TABLE I

C^{11} LABELED PRODUCTS OF REACTION OF ATOMIC C^{11} WITH ETHYLENE YIELDS AS % OF TOTAL GASEOUS ACTIVITY

Each yield represents the average of at least three runs. Errors indicated are a measure of reproducibility. C_4 or lighter hydrocarbons not mentioned <1% (or <5% for moderated runs.)

	Composition of reacting gas (Total press. 1 atm)		
C^{11} Product	C_2H_4	C_2H_4 (98.5%) O_2 (1.5%)	C_2H_4 (4.5%) O_2 (0.2%) Ne (95.3%)
Carbon monoxide[a]	0.9 ± 0.3	9.8 ± 2.0	24 ± 5
Ethylene	1.5 ± 0.5	2.0 ± 1.0	...
Acetylene	38.0 ± 3.5	36.6 ± 1.5	31 ± 5
Cyclopropane	3.2 ± 0.7	<1	...
Propylene	3.7 ± 0.6	4.7 ± 0.5[b]	...
Allene	18.0 ± 2.0	15.3 ± 0.8	17 ± 4
Methylacetylene	4.0 ± 1.5	3.7 ± 1.0	...
Vinylacetylene	11.2 ± 1.5	10.6 ± 3.5	...

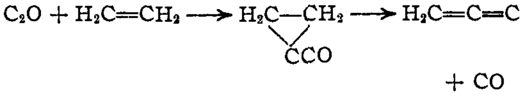
[a] These values may include a small yield of methane. [b] Probably includes an indeterminate amount of CO_2

manner[5] to form cyclopropane-C^{11}. The vinylacetylene found presumably results from the secondary reaction of a two carbon fragment, possibly CC^{11}, formed by decomposition of an excited complex resulting from C–H or C=C insertion.

Column III indicates that the major products obtained from atomic carbon thermalized by neon moderator, are qualitatively similar to those from high kinetic energy carbon. Furthermore, thermalization does not significantly change the relative yield of allene to acetylene. This has been verified by a detailed analysis using the kinetic theory of hot atom reactions,[6] on data from ethylene runs containing various fractions of neon, helium or xenon moderator. Apparently the chemical potential and reactivity of thermal atomic carbon are so high that the addition of kinetic energy makes little, if any, difference to the modes by which it can become chemically combined. In this respect it differs markedly from atomic hydrogen.[6,7] It should be noted, however, that the reaction probability of carbon with ethylene relative to that with oxygen, appears lower at thermal energies.

In a recent communication Bayes[8] reported that the photolysis of C_3O_2 at 2537 Å., in the presence of ethylene, yields allene and carbon monoxide. It was suggested that the C_3O_2 may be dissociated into CO and atomic carbon which reacted to form the allene. This hypothesis was inconsistent with our results that reaction of atomic carbon with ethylene yields acetylene and other major products, as well as allene. Furthermore, we find that addition of small amounts of oxygen increases the CO yield, whereas Bayes' system was unaffected by 18% O_2. Bayes suggested two possible reasons for the discrepancy[8]: (1) that the reactions observed by us were characteristic of hot, but not of thermal, carbon atoms; (2) that the reactive species produced in the photolysis of C_3O_2 was actually C_2O instead of C.

With factor (1) being excluded by our results with neon moderator, it can be concluded that C_2O is the active species produced by photolysis of C_3O_2.[9] Apparently C_2O adds to double bond in a manner similar to atomic carbon and C_2H^5,



(III)

However, atomic carbon is a more energetic and less specific reagent undergoing a wider range of reactions and yielding more products.

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(5) W. von E. Doering, *et al.*, *J. Am. Chem. Soc.*, **78**, 3224 (1956); H. M. Frey and G. B. Kistiakowsky, *J. Am. Chem. Soc.*, **79**, 6373 (1957).

(6) P. J. Estrup and R. Wolfgang, *J. Am. Chem. Soc.*, **82**, 2665 (1960).

(7) D. Urch and R. Wolfgang, *J. Am. Chem. Soc.*, **83**, 2982 (1961).

(8) K. Bayes, *J. Am. Chem. Soc.*, **83**, 3712 (1961).

(9) The production of C_2O rather than C by photolysis of C_3O_2 with 2537 Å. radiation also seems more likely on the basis of energy considerations. The heat of formation of C_3O_2 can be estimated, using bond strengths determined from bond length and force constant data [see for example A. D. Walsh, *Trans. Faraday Soc.*, **43**, 60 (1947), and L. H. Long and A. D. Walsh, *ibid.*, **43**, 342 (1947)], as not less than about 690 kcal. On this basis the reaction $C_3O_2 \rightarrow C + 2CO$ is endothermic by about 175 kcal. or more, even if the C atom is produced in the triplet ground state in violation of the spin conservation rule. The 2537 Å. radiation supplies only 112 kcal.

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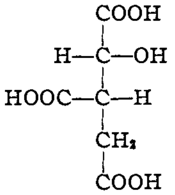
RECEIVED OCTOBER 28, 1961

THE ABSOLUTE CONFIGURATION OF NATURALLY OCCURRING ISOCITRIC ACID[1]

Sir:

In a recent communication from this laboratory[2] a structure determination was reported of the isomorphous monopotassium and monorubidium salts of the lactone of *d*-isocitric acid prepared for us from the Crassulacean plant *Bryophyllum calycinum* by Dr. H. B. Vickery and Dr. D. G. Wilson[3] of the Connecticut Agricultural Experiment Station. From this work we deduced that the configuration of the acid was either D_sL_g isocitric acid (I) or its optical enantiomorph L_sD_g isocitric acid. This



I

result was in complete agreement with the work of Gawron[4] and his co-workers who had come to the same conclusion both on physical, chemical and synthetic grounds. Because Greenstein and his

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(1) Work supported by a grant (A2884) from the National Institutes of Health, U. S. Public Health Service. A preliminary account of this work was presented at the Boulder, Colo., meeting of the American Crystallographic Association, August, 1961.

(2) J. P. Glusker, A. L. Patterson, W. E. Love and M. L. Dornberg, *J. Am. Chem. Soc.*, **80**, 4426 (1958).

(3) H. B. Vickery and D. G. Wilson, *J. Biol. Chem.*, **233**, 14 (1958).

(4) (a) O. Gawron and A. J. Glaid, III, *J. Am. Chem. Soc.*, **77**, 6638 (1955); (b) O. Gawron, A. J. Glaid, III, A. LoMonte, and S. Gary, *ibid.*, **80**, 5856 (1958).

co-workers[5] had ascribed the configuration $\mathrm{L_s}$ to the α-carbon, both Gawron's group and the report from this laboratory gave the configuration of isocitric acid as $\mathrm{L_sD_g}$, the optical enantiomorph of I. However, a series of papers by Katsura and Kaneko and their co-workers[6] have reported independent determinations by classical methods of the configurations of the α and β carbons of *d*-isocitric acid. They ascribe the configuration I to isocitric acid in contradiction to Greenstein's result, but in agreement with the *threo* configuration required by Gawron's work and our own. Although this latter fact was a strong indication that the Katsura absolute configuration was correct, it seemed worth while for us to obtain an independent check on this very important result by X-ray dispersion techniques as we had already planned.[2]

TABLE I

SOME DISPERSION DATA FOR POTASSIUM AND RUBIDIUM MONO-SALTS OF ISOCITRIC LACTONE

Values of $100\,(|F_+|^2 - |F_-|^2)/{}^1/_2(|F_+|^2 + |F_-|^2)$

	Mo Kα-Rb salt		Cu Kα-K salt		Cr Kα-K salt	
(*hkl*)	Calcd.	Obsd.	Calcd.	Obsd.	Calcd.	Obsd.
(111)	−38.0	−39.3	−26.5	−28.9	−50.2	−54.0
(282)	+27.8	+29.9	+45.1	+41.5	+82.9	+78.8
(331)	−15.3	−17.7	−16.2	−13.5	−31.1	−27.9
(241)	+15.5	+11.9	+12.5	+ 8.0	+23.7	+18.1
(243)	−22.0	−19.4	−25.6	−21.1	−48.8	−45.4
(212)	−18.0	−15.5	−15.8	−13.2	−30.2	−23.3
(141)	− 8.1	− 8.6	−14.6	−14.5	−27.8	−29.0
	$\Delta f' = -0.9^a$		$\Delta f' = +0.2^b$		$\Delta f' = +0.1^b$	
	$\Delta f'' = +3.2^a$		$\Delta f'' = +1.2^b$		$\Delta f'' = +2.3^b$	

[a] Ref. 10. [b] Extrapolated from ref. 10.

We have therefore made an absolute determination of the two isomorphous lactone salts by the method of Bijvoet[7] and find that the Crassulacean *d*-isocitric acid has the configuration I in agreement with Katsura. Thus this acid can be described as $\mathrm{D_sL_g}$ isocitric acid, as *threo*-$\mathrm{D_s}$-isocitric acid,[8] or in the Cahn–Ingold–Prelog notation[9] as (1R:2S) - 1 - hydroxy - 1,2,3 - propanetricarboxylic acid.

Diffraction measurements were made on two different crystals of the rubidium salt using Mo Kα radiation and on two different crystals of the potassium salt using Cr Kα radiation. Measurements also were made on one of the latter with Cu Kα radiation. In the table, results of typical experiments are shown. Observed and calculated values of the quantity $100(|F_+|^2 - |F_-|^2)/{}^1/_2(|F_+|^2 + |F_-|^2)$ are shown for 21 of the 47 experiments carried out. In this expression $|F_+|$ corresponds to the reflection *hkl* and its space group equivalents $(h\bar{k}\bar{l}, \bar{h}k\bar{l}, \bar{h}\bar{k}l)$ while $|F_-|$ corresponds to $\bar{h}\bar{k}\bar{l}$ and its equivalents $(\bar{h}kl, h\bar{k}l, hk\bar{l})$. The table also includes the values of the dispersion constants $\Delta f'$ and $\Delta f''$ used in the structure factor calculations.[10] The atomic coördinates, which will be presented elsewhere, are available on request from the undersigned. In all experiments at least two equivalent reflections of each type were measured. In some experiments all four equivalent reflections were available. For example in the case of the reflection 412 (K:crystal #1:Cr Kα) the counts were: $|F^-|^2$ −7,780, 7,750, 7,540, 7,560: $|F_+|^2$ −11,140, 11,560, 11,190, 10,860. In no case was a dispersion effect observed which differed in sign from that calculated. Thus it is quite clear that the Katsura configuration on which our calculation was based is correct.

We are very much indebted to Dr. H. B. Vickery, not only for his provision of these and other crystals, but also for his continued interest in and discussion of this work.

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(6) (a) T. Kaneko, H. Katsura, H. Asano, and K. Wakabayashi, *Chem. and Ind.*, 1187 (1960); (b) T. Kaneko and H. Katsura, *ibid.*, 1188 (1960); (c) H. Katsura, *J. Chem. Soc. Japan*, **82** [1], 91 (1961); (d) H. Katsura, *ibid.*, **82** [1], 92 (1961); (e) H. Katsura, *ibid.*, **82**, [1], 98 (1961).

(7) J. M. Bijvoet, A. F. Peerdeman, and A. J. van Bommel, *Nature*, **168**, 271 (1951).

(8) *Cf.* H. B. Vickery, *Science*, in press.

(9) (a) R. S. Cahn and C. K. Ingold, *J. Chem. Soc.*, 612 (1951); (b) R. S. Cahn, C. K. Ingold and V. Prelog, *Experientia*, **12**, 81 (1956).

(10) C. H. Dauben and D. H. Templeton, *Acta Cryst.*, **8**, 841 (1955).

(11) American Cancer Society Post-Doctoral Research Fellow (PF-87).

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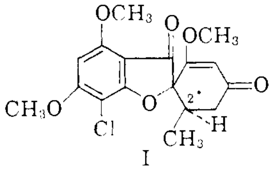
A STEREOSPECIFIC TOTAL SYNTHESIS OF GRISEOFULVIN

Sir:

The synthesis of the orally active antifungal antibiotic griseofulvin (I) presents interesting structural and stereochemical problems. These problems are well illustrated by one of the two previous syntheses[1,2] of this substance: both epimers at the 2′ carbon are obtained while the intermediacy of the β-diketone II (griseofulvic acid) leads to the two possible enol ethers with diazomethane.[1]



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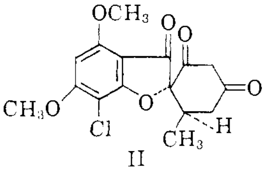

II

An interesting solution to these difficulties, based on a biogenetically likely pathway, has been recorded.[2]

We now report a one-step total synthesis of *dl*-griseofulvin which provides a model for the synthesis of poly-β-dicarbonyl compounds or their enol ethers.

Reaction of the known 7-chloro-4,6-dimethoxycoumaranone (III)[3] with methoxyethynylpropenyl ketone (IV), in the presence of potassium *tert*-

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(1) A. Brossi, M. Baumann, M. Gerecke and E. Kyburz, *Helv. chim. acta*, **43**, 2071 (1960).

(2) (a) A. C. Day, J. Nabney and A. J. Scott, *J. Chem. Soc.*, 4067 (1961). (b) See also C. H. Kuo, R. D. Hoffsommer, H. L. Slates, D. Taub and N. L. Wendler, *Chemistry and Industry*, 1627 (1960).

(3) J. MacMillan, T. P. C. Mulholland, A. W. Dawkins and G. Ward *ibid.*, 429 (1954).