made in order to provide reasonable agreement with experiment, once such agreement is achieved, it is possible to make quantitative predictions of the stereochemistries of reactions with similar substituents.

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Functionalized 1,2-Dioxetanes as Potential Phototherapeutic Agents: The Synthesis of Carboxylate, Carbonate, Carbamate, and Ether Derivatives of 3-(Hydroxymethyl)-3,4,4-trimethyl-1,2-dioxetane

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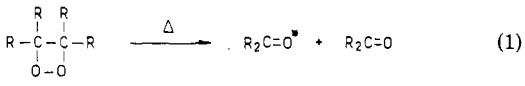
With gentle and efficient synthetic methods, 3-(hydroxymethyl)-3,4,4-trimethyl-1,2-dioxetane (1) can be transformed with appropriate electrophiles in moderate to good yields into functionalized derivatives of dioxetane 1. As electrophiles served carboxylic acids, chlorocarbonates, isocyanates, trialkyloxonium salts, and trialkylsilyl chlorides. With 1 these afford respectively dioxetanes with carboxylate, carbonate, carbamate, ether, and silyl ether functionalities. Nucleophilic activation of the hydroxymethyl substituent in the dioxetane 1 can be achieved under mild conditions by pyridine, 4-(dimethylamino)pyridine, potassium hydride, or butyllithium. Such functionalized dioxetanes serve as chemical sources of triplet excited carbonyl compounds which should find interesting utilization in photobiology and photomedicine, e.g., as potential phototherapeutic agents.

1,2-Dioxetanes have the unique property of generating electronically excited carbonyl products on thermal activation (eq 1), usually triplet states.[1] Thus, these unusual



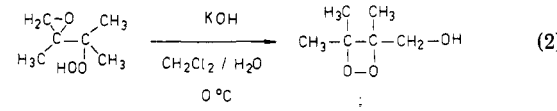
(1)

compounds represent latent excited states, which when appropriately functionalized, would permit releasing on command excited carbonyl fragments for biological, chemical, and physical explorations. Although some functionalized dioxetanes exist,[2] only few attempts have been realized in which dioxetanes with chemical handles have been functionally transformed.[3,4] This synthetic methodology should prove more effective and convenient in derivatizing biomolecules such as sugars, steroids, fatty acids, nucleic acids, amino acids, peptides, etc. by attaching 1,2-dioxetanes through their chemical handles than converting such substrates themselves into 1,2-dioxetanes. Certainly this synthetic modus should provide scope and diversity.

Our specific goal was to expand the still limited[3,4] functional group chemistry of 1,2-dioxetanes so as to permit preparing appropriate biodioxetanes for assessing the photochemical genotoxic potential of such carriers of triplet excited states. Despite their labile nature toward heat, light, bases and nucleophiles, acids and electrophiles, and paramagnetic species such as free radicals and transition-metal ions, etc.,[3a] we demonstrate in the present report that moderately stable 1,2-dioxetanes are sufficiently persistent for functional group manipulation, provided that gentle and efficient synthetic transformations are employed. In fact, the scope and diversity of the synthetic conversions that can be performed on these labile materials is impressive (Scheme I).

Results and Discussion

The moderately stable dioxetane that served as vehicle for the functional group chemistry performed herein is the 3-(hydroxymethyl)-3,4,4-trimethyl-1,2-dioxetane (1), readily available via base-catalyzed cyclization of the 2,3-dimethyl-1,2-epoxy-3-hydroperoxybutane (eq 2).[5] Instead



(2)

of using the recommended tetramethylammonium hydroxide as the phase-transfer base, we found that merely KOH in CH_2Cl_2/H_2O afforded higher yields and purer products.

Previously we showed[3b] that the 1,2-dioxetane 1 could readily be esterified with carboxylic or sulfonic acids. For this purpose the Brewster–Ciotti[6] (benzenesulfonyl chloride in pyridine) and the Mitsunobu[7] (diethyl azocarboxylate and triphenylphosphine) procedures proved especially helpful as mild reagents in converting dioxetane 1 with the appropriate carboxylic or sulfonic acid to the

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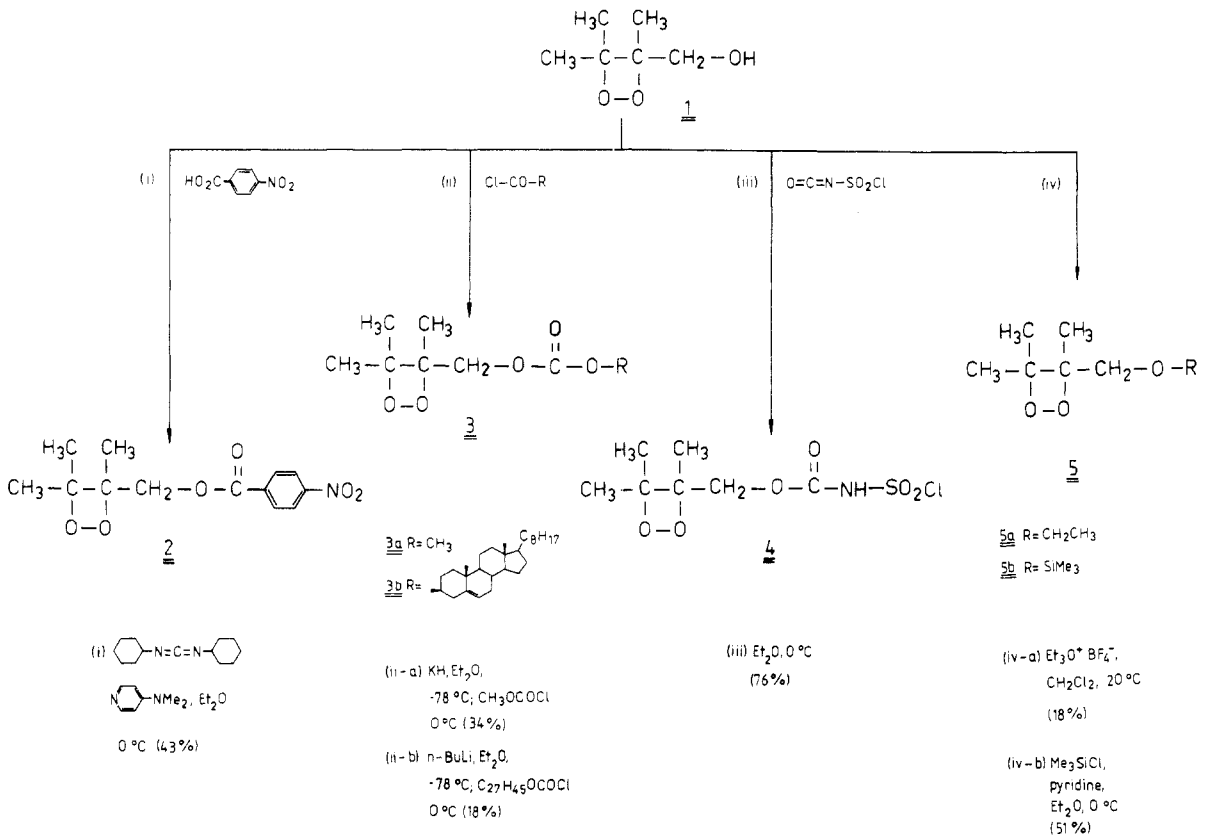
Scheme I



corresponding carboxylates or sulfonates. For such direct esterification usually the mild carbodiimide method is quite effective;[8] however, for the dioxetane **1** the yields were consistently poorer than with the other methods.[6,7] Yet, when *p*-(dimethylamino)pyridine was added in catalytic amounts (Scheme I, conditions i), reasonable yields (42%)[9] of the *p*-nitrobenzoate **2** could be achieved with dicyclohexylcarbodiimide in ether. Also the carbonates **3a,b** could be obtained readily (Scheme I) by first converting the alcohols methanol and cholesterol, respectively, into their chlorocarbonates and subsequently attaching the latter to the corresponding potassium or lithium salts of the hydroxydioxetane **1**. In the case of carbonate **3a**, potassium hydride in ethyl ether at −78 °C (Scheme I, conditions ii–a) served for the derivatization. For carbonate **3b**, the hydroxydioxetane **1** was converted into its lithium alcoholate with *n*-BuLi in Et_2O at −60 °C, followed by addition of the cholesteryl chlorocarbonate at 0 °C (Scheme I, conditions ii–b).

What these dioxetane-substituted carbonates **3a,b** illustrate is that in principle biomolecules with hydroxylic groups, e.g., sugars, steroids, terpenes, fatty alcohols, etc., can be attached to hydroxydioxetane **1** via the carbonate linkage. Such derivatization should prove its usefulness in future biological studies.

Of particular interest is the chlorosulfonyl-functionalized, dioxetane-substituted carbamate **4**, produced essentially quantitatively by addition of the very reactive chlorosulfonyl isocyanate in ethyl ether at 0 °C (Scheme I, conditions iii). With the help of the chlorosulfonyl group as reactive chemical handle, it should be possible to attach the carbamate **4** to biomolecules with nucleophilic sites (amino, carboxy, hydroxy, sulfhydryl, etc.), thus potentially providing a variety of novel functionalized dioxetanes. Dioxetane **4** might prove especially useful in derivatizing enzymes, antibodies, receptors, etc. with latent excited states.[4]

Finally, the ether-functionalized dioxetanes **5a,b** were prepared in good yields. A bit unexpected was the fact that the triethyloxonium salt (Scheme I, conditions iv–a) reacted exclusively at the hydroxy site and not at the electron-rich peroxide linkage of the dioxetane **1**, affording **5a**. An interesting peroxyoxonium salt could have resulted. How useful such ether-functionalized dioxetanes will turn out to be for biological investigations remains to be seen; however, the conversion **1** → **4a** illustrates that dioxetanes are sufficiently stable to survive such transformations.

Also the silylation of the hydroxydioxetane **1** with trimethylsilyl chloride and pyridine as a base catalyst in ethyl ether at 0 °C (Scheme I, conditions iv–b) proceeded smoothly, affording the silyl ether substituted dioxetane **5b** in high yield. This dioxetane is sufficiently volatile to permit purification by high-vacuum distillation. In given instances such silylation might be helpful in providing volatile dioxetanes.

In summary, by means of the set of dioxetanes **2–5** (Scheme I) presented here, all available via straightforward derivatization of the dioxetane **1** with routine chemical transformations, but under gentle and selective conditions, the feasibility of preparing functionalized dioxetanes has been demonstrated. In the present case the chemical linkages that proved successful were the carboxylate, carbonate, carbamate, and ether functions, which by means of appropriate electrophilic agents were attached to the nucleophilic hydroxyl group of dioxetane **1**. The reverse methodology can be achieved through "umpolung", in which the hydroxyl group of dioxetane **1** can be converted into an electrophilic handle and anchored to nucleophilic sites, especially those of biomolecules.[3a]

(8) Neises, B.; Steglich, W. *Angew. Chem., Int. Ed. Engl.* **1978**, *17*, 522.
(9) Isolated yield of analytically pure material; the crude yield was much higher, but on low-temperature column chromatography product loss ensued through on-column decomposition.

Experimental Section

General Aspects. Boiling and melting points are uncorrected, the latter were taken on a Reichert Thermovar Kofler apparatus. Infrared (IR) spectra were obtained on a Beckman Acculab 4 spectrophotometer. ^1H NMR spectra were run either on an Hitachi-Perkin-Elmer R 24 B (60 MHz), Varian EM 390 (90 MHz), or Bruker WM 400 (400 MHz) spectrometer, with Me_4Si as internal standard, and ^{13}C NMR spectra on a Bruker WM 400 (100.6 MHz) spectrometer with $CDCl_3$ or Me_4Si as internal standard; the chemical shifts (δ) are reported in ppm. Mass spectra (MS) were measured on a Varian MAT CH 7 spectrometer, with inlet temperature below 100 °C.

Combustion analyses for elemental composition were obtained in-house. Thin-layer chromatography (TLC) was run on Polygram SIL/G/UV (40 × 80 mm) from Machery and Nagel Co. Column chromatography utilized silica gel 32–64 mesh ASTM (activity grade III).

Commercial reagents and solvents were purchased from standard chemical suppliers and purified to match the reported physical and spectral data. Known compounds were prepared according to the literature procedures and purified to match the reported physical and spectral data. Unless otherwise stated, stirring was performed magnetically, room temperature was ca. 20 °C, drying after aqueous workup was carried out over anhydrous $MgSO_4$, and rotary evaporation was performed at aspirator pressure (15–20 Torr) at 0 °C.

3-(Hydroxymethyl)-3,4,4-trimethyl-1,2-dioxetane (1). *CAUTION*: Dioxetanes are thermally labile peroxides and thus potentially dangerous materials (*EXPLOSIVE*) so that all precautionary measures such as safety shield, face mask, and heavy gloves should be used when working with them!

Into a 2000-mL round-bottomed flask, equipped with a mechanical stirrer, was placed a solution of 20.6 g (156 mmol) of 2,3-dimethyl-1,2-epoxy-3-hydroperoxybutane[5] in 300 mL of CH_2Cl_2, and while the mixture was cooled by means of an ice bath and stirred, a solution of 56.6 g (1.01 mol) of KOH in 120 mL of H_2O, previously cooled to 0 °C in an ice bath, was added. The mixture was stirred vigorously at 0 °C for 5.5 h, the organic phase separated, and the aqueous phase extracted with CH_2Cl_2 (4 × 30 mL); the combined organic layers were washed with saturated brine (30 mL) and dried. An aliquot (ca. 5% dioxetane) of the yellow CH_2Cl_2 solution (*CAUTION*: when working with dioxetanes, only samples containing less than 1.0 g of crude material by theory should be utilized in the workup!) was rotary evaporated, affording 845 mg (78%) of a yellow oil, which on recrystallization (twice) from petroleum ether (30–50) gave 785 mg (73%) of yellow needles: mp 34–35 °C (lit.[5] mp 35 °C); TLC (silica gel) [1:1 ethyl ether/petroleum ether (bp 30–50 °C)] R_f 0.42, [CH_2Cl_2] R_f 0.07; IR (CCl_4) 3570, 3000, 2975, 2930, 2880, 1380, 1170, 1145, 1070, 1045, 870 cm^{-1}; ^1H NMR ($CDCl_3$, 90 MHz) δ 1.35 (s, 3 H, CH_3), 1.45 (s, 3 H, CH_3), 1.65 (s, 3 H, CH_3), 2.30 (br s, 1 H, OH) [AB system, δ_A 3.71, δ_B 4.20 (J_{AB} = 12.0 Hz, 2 H, CH_2O)]; ^{13}C NMR ($CDCl_3$, 100.6 Hz, −20 °C) δ 17.24 (q, CH_3), 21.58 (q, CH_3), 24.01 (q, CH_3), 64.72 (t, CH_2O), 89.14 (s, COO), 90.29 (s, COO); MS (70 eV) m/e 132 (1%, M^+), 100 (4%, M − O_2), 74 (4%, M − acetone), 58 (12%), 43 (100%).

3-[((*p*-Nitrobenzoyl)oxy)methyl]-3,4,4-trimethyl-1,2-dioxetane (2). Into a 100-mL, round-bottomed flask, equipped with a magnetic spin bar and a 25-mL dropping funnel, was placed 560 mg (3.35 mmol) of *p*-nitrobenzoic acid in 10 mL of CH_2Cl_2 and the mixture cooled to 0 °C by means of an ice bath. Within 5 min a solution of 198 mg (1.50 mmol) of dioxetane 1 in 2 mL of CH_2Cl_2 was added, followed by 840 mg (4.08 mmol) of dicyclohexylcarbodiimide and 120 mg (1.00 mmol) of 4-(dimethylamino)pyridine, and the mixture stirred at 0 °C for 1 h. The solids of the yellow reaction mixture were removed by filtration, the filtrate was concentrated to ca. 15-mL volume by means of rotary evaporation, the solids were removed by filtration, and the filtrate was washed with saturated aqueous $NaHCO_3$ solution (15 mL), with H_2O (20 mL), and with saturated brine (20 mL). After drying over anhydrous Na_2SO_4, the organic phase was rotary evaporated and the residue chromatographed on silica gel (activity grade III, 60:1 adsorbent/substrate ratio, CH_2Cl_2, −35 °C). The peroxidic fractions (spotted by means of peroxide test on TLC with KI/HOAc spray) were combined, rotary evaporated, and extracted with bp 30–50 °C petroleum ether (3 × 30 mL). The combined extracts were rotary evaporated and recrystallized from 1:3 CH_2Cl_2/petroleum ether (bp 30–50 °C), yielding 180 mg (43%) of yellow needles, mp 72–73 °C (lit.[3b] mp 70–71 °C).

3-[(((Methyloxy)carbonyl)oxy)methyl]-3,4,4-trimethyl-1,2-dioxetane (3a). A 50-mL, round-bottomed flask, equipped with a nitrogen inlet and outlet and a magnetic spin bar, was charged with 117 mg (2.92 mmol) of KH in 10 mL of anhydrous Et_2O under a nitrogen atmosphere. Under vigorous stirring was added at once a solution of 389 mg (29.5 mmol) dioxetane 1 in 1 mL of anhydrous Et_2O, with the reaction temperature kept at ca. −70 °C by means of external cooling with a methanol–dry ice bath. Gas evolution (hydrogen) could be observed, and the yellow reaction mixture decolorized to pale yellow. After 30 min a solution of 557 mg (5.89 mmol) of methyl chloroformate in 2 mL of anhydrous Et_2O was added at ca. −70 °C, stirred for 30 min, and allowed to warm up to 0 °C. To the reaction mixture was added 20 mL of 5% aqueous HCl, the organic phase subsequently washed with saturated aqueous $NaHCO_3$ (20 mL) and with H_2O (10 mL), dried, and rotary evaporated, giving 417 mg (75%) of a yellow oil. Flash chromatography on silica gel (120:1 adsorbent/substrate ratio; CH_2Cl_2; −30 °C) afforded 191 mg (34%) of yellow needles, mp 48–49 °C; peroxide content > 99% by iodometry: TLC (silica gel) [CH_2Cl_2] R_f 0.47; IR (CCl_4) 2990, 2960, 2942, 1755, 1442, 1390, 1380, 1370, 1275, 1260, 1150, 1115, 975 cm^{-1}; ^1H NMR ($CDCl_3$, 90 MHz) δ 1.40 (s, 6 H, CH_3), 1.59 (s, 3 H, CH_3), 3.75 (s, 3 H, OCH_3) [AB signal, δ_A 4.69, δ_B 4.24 (J_{AB} = 11.3 Hz, 2 H, CH_2O)]; ^{13}C NMR ($CDCl_3$, 100.6 MHz) δ 17.98 (q, CH_3), 22.25 (q, CH_3), 22.70 (q, CH_3), 55.19 (q, CH_3), 69.20 (t, CH_2O), 88.57 (s, COO), 89.10 (s, COO), 155.41 (s, C=O); MS (70 eV), m/e 158 (0.08%, M − O_2), 132 (5%, M − acetone), 104 (0.5%), 90 (2%), 82 (3%), 59 (8%), 43 (100%). Anal. Calcd for $C_8H_{15}O_5$ (191.2): C, 50.25; H, 7.91. Found: C, 50.28; H, 7.49.

3-[(((5-Cholesten-3β-yloxy)carbonyl)oxy)methyl]-3,4,4-trimethyl-1,2-dioxetane (3b). A 100-mL, three-necked, round-bottomed flask, equipped with a magnetic spin bar, a 25-mL dropping funnel (pressure equalized), and a nitrogen inlet and outlet tubes, was charged with 396 mg (3.00 mmol) of dioxetane 1 in 20 mL of anhydrous Et_2O, and while the mixture was stirred and cooled at −60 °C (methanol–dry ice bath), *n*-BuLi in *n*-hexane (1.07 mL, 2.08 M) was added dropwise within 10 min. After the mixture was stirred for 5 min at −60 °C, the dry ice bath was replaced by an ice bath, and the reaction mixture was allowed to warm up to 0 °C and stirred for 10 min. All at once was added a solution of 1.00 g (2.23 mmol) cholesteryl chloroformate in 10 mL of anhydrous Et_2O while the mixture was stirred and cooled at 0 °C for 15 min. A solution of 110 mg (1.00 mol) of triethylamine in 10 mL of anhydrous Et_2O was added and stirred at 0 °C for an additional 30 min. The reaction mixture was acidified carefully with 2 N HCl to pH ca. 5 and washed with H_2O (2 × 20 mL). The organic phase was dried over anhydrous $Na_2CO_3/MgSO_4$ and rotary evaporated. After twofold flash chromatography on silica gel (first with a 21:1 adsorbent/substrate ratio, 2:1 CH_2Cl_2/petroleum ether (bp 30–50 °C), −20 °C, and second with a 56:1 adsorbent/substrate ratio, 1:1 CH_2Cl_2/petroleum ether (bp 30–50 °C), −25 °C) of the yellow residue there was obtained 267 mg (18%) of pale yellow needles, mp 95–99 °C, which on recrystallization from petroleum ether (bp 30–50 °C) gave the pure dioxetane **3b**: mp 97–104 °C dec; TLC (silica gel) [1:2 Et_2O/petroleum ether (bp 30–50 °C)] R_f 0.81; IR (CCl_4) 3030, 2950, 2885, 1750, 1470, 1440, 1390, 1375, 1320, 1270, 1250, 1150, 1120, 1025, 995, 975 cm^{-1}; ^1H NMR ($CDCl_3$, 90 MHz) δ 0.97–2.56 (m, 44 H, cholesteryl), 1.40 (s, 3 H, CH_3), 1.43 (s, 3 H, CH_3), 1.61 (s, 3 H, CH_3) [AB system, δ_A 4.46, δ_B 4.71 (J_{AB} = 11.3 Hz, 2 H, CH_2O)], 5.36–5.57 (m, 1 H, =CH); ^{13}C NMR ($CDCl_3$, 100.6 MHz) δ 11.78 (q, CH_3), 18.06, 18.61, 19.23, 20.90, 22.25, 22.55, 22.88, 23.74, 23.95, 24.21, 27.50, 28.02, 28.21, 31.63, 31.79, 35.78, 36.05, 36.38, 36.66, 37.82, 39.42, 39.50, 42.15 (s), 49.71 (d), 55.86 (d), 56.49 (d), 68.87 (t, CH_2O), 78.37 (d), 88.65 (s, COO), 89.15 (s, COO), 123.17 (d, =CH), 138.95 (s, =C), 154.22 (s, C=O); MS (70 eV), m/e 220 (4%), 205 (19%), 177 (3%), 121 (21%), 119 (63%), 117 (62%), 58 (27%), 57 (33%), 43 (100%). Anal. Calcd for $C_{34}H_{56}O_5$ (544.8): C, 74.96; H, 10.36. Found: C, 75.20; H, 10.67.

3-[(((*N*-(Chlorosulfonyl)amino)carbonyl)oxy)methyl]-3,4,4-trimethyl-1,2-dioxetane (4). A 50-mL, round-bottomed

flask, equipped with a magnetic spin bar and a dropping funnel with a $CaCl_2$ drying tube, was charged with a solution of 2.46 g (17.4 mmol) of chlorosulfonyl isocyanate in 20 mL of anhydrous Et_2O. While the mixture was stirred vigorously and cooled to 0 °C by means of an ice bath, a solution of 2.29 g (17.4 mmol) of dioxetane 1 in 20 mL of anhydrous Et_2O was added dropwise within 30 min. A 10% aliquot of the reaction mixture was removed and rotary evaporated, affording 475 mg (100%) of a viscous, yellow oil, which exhibited no significant impurities by means of ^1H NMR. Recrystallization twice from 1:1 Et_2O/petroleum ether (bp 30–50 °C) led to 361 mg (76%) of yellow powder: mp 90–91 °C; TLC (silica gel) [CH_2Cl_2] R_f 0.50 (with strong tailing); IR (CCl_4) 3360, 3000, 2980, 1780, 1620, 1435, 1383, 1290, 1193, 1175, 1155 cm^{-1}; ^1H NMR ($CDCl_3$/acetone-d_6, 90 MHz) δ 1.44 (s, 3 H, CH_3), 1.47 (s, 3 H, CH_3), 1.63 (s, 3 H, CH_3), 4.76 (s, 2 H, CH_2O), 10.00–10.50 (s, 1 H, NH); ^{13}C NMR ($CDCl_3$, 100.6 MHz) δ 17.58 (q, CH_3), 21.92 (q, CH_3), 23.83 (q, CH_3), 69.02 (t, CH_2O), 89.06 (s, COO), 89.82 (s, COO), 149.06 (s, C=O); MS (70 eV), m/e 215 (0.03%, M - acetone), 202 (0.06%), 149 (0.2%), 74 (2%), 64 (6%), 58 (28%), 43 (100%). Anal. Calcd for $C_7H_{12}NO_6SCl$ (273.7): C, 30.72; H, 4.42; N, 5.12. Found: C, 30.80; H, 4.41; N, 4.98.

3-(Ethoxymethyl)-3,4,4-trimethyl-1,2-dioxetane (5a). A 100-mL, round-bottomed flask, equipped with a magnetic spin bar and a dropping funnel protected with a $CaCl_2$ drying tube, was charged with a solution of 823 mg (6.24 mmol) of dioxetane 1 in 30 mL of anhydrous CH_2Cl_2 and ca. 4.5 g of anhydrous Na_2CO_3. While the mixture was stirred and the reaction temperature maintained at 0 °C by means of cooling with an external ice bath, a solution of 1.51 g (7.95 mmol) of triethyloxonium tetrafluoroborate in 10 mL of anhydrous CH_2Cl_2 was added within 5 min. After the addition, the ice bath was removed and the reaction mixture allowed to stir at ca. 20 °C for 4 h. Again the reaction mixture was cooled to ca. 0 °C by means of an ice bath and the organic phase separated and washed with concentrated aqueous NH_3 (5 mL), followed by a washing with H_2O (20 mL) and drying. The yellow solution was concentrated to one-third its volume by means of rotary evaporation and flash chromatographed on silica gel (20:1 adsorbent/substrate ratio, CH_2Cl_2, -20 °C). The peroxidic eluates (spotted by means of KI–HOAc) were combined and rotary evaporated (-10 °C at 17 Torr), leading to 183 mg (18%) of a yellow, pungent-smelling oil; peroxide content > 97% by means of iodometry: TLC (silica gel) [CH_2Cl_2] R_f 0.67; IR (CCl_4) 2980, 2935, 2900, 2870, 1470, 1455, 1440, 1410, 1380, 1370, 1260, 1230, 1150, 1113, 1022, 880 cm^{-1}; ^1H NMR ($CDCl_3$, 90 MHz) δ 1.20 (t, J = 2.3 Hz, 3 H, CH_3CH_2), 1.43 (s, 3 H, CH_3), 1.46 (s, 3 H, CH_3), 1.59 (s, 3 H, CH_3), 3.55 (q, J = 2.3 Hz, 2 H, CH_2CH_3) [AB system, δ_A 4.62, δ_B 3.66 (J_{AB} = 9.3 Hz, 2 H, CH_2O); ^{13}C NMR ($CDCl_3$, 100.6 Hz) δ 14.97 (q, CH_3CH_2), 18.46 (q, CH_3), 22.28 (q, CH_3), 23.95 (q, CH_3), 66.96 (t, CH_2OEt), 72.88 (t, OCH_2CH_3), 89.05 (s, COO), 89.47 (s, COO); MS (70 eV), m/e 161 (0.07%, M + 1), 159 (0.06%, M - 1), 131 (0.1%, M - C_2H_5), 129 (0.2%, M - O_2), 103 (0.3%, M + 1 - acetone), 102 (0.1%, M - acetone), 87 (2%), 59 (25%), 58 (32%), 57 (7%), 43 (100%).

3-[((Trimethylsilyl)oxy)methyl]-3,4,4-trimethyl-1,2-dioxetane (5b). A 100-mL, round-bottomed flask, equipped with a magnetic spin bar and a 25-mL dropping funnel protected with a $CaCl_2$ drying tube, was charged with 1.09 g (10.1 mmol) of trimethylsilyl chloride in 20 mL of anhydrous CH_2Cl_2. While the mixture was stirred and cooled to 0 °C by means of an ice bath, 797 mg (10.1 mmol) of pyridine was first added and then dropwise within 10 min a solution of 666 mg (5.04 mmol) of dioxetane 1 in 20 mL of anhydrous CH_2Cl_2. After a 40-min reaction time under these conditions, the clear yellow solution was concentrated to a 5-mL volume by means of rotary evaporation and flash chromatographed over alumina (69:1 adsorbent substrate ratio, 1:1 CH_2Cl_2/petroleum ether (bp 30–50 °C), -30 °C), affording 525 mg (51%) of a yellow, pleasant-smelling oil; peroxide content > 97% by means of iodometry: TLC (silica gel) [CH_2Cl_2] R_f 0.77; IR (CCl_4) 3000, 2955, 2920, 2870, 1470, 1375, 1252, 1152, 1095, 980, 877, 842 cm^{-1}; ^1H NMR ($CDCl_3$, 90 MHz) δ 0.16 (s, 9 H, $SiMe_3$), 1.45 (s, 6 H, CH_3), 1.64 (s, 3 H, CH_3) [AB system, δ_A 4.18, δ_B 3.81 (J_{AB} = 10.2 Hz, 2 H, CH_2O)]; ^{13}C NMR ($CDCl_3$, 100.6 MHz) δ -0.72 (q, $SiMe_3$), 18.00 (q, CH_3), 22.19 (q, CH_3), 24.16 (q, CH_3), 65.05 (t, CH_2O), 89.13 (s, COO), 89.98 (s, COO); MS (70 eV), m/e 147 (0.6%, M - acetone), 131 (25%, M - $SiMe_3$), 115 (2%, M - $OSiMe_3$), 73 (42%, $SiMe_3$), 58 (18%), 43 (100%).

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Registry No. 1, 84114-76-1; 2, 92507-36-3; 3a, 108560-91-4; 3b, 108536-11-4; 4, 108536-12-5; 5a, 108536-13-6; 5b, 108536-14-7; 2,3-dimethyl-1,2-epoxy-3-hydroperoxybutane, 108536-15-8; p-nitrobenzoic acid, 62-23-7; 4-(dimethylamino)pyridine, 1122-58-3; methyl chloroformate, 79-22-1; cholesteryl chloroformate, 7144-08-3; chlorosulfonyl isocyanate, 1189-71-5.

Stabilization Energies and Structures of Substituted Methyl Radicals

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The energies and structures of a large number of substituted methyl radicals and methanes have been calculated at the fully geometry optimized UHF and ROHF 4-31G levels. The radical stabilization energies (RSE's) of the various substituents have been calculated according to the isodesmic reaction $X_n\dot{C}H_{3-n} + CH_4 \rightarrow X_nCH_{4-n} + \dot{C}H_3$. These RSE's are compared with other radical stabilization scales and with various types of experimental data derived from radical reactions and provide a scale for evaluating the extent of substituent stabilization in radical-forming reactions.

Over the past decade considerable attention has been devoted to attempts to determine the relative extents of stabilization, or destabilization, of a radical center by an attached substituent and the nature of the orbital interactions between the orbitals of the substituent and the singly occupied molecular orbital (SOMO) of the radical center. The vast majority of these efforts have involved kinetic studies including the following: (1) hydrogen atom

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