmpe solution coordination environment (B), in accord with the solid-state crystallographic



B

results. In principle, the remaining magnetic nonequivalences as well as scalar coupling would be resolvable in the absence of the severe line broadening. Preliminary line-shape analysis indicates that exchange with free dmpe is slower than the site permutation process(es) within the coordinated dmpe. Presumably the latter involve reversible single phosphorus atom dissociation and/or "spinning" of the dmpe about the local C_2 axis together with inversion of the five-membered chelate ring. Evidence for the high chemical lability of the uranium-coordinated dmpe is provided by displacement reactions. Thus, NMR experiments indicate that 1 reacts rapidly with THF, CO, and N_2 to yield free dmpe and complex mixtures of U(III) and U(IV) products. The nature of these products is under investigation.

This study underscores the ready accessibility of organouranium phosphine complexes, as exemplified by a hydrogenolysis route to a trivalent diphosphine hydride, and suggests that such species will have a rich chemistry. Particularly noteworthy in the present case is the marked lability of the chelating bis(phosphine) and the formation of a *trivalent* product from reaction 2. Although the reaction mechanism has not been investigated in detail (reactions 1 and 2 likely proceed via unstable chloro- and alkylhydrides, respectively[2,3]), the absence of a divalent product analogous to the group 4B $Zr(C_5H_5)_2(dmpe)$[8b] is further evidence for a greater stability of formal oxidation states higher than +2 among the early actinides.[2,3]

Acknowledgment. We thank the National Science Foundation (CHE8009060) for generous support of this research.

Supplementary Material Available: Tables of fractional coordinates and anisotropic thermal parameters (2 pages). Ordering information is given on any current masthead page.

(14) Fagan, P. J.; Manriquez, J. M.; Marks, T. J.; Day, V. W.; Vollmer, S. H.; Day, C. S. *J. Am. Chem. Soc.* **1980**, *102*, 5393-5396.

(15) (a) Manriquez, J. M.; Fagan, P. J.; Marks, T. J.; Day, C. S.; Day, V. W. *J. Am. Chem. Soc.* **1978**, *100*, 7112-7114. (b) Fagan, P. J.; Manriquez, J. M.; Vollmer, S. H.; Day, C. S.; Day, V. W.; Marks, T. J. *J. Am. Chem. Soc.* **1981**, *103*, 2206-2220.

(16) The first number in parentheses following an averaged value of a bond length or angle is the root-mean-square estimated standard deviation of an individual datum. The second and third numbers, when given, are the average and maximum deviations from the averaged value, respectively. The fourth number represents the number of individual measurements which are included in the average value.

(17) Intra-dmpe couplings are expected to be on the order of only a few Hz. See ref 8b. Also see: Akhtar, M.; Ellis, P. D.; MacDiarmid, A. G.; Odom, J. D. *Inorg. Chem.* **1972**, *11*, ,2971-2921.

Total Synthesis of (±)-Triptonide and (±)-Triptolide

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Received August 24, 1981

Because the promising anticancer compound triptolide 1[1] and congeners remain scarcely accessible from the natural source, interest in a practical total synthesis of these substances continues at a high level. Herein we report a new, efficient route to an established key intermediate in previous total syntheses of triptolide (1) and triptonide (2),[2] viz., 7-oxo-14-methoxyisodehydroabietenolide (3). The present sequence features two new methods of butenolide construction, one of which finds subsequent utilization in the assemblage of the benzenoid nucleus as an integral part of the synthesis rather than its origination in aromatic starting materials, as in prior approaches.[2] In addition, the pathway

(1) (a) Kupchan, S. M.; Court, W. A.; Dailey, R. G., Jr.; Gilmore, C. J.; Bryan, R. F. *J. Am. Chem. Soc.* **1972**, *94*, 7194. (b) Kupchan, S. M.; Schubert, R. M. *Science, (Washington, D.C.)* **1974**, *185*, 791. (c) *K'o Hseuh T'ung Pao* **1977**, *22*, 458; *Chem. Abstr.* **1978**, *88*, 177077y.

(2) (a) Racemic triptonide and triptolide, Buckanin, R. S.; Chen, S. J.; Frieze, D. M.; Sher, F. T.; Berchtold, G. A. *J. Am. Chem. Soc.* **1980**, *102*, 1200. (b) *l*-Triptolide and *l*-triptonide: van Tamelen, E. E.; Demers, J. P.; Taylor, E. G.; Koller, K. *Ibid.* **1980**, *102*, 5424.

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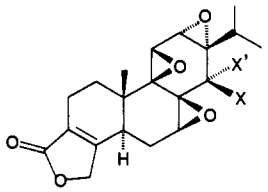
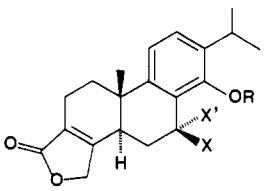


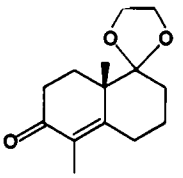
1 X=OH,X'=H
2 X=X'=O



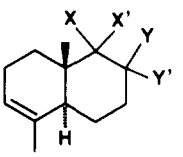
3 X,X'=O; R=CH_3
17 X,X'=H; R=CH_3
24 X,X'=O; R=H
25 X=OH,X'=H; R=H

described herein requires fewer steps and proceeds in an overall yield 40–50 times that realized earlier in this laboratory.[2b]

By a sequence[3a] entailing a slight variation in the original procedure,[3b] bicyclic diketone monoethylene ketal **4**[4] was converted into octalin ketal **5** (90–92%) in a "one-pot" sequence involving initial treatment with Li/NH_3 (THF, −78 °C, 0.8 equiv of *t*-BuOH, 15 min), subsequent reaction with diethyl chlorophosphate (THF, 0 °C, 30 min) after excess Li quench (isoprene) and NH_3 removal, and finally, enol phosphate reduction with Li ($EtNH_2$, THF, *t*-BuOH, 0 °C, 12 h). After generation of the parent

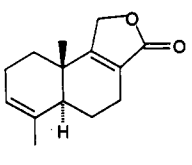


4

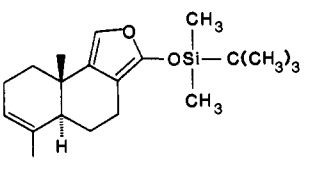


5 X,X'=OCH_2CH_2O, Y=Y'=H
6 X,X'=O; Y,Y'=H
7 X,X'=O; Y,Y'=$C(SCH_3)_2$

octalone (3 M H_2SO_4, THF, 25 °C, 24 h, 90%) **6**,[21] the reaction mixture was subjected to reaction with carbon disulfide[5] (6 equiv) in the presence of 2.5 equiv of lithium 4-methyl-2,6-di-*tert*-butylphenoxide (THF, 25 °C, 48 h) followed by addition of methyl iodide (6 eq, THF, 25 °C, 24 h), affording the ketene dithioacetal **7**[21] (quantitative yield after column chromatography). Subjection of **7** to the action of dimethylsulfonium methylide[6] (1:1 Me_2SO–THF, −10–25 °C) followed by direct acid hydrolysis (1:6 6 M aqueous HCl–MeOH, 25 °C, 15 h) produced the unsaturated lactone **8**[21] (84%).[7]

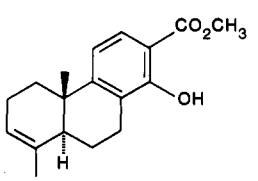


8

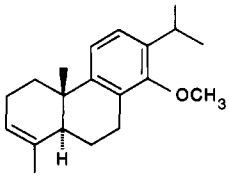


9

In preparation for construction of the benzenoid ring in **3** and its precursors, butenolide **8** was transformed into the corresponding α-(*tert*-butyldimethylsiloxy)furan **9** via initial generation of its furanoid dienolate with $(i\text{-Pr})_2$NLi–HMPA[8a] (THF, −78 °C, 25 min) followed by subsequent reaction with *tert*-butyldimethylsilyl chloride[8b] (THF, −78–0 °C, 1 h). Compound **9** was subjected without further purification to a Diels–Alder reaction with methyl acrylate[9] (5 equiv, benzene, 65–70 °C, 48 h, sealed tube) which was followed by spontaneous aromatization of the intermediate adduct (5:1 MeOH–6 M HCl, 25 °C, 1 h) to give salicyclic ester **10**[21] in 86–93% yield from butenolide **8**.[9c] Conversion of **10** to *o*-isopropylphenyl methyl ether **11**[21] was accomplished by successive treatment with methyl iodide/NaH (THF, 25 °C, 48 h), methyllithium (THF, −15 °C, 5 min), methanesulfonyl chloride/Et_3N (8 equiv, CH_2Cl_2, 0–25 °C, 1 h), and finally Li/NH_3 (7 equiv, THF, −78 °C, 15 min) (65–70% overall yield).[10] Olefin **11** represents the pivotal key intermediate utilized not only for the preferred pathway to **3**, described next, but also secondary routes.[12]



10



11

In order to set the stage for formation of a new carbon–carbon bond at C-3 by means of a [2,3]-sigmatropic rearrangement of a carbene,[17] olefin **11** was converted to allylic alcohol **12** by a

(3) (a) Miller, R. B.; Behare, E. S. *J. Am. Chem. Soc.* **1974**, *96*, 8102. (b) Ireland, R. E.; Pfister, G. *Tetrahedron Lett.* **1969**, 2145. Ireland, R. E.; Muchmore, D. C.; Hengartner, U. *J. Am. Chem. Soc.* **1972**, *94*, 5098.

(4) Prepared by a three-step sequence for 2-methyl-1,3-cyclohexanedione and 2-chloroethyl ethyl ketone. See: (a) Bauduin, G.; Christol, H.; Pietrasanta, Y. *Bull. Soc. Chim. Fr.* **1973**, 359. (b) Wieland, P.; Ueberwasser, H.; Anner, G.; Miescher, K. *Helv. Chim. Acta* **1953**, *36*, 376. (c) McMurry, J. E. *J. Am. Chem. Soc.* **1968**, *90*, 6821. (d) Kitahara, Y.; Yoshikoshi, A.; Oida, S. *Tetrahedron Lett.* **1964**, 1763.

(5) Corey, E. J.; Chen, R. H. K. *Tetrahedron Lett.* **1973**, 3817.

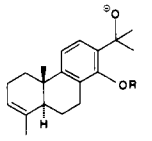
(6) Corey, E. J.; Chaykovsky, M. *J. Am. Chem. Soc.* **1965**, *87*, 1353.

(7) Cf.: Garst, M. E.; Spencer, T. A. *J. Am. Chem. Soc.* **1973**, *95*, 250.

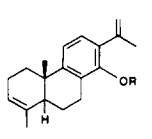
(8) (a) Herman, J. L.; Kieczykowski, G. R.; Schlessinger, R. H. *Tetrahedron Lett.* **1973**, 2433. (b) Rathke, M. W.; Sullivan, D. F. *Synth. Commun.* **1973**, *3*, 67.

(9) (a) Asaoka, M.; Miyake, K.; Takei, H. *Chem. Lett.* **1977**, 167. (b) Brownbridge, P.; Chan, T. H. *Tetrahedron Lett.* **1980**, 3423. (c) Only ca. 5% of the corresponding regioisomer was isolated from the Diels–Alder sequence.

(10) Direct reductive deoxygenation[11] of either i or ii with Li/NH_3 after CH_3Li addition failed, while attempts to produce iii or iv via dehydration of these intermediates using a variety of standard acid catalysts (H_3PO_4, *p*-TsOH, P_2O_5, $SOCl_2$) led to simultaneous formation of varying amounts of the corresponding $\Delta^{4,5}$-olefin.



i R=H
ii R=Me



iii R=H
iv R=Me

(11) Huffman, J. W.; Pandian, R. *J. Org. Chem.* **1979**, *44*, 1851. Hall, S. S.; Lipsky, S. D. *Ibid.* **1973**, *38*, 1735.

(12) Two additional routes to anisolic butenolide **17** from **11** were developed. However, they proceeded in lower overall yield due to difficulties in oxidatively decarboxylating intermediates of the type **18** or **19**. Compound **18** was prepared by reaction of **11** with diethyl oxomalonate[13] (2.5 equiv, toluene, sealed tube, 165–170 °C, 48 h). Both **18** and the corresponding $\Delta^{4,5}$-olefin **20** were isolated in a 1:3 ratio, respectively, in 91% overall yield. Extensive experimental modifications in solvent, temperature, and time of reaction or use of various Lewis acid catalysts[14] were ineffective in improving this olefin isomer distribution. Subsequent diester hydrolysis (NaOH, Me_2SO, 25 °C, 20 h), oxidative decarboxylation ($NaIO_4$, MeOH–H_2O, 25 °C, 3 days), and esterification (CH_2N_2, ether, 0 °C) gave a ca. 1:1 mixture of **21** and **22** (42% overall). Epoxidation (MCPBA, 25 °C, CH_2Cl_2, 24 h) and base-initiated epoxide opening with concomitant lactone formation on workup (LDA, −78 °C, THF, 45 min, then H_3O^+) gave **17** in 5% overall yield from **11**. In addition, *p*-toluenesulfonyl chloride promoted esterification of allylic alcohol **14** with methoxyacetic acid[15] (4 equiv, *p*-TsCl, pyridine, 2 h, 0 °C, then lactic acid, 2 h, 0 °C) followed by [3,3]-sigmatropic rearrangement[16] of the resulting mixed silyl ketene acetal (LDA–HMPA, THF, −78 °C, 30 min; *t*-$BuMe_2SiCl$, THF, −78–0 °C, 1 h; then 25 °C, 1 h) afforded α-methoxy acid **19** in 70–80% overall yield. This crude product was oxidatively decarboxylated[16b] directly by oxygenation of the acid dianion (4 equiv of tetramethylpiperidide–HMPA, 0 °C, THF, 90 min) with O_2 (−78 °C, ether, 20 min) followed by treatment with acid (CH_3SO_3H, −78–25 °C, 1 h) to afford **21**[21] in 25–30% yield. Ultimately, epoxidation to give **23** followed by base-promoted epoxide opening as before afforded **17** (75% from **20**) in 10% overall yield from **11**.

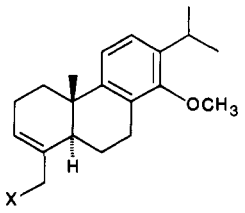
(13) Salomon, M.; Pardo, S. N.; Salomon, R. G. *J. Am. Chem. Soc.* **1980**, *102*, 2473.

(14) Snider, B. B. *Acc. Chem. Res.* **1980**, *13*, 426.

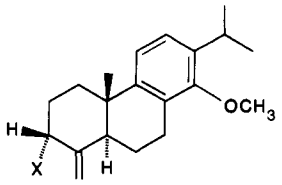
(15) Brewster, J. H.; Clotti, C. J., Jr. *J. Am. Chem. Soc.* **1955**, *77*, 6214.

(16) (a) Ireland, R. E.; Mueller, R. H.; Willard, A. K. *J. Am. Chem. Soc.* **1976**, *98*, 2868. (b) Whitesell, J. K.; Helbling, A. M. *J. Org. Chem.* **1980**, *45*, 4135.

precedented sequence[3a] involving epoxidation (MCPBA, CH_2Cl_2, 25 °C, 6 h, 100%) followed by base-promoted elimination in the oxide moiety (LDA, THF, 25 °C, 24 h, 91%; or tetramethylpiperidide–HMPA, THF, −15 °C, 14 h; 86%). Thionyl chloride

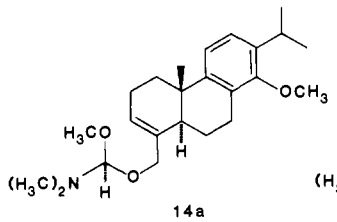


13 X=Cl
14 X=OH

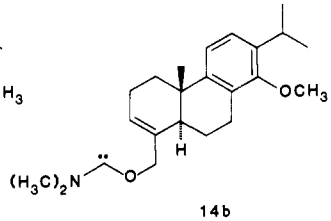


12 X=OH
15 X=$CONMe_2$
18 X=$HOC(CO_2Et)_2$
19 X=$CH_3OCH(CO_2H)$
21 X=CO_2Me

induced rearrangement ($SOCl_2$–pyridine, ether, 0 °C, 2 h) of alcohol **12** gave allylic chloride **13** (83–85%) (contaminated with 5–7% of the corresponding C-3 allylic chloride); displacement of halogen by acetate (KOAc, Me_2SO, 70–75 °C, 24 h) followed by methanolysis (NaOMe, MeOH, 25 °C, 2 h) gave alcohol **14**[21] (70–74%). On being heated with dimethylformamide dimethylacetal[17] (5–10 equiv, xylene, reflux, 4-Å sieves (–MeOH), 3 days), alcohol **14** generated, via unisolated intermediates **14a** and **14b**, the allylic amide **15**[21] (80%). Oxidation (MCPBA,

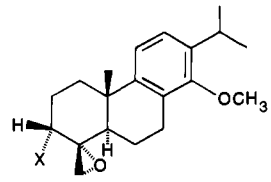


14a

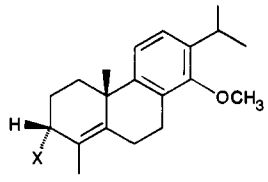


14b

CH_2Cl_2, 25 °C, 30 h) to epoxy amide **16** (100%) followed by lithium hexamethyldisilazide induced β elimination (3 equiv, THF, 0 °C, then 25 °C for 2 h) gave the intermediate α,β-unsaturated amide, which on direct acid hydrolysis (1 M HCl, 10 min) yielded (80%) butenolide **17**.[21]



16 X=$CONMe_2$
23 X=CO_2Me



20 X=$HOC(CO_2Et)_2$
22 X=CO_2Me

Benzylic oxidation (CrO_3, 80% AcOH–H_2O, 35–40 °C, 2–3 h) of **17** to the desired 7-oxobutenolide **3**[21] (25%, 42% based on starting material consumed) was managed as described before,[2b] the product resulting from this step being indistinguishable (IR, NMR, MS, mp, mmp) from the substance[2a,18] which served as an intermediate in the synthesis of (±)-triptonide. The nature[19] and order of the remaining oxidation steps in the present approach to (±)-triptonide (22% overall yield) paralleled those reported for the synthesis of *l*-triptonide.[2b,20] In view of the prior conversion of (±)-triptonide to (±)-triptolide,[2a] the work described herein constitutes a new total synthesis of (±)-triptolide as well.

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Registry No. 1, 73414-46-7; **2**, 73465-88-0; **3**, 73414-42-3; **4**, 31062-32-5; **5**, 80325-82-2; 6, 80325-83-3; **7**, 80325-84-4; **8**, 80325-85-5; **9**, 80325-86-6; **10**, 80325-87-7; **11**, 80325-88-8; **12**, 80325-89-9; **13**, 80325-90-2; **14**, 80325-91-3; **15**, 80325-92-4; **16**, 80325-93-5; **17**, 73414-41-2; **18**, 80325-94-6; **19**, 80325-95-7; **20**, 80325-96-8; **21**, 80325-97-9; **22**, 80325-98-0; **23**, 80325-99-1; **24**, 73414-43-4; **25**, 73414-44-5.

(17) (a) Büchi, G.; Cushman, M.; Wüest, H. *J. Am. Chem. Soc.* **1974**, *96*, 5563. (b) Chan, K.; Saucy, G. *J. Org. Chem.* **1977**, *42*, 3828.

(18) We thank Professor Glenn A. Berchtold for generous samples of (±)-triptonide and oxobutenolide **3** for comparison purposes.

(19) (a) Becker, H. -D.; Bremholt, T.; Alder, E. *Tetrahedron Lett.* **1972**, 4205. (b) Sher, F. T.; Berchtold, G. A. *J. Org. Chem.* **1977**, *42*, 2569 (c) Frieze, D. M.; Berchtold, G. A.; Blount, J. F. *Tetrahedron Lett.* **1978**, 4607. (d) For a different method of constructing models for the polyepoxide ketone moiety of the triptolide family, see: Koike, H.; Tokoroyama, T. *Ibid.* **1978**, 4531.

(20) Demethylation (BCl_3, CH_2Cl_2, 25 °C, 24 h, 82%) of **3** to give **24**[21] (X, X' = O; R = H) followed by $NaBH_4$ reduction (EtOH, 25 °C, 2 h, 97%) gave alcohol **25**, which was subjected immediately to treatment with $NaIO_4$ (4:1 MeOH–H_2O, 25 °C, 5 h), alkaline H_2O_2 (9:1 MeOH–water, 25 °C, 12 h), and finally 3,5-dinitroperbenzoic acid (CH_2Cl_2, Na_2HPO_4, 25 °C, 36 h) to complete this total synthesis of (±)-triptonide, which was indistinguishable from an authentic sample of (±)-triptonide[2a,18] (NMR, MS, IR, mp, TLC).

(21) **17**: mp 175.5–176 °C; IR (CCl_4) 2962, 1763, 1678, 1033 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.03 (s, 3 H, CH_3), 1.22 (d, 3 H, J = 6.8 Hz, $CHMe_2$), 1.23 (d, 3 H, J = 6.8 Hz, $CHMe_2$), 3.30 (sept, 1 H, J = 6.8 Hz, $CHMe_2$), 3.74 (s, 3 H, —OCH_3), 4.78 (m, 2 H, —OCH_2—), 7.11 (s, 2 H, ArH); ^{13}C NMR ($CDCl_3$) δ 174.0 (C=O), 162.9 (C=C), 155.5, 144.1, 139.1, 128.0 (aryls), 124.8 (C=C), 124.0, 120.2 (aryls), 70.4 (—OCH_2—), 60.4 (—OMe). **3**: mp 181–182 °C; IR (CCl_4) 2968, 1768, 1685, 1029 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.13 (s, 3 H, CH_3), 1.20 (d, 3 H, J = 6.9 Hz, $CHMe_2$), 1.26 (d, 3 H, J = 6.9 Hz, $CHMe_2$), 3.41 (sept, 1 H, J = 6.9 Hz, $CHMe_2$), 3.83 (s, 3 H, —OCMe), 4.76 (m, 2 H, —OCH_2—), 7.19 (d, 1 H, J = 8.2 Hz, Ar H), 7.47 (d, 1 H, J = 8.2 Hz, Ar H); ^{13}C NMR ($CDCl_3$) δ 194.7 (C=O), 173.1 (C=O, ester), 160.1 (C=C), 158.0, 150.4, 141.6, 131.6, 125.2 (Aryls), 124.6 (C=C), 118.5 (Aryl), 69.8 (—OCH_2—), 62.4 (—OMe). **24**: mp 175.5–176 °C; IR (CCl_4) 1755, 1683, 1427, 1246, 1018 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.14 (s, 3 H, CH_3); 1.23 (d, 3 H, J = 6.9 Hz, $CHMe_2$), 1.25 (d, 3 H, J = 6.9 Hz, $CHMe_2$), 2.78 (dd, 2 H, J = 8.1 and 9.5 Hz, C-7 CH_2CO), 3.28 (sept, 1 H, J = 6.9 Hz, $CHMe_2$), 4.76 (m, 2 H, —OCH_2—), 6.87 (d, 1 H, J = 7.9 Hz, Ar H), 7.42 (d, 1 H, J = 7.9 Hz, Ar H), 13.0 (s, 1 H, Ar OH, D_2O exch.); ^{13}C NMR ($CDCl_3$) δ 202.3 (C=O), 173.2 (C=O, ester), 161.8 (aryl), 159.8 (C=C), 149.3, 135.9, 133.6 (aryls), 125.9 (C=C), 114.8, 113.6 (aryl), 69.9 (—CH_2O—). **6**: bp 72–73 °C (0.03 mm); ^1H NMR ($CDCl_3$) δ 1.09 (s, 3 H, CH_3), 1.68 (br s, 3 H, C=C—CH_3), 5.37 (m, 1 H, C=C—H). **7**: mp 53–55 °C; IR (CCl_4) 2923, 1698, 1436, 1261 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.02 (s, 3 H, CH_3), 1.67 (br s, 3 H, C=C—CH_3), 2.31 (s, 3 H, —SCH_3), 2.35 (s, 3 H, —SCH_3), 5.40 (m, 1 H, C=C—H); ^{13}C NMR ($CDCl_3$) δ 205.7 (C=O) 141.9, (C=$C(SMe)_2$), 139.4 (C=C($SMe)_2$), 132.2 (C=C—Me), 121.5 (HC=C), 47.2 (—SMe), 45.9 (—SMe). **8**: mp 116–116.5 °C; IR (CCl_4) 2925, 1763, 1677, 1236, 1024 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.08 (s, 3 H, CH_3), 1.71 (br s, 3 H, C=CCH_3), 4.75 (t, 2 H, $J \simeq$ 2.3 Hz, —OCH_2—), 5.38 (m, 1 H, C=CH); ^{13}C NMR ($CDCl_3$) δ 174.2 (C=O, ester), 169.5 (C=C—CO) 132.9 (MeC=C), 123.5 (C=C—CO), 120.8 (HC=C), 68.6 (—CH_2O—). **10**: mp 114–114.5 °C; IR (CCl_4) 2954, 1672, 1618, 1440, 1330, 1148 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.04 (s, 3 H, CH_3), 1.73 (br s, 3 H, C=CCH_3), 3.92 (s, 3 H, —OCH_3), 5.44 (m, 1 H, C=CH), 6.89 (d, 1 H, J = 8.5 Hz, Ar H), 7.63 (d, 1 H, J = 8.5 Hz, Ar H), 11.0 (s. 1 H, Ar OH, D_2O exch); ^{13}C NMR ($CDCl_3$) δ 171.0 (C=O) 159.7, 155.4, 134.5, 126.3, 124.2, 121.2, 114.9 (C=C and aryls), 52.0 (OCH_3). **11**: IR (CCl_4) 2962, 1485, 1413, 1260, 1033 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.03 (s, 3 H, CH_3), 1.21 (d, 6 H, J = 6.9 Hz, $CHMe_2$), 1.72 (br s, 3 H, C=CCH_3), 3.31 (sept, 1 H, J = 6.9 Hz, $CHMe_2$), 3.73 (s, 3 H, —OMe), 5.46 (m, 1 H, C=CH), 7.08 (s, 2 H, Ar H); ^{13}C NMR ($CDCl_3$) δ 155.2, 146.5, 138.1 (aryls), 134.7 (C=CMe), 128.7, 123.4 (aryls), 121.3 (C=CMe), 120.1 (aryl), 60.4 (—OCH_3). **14**: IR (CCl_4) 3616, 3350, 2962, 1485, 1412, 1260, 1033 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.03 (s, 3 H, CH_3), 1.22 (d, 6 H, J = 7.0 Hz, $CHMe_2$), 3.29 (sept, 1 H, J = 7.0 Hz, $CHMe_2$), 3.71 (s, 3 H, —OMe), 4.04 and 4.21 (AB quartet, 2 H, J = 13 Hz, —CH_2O—), 5.73 (m, 1 H, C=CH), 7.07 (s, 2 H, Ar H); ^{13}C NMR ($CDCl_3$) δ 155.1, 145.9, 138.2, 128.6, 123.7, 123.4, 120.2 (aryl and C=C), 65.5 (CH_2OH), 60.4 (—OMe). **15**: mp 147–147.5 °C; IR (CCl_4) 2962, 2934, 1649, 1485, 1412, 1033 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.01 (s, 3 H, CH_3), 1.20 (d, 6 H, J = 6.9 Hz; $CHMe_2$), 2.90 (s, 3 H, NCH_3), 3.08 (s, 3 H, NCH_3), 3.28 (sept, 1 H, J = 6.9 Hz, $CHMe_2$), 3.62, (dd, 1 H, J = 1.7 Hz, 3.9 Hz, $CHCONMe_2$), 4.86 (t, 1 H, J = 1.5 Hz, C=CH), 5.00 (s, 1 H, C=CH) 7.02 (s, 2 H, Ar H); ^{13}C NMR ($CDCl_3$) δ 173.1 (C=O), 154.6 (aryl), 148.3 (C=C), 146.0, 137.7, 128.3, 123.4, 121.5 (aryls), 110.7 (C=C), 60.2 (—O-CH_3), 45.7 (NCH_3), 43.4 (NCH_3). **21**: mp 89–92 °C; IR (CCl_4) 2962, 1735, 1649, 1193, 1170, 1032 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.00 (s, 3 H, CH_3), 1.21 (d, 6 H, J = 6.9 Hz, $CHMe_2$), 3.29 (sept, 1 H, J = 6.9 Hz, $CHMe_2$), 3.36 (1 H, $CHCO_2Me$), 3.65 (s, 3 H, ester —OCH_3), 3.72 (s, 3 H, Ar OMe), 4.86 (t, 1 H, J = 1.5 Hz, C=CH), 5.06 (s, 1 H, C=CH), 7.05 (s, 2 H, Ar H); ^{13}C NMR ($CDCl_3$) δ 173.7 (C=O), 155.1 (aryl), 147.1 (C=C), 145.7, 138.2, 128.4, 123.7, 121.3 (aryls), 111.4 (C=C), 60.3 (Ar OCH_3), 51.8 (CO_2CH_3).