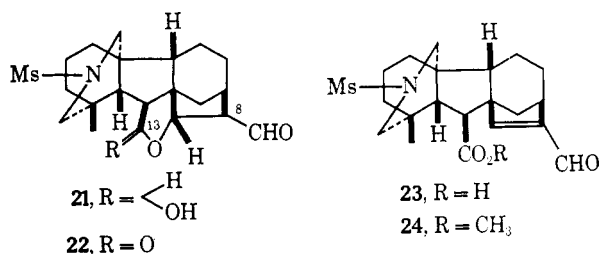6, mp 236–238°. The Wittig reaction of the acetate **8** followed by alkaline hydrolysis gave the olefin **9**, mp 198–199.5° (60% yield), which on oxidation (CrO₃–H₂SO₄ in acetone), followed by dehydration (SOCl₂ in methylene chloride and pyridine, −73°, 2 min) was converted to the conjugated enone **11**, mp 212–213° (83% from **9**), *via* the ketol **10**, mp 208–210°. Hydrocyanation of **11** with diethylaluminum cyanide[6] in methylene chloride–benzene (5:1) gave exclusively the *cis*-cyano ketone **12**, mp 214–215°, in 87% yield. The dipole moment of **12** supports the assigned 4β,9aβ configuration with ring C chair conformation (**12**; calcd, 4.24 D; found, 3.8 D). Reduction of **12** with aluminum isopropoxide gave a 5:1 mixture of the epimeric alcohols **13** and **14**. Acid treatment (TsOH in benzene) converted the *cis*-hydroxy nitrile **14** into a basic iminolactone, mp 188–190°, the major *trans* isomer **13**, mp 161–162° (71%), remaining unchanged and thus being readily separated. Compound **13** was transformed into the angular formyl derivative **15**, mp 150–154° (81%), by the sequence of reactions: reduction (*i*-Bu₂AlH), hydrolysis (NaOAc–HOAc in aqueous THF), and tetrahydropyranylation of the 7-hydroxyl. Formylolefination[7] of **15** with sodium diethyl β-(cyclohexylamino)vinylphosphonate followed by acid hydrolysis gave the *trans*-α,β-unsaturated aldehyde **16** (87%), mp 191–194°. For selective ozonization, compound **16**, after tosylation (**17**), was converted (Ac₂O and ZnCl₂) into the diacetoxy tosylate **18** (79%), mp 118–126°. This compound was now ozonized and reduced (Zn–HOAc) to give the desired aldehyde **19**, which without purification was subjected to a unique cyclization method devised particularly for construction of the B–C–D ring system of gibbane with requisite functionalities. Thus, the crude **19** was treated with 3 equiv of potassium hydroxide (in dry MeOH–THF, −8°, 5 min) giving the intermediate **20**, which on treatment with 2 equiv of pyrrolidine in methanol–N-methylpyrrolidone followed by hydrolysis with 50% acetic acid gave a mixture of hexacyclic hemiacetals **21** (epi-
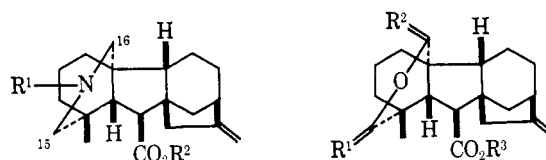

25, R¹ = Ms; R² = H
26, R¹ = R² = H(HCl salt)
27, R¹ = COCF₃; R² = H
28, R¹ = COCF₃; R² = CH₃
29, R¹ = H; R² = CH₃

30, R¹ = $\langle$ $^{OH}_{H}$; R² = H₂; R³ = CH₃
31, R¹ = H₂; R² = $\langle$ $^{OH}_{H}$; R³ = CH₃
32, R¹ = H₂; R² = O; R³ = CH₃
33, R¹ = H₂; R² = O; R³ = H

yield from **16** through nine steps), mp 163–164°, construction of the A–B–C–D ring parts thus being completed. Reduction (Li in liquid NH₃) of **25** gave the amino acid isolated as its hydrochloride **26** (56%), mp >300°. Attempted selective methylation of the carboxylic function in **26** with diazomethane failed and, therefore, the secondary amino group had to be first reprotected by treating **26** with trifluoroacetic anhydride giving **27**, which was then methylated (**28**) and hydrolyzed selectively to the ester **29** (reflux with 3 *N* K₂CO₃ in methanol, 1.5 hr). Dehydrogenation of the secondary amine **29** with lead tetraacetate yielded a mixture of azomethine isomers [Δ$^{15(N)}$ and Δ$^{(N)16}$ in **29**], which was converted into the hemiacetals **30** and **31** according to the method developed by ApSimon, *et al.*[9] The crude mixture of the hemiacetals was oxidized with the Collins reagent[8] to a mixture of lactones, which was separated by preparative tlc affording *dl*-gibberellin A₁₅ methyl ester **2**, mp 168–170°, *m/e* 344, and the less polar isomeric lactone **32**, mp 114–116°, *m/e* 344, each in *ca.* 5% overall yield from **27** (through five steps). Demethylation of **2** and **32** was effected without double bond migration by treatment with lithium iodide in refluxing collidine[10] in the presence of triphenylphosphine[11] giving *dl*-gibberellin A₁₅, **1** (over 40% yield), mp 236–237°, *m/e* 330, and its lactone isomer **33** (over 32% yield), mp 197–198°, *m/e* 330. The synthetic materials **1** and **2** have been rigorously proved to be the racemic forms of gibberellin A₁₅ and its methyl ester, respectively, by identity of their ir (in CHCl₃) and mass spectra, and also by their chromatographic behavior (tlc and glc) relative to that of authentic specimens.[12]

(9) J. W. ApSimon, O. E. Edwards, and R. Howe, *Can. J. Chem.*, 40, 630 (1962).

(10) F. Elsinger, J. Schreiber, and A. Eschenmoser, *Helv. Chim. Acta*, 43, 113 (1960).

(11) Undesirable migration of the double bond from *exo* to *endo* can be prevented effectively by addition of triphenylphosphine.

(12) The authors are very grateful to Professor J. R. Hanson for kindly providing us with the authentic sample of gibberellin A₁₅.

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21, R = $\langle$ $^{H}_{OH}$
22, R = O

23, R = H
24, R = CH₃

meric both at C₈ and C₁₃). This mixture was oxidized selectively with the Collins reagent[8] to a mixture of the formyl lactones **22** (epimeric at C₈). Ring opening of **22** with base (aqueous K₂CO₃) eliminates C₈ asymmetry giving the crystalline pentacyclic carboxylic acid **23** [the methyl ester **24**, mp 184–186°, λ$_{max}^{EtOH}$ 253.5 mμ (ε 13,050)]. The Wolff–Kishner reduction of **23** yielded the *exo*-methylene carboxylic acid **25** (30% overall

show that the 9aβ-hydroxyl is hydrogen bonded with the 7β-acetyl in **8** and with the vinyl in **10**; (ii) facile β-lactone formation between the 9aβ-hydroxyl and the 10β-formyl group was observed on oxidation of **7** with the Collins reagent (J. C. Collins, W. W. Hess, and F. J. Frank, *Tetrahedron Lett.*, 3363 (1968)).

(6) (a) W. Nagata, M. Yoshioka, and S. Hirai, *Tetrahedron Lett.*, 461 (1962); (b) W. Nagata and M. Yoshioka, *ibid.*, 1913 (1966).

(7) W. Nagata and Y. Hayase, *ibid.*, 4359 (1968); *J. Chem. Soc.*, 1400 (1969).

(8) See Collins, *et al.*, ref 5b.

Free-Radical Rearrangement of Enol Sulfonates

Sir:

Enol esters of sulfonic acids, which are readily available by a recently published synthesis,[1] are com-

paratively stable under heterolytic reaction conditions like solvolysis or hydrolysis. We have observed, however, that these compounds readily undergo homolysis and a subsequent free-radical rearrangement.

When *trans*-stilbenyl tosylate 1a[1a] [mp 134–135°; uv max (EtOH), 226, 285 nm (ε 22,000, 21,000); nmr
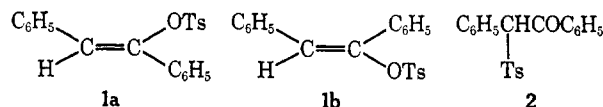
(CDCl$_3$) δ 6.50 (s, 1, CH=C)] is heated at 100° for 48 hr or irradiated with a tungsten-filament lamp at room temperature for 24 hr, both in evacuated ampoules and in acetonitrile, it is converted to a mixture of the β-ketosulfone 2 [mp 153–154°; uv max (CH$_3$CN) 233, 240 nm (ε 18,500, 14,000); nmr (CDCl$_3$) δ 6.17 (s, 1, COCH)] (in 7 and 37%, respectively) and the cis isomer 1b [mp 91–92°; uv max (EtOH) 225, 272 nm (ε 25,000, 11,000); nmr (CDCl$_3$) δ 6.60 (s, 1, CH=C)] (in 5 and 7%, respectively). However, after longer reaction times, 144 hr at 100° or 76 hr irradiation, only the sulfone 2 is obtained in ca. 80% yield. Traces of hydroquinone completely inhibit the thermal reaction and slow down the photochemical one.[2] On the other hand addition of traces of benzoyl peroxide considerably enhanced the rate of the thermal reaction; already after 1.5 hr at 100° both the sulfone 2 and the cis isomer 1b are formed in 17 and 7% yield, and after 24 hr the yield of 2 increases to 87%.

When the cis isomer 1b is subjected to the same reaction conditions smaller yields of the sulfone 2[3] are obtained accompanied by the trans isomer 1a; e.g., heating at 100° for 144 hr (under which condition the trans isomer 1a yields the sulfone 2 only) gave 33% of the sulfone 2 and 57% of the trans isomer 1a. Similarly after 76 hr irradiation of 1b, a mixture of 2 and 1a in 25 and 65% yield, respectively, is obtained. In this case, too, hydroquinone suppresses and benzoyl peroxide enhances the reaction rates.

These results indicate that both the 1,3 rearrangement of the sulfone group and the cis–trans isomerization are free-radical chain reactions,[4,5] which can be repre-

Scheme I
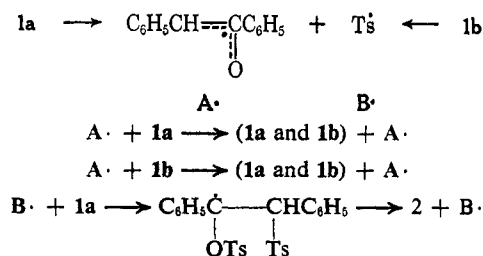
sented by Scheme I. Accordingly, both the cis- and the trans-enol tosylates 1a and 1b can transfer the tosyl group to the enol radical A·, but only the trans isomer 1a is susceptible to attack by the tosyl radical B·.

A number of other aliphatic and aromatic enol tosylates were likewise subjected to the rearrangement conditions. The experimental results are listed in Table I. Those enol tosylates having the methylene

Table I

Starting material	Product	% yield[a] after 3 hr at 100°[b]	140°[c]
(structure)[d,e]	C$_6$H$_5$COCH$_2$Ts[f]	95	95
(structure)[g]	MeCOCH$_2$Ts[f]	95	95
(structure)[d,h]	EtCOCHMe(Ts)[i]	40	90
(structure)[d,j]	(structure)[k]	0	40
(structure)[l]	(structure)[m]	0	60

[a] As determined from the nmr spectrum of the total product. [b] In the presence of benzoyl peroxide. [c] In the presence of t-butyl peroxide. [d] Reference 1a. [e] Mp 49–50°; uv max (C$_6$H$_{12}$) 227, 245 nm (ε 20,000, 15,000); nmr (CDCl$_3$) δ 5.40 (d, 1, J = 3Hz, C=CH_2), 5.09 (d, 1, J = 3 Hz, C=CH_2). [f] L. Field, J. E. Lawson, and J. W. McFarland, J. Amer. Chem. Soc., 78, 4389 (1956). [g] Uv max (EtOH) 227, 265 nm (ε 13,000, 600); nmr (CDCl$_3$) δ 4.67 (s, 2, C=CH_2), 1.87 (s, 3, CH_3). [h] Oil; nmr (CDCl$_3$) δ 5.10 (q, 1, J = 7 Hz, C=CH), 2.27 (q, 2, J = 7.5 Hz, CH$_3$CH_2), 1.38 (d, 3, J = 7 Hz, CH_3CH$_2$), 0.99 (t, 3, J = 7.5 Hz, CH_3CH=C). [i] Mp 71–72°; uv max (EtOH) 227, 265 nm (ε 13,500, 800); nmr (CDCl$_3$) δ 4.18 (q, 1, J = 7 Hz, COCHCH$_3$), 2.37 (q, 2, J = 7 Hz, CH$_3$CH_2), 1.38 (d, 3, J = 7 Hz, CH_3CH), 1.06 (t, 3, J = 7 Hz, CH$_2$CH_3). [j] Oil; nmr (CDCl$_3$) δ 5.37 (m, 1, C=CH). [k] M. S. Newman, B. J. Magerlein, and W. B. Wheatley, J. Amer. Chem. Soc., 68, 2112 (1946). [l] Mp 59–60°; uv max (EtOH) 226 nm (ε 15,500); nmr (CDCl$_3$) δ (5.14 (t, 1, J = 7.5 Hz, C=CH). [m] Mp 147–148°; uv max (EtOH) 228, 262 (ε 13,000, 700); nmr δ 4.29 (m, 1, CHCO).

(1) (a) N. Frydman, R. Bixon, M. Sprecher, and Y. Mazur, Chem. Commun., 1044 (1969); (b) P. E. Peterson and J. M. Indelicato, J. Amer. Chem. Soc., 90, 6515 (1968); (c) S. A. Sherrod and R. G. Bergman, ibid., 91, 2115 (1969); (d) W. M. Jones and D. D. Maness, ibid., 91, 4314 (1969); (e) P. J. Stang and R. Summerville, ibid., 91, 4600 (1969); (f) G. Capozzi, G. Melloni, G. Modena, and M. Piscitelli, Tetrahedron Lett., 4039 (1968).

(2) It is assumed that hydroquinone decomposes after longer irradiation periods.

(3) Satisfactory analyses and ir, uv, nmr, and mass spectra were obtained for all new compounds reported.

(4) Migrations of a sulfonyl group from the N to the C atoms in N-alkyl-N-vinylsulfonamides under the influence of γ radiation or peroxides are postulated to involve free-radical chain reactions: F. W. Stacey, J. C. Sauer, and B. C. McKusick, J. Amer. Chem. Soc., 81, 987 (1959). Thermal rearrangements of α-alkoxystyrenes to α-alkylacetophenones are also suggested to proceed by the same mechanism, although they are not suppressed by radical inhibitors: K. B. Wiberg, T. M. Shryne, and R. R. Kintner, ibid., 79, 3160 (1957), and previous publications.

(5) Rearrangements of a sulfonyl group from O to C atoms were observed on heating in the presence of aluminum chloride or on irradiation with a mercury arc of phenyl and naphthyl sulfonates: V. Balasubramanian and V. Baliah, J. Indian Chem. Soc., 36, 391 (1959); V. Baliah and M. Uma, Rec. Trav. Chim. Pays-Bas, 80, 139 (1961); J. L. Stratenus and E. Havinga, ibid., 85, 434 (1966). Rearrangement of the sulfonyl group from C to O atoms was observed when some β-keto sulfones were irradiated with mercury arc yielding i.a. enol sulfonates: C. L. McIntosh, P. de Mayo, and R. W. Yip, Tetrahedron Lett., 37 (1967).

group gave the β-ketosulfones even under milder conditions; e.g., α-tosyloxystyrene, when left in ether containing traces of ether peroxides, rearranges quantitatively to the α-tosylacetophenone. On the other hand, the rearrangement of cyclic enol tosylates requires higher temperatures; the β-ketosulfones are obtained only after heating at 140° in the presence of catalytic amounts of t-butyl peroxide. The enol tosylates derived from diphenylacetaldehyde and cyclohexylaldehyde which do not possess β hydrogens are stable even under the latter conditions.

The rearrangements could also be carried out in other solvents, both polar and nonpolar, like methanol, 2-propanol, benzene, or carbon tetrachloride. However in bromotrichloromethane the enol tosylates gave trichloromethyl ketones[6] or their decomposition products, the dichloromethylene ketones. Thus, 1a and 3 were converted in this solvent to 4[3] [oil; uv max

$$C_6H_5CHCOC_6H_5 \qquad MeCOCH=C(Cl)_2$$
$$\underset{CCl_3}{|}$$

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4   5

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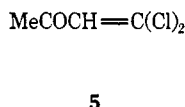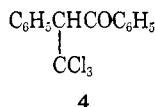
(EtOH) 252 nm (14,000); nmr (CDCl₃) δ 5.74 (s, 1, COCH)] (30%) and 5[6b] (24%), respectively, after heating for 3 hr at 100° with benzoyl peroxide.

When an acetonitrile solution of the dienol tosylate 6a[7] [mp 138–139°; uv max (EtOH) 226 nm (ε 24,000); nmr (CDCl₃) δ 5.67 (s, 1, H at C-4), 5.38 (m, 1, H at C-6), 0.86 (s, 3, H at C-19)] was heated in an evacuated
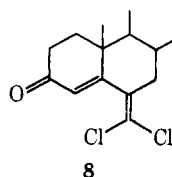

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6   a, R = CH₃C₆H₄   7
        b, R = CH₃

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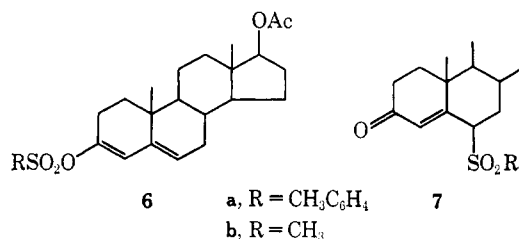
tube at 100° for 25 hr, it rearranged in 90% yield to the 6β-tosyl derivative 7a [mp 185–186°; uv max 227 nm (ε 27,000); nmr (CDCl₃) δ 5.56 (s, 1, H at C-4), 3.84 (d, 1, $J = 7.5$ Hz, H at C-6), 1.49 (s, 3, H at C-19)].

This 1,5-rearrangement also appears to proceed by a free-radical mechanism, since its rate was enhanced by the addition of benzoyl peroxide (90% yield after 2.5 hr) and inhibited by traces of hydroquinone.

Heating 6a in ether solution containing ether peroxides also results in 7a. The same rearrangement also took place on irradiation of 6a with a filament lamp (70% after 21 hr) or stronger light sources, such as Westinghouse sun lamps (60% after 1 hr) and Philips germicidal lamps (40% after 2.5 hr), the two latter emitting at 300–400 nm and 254 nm, respectively.

In this case too, other solvents did not interfere with the rearrangement, except trichlorobromomethane, which reacted with the dienol tosylate 6a when heated at 100° yielding ca. 85% of the dichloromethylene derivative 8,[6c,8] and only 10% of the 6β-sulfone 7a.

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8

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The dienol mesylate 6b[9] [mp 138–139°; uv max (C₆H₁₂)

241 nm (ε 23,000); nmr (CDCl₃) δ 5.97 (s, 1, H at C-4), 5.53 (m, 1, H at C-6), 0.98 (s, 3, H at C-19)] similarly but somewhat less readily gave the 6β-mesyl derivative 7b [mp 241–242°; uv max (EtOH) 243 nm (ε 12,000); nmr (CDCl₃) δ 6.00 (s, 1, H at C-4), 3.95 (d, 1, $J = 7.5$ Hz, H at C-6), 1.39 (s, 3, H at C-19)].

Heating in the presence of benzoyl peroxide at 100° for 5.5 hr gave 90% of 7b, but in the absence of peroxide or upon irradiation with a filament lamp the starting mesylate was recovered unchanged.

The two main factors influencing the free-radical rearrangement of enol sulfonates are, thus, the relative stabilities of the free radicals obtained by homolysis of the O–S bonds and the stereochemical accessibility of the β-carbon atom of the enol sulfonates to an attack by the sulfonyl radical.

(10) Taken in part from the Ph.D. Thesis of Norbert Frydman to be submitted to the Feinberg Graduate School of the Weizmann Institute of Science.

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Singlet Oxygen Sources in Ozone Chemistry. Decomposition of Oxygen-Rich Intermediates

Sir:

We have recently shown that decomposition of the triphenyl phosphite–ozone adduct[1] provides a convenient method for accomplishing chemical oxygenations involving singlet oxygen.[2–5] This result suggested that a number of known reactions of ozone with such substrates as sulfides, sulfoxides, amines, and phosphines are also potential sources of singlet oxygen.

We now wish to report that ozonization of even relatively unreactive substrates including hydrocarbons, ethers, and alcohols, where oxygen-rich intermediates, possibly hydrotrioxides, are formed, can also be expected to lead to sources of singlet oxygen. Evidence is presented that this prediction is realized in the cases of isopropyl alcohol and isopropyl ether.

Hydrotrioxides have been postulated as intermediates or unstable products in the ozonization of such diverse substrates as hydrocarbons,[6–8] silanes,[9] ethers,[10,11] alcohols,[7] amines,[12,13] aldehydes,[14] and diazo compounds.[15] Evidence has also been presented confirming

(1) Q. E. Thompson, *J. Amer. Chem. Soc.*, 83, 846 (1961).
(2) R. W. Murray and M. L. Kaplan, *ibid.*, 90, 537 (1968).
(3) R. W. Murray and M. L. Kaplan, *ibid.*, 90, 4161 (1968).
(4) E. Wasserman, R. W. Murray, M. L. Kaplan, and W. A. Yager, *ibid.*, 90, 4160 (1968).
(5) R. W. Murray and M. L. Kaplan, *ibid.*, 91, 5358 (1969).
(6) G. A. Hamilton, B. S. Ribner, and T. M. Hellman, "Oxidation of Organic Compounds," Vol. III, Advances in Chemistry Series, No. 77, American Chemical Society, Washington, D.C., p 15.
(7) M. C. Whiting, A. J. N. Bolt, and J. H. Parish, "Oxidation of Organic Compounds," Vol. III, Advances in Chemistry Series, No. 77, American Chemical Society, Washington, D.C., p 4.
(8) J. E. Batterbee and P. S. Bailey, *J. Org. Chem.*, 32, 3899 (1967).
(9) J. D. Austin and L. Spialter, "Oxidation of Organic Compounds," Vol. III, Advances in Chemistry Series, No. 77, American Chemical Society, Washington, D.C., p 26.
(10) R. E. Erickson, R. T. Hansen, and J. Harkins, *J. Amer. Chem. Soc.*, 90, 6777 (1968).
(11) C. C. Price and A. L. Tumolo, *ibid.*, 86, 4691 (1964).
(12) P. S. Bailey, D. A. Mitchard, and A.-I. Y. Khashab, *J. Org. Chem.*, 33, 2675 (1968).
(13) P. S. Bailey and J. E. Keller, *ibid.*, 33, 2680 (1968).
(14) H. M. White and P. S. Bailey, *ibid.*, 30, 3037 (1965).
(15) P. S. Bailey, A. M. Reader, P. Kolsaker, H. M. White, and J. C. Barborak, *ibid.*, 30, 3042 (1965).

(6) Analogous free-radical addition reactions of trichlorobromomethane to enol acetates and enol ethers are well known; cf. (a) C. Walling, "Free Radicals in Solutions," John Wiley & Sons, Inc., New York, N. Y., 1957, pp 247–272; (b) S. Searles, R. A. Sanchez, R. L. Soulen, and D. G. Kundiger, *J. Org. Chem.*, 32, 2655 (1967); (c) S. Liisberg, W. O. Godtfredsen, and S. Vangedal, *Tetrahedron*, 9, 149 (1960).
(7) Prepared in 80% yield from testosterone acetate and tosyl anhydride in dimethylformamide; cf. ref 1a.
(8) J. Libman, M. Sprecher, and Y. Mazur, *J. Amer. Chem. Soc.*, 91, 2062 (1969).
(9) Prepared in 60% yield from testosterone acetate and mesyl anhydride in dimethylformamide.