J. Org. Chem. **1982**, *47*, 3647–3649 **3647**

Bis(carbomethoxy)maleic Anhydride

H. K. Hall, Jr.,* R. C. Sentman, and P. Nogues

Chemistry Department, University of Arizona, Tuscon, Arizona 85721

Received February 10, 1982

Bis(carbomethoxy)maleic anhydride (1) was synthesized by phosphoric anhydride induced demethoxylation of tetramethyl ethylenetetracarboxylate. With *p*-methoxystyrene, anethole, divinylbenzene, and diphenylethylene, 1 formed 2:1 Diels–Alder adducts. With styrene and isobutyl vinyl ether, 1 underwent an inverse electron-demand Diels–Alder reaction leading to 3,4-dihydro-2*H*-pyran derivatives. In the Diels–Alder reaction with butadiene, 1 was 100 times less reactive than (carbomethoxy)maleic anhydride. A radical-initiated alternating copolymer was obtained at 80 °C with styrene.

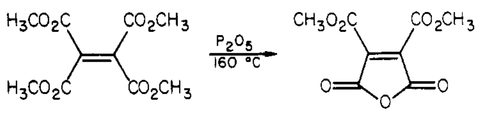
Introduction

Recently we reported the synthesis and homopolymerization of (carbomethoxy)maleic anhydride (CMA)[1] the first trisubstituted ethylene reported to homopolymerize. It was also extremely reactive in [4 + 2] cycloadditions.[2] This high reactivity is ascribed to the fact that two of the substituents are confined into a ring, reducing steric hindrance sufficiently to permit oligomerization and permitting extensive delocalization of a growing radical. These factors are also effective among the 1,2-disubstituted olefins, where maleic anhydride and maleimide are much more reactive monomers in copolymerizations than the acyclic 1,2-disubstituted olefins.

The literature did not provide any examples of a maleic anhydride derivative carrying two electron-withdrawing groups, which would also be a potential comonomer. Recently though, Vogl and co-workers[3] reported the copolymerization of dimethylmaleic anhydride with vinyl ethers. We have studied the synthesis and reactivity of bis(carbomethoxy)maleic anhydride (BCMA).

Results

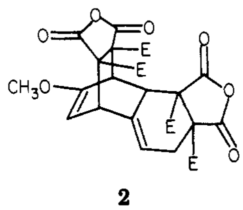
Synthesis. Bis(carbomethoxy)maleic anhydride was prepared from tetramethyl ethylenetetracarboxylate (eq 1) in moderate yield by heating the latter in the presence of phosphorus pentoxide at 160 °C for 24 h. BCMA is isolated by vacuum distillation and purified by recrystallization from diethyl ether. This procedure is similar to that used to prepare CMA[1] and had previously been reported for the synthesis of α-(trichloromethyl)maleic anhydride.[4]



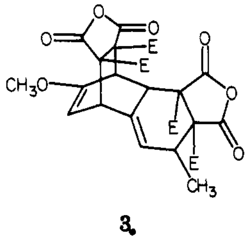
1

(1)

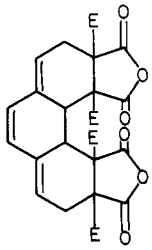
Cycloaddition Reactions. BCMA was mixed with various electron-rich olefins and the products of the spontaneous reactions were examined.



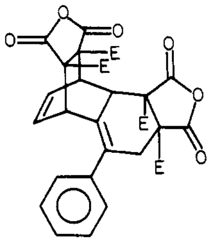
2



3

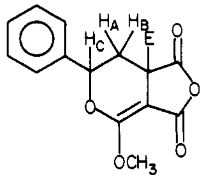


4

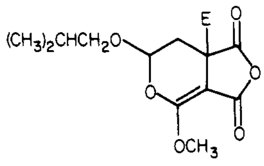


5

With most styrenes including *p*-methoxystyrene, anethole, divinylbenzene, and diphenylethylene, double Diels–Alder adducts, the so-called "Wagner-Jauregg adducts",[5] were obtained (2–5, E = $COOCH_3$). The NMR spectra do not indicate if one or more isomers are formed. With styrene itself and isobutyl vinyl ether, an inverse electron demand Diels–Alder reaction occurs involving one of the carbonyl groups in the [4 + 2] cycloaddition, leading to the dihydropyran derivatives 6 and 7, respectively. The NMR spectrum indicates that only one stereoisomer of 6 is formed. With 2,5-dichlorostyrene no reaction occurs.

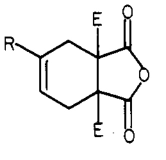


6



7

Isoprene and butadiene added smoothly to BCMA to give the expected cycloadducts 8a and 8b, respectively.



8a, R = CH_3
b, R = H

The latter reaction followed second-order kinetics. The second-order rate constant is 7×10^{-5} M^{-1} s^{-1}, compared to 5.8×10^{-3} M^{-1} s^{-1} for CMA[2] and 1.2×10^{-3} M^{-1} s^{-1} for tetracyanoethylene.

Radical-Induced Copolymerization. While no polymer forms spontaneously in any of these reactions, 1:1 copolymer is formed with styrene in the presence of AIBN

---

[1] Hall, H. K., Jr.; Rhoades, J. W.; Nogues, P.; Wai, G. K. C. *Polym. Bull. (Berlin)* **1981**, *4*, 629.

[2] Hall, H. K., Jr.; Nogues, P.; Rhoades, J. W.; Sentman, R. C.; Detar, M. *J. Org. Chem.* **1982**, *47*, 1451.

[3] Florianczyk, T.; Sullivan, C.; Janovic, Z.; Vogl, O. *Polym. Bull. (Berlin)* **1981**, *5*, 521.

[4] Bowman, R. E.; Closier, M. D.; Islip, P. J. *J. Chem. Soc.* **1964**, 3841.

[5] Wagner-Jauregg, Th. *Synthesis*, **1980**, 769.

0022-3263/82/1947-3647$01.25/0

at 80 °C. A mixture of 50% polymer, 50% pyran **6** is formed. At lower temperatures the yield of polymer decreases until at 60 °C only pyran is isolated.

Left for several weeks at room temperature or several days at higher temperature, the pyran **6** is slowly converted to copolymer. Molecular weights of copolymer so formed are extremely low, and the copolymers are soluble in diethyl ether.

No copolymer is formed under analogous conditions with *p*-methoxystyrene. BCMA is incorporated into 2:1 adduct, and any remaining methoxystyrene homopolymerizes.

Discussion

BCMA undergoes two consecutive Diels–Alder additions with the electron-rich styrenes. This reaction has recently been reviewed by Wagner-Jauregg.[5] In most examples, including *p*-methoxystyrene, anethole, and diphenylethylene, the second cycloaddition occurs on the cis-diene system in the ring. In the case of divinylbenzene the second [4 + 2] cycloaddition occurs on the second exocyclic vinyl group and an endocyclic double bond, and not on the cis-diene system in the six-membered ring formed after the first addition. With diphenylethylene only a 2:1 adduct is formed, in spite of the presence of more cis-diene systems in the final product.

The inverse electron demand Diels–Alder reaction observed with styrene and isobutylvinyl ether is analogous to the reactions described in previous papers.[6,7] Several methyl acrylate esters with one additional electron-withdrawing group in the α position behave as heterodienes in the reaction with electron-rich olefins.

BCMA is not nearly as reactive as its trisubstituted analogue CMA, which was more reactive than tetracyanoethylene. The lower reactivity of BCMA compared to CMA can be ascribed to greater steric interactions.

Finally, BCMA is one of the very few (nonfluorinated) tetrasubstituted ethylenes capable of copolymerization.

Experimental Section

Instrumentation. The melting points were determinated in a Thomas-Hoover melting point apparatus and are uncorrected. Nuclear magnetic resonance (NMR) spectra were recorded on a Varian T-60 or a Varian EM-360 spectrometer at 60 MHz. Infrared (IR) spectra were obtained with a Perkin-Elmer grating infrared spectrophotometer. Elemental analyses were performed by the University of Arizona, Analytical Center, Tuscon, AZ.

Chemicals. *p*-Methoxystyrene, diphenylethylene, and anethole were obtained with Aldrich; divinylbenzene was obtained from Pfaltz and Bauer. All reactants were distilled from calcium hydride. All solvents were dried and distilled according to standard procedures before use.

Bis(carbomethoxy)maleic Anhydride (1). Tetramethyl ethylenetetracarboxylate[8,9] (15.0 g) and 10 g of phosphorus pentoxide were mixed in a closed flask and heated to 160 °C for 24 h. The solid black residue was allowed to cool and then vacuum distilled, bp 105–110 °C (0.05 mmHg). The crude BCMA was recrystallized from diethyl ether; mp 75–76 °C; yield 3.4 g (27%); NMR ($CDCl_3$) δ 4.0 (s) IR (KBr) 1860, 1790 (anhydride), 1720 (ester carbonyl), 1660 (C=C) cm^{-1}. Anal. Calcd for $C_8H_6O_7$: C, 45.0; H, 2.84. Found: C, 45.2; H, 2.9.

General Reaction Procedures. Equimolar amounts of BCMA and olefin were mixed in bulk or in the appropriate solvent in reaction vessel equipped with a vacuum valve. The mixture was degassed by using the freeze–thaw method and placed in a thermostated bath at the desired temperature (±1 °C). When the reaction was finished, the adducts were isolated and recrystallized from ether. The residue usually consisted of starting material.

2:1 Adduct of BCMA and *p*-Methoxystyrene 2. Equimolar amounts of BCMA and *p*-methoxystyrene were reacted in bulk at 60 °C for 18 h, and the product was recrystallized from ether at −50 °C; NMR ($CDCl_3$) δ 2.7 (m, 2 H), 3.0–3.5 (m, 3 H), 3.6 (s, 3 H), 3.8, 3.9, 3.95, 4.0 (4 s, 12 H), 5.2 (m, 1 H), 6.1 (m, 1 H). Anal. Calcd for $C_{25}H_{22}O_{15}$: C, 53.38; H, 3.94. Found: C, 53.07; H, 3.76.

2:1 Adduct of BCMA and Divinylbenzene 4. Equimolar amounts (0.25 mmol) of BCMA and divinylbenzene were mixed with 4 mL of ether and left at room temperature for 2 days; yield 10%; NMR (acetone-d_6) δ 2.95 (m, 4 H), 3.1–3.6 (m, 2 H), 3.8–4.0 (4 s, 12 H), 6.0–6.4 (m, 4 H); IR (KBr) 1855, 1780 (anhydride), 1760, 1720 (ester carbonyl), 1630 (C=C) cm^{-1}. Anal. Calcd for $C_{26}H_{22}O_{14}$: C, 55.9; H, 3.9. Found: C, 56.0; H, 4.1.

2:1 Adduct of BCMA and Anethole 3. Equimolar amounts (0.25 mmol) of BCMA and anethole were mixed with 1 mL of ether. After 3 days at room temperature, white crystals were obtained: yield 20%; NMR (acetone-d_6) δ 1.55 (d, J = 7 Hz, 3 H), 2.95 (br, 2 H), 3.5 (s, 3 H), 3.8–4.2 (m + 4 s, 14 H), 5.25 (dd, 1 H), 5.9 (m, 1 H); IR (KBr) 1860, 1785 (anhydride), 1765, 1750, 1730 (ester carbonyl), 1635 (C=C) cm^{-1}. Anal. Calcd for $C_{26}H_{24}O_{15}$: C, 54.2; H, 4.2. Found: C, 54.1; H, 4.1.

2:1 Adduct of BCMA and Diphenylethylene 5. Equimolar amounts (0.5 mmol) of BCMA and diphenylethylene were mixed with 3 mL of ether. After 4 weeks at room temperature, crystals form: yield 15%; NMR (acetone-d_6) δ 3.0–3.6 (m, 3 H), 3.7, 3.8, 3.85, 4.07 (4 s, 12 H), 4.2–4.5 (m, 2 H), 6.4–7.0 (m, 2 H), 7.2–7.7 (m, 5 H); IR (KBr) 1865, 1795 (anhydride), 1760, 1740, 1730 (ester carbonyl) cm^{-1}. Anal. Calcd for $C_{30}H_{24}O_{14}$: C, 59.2; H, 4.0. Found: C, 59.4; H, 4.1.

2-Phenyl-4-(methoxycarbonyl)-6-methoxy-3,4-dihydro-2*H*-pyran-4,5-dicarboxylic Anhydride (6). Equimolar amounts (0.25 mmol) of BCMA and styrene were mixed with 3 mL of ether. After 2 days at room temperature, crystals were formed at 0 °C. The NMR spectrum indicates only one isomer is present; yield 40%; NMR (acetone-d_6) δ 2.4 (q, 1 H, J_{AB} = 14 Hz, J_{AC} = 12 Hz), 2.9 (q, 1 H, J_{BC} = 3.6 Hz), 3.85, 4.0 (2 s, 6 H), 5.85 (dd, 1 H), 7.6 (m, 5 H); IR (KBr) 1830, 1765 (anhydride), 1740 (ester carbonyl), 1600 (phenyl) cm^{-1}. Anal. Calcd for $C_{16}H_{14}O_7$: C, 60.4; H, 4.4. Found: C, 60.1; H, 4.6.

2-Isobutoxy-4-(methoxycarbonyl)-6-methoxy-3,4-dihydro-2*H*-pyran-4,5-dicarboxylic Anhydride (7). Equimolar amounts of BCMA and isobutyl vinyl ether (0.50 mmol) were mixed in 2 mL of acetonitrile. After 18 h at room temperature, the solvent was removed by vacuum. The oily residue was dissolved in ether and separated into two layers by the addition of petroleum ether. The oil was dried under vacuum. The fact that the residue did not crystallize and excessive splitting in the NMR spectrum indicate that more than one isomer is present; yield, 40%; NMR ($CDCl_3$) δ 1.4 (2 d, 6 H), 2.5–2.8 (m, 1 H), 3.30 (m, 2 H), 3.80 (br s, 6 H), 4.10–4.45 (m, 2 H), 5.85 (m, 1 H); IR (NaCl, $CDCl_3$) 1850, 1780 (anhydride), 1745 (ester carbonyl) cm^{-1}. Anal. Calcd for $C_{14}H_{18}O_8$: C, 53.50; H, 5.77. Found: C, 53.37; H, 5.92.

1-Methyl-4,5-bis(methoxycarbonyl)cyclohex-1-ene-4,5-dicarboxylic Anhydride (8a). Equimolar amounts (0.25 mmol) of BCMA (54 mg) and isoprene (25 μL) in 1 mL of chloroform were allowed to react for 24 h. The solvent was removed and the product recrystallized from diethyl ether; yield 32 mg, 44%; mp 64–65 °C; NMR ($CDCl_3$) δ 1.8 (m, 3 H), 2.75 (m, 4 H), 3.8 (s, 6 H), 5.6 (m, 1H). Anal. Calcd for $C_{13}H_{14}O_7$: C, 55.32; H, 5.00. Found: C, 55.13; H, 5.01.

4,5-Bis(methoxycarbonyl)cyclohex-1-ene-4,5-dicarboxylic Anhydride (8b). BCMA (42.82 mg, 0.25 mmol) was dissolved in 0.8 mL of acetone-d_6, mixed with 0.2 mL of a stock solution of 0.5 M butadiene in acetone, and left at 25 °C for 48 h. Acetone was removed under aspirator vacuum, and the residue was recrystallized from ether/pentane at −60 °C with filtration while still cold; yield 42.3 mg (75%); mp 54–56 °C (discolors at 35 °C); NMR ($CDCl_3$) δ 6.0 (m, 2 H), 4.8 (s, 6 H), 2.8 (m, 4 H). Anal. Calcd for $C_{12}H_{12}O_7$: C, 53.73; H, 4.47. Found: C, 53.98; H, 4.18.

Copolymer of BCMA and Styrene. Equimolar amounts (1 mmol) of BCMA and styrene were dissolved in 2 mL of acetonitrile with 0.02 g of AIBN. The system was degassed by the freeze–thaw procedure and heated to 80 °C for 18 h. The polymer was pre-

---

(6) Hall, H. K. Jr.; Rasoul, H. A. A.; Gillard, M.; Abdelkader, M.; Nogues, P.; Sentman, R. C. *Tetrahedron Lett.* **1982**, 603.

(7) Rasoul, H. A. A.; Hall, H. K., Jr. *J. Org. Chem.* **1982**, *47*, 2080.

(8) Hall, H. K., Jr.; Daly, R. C. *Macromolecules* **1975**, *8*, 22, 959.

(9) Corson, B. B; Benson, W. L. "Organic Syntheses"; Wiley: New York, 1943; Collect. Vol. II, 273.

cipitated in ether, redissolved in chloroform, and reprecipitated in ether; yield 47%. (Evaporation of the first ether fraction yielded 33% of pyran.) Anal. Calcd for $C_{16}H_{14}O_7$: C, 60.38; H, 4.43. Found: C, 59.56; H, 4.45.

Acknowledgment. We thank the National Science Foundation, Grant No. DMR-81-06018 and the U.S. Army Research Office, Grant DAAG-29-77-G-0231, for support of this work.

Registry No. 1, 82522-55-2; 2, 82522-57-4; 3, 82522-59-6; 4 82522-58-5; 5, 82522-60-9; 6, 82522-61-0; 7, 82522-62-1; 8a, 82522-63-2; 8b, 82522-64-3; tetramethyl ethylenetetracarboxylate, 1733-15-9; *p*-methoxystyrene, 637-69-4; divinylbenzene, 105-06-6; anethole, 104-46-1; diphenylethylene, 530-48-3; styrene, 100-42-5; isobutyl vinyl ether, 109-53-5; isoprene, 78-79-5; butadiene, 106-99-0; BCMA styrene polymer, 82522-56-3.

Diels–Alder Reaction of Some Trimethylsilyloxy 1,3-Dienes

J. Bélanger, N. L. Landry, J. R. J. Paré, and K. Jankowski*

Département de Chimie, Université de Moncton, Moncton, N.B., E1A 3E9, Canada

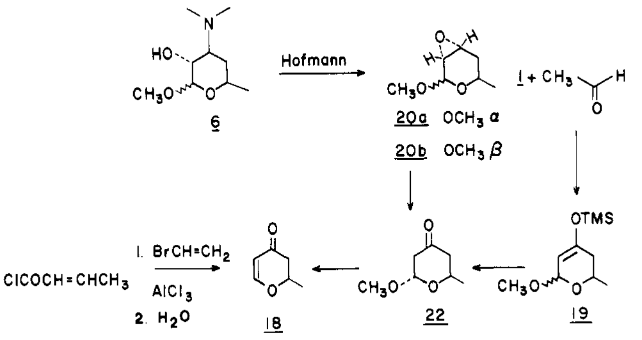
Received November 20, 1981

The thermal condensation of five trimethylsilyloxy 1,3-dienes with ethyl mesoxalate led to dihydropyran adducts. The trimethylsilyloxy radical was then removed by hydrolysis. The Danishefsky diene 1 was used to synthesize, with acetaldehyde, the 2,3-dihydro-2-methyl-4-pyrone (18), which was also obtained by two other independent ways.

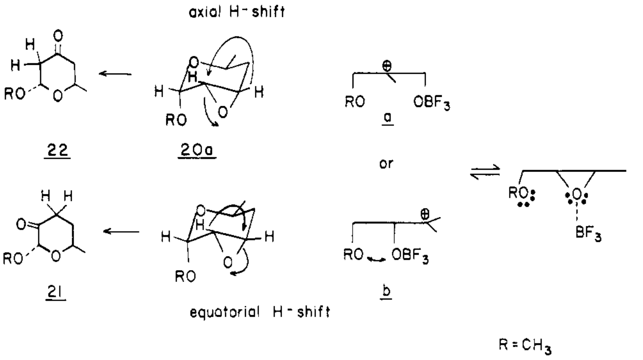
The trimethylsilyloxy 1,3-dienes are not very popular dienes used in the Diels–Alder condensation. Recently, however, Danishefsky[1,2] reported a synthesis of an interesting diene, 1-methoxy-3-[(trimethylsilyl)oxy]-1,3-butadiene (1), via the enolization of the corresponding enone and silylation, already available from Aldrich Chemical Co. The progress in the silylation of enolates of vinyl ketones,[3] on the other hand, has aroused an additional interest in this synthesis. For example, Yamamoto,[4] Danishefsky again,[5,6] and Anderson[7] are using the trimethylsilyloxy dienes instead of more conventional alkoxy dienes in their synthesis.

We have been interested in a total sugar synthesis via Diels–Alder condensation of carbonyl dienophiles, particularly ethyl mesoxalate, with dienes. This reaction leads to dihydropyran derivatives. Although acetaldehyde remains the simplest dienophile leading toward the 6-deoxy sugars via Diels–Alder condensation, most similar syntheses have been done with the more reactive carbonyl groups, such as glyoxalate or mesoxalate[6a–c] or, more recently, high-pressure reaction on nonconjugated aldehydes.[6d] We have made a condensation of the following dienes: 1-[(trimethylsilyl)oxy]-1,3-butadiene (2), 2-[(trimethylsilyl)oxy]-1,3-butadiene (3), 3-[(trimethylsilyl)oxy]-1,3-pentadiene (4), 2-[(trimethylsilyl)oxy]-1,3-cyclohexadiene (5) and Danishefsky's diene 1 with ethyl mesoxalate. The last diene has also been condensed to acetaldehyde in order to confirm the structure of methyl desosaminide (6) degradation product. The thermal condensation of 1 and acetaldehyde leads, in principle, to an interesting 6-deoxy sugar precursor. Finally, the condensation of 1-methoxy-1,3-cyclohexadiene 7 leads to a model cage compound, 8. The trimethylsilyloxy enol ethers have been successfully unblocked to the corresponding ketones via hydrolysis. These ketones could be used for preparation of an interesting variety of sugars via reductive or alkylating routes.

Scheme I



Scheme II



The trimethylsilyloxy 1,3-dienes react relatively well with ethyl mesoxalate in thermal reaction. However, the catalysis of this condensation via Lewis acids (e.g., aluminum chloride) does not work under various conditions

---

[1] After submission of this work we were informed by the Referee of our paper that he was completing a synthesis of compound 18 using a Diels–Alder BF_3-catalyzed reaction between the diene 1 and acetaldehyde (yield 17%, compare to 5% of thermal reaction described by us). There is apparently less of a complexation of the methoxy group of the diene 1 by a Lewis acid catalyst than expected.[5d,e]

(2) S. Danishefsky and T. Kitahara, *J. Am. Chem. Soc.*, **96**, 7807 (1974).

(3) (a) H. O. House, L. J. Czuba, M. Gall, and H. D. Olmstead, *J. Org. Chem.*, **34**, 2324 (1969); (b) M. W. Rathke and D. F. Sullivan, *Synth. Commun.*, **3**, 67 (1973).

(4) K. Yamamoto, S. Suzuki, and J. Tsuji, *Chem. Lett.*, 649 (1978).

(5) (a) S. Danishefsky, R. K. Singh, and R. B. Gammill, *J. Org. Chem.*, **43**, 379 (1978); see also ref 3 of this paper; (b) S. Danishefsky, M. P. Prisbylla, and S. Hiner, *J. Am. Chem. Soc.*, **100**, 2919 (1978); (c) S. Danishefsky, J. F. Kerwin, Jr., and S. Kobayashi, *J. Am. Chem. Soc.*, **104**, 358 (1982); (d) S. Danishefsky and J. F. Kerwin, Jr., *J. Org. Chem.*, in press; (e) *ibid.*, submitted; (f) S. Danishefsky, N. Kato, D. Askin, and J. F. Kerwin, Jr., *J. Am. Chem. Soc.*, in press.

(6) (a) O. A. Sharygina and S. M. Makin, *Khim. Farm. Zh.*, **3**, 17 (1969); (b) S. David and J. Eustache, *J. Chem. Soc., Perkin Trans. 1*, 2230 (1979); (c) A. Konowal, J. Jurczak, and A. Zamojski, *Rocz. Chem.*, **42**, 2045 (1968); (d) M. Chmielewski and J. Jurczak, *J. Org. Chem.*, **46**, 2230 (1981).

(7) D. R. Anderson and T. H. Koch, *J. Org. Chem.*, **43**, 2726 (1978).