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SYNTHESES AND PROPERTIES OF H-1,2,3-TRIAZOLES[a]

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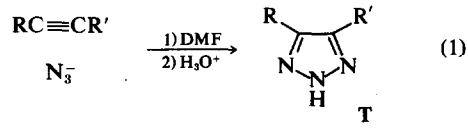
Abstract—About twenty new H-1,2,3-triazoles (T) were readily synthesized by nucleophilic attack of sodium azide on activated acetylenes in dimethylformamide. Typical activating groups were COR, COOR, $O_2NC_6H_4$, $PO(OC_2H_5)_2$, COT, and $(C_6H_5)_3P^+$. Propynyl 4-triazolyl ketone or phenylethynyl 4-triazolyl ketone may be converted to acylic adducts (triazolylketoenamines), biheteroaromatic systems (isoxazolytriazoles, pyrazolytriazoles), as well as to ditriazolyl ketones. Certain T properties were examined in detail. The apparent pK's for our group of *ca* 30 triazoles were in the range 4·95–9·45 in ethanol-water (v/v 1/1) at 25°. The Hammett correlation for five 4-aryl-T was $\log K_a = 0{\cdot}89\sigma^- - 9{\cdot}21$ and for seven 4-aryl-5-carbethoxy-T was $\log K_a = 1{\cdot}45\sigma - 6{\cdot}95$. The UV spectra of T are similar to those of other heteroaromatic and phenyl compounds; interesting analogies between triazolyl and phenyl, e.g., "ortho" crowding effects, appear to be indicated in the spectra of compounds related to biphenyl, stilbene and benzophenone. With regard to structure assignment on the basis of spectra, characteristic features of UV and IR spectra of the H-1,2,3-triazoles are discussed.

In 1964 a simple and convenient synthesis of H-1,2,3-triazoles (T) was reported.[1] Yet apart from one further paper,[2] it still seems generally unfamiliar. This route has given us access to a wide



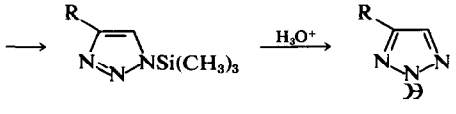
T (1)

variety of new T and made possible or stimulated a thorough investigation of many aspects of their chemistry. In related papers, we discuss a novel redox synthesis of T from alkenes,[3] orientation in the nucleophilic attacks of the anion (T^-) of T,[4] the properties of novel triazole ylids,[5a] and mass spectral fragmentation patterns of 1,2,3-triazoles.[5b] In this paper, we develop process 1 in depth as a major synthesis of T, and look carefully at the pK's and spectral properties of this important heterocyclic family.

Direct access routes to T appear to be limited to special combinations of reagents.[6–8] Several additions of hydrazoic acid to alkynes are known; where high pressure and heat are required, the method is not attractive.[9] The reaction of Pb(IV) acetate azide with phenylmethylsilylacetylene yielded several products, among them the expected T (45%).[10] The formation of 4-OH-5-$CONH_2$-T from azide ion and malonamide appears to be an isolated instance of the Dimroth reaction of active methylene compounds with organic azides.[11] Recently, we have catalogued a number of examples in which T results from the attacks of azide ion on alkenes containing electron-withdrawing groups, e.g., CN, $O_2NC_6H_4$, etc.[3] All of these syntheses lack the breadth of process 1.

We class as indirect those routes to T which go through N-substituted triazoles. The additions of silyl,[12] tosyl,[13a] tin,[13b] and acyl azides to alkynes,[8] or of acyl azides to certain phosphorus ylids[14] yield 1- or 3-substituted triazoles which readily yield T on hydrolysis. In general, N-alkyl or -aryl groups are not as easy to remove, but examples are known in which hydrogenolysis or hydrolysis have shorn these groups away to give T.[8,15] With regard to scope and utility, we find the trimethylsilyl azide synthesis complementary to the present one in that it works poorly with alkynes containing electron-withdrawing substituents and well with others. To fill out several of our series, we have used it here:

$RC{\equiv}CH + (CH_3)_3SiN_3$



(2)

R = 4-XC_6H_4, (X = H, CH_3O, CH_3, Cl)

Azide-acetylene synthesis of triazoles. The synthesis of triazoles by the addition of azide ion to activated alkynes in an aprotic solvent (DMF) was discovered about ten years ago.[1] While

[a]Taken from the Ph.D. thesis of Y. T., Illinois Institute of Technology, May 1972.

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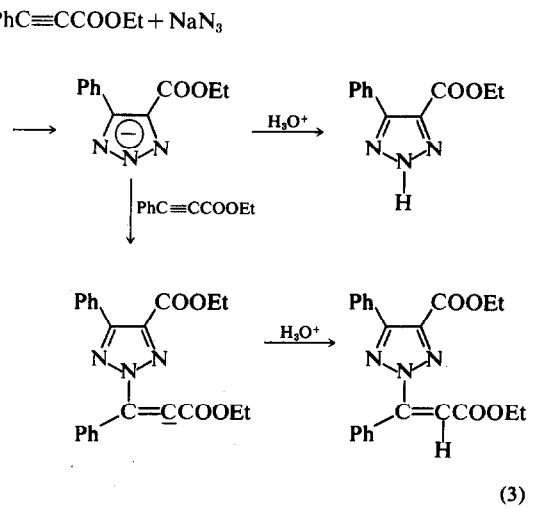
our work in this area was in progress, four more examples of this synthesis were published.[2] To illustrate its scope, we have collected all of the available examples of this method in Table 1.

Perhaps the most outstanding feature of process 1 is the pronounced effect of the alkyne substituents on the rate and often the yield of triazole. In DMF, process 1 for acetylene dicarboxylic ester (**ADE**) is complete (< 5 min) at −20° while for *p*-chlorophenylacetylene the process has hardly begun (1%) after 5 days at 153°. On the basis of our experience, it is possible to identify the electron-withdrawing groups, RCOO, RCO, $(C_6H_5)_3P^+$, $(C_2H_5O)_2PO$, and probably CN as activating. Judging by the yields of products, we find a drop in activation between *p*-nitro- and *p*-chlorophenyl groups. In fact, we have found that prolonged heating at reflux of sodium azide and tolan, perfluorotolan, or phenylacetylene in DMF do not give triazoles. Woerner and Reimlinger, however, did produce triazoles from acetylene, phenylacetylene and tolan, but not ethoxyacetylene, in DMSO as solvent (Table 1).[2] It seems probable that a detailed investigation will turn up one or more solvents in which syntheses of triazoles from other "unreactive" alkynes will become feasible. In what follows, we shall make or emphasize some points which may not be apparent from Table 1 or the Experimental.

Our normal synthetic procedure was to add the acetylene gradually onto a suspension of sodium azide. Fast addition or sudden mixing of the acetylene into the suspension gave rise to by-products, such as adducts, which are obtained by a successive reaction of the triazole anion with more acetylene (Eq. 3).[4] Such a coproduct was obtained in the reaction of ethyl phenylpropiolate with sodium azide in 13% yield, when both reactants were added at the same time at 60°. Therefore, if the purpose is to prepare H-1,2,3-triazole, an excess of sodium azide and rapid stirring of the reaction solution are desirable, since sodium azide is sparingly soluble in DMF. Finally, prolonged heating of the reaction mixture at elevated temperatures appears to give rise to a lower yield and higher contamination of the product.

Some of the "special" alkynes, e.g., ethynylphosphites or -phosphonium salts, derive from our interest in nucleophilic substitution at an acetylenic carbon.[16,17] Certain of these **T** syntheses could be performed in a single vessel, provided that an appropriate haloalkyne was available: haloalkynes are readily synthesized from acetylenes; the displacement of halide ion by phosphine[17] followed by azide addition leads to ylids, from which the phosphorus moiety can be removed by hydrolysis (Eq. 4). These constitute a new and interesting class of ylids whose chemistry is described elsewhere.[5]



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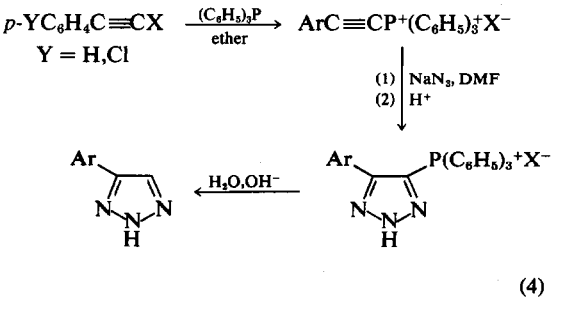
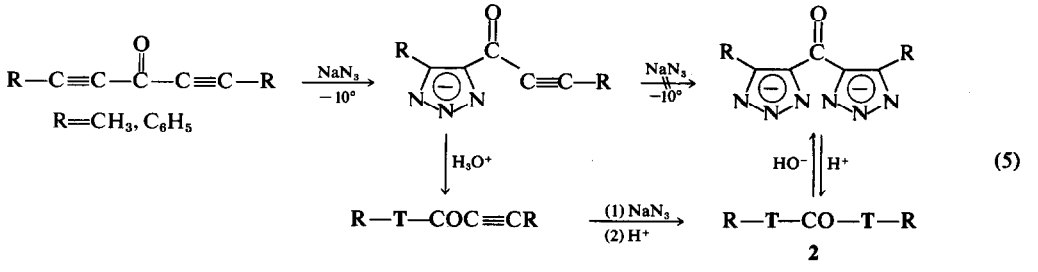


(4)

Diethynyl ketones are active substrates:[18] the addition of the first azide ion is complete in 10 min at −10°, under conditions where the second addition scarcely proceeds:



(5)

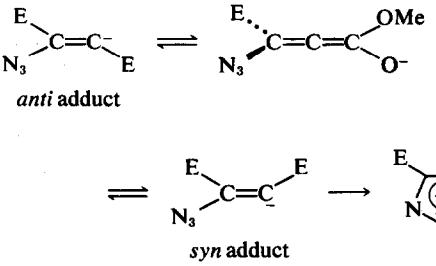
Table 1. H-1,2,3-Triazoles (4-R, 5-R′-C_2N_3H), preparation and physical constants[a]

T[a]	4-R[b]	5-R′[b]	Triazole Formula	Calcd, % C	Calcd, % H	Found, % C	Found, % H	Prep. Method (% yield)	Conditions Temp °C (Hr)	m.p. °C	pK[c]	M.W.[d] (obs.)	M.W. (calc.)	T λ_{max}^{EtOH} nm	T ϵ_{max} × 10^{-4}	T⁻ or T⁼ λ_{max}^{EtOH}	T⁻ or T⁼ ϵ_{max} × 10^{-4}
1a	H[e]	H						I(11)[e]	~105 (72)	liq.							
b	CHO	H	$C_3H_3N_3$					I(–)	90 (2)	137–140[f]	6·63[m]			237[m]	0·74[m]		
c	*n*-C_3H_7CO[g]	H						I(86)[g]	40 (1·5)	119–121							
d	CH_3O_2C[e]	H						I(49)[e]	25 (1)	145							
e	C_6H_5	H	$C_8H_7N_3$					III(25)		147–148	9·19 ± 0·07	141	145	246[i]	1·54[i]	261	1·65
								I(40)[e]	120 (160)[e]	148[e]	7·91 ± 0·03[i]	146	145				
f	*p*-$CH_3C_6H_4$	H	$C_9H_9N_3$	67·91	5·70	67·76	5·73	III(46)		157	9·34 ± 0·14	154	159	252	1·46	263	1·66
g	*p*-$CH_3OC_6H_4$	H	$C_9H_9N_3O$	61·71	5·18	61·84	5·19	III(18)		171–171·5	9·45 ± 0·25	174	175				
h	*p*-ClC_6H_4	H	$C_8H_6N_3Cl$	53·51	3·37	53·38	3·37	III(22)		161–161·5	9·05 ± 0·11	179	179·5				
								I(1)	153 (120)	160–162							
i	*p*-$O_2NC_6H_4$	H	$C_8H_6N_4O_2$	50·53	3·18	50·84	3·12	I(56)	120 (10)	190–191	8·09 ± 0·03	193	190	304	1·60	350	1·71
j	C_6H_5CO[g]	H						I(82)[g]	40 (1·5)	123–124							
k	CH_3	$CH_3C{\equiv}CCO$	$C_7H_7N_3O$	56·35	4·73	56·16	4·69	I(78)	~5 (0·5)	160–162	7·25 ± 0·02[n]	148	149	260	0·76	293	1·05
l	CH_3	CH_3TCO	$C_7H_8N_6O$	43·77	4·17	43·56	4·08	I(76)	60 (0·4)	244–245	7·42 ± 0·11	198	192	263·5	1·17	291	1·49
											9·35 ± 0·15						
m	CH_3O_2C	CO_2CH_3	$C_6H_7N_3O_4$					I(60)	0 (0·5)	130–131[h]	4·95 ± 0·01[n]	186	185			247	0·81
n	C_6H_5	CHO	$C_9H_7N_3O$					I(83)	65 (17)	189–189·5[f]	6·42 ± 0·01	173	173	275	0·55	225	2·52
																290	0·72
o	H_3C_6	C_6H_5						I(16)[e]	140 (20)	140							
p	C_6H_5	CN[g]						I(80)[g]	90 (1·5)	166–167							
q	C_6H_5	H_2NCO[g]						I(53)[g]	90 (1·5)	273–274							
r	C_6H_5	$C_2H_5O_2C$	$C_{11}H_{11}N_3O_2$					I(91)	90 (2)	91–92[g]	7·05 ± 0·01	221	217	240	0·97	262	1·00
s	$C_6H_4OCH_3$-*p*	$C_2H_5O_2C$	$C_{12}H_{13}N_3O_3$	58·31	5·30	58·42	5·03	I(76)	90 (2·5)	6–10	7·38 ± 0·02	251	247				
t	C_6H_4Cl-*p*	$C_2H_5O_2C$	$C_{11}H_{10}N_3O_2Cl$	52·51	4·01	52·72	3·95	I(–)	55 (2)	172–172·5	6·50 ± 0·01	254	251·5	252	1·04	268	1·11
u	C_6H_4Cl-*o*	$C_2H_5O_2C$	$C_{11}H_{10}N_3O_2Cl$	52·51	4·01	52·65	4·02	I(86)	~75 (3)	liq.	6·55 ± 0·01	263	251·5				
v	$C_6H_4NO_2$-*p*	$C_2H_5O_2C$	$C_{11}H_{10}N_4O_4$					I(69)[j]	60 (1)	170–171	5·85 ± 0·01	261	262	290	1·24	326	1·28
w	$C_6H_4NO_2$-*o*	$C_2H_5O_2C$	$C_{11}H_{10}N_4O_4$					(IV)		27–41	6·70 ± 0·02	288	262				
x	$C_6H_4NO_2$-*m*	$C_2H_5O_2C$	$C_{11}H_{10}N_4O_4$					(IV)		105–106	6·00 ± 0·01	270	262	249	1·67	266	1·90
y	C_6H_5	$C_6H_5C{\equiv}CCO$	$C_{17}H_{11}N_3O$	74·81	3·99	74·75	3·99	(I)(72)	~10 (0·5)	131–132	6·40 ± 0·01	276	273	300	2·34	320	1·62
														226·5	2·56	277	2·07
																226	2·61
z	C_6H_5	C_6H_5TCO	$C_{17}H_{12}N_6O$	64·51	3·82	64·28	3·95	(I)(77)	20 (0·5)	121–122(dec)	6·35 ± 0·12	314	316	288	0·96	302·5	0·96
											8·35 ± 0·11			225·5	2·27	230·5	2·52
aa	C_6H_5	$C_6H_5CH{=}CHCO$	$C_{17}H_{13}N_3O$	74·11	4·76	74·30	4·73	(I)(65)	~0 (0·5)	150–151	6·80 ± 0·02	279	275				
bb	C_6H_4Cl-*p*	$(C_6H_5)_3P^+$						(II)(94)	60 (2·5)	278–280(dec)							
cc	C_6H_5	$(C_2H_5O)_2P(O)$	$C_{12}H_{16}N_3O_3P$[k]	51·21	5·53	50·96	5·56	(I)(71)[k]	70 (4)	liq.							
dd	C_6H_5	$(C_6H_5)_3P^+$						(II)(93)	60 (3)	240–241							

[a]The preparative methods are: I—addition of azide ion to alkyne in DMF (except as noted) according to Eq. 1; II—addition of azide ion to the indicated ethynylphosphonium salt yields a triazolyl ylid. (On hydrolysis, **1dd** yields **1e** and **1bb** yields **1hh**. See Ref 5); III—addition of trimethylsilyl azide to alkyne in toluene (Eq. 2); IV—addition of azide to alkene in DMF (*Ref* 3). Triazoles prepared according to 1 by other workers are included. [b]These substituents in the product triazole are those of the starting 1,2-alkyne, except for method IV, in which they derive from a 1,2-alkene. [c]Average deviation at 25 ± 2° for duplicate runs. In two cases, the compound has two p*K*'s. [d]The observed molecular weight was determined from the equivalence point in the p*K* determination in this work. [e]Ref 2. The solvent was DMSO. For C_2H_2, p = 8 atm. [f]J. C. Sheehan and C. A. Robinson, *J. Am. Chem. Soc.*, 71, 1436 (1949), report mp 141–142° for **1b** and 186·5–187·5° for **1n**. [g]Ref 1. For 4-phenyl-5-carbethoxytriazole, Ref 1 reports 92–93°. [h]Ref 2 reports mp 132°. [i]The solvent was water for which Ref 8 cites p*K* = 7·68. [j]Also prepared by method IV, Ref 3. [k]This product was difficult to purify. The yield refers to the triazole derivative, diethyl 5-(2-benzyl-4-phenyl-triazolyl)phosphonate. [l]D. Dal Monte, A. Mangini, and F. Montanari, *Gazz. Chim. Ital.* 88, 1035 (1958) gives λ_{max} 262 (log ε 4·31). [m]These data are for water at 20° (G. B. Barlin, *J. Chem. Soc. B* 641 (1967). [n]In water, p*K* = 4·44 ± 0·01. [o]In water, p*K* = 6·46 ± 0·02.

The reaction of two negative ions after the first stage should be less favorable; moreover, T^- may cross-conjugate with the surviving triple bond and may thus decrease the tendency for further nucleophilic attack of azide. Once acidified, however, **T** (neutral) reacts readily with sodium azide. As expected, diphenylethynyl ketone is more active, i.e., azide addition proceeds under milder conditions than for dipropynyl ketone in this synthesis (Table 1).

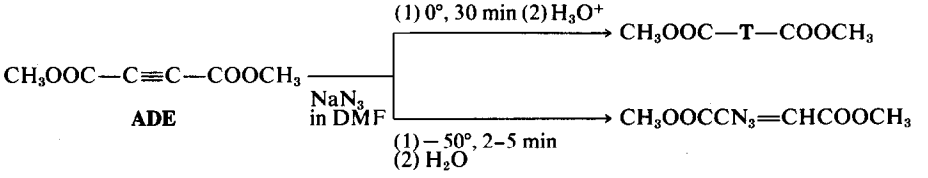
In regard to the mechanism of process 1, we record some preliminary observations on one system. **ADE** and sodium azide in DMF at $-20°$ give a red solution immediately. Above 0° the color is deeper and the yield of H-1,2,3-triazole lower. On dropwise addition of the acetylene, the red color forms and disappears gradually, appearing with each drop and then fading. Finally, the red-purple color remains. The colored species may be the azidoethylene anion, $RC(N_3)=\bar{C}R'$, or a precursor charge transfer complex, as has been found in the case of phosphine-activated alkyne interactions.[19] Apart from the question of the colored species, there is sound, albeit indirect, support for the intermediacy of the azidovinyl anion. When the reaction time was shortened to several minutes at $-50°$ and water was added, small amounts of *cis* and *trans*-dicarbomethoxyazidoethylenes were isolated:



(7)

Once the *syn*-adduct is formed, cyclization should be very fast because of accessibility and because of the stability of the triazolide. Moreover, conjugation with the side chain carbonyl, which is present in the open structure, is equally present in the ring (Eq. 7).

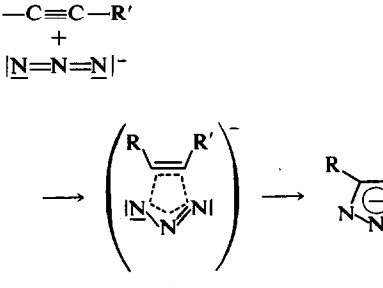
As an alternate to the above nucleophilic addition, an "aromatic" dipolar cycloaddition is also *syn* and "allowed" (Eq. 8).[6] The six "involved" electrons become σ bonds leaving an "aromatic" product, which is still stabilized by six π electrons. Azide, of course, is a powerful dipolarophile. Nevertheless, we prefer the ionic mechanism for process 1 for several reasons. 1,3-Dipolar additions, e.g., aryl azides to alkenes, are not usually as



(6)

It is known that sodium azide and **ADE** in 90% methanol in the presence of acetic acid at *ca.* 25° also gave the *cis* and *trans* azidoethylene.[20] Normally, the yield of T^- in this reaction in DMF is > 60% and we know this to be pale yellow (λ_{max} 248 nm). Therefore, the permanent colored material (< 5%) cannot be this species.

As is well known, most simple nucleophilic additions to acetylene show an *anti* preference, although the possibility of ring closure, e.g., to pyrazoles, isoxazoles, etc., often leads to overall *syn* addition[19]—see next section. In either case, these additions are generally considered to proceed through several steps. With respect to azide as a nucleophile on **ADE**, the observed rate law for 90% acetic acid is $v = k[HN_3][\mathbf{ADE}]$.[20] We presume that addition of azide to acetylene starts with *anti* addition. Were the *anti* anion rigid and of the geometry indicated in Eq. 7, no triazole would form;[19] but when conjugating electron-withdrawing groups are present, the barrier to isomerization may be reduced considerably and isomerization may proceed through an allenic form:[19]



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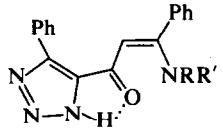
(8)

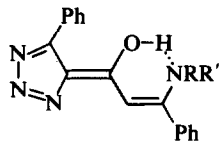
susceptible to the large solvent and substituent effects that have been found in this process.[21] When proton donors are present, we found that the reactivity of the azide ion was diminished and that azido ethylenes were also formed (Eq. 6). Minimally this indicates that the azidovinyl anion is produced, a finding consistent with the ionic mechanism. For these reasons, we believe process 8 does not apply here.

D. *Ethynylketotriazoles and their reactions*

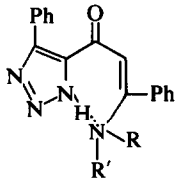
Ethynylketotriazoles (**1l**, **1z**) have three chemically active sites in C≡C, C=O and T. As we have seen in Eq. 5, azide ion adds to form ditriazolylketones (**2**). In Table 2 we list other products, triazolylenamines (**3**), triazolylpyrazoles (**4**) and triazolylisoxazoles (**5**) by the addition of amines, hydrazine and hydroxylamine, respectively. Hydrazine and hydroxylamine can conceivably attack at the carbonyl site, but previous work indicates that attack under basic conditions generally favors the acetylenic carbon.[18] Moreover, the UV spectrum appears to be more consistent with **5** than with the alternative **6** (see below). In passing, we note that the acidity of the eneamine (**3**) is unexpectedly low, that there is a fairly intense $(P—OH)^+$ peak in its mass spectrum, and that its IR CO peak is weak or absent. These observations indicate that the tautomer **3′** may predominate.



3a: R=R′=Et,
b: R=H, R′=C_6H_5NH



3′



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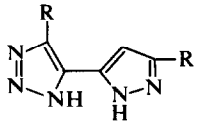
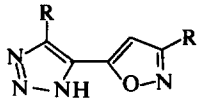
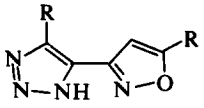


4a: R=Ph;
b: R=Me



5a: R=Ph;
b: R=Me



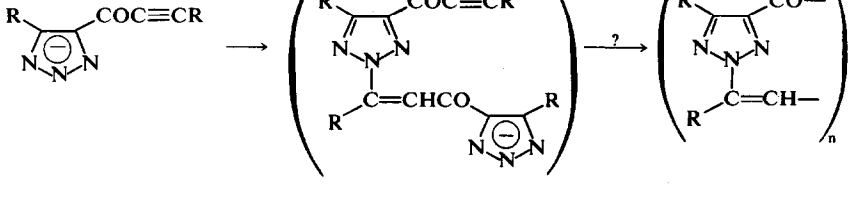
6

(9)

In the presence of base, triazoles form T^- which are potential nucleophiles. Thus, ethynylketotriazoles undergo changes in the presence of base; e.g., their solubility in methanol decreases and their IR spectra lose ν(C≡C) and ν(NH). Since the material(s) which formed have elementary C—H analyses which are lower than those expected for the products of Eq. 10, we speculate that the reactants may have been degraded by base. Indeed, such observations attracted our attention to the potential of triazolides as nucleophiles.[4]

Triazole acidity constants. H-1,2,3-Triazoles are weak acids, falling in the middle range of 5-membered conjugated ring systems between the group of cyclopentadiene, pyrrole, pyrazole, and imidazole with pK *ca* 15 and tetrazole with pK *ca* 5 in water.[22] There is, of course, considerable variation within any given ring system; our pK range of 5-9·5 (Table 1) could be expanded with the inclusion of other T, e.g., 4,5-dicyanotriazole with pK = 2·5.[23] The compounds of this work will be grouped for purposes of discussion into three categories, that is 4-aryl, 4-aryl-5-carbethoxy, and miscellaneous—H-1,2,3-triazoles.

Our pK's were determined by potentiometric titration at 25 ± 2°—the uncertainty arising solely from the possible variation of temperature of measurement is probably < |±0·01| unit.[22,24] These pK's are apparent rather than thermodynamic: corrections and adjustments for medium effects and the mixed solvent were considered to have cumulative uncertainties[24] comparable to those in our pK's and were not made. The estimated uncertainties given in Tables 1 and 2 were made by a straightforward procedure outlined in the experimental section. To ensure adequate solubility of these compounds, we used an ethanol-water (v/v 1/1) solvent. Now, it is known that the admixture of ethanol or DMF to an acid in water raises its pK;[24] for benzotriazole, pK = 8·98 in ethanol-water is higher than pK = 8·6 reported for water.[22] Likewise, we find the change in pK or ΔpK, for 4,5-dicarbomethoxy-1,2,3-triazole, 4-methyl-5-propiolylketo-1,2,3-triazole and 4-phenyltriazole in ethanol-water (v/v 1/1) *versus* water to be 0·51, 0·79 or 1·29, respec-



(10)

Table 2. Products, (5-R)-T-(R′-4), from ethynylketotriazoles, 4-R′-T-(COC≡CR′)

Compound	5-R	4-R′	Formula	Calcd, % C	Calcd, % H	Found, % C	Found, % H	p*K*	m.p. °C	M.W. (obs.)	M.W. (calc.)	T λ_{max}^{EtOH} nm	T ϵ_{max} $\times 10^{-4}$	T⁻ λ_{max}^{EtOH} nm	T⁻ ϵ_{max} $\times 10^{-4}$
3a	$C_6H_5C(N(C_2H_5)_2)=CHCO$	C_6H_5	$C_{21}H_{22}N_4O$	72·81	6·40	72·79	6·58	8·60 ± 0·03	272–273	358	346	344	2·98	344	3·33
														234	1·89
3b	$C_6H_5C(NHC_6H_5)=CHCO$	C_6H_5	$C_{23}H_{18}N_4O$	75·39	4·94	75·16	4·79	7·75 ± 0·02	193–194	373	365	380	3·54	380	4·22
												226·5	2·52	243	2·54
4a	(3′-phenylpyrazolyl)	C_6H_5	$C_{17}H_{12}N_5$	71·08	4·56	71·01	4·30	8·20 ± 0·03	207	275	277	253·5	3·28	251	2·98
4b	(3′-methylpyrazolyl)	CH_3	$C_7H_9N_5$	51·34	5·36	51·53	5·55	9·57 ± 0·15	261–263	162	167	238	1·11	252	1·43
5a	(3′-phenylisoxazolyl)	C_6H_5	$C_{17}H_{12}N_4O$	70·82	4·19	70·37	4·11	7·01 ± 0·01	152–153	288	288	235	238	291	1·36
														237	3·80
5b	(3′-methylisoxazolyl)	CH_3	$C_7H_8N_4O$	51·22	4·91	51·06	5·07	8·11 ± 0·03	193–194	165	164	254	1·54	264	1·45

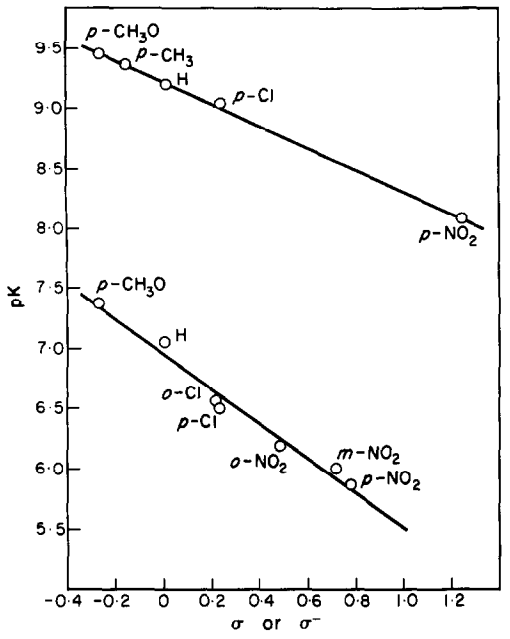
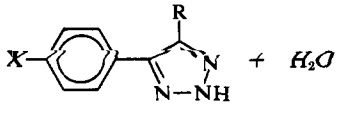


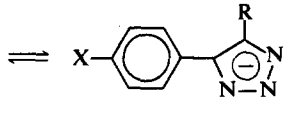
Fig 1. Hammett plots of apparent pK values in 50% ethanol–water (v/v 1/1): upper line, 4-XC_6H_4-T-H *versus* σ^-; lower line, XC_6H_4-T-$COOC_2H_5$ *versus* σ.

tively. Evidently, the effect of solvent becomes larger as the pK increases, and this tendency is likely to be applicable to all of our triazoles for the two solvents.

Correlations of the pK's of two families of acids are shown in Fig 1. For process 11, the pK's of 4-aryl-1,2,3-triazoles show a better correlation with



R=H, R=COOEt



(11)

σ^- than σ (Eq. 12),[25] probable errors being given in Eq. 12. Because of the small number of substituents overall, it is premature to make much of the

$$\log K_a = (0{\cdot}89 \pm 0{\cdot}02)\sigma^- - (9{\cdot}21 \pm 0{\cdot}12) \quad (12)$$

fact that σ^- rather than σ was used for the p-NO_2 group in Eq. 12. Turning to the 4-aryl-5-carbethoxy-1,2,3-triazoles, the presence of the CO function enhances the acidity by *ca* 2·15 units, presumably by stabilizing charge in T^-. For this family, the correlation (Eq. 13) involves σ and has

$$\log K_a = (1{\cdot}45 \pm 0{\cdot}10)\sigma - (6{\cdot}95 \pm 0{\cdot}05) \quad (13)$$

$\rho = 1{\cdot}44$ (σ values for two ortho substituents were taken from Solomon and Filler[26]).

The remaining group of triazoles covers a wide variety of compounds and we can only comment on a few aspects of the relation of pK to structure. With respect to the ethynylketotriazoles, —C≡C—CO—T—, the phenyl- are stronger acids than the Me-substituted triazoles, e.g. **1k** *vs* **1z**. A similar substituent effect holds for the symmetrical ditriazolyl ketones which have two dissociation constants: di(4-phenyl)triazolyl ketone (**1z**) has pK's 6·35 and 8·35; di(4-methyl)triazolyl ketone (**11**) has pK's 7·42 and 9·35. The phenylethynyl-(**1y**) is a stronger acid than the styrylketotriazole (**1aa**), presumably because the triple bond is more electron-withdrawing than the double bond.

An interesting case is that of 5-(4-phenyl-1,2,3-triazolyl)-α-diethylamino-β-styrylketone (**3a**), which has an unexpected high pK = 8·60 as compared with the pK = 6·80 of 4-phenyl-5-styrylketo-1,2,3-triazole (**1aa**) and pK = 7·75 of 5-(4-phenyl-1,2,3-triazolyl)-2′-N-anilino-1′-styrylketone (**3b**). Compound **3a** is an enaminoketone and the diethylamino group presumably releases electronic charge to the CO group; since this is conjugated with the triazole group, the diethylamino group may reduce the acidity somewhat. But the difference of 1·80 in pK between **1aa** and **3a** seems to us to be too large for the relatively remote —NEt_2. We therefore considered a number of hydrogen-bonded tautomers, e.g., **3′** and **3″**. All of these would make for more difficult dissociation of the proton, but we are inclined to favor those related to **3′** in which the H atom is bonded or H-bonded to oxygen, for the following reasons. First, **3a** shows no CO absorption in the region 1520–1800 cm^{-1}, unlike ordinary *cis*-dialkylaminoalkenones which lack (T).[27] Second, the mass spectra of both **3a** and **3b** have intense $(P—OH)^+$ peaks.[5]

Physical data have rarely been discussed in the area of *bis*-heterocyclics. Pyrazolyl in **4a** with pK = 8·2 does not increase the acidity of the attached **T** as much as isoxazoyl in **5a** with pK = 7·01. This observation is consistent with the fact that protonated isoxazole is more acidic than protonated pyrazole;[22] the lowest energy UV band occurs at a slightly higher wavelength for isoxazole than for pyrazole,[28] and theoretical calculations indicate that isoxazolyl- is more electron-withdrawing than pyrazolyl-substitition.[29] Further discussion of the pK's, pK correlations and related physical data is given in the Ph.D. thesis of the first author.

UV spectra. The UV spectrum of the parent H-1,2,3-triazole has a max absorption at 210 nm (ϵ_{max} 4400) in ethanol, not very different from the spectra of pyrrole, pyrazole and imidazole.[28] Alkyl substitution produces small changes in both the

intensity and position of the 210 nm absorption but 4-aryl or -CO substitution produces more intense bands shifted to higher wavelengths.[8,9,28] The bathochromic shifts on mono- and di-substitution in a variety of triazoles are well illustrated by the compounds in Tables 1 and 2. Spectral data of **T**⁻ are rarely recorded. Nevertheless, such data have often been used to make structural assignments in the **T** series[8,30] and the present data should help to simplify this task.

A similarity in the spectra of phenyltriazole and biphenyl was first pointed out by Hartzel and Benson.[9] Apart from the bathochromic shift from **T** to **T**⁻, this analogy seems to hold for the 4-aryltriazole anions too (Fig 2). A 4,5-disubstituted tri-

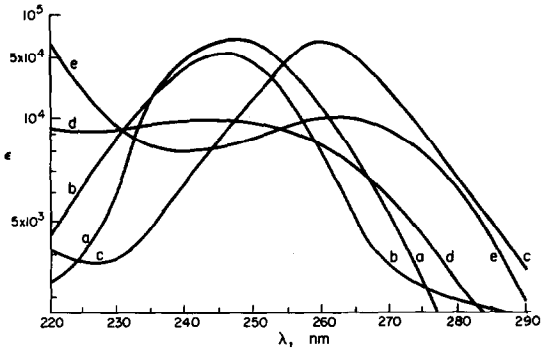
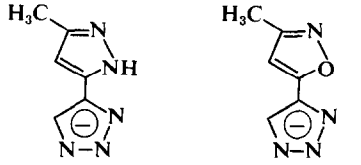


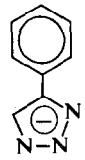
Fig 2. UV Spectra: a, biphenyl; b, 4-phenyl-1,2,3-triazole; c, 4-phenyl-1,2,3-triazole anion; d, 4-phenyl-5-carbethoxy-1,2,3-triazole; e, 4-phenyl-5-carbethoxy-1,2,3-triazole anion.

azole also presents a possible analogy with a hindered *cis*-alkene. Thus, λ_{max} of 4-phenyl-5-carbethoxy-1,2,3-triazole (λ_{max} 240, ϵ 9700) is of lower intensity than λ_{max} of 4-phenyl-1,2,3-triazole (λ_{max} 246, ϵ 15400); this may be rationalized if the phenyl and ester group are forced out of the plane of the triazole ring, because of steric interactions.[31] Such effects have been decomented for several series, e.g. biphenyls and stilbenes.[31] Likewise, in the triazolylcarbonyl compounds and their anions crowding effects that are present in acetophenones and benzophenones[31] show up in the series **1n**, **1y**, and **1z** in which λ_{max} and ϵ do not follow the anticipated order. On this basis, the substitution of a smaller group, e.g., Me (**1k** and **1l**) for phenyl, (**1y** and **1z**), should lead to less pronounced effects, as we observe (Table 1).

The UV spectra of biheteroaromatic systems and their anions provide variations on a theme (Table 2). The UV spectrum of 4′-methyltriazolyl-3-methylpyrazole (**4b**), for example, is similar to that of 2,4′-dimethylbiphenyl (λ_{max} 239·5, ϵ 11800).[32a] Likewise, the spectra of the following anions are similar:



λ_{max} 238, ϵ 11100 λ_{max} 264, ϵ 14500



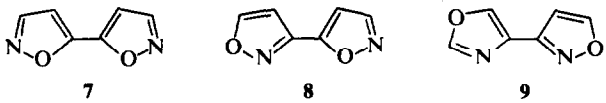
λ_{max} 264, ϵ 16500

These observations indicate a remarkable similarity between heteroaromatic compounds and hydrocarbon aromatic compounds.

Substitution of phenyl for methyl, as in **4a** and **5a**, again indicate complicated changes of the kind seen for *ortho*-phenylbiphenyl structures. The pyrazolyltriazole (**4a**) spectrum (λ_{max}^{EtOH} 253·5, log ϵ 4·5) falls between that of 2,3′-diphenylbiphenyl ($\lambda_{max}^{C_6H_{12}}$ 236, log ϵ 4·6) and that of 3,4′-diphenylbiphenyl ($\lambda_{max}^{C_6H_{12}}$ 267 nm, log ϵ 4·6).[32b] The isoxazolyltriazole (**5a**) spectrum (λ_{max} 235 nm log ϵ 4·4; λ (shoulder) ~ 268 nm) is similar to that of 2,4′-diphenylbiphenyl ($\lambda_{max}^{C_6H_{12}}$ 248, log ϵ 4·4; $\lambda_{max}^{C_6H_{12}}$ 276, log ϵ 4·3).[32c] Some of these spectra are given in Fig 3 and UV data for various dimethyl- or *bis*-diphenyl-biphenyls have been given by other workers.[28,31,32]

As indicated earlier, we favored **5** over **6** as the structure of our oxazole products. The chief support for this assignment derives from the kind of spectral analogies that we have just considered. Fortunately, UV data of model compounds are available.[33] Clearly, the data for **5b** (λ_{max} 254, ϵ 15400), the structure we chose, are bracketed by those of **7** and **8** and rather different from those of **9**, which is structurally more related to **6**.

C_6H_5—T—CHO **1n**		C_6H_5—T—CO—T—C_6H_5 **1z**		C_6H_5—T—COC≡CC_6H_5 **1y**	
neutral	275 (5500)	neutral	288 (9600)	neutral	300 (23400)
			225·5 (22700)		226·5 (25600)
anion	225 (25200)	dianion	302·5 (9600)	anion	320 (16200)
	290 (7200)		230·5 (25200)		277 (20700)
					226 (26100)



7 8 9

λ_{max} 260 (ϵ 16300) 242 (ϵ 12100) 210 (ϵ 9500)

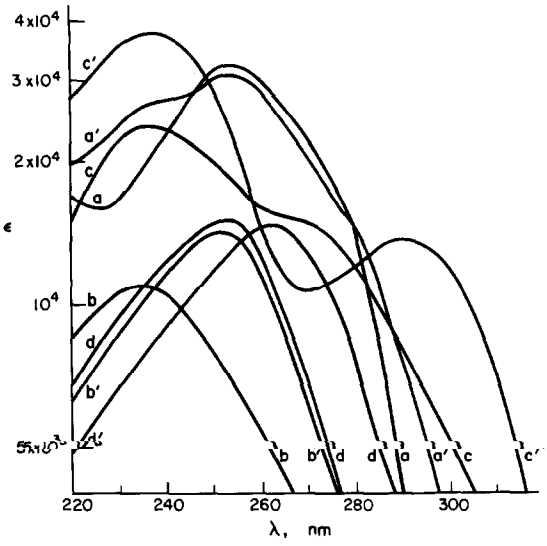


Fig 3. UV spectra of several biheteroaromatics and their anions: a and a', 4-phenyl-5-(3'-phenylpyrazolyl-5')-1,2,3-triazole and its anion; b and b', 4-methyl-5-(3'-methylpyrazolyl-5')-1,2,3-triazole and its anion; c and c', 4-phenyl-5-(3'-phenylisoxazolyl-5')-1,2,3-triazole and its anion; d and d', 4-methyl-5-(3'-methylisoxazolyl-5')-1,2,3-triazole and its anion.

IR Spectra. Borello, *et al.*, has given IR spectra and made band assignments to the parent 1,2,3-triazole as well as to several 2-aryl-1,2,3-triazoles.[34] As a group, the spectra of our H-1,2,3-triazoles have several characteristic features which aid in structure identification (Table 3). An absorption in the region 3100–3200 cm^{-1} usually indicates an imino proton. The peaks in the region 1400–1470 and 1440–1450 cm^{-1} do not depend on substituents and are generally diagnostic for triazoles, unless alkyl group absorptions interfere. The absorptions at 970–1030 and 1075–1145 cm^{-1} are strong, sometimes sharp, and easily recognizable.

As for T^- few IR data are available. The anions of the ketotriazoles, for example, show a large shift in the carbonyl absorption from ~ 1710 to ~ 1650 cm^{-1} (Fig 4), analogous to that observed in ketopyrroles.[35]

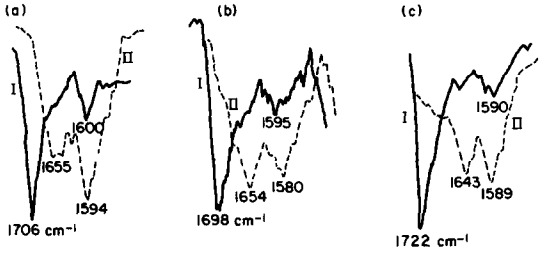


Fig 4. IR spectra of 4-aryl-5-carbethoxy-1,2,3-triazoles-(I) and their anions (II) in the region of 1550–1750 cm^{-1} (nujol): (a) 4-p-nitrophenyl-5-carbethoxy-1,2,3-triazole; (b) 4-p-chlorophenylcarbethoxy-1,2,3-triazole; (c) 4-phenyl-5-carbethoxy-1,2,3-triazole.

EXPERIMENTAL*

PMR spectra were obtained on a Varian A-60 instrument, and are reported in δ, ppm relative to internal TMS. The line frequencies are estimated to be precise to within 0·5 Hz; s, d, t, m are used to indicate singlet, doublet, triplet, multiplet, respectively. IR spectra were recorded on a Beckman IR-8 Spectrometer. Soln spectra were measured in a matched set of 0·1 mm path length sodium chloride cells. UV and visible spectra were recorded on a Beckman DK-2 Spectrophotometer. The solvent was EtOH or MeOH-NaOMe and λ is always given in nm. Mass spectra were recorded on a Varian CH-7 Mass Spectrometer. Refractive indexes were determined by a thermostated Abbé refractometer. All m.ps were taken in capillary tubes on a Mel-Temp instrument and are uncorrected. Microanalyses were performed by M-H-W Laboratories, Garden City, Michigan.

Preparation of 4-aryl-1,2,3-triazoles (1a–h), from trimethylsilyl azide and arylacetylenes.[12] An equimolar soln of phenylacetylene and trimethylsilyl azide in toluene was heated at reflux for 3 days. Several drops of water, enough to hydrolyze the silyltriazole, were then added. After heating for an additional 12 hr, the soln was cooled to ~ 20°. White crystals which appeared were filtered off, washed twice with CCl_4, and recrystallized from aqueous MeOH. Data on these compounds are given in Tables 1 and 3.

General procedures for process 1. In what follows we outline one method for 4-aryl-5-carbethoxy-1,2,3-triazoles and their purification (*Workup 1*). Variations for other compounds follow with *Workup 2* given with 1i. Data already listed in Tables 1–3 will generally be omitted. To a stirred solution of sodium azide (0–5% excess) in DMF at 55–90° and swept by dry nitrogen was added the ethyl phenylpropiolate*,[36] (0·44–1·24 g) in dry DMF. The

*Several compounds were available from past or ongoing projects: from Dr. G. S. Krishnamurthy, several ethyl phenylpropiolates;[37] from Dr. R-R. Lii, *p*-methoxy, *p*-methyl, *p*-nitro, and *p*-chloro-phenylacetylene;[38] from Dr. A. Fujii, diethyl phenylethynylphosphonate;[16] from Dr. J. L. Dickstein, phenylethynyltriphenylphosphonium halides;[17] from Mr. K. G. Migliorese, dipropynylketone; from Mr. G. Shimek, ethyl *o*-chlorocinnamate.

Table 3. Characteristic IR spectral regions of H-1,2,3-triazoles[a]

	Solvent	970–1030 cm^{-1}	1075–1145 cm^{-1}	1400–1410 cm^{-1}	1440–1450 cm^{-1}	3100–3300[b] cm^{-1}
1e	Nujol	982 s	1089 s			3145
q	Nujol	986 s	1088 m			3135
f	Nujol	982 s	1076 s			3143
h	Nujol	982 s	1104 s			3140
r	KBr	1031 m	1104 s	1400 w	1451 w	3120
s	film	1025 s	1145 s	1410 w	1445 w	3150
t	KBr	1000 s	1100 s	1408 w	1448 w	3205
u	film	1025 s	1080 s	1410 w	1450 w	3180
v	KBr	1002 s	1110 s	1411 w	1448 w	3200
x	KBr	1020 w	1100 m	1403 w	1448 m	3100
m	KBr	980 m	1070 s			3200
y	CCl_4	990 s	1075 m	1410 w	1445 m w	3120
1aa	$CHCl_3$			1412 m	1451 m	3230
1k	film	985 m	1135 s	1412 w		3150
1z	Nujol	1000 s	1125 m	1410 w	1445 s	3120
1l	Nujol	975 s	1120 m			3150
3a	Nujol	987 s	1088 s			3150
3b	Nujol	995 s	1122 s			3150
4a	KBr	978 s	1080 s	1405 w	1445 m	3150
4b	Nujol	970 s	1130 s			3150
5a	Nujol	1005 s	1125 s		1450	3150

[a]The compounds with numbers in column 1 are identified in Tables 1 and 2. s, m, and w mean strong, medium and weak.

[b]The peaks in this region are broad and may be solvent dependent.

stirred mixture was kept at the reaction temperature for 1–3 hr. *Workup* 1. To facilitate purification at a later stage, the DMF was removed at *ca* 60° under reduced pressure (2–5 nm) and the residue was taken up in water. The soln was then acidified with 10% HCl, and extracted with ether several times. The extract was washed twice with a small amount of water, dried over $MgSO_4$, and evaporated to deposit the triazole. The crude solid was recrystallized from water. Details of preparation and properties are given below and in Tables 1–3.

4-*Phenyl-5-carbethoxy*-1,2,3-*triazole* (**1r**) had: NMR ($CDCl_3$) δ 1·31 (t, 7·1 Hz, 3H), 4·35 (q, 7·1 Hz, 2H), 7·42 (m, 3H), 7·78 (m, 2H), 9·00 (broad, 1H); IR (KBr) 1730 cm^{-1}.

4-p-*Methoxyphenyl-5-carbethoxy*-1,2,3-*triazole* (**1s**), a liquid, was treated with NaOMe in MeOH-water to make the Na salt. This soln was washed twice with ether and reacidified with HCl. Extraction with ether and washing of the ether layer with water followed. Finally, removal of the ether gave purified triazole: NMR ($CDCl_3$) δ 1·27 (t, 7·1 Hz, 3H), 3·79 (s, 3H), 4·35 (q, 7·1 Hz, 2H), 6·93 (d, 8·7 Hz, 2H), 7·80 (d, 8·7 Hz, 2H), 11·10 (broad 1H); IR (neat) 1714 cm^{-1}.

4-p-*Nitrophenyl-5-carbethoxy*-1,2,3-*triazole* (**1v**), prepared from ethyl-*p*-nitropropiolate, was identical to a sample which was prepared from ethyl-*p*-nitrocinnamate.[3]

4-p-*Chlorophenyl-5-carbethoxy*-1,2,3-*triazole* (**1t**) had: NMR (d-acetone) δ 1·33 (t, 7·1 Hz, 3H), 4·37 (q, 7·1 Hz, 2H), 7·51 (d, 8·6 Hz, 2H), 7·94 (d, 8·6 Hz, 2H); IR (KBr) 1710 cm^{-1}.

4-o-*Chlorophenyl-5-carbethoxy*-1,2,3-*triazole* (**1u**) was purified by the same method as that of **1s** and had: NMR (d-acetone) δ 1·14 (t, 7·1 Hz, 3H), 4·25 (q, 7·1 Hz, 2H), 7·52 (s, 4H); IR (neat) 1730 cm^{-1}.

4-p-*Chlorophenyl*-1,2,3-*triazole* (**1h**). This compound was prepared from *p*-chlorophenylacetylene[37] and sodium azide as described below for **1i**. Workup (with methylene chloride instead of ether) left a brown gummy residue which was chromatographed on silica gel and eluted with methylene chloride to give **1h** in low yield (1%).

4-p-*Nitrophenyl*-1,2,3-*triazole* (**1i**). A soln of *p*-nitrophenylacetylene[38] (0·240 g, 1·63 mmol) and sodium azide (0·106 g, 1·63 mmol) in DMF (10 ml) were heated at 120° with stirring for 10 hr, cooled and evaporated to dryness *in vacuo*. *Workup 2*. The residual solid was washed with ether and dissolved in water. After the water soln was acidified with hydrochloric acid, a light brown solid was precipitated and filtered off. The filtrate was extracted with ether, washed with several small portions of water, and the extract was evaporated, leaving a light brown solid. This solid and the precipitate were recrystallized from water to give a light yellow solid (0·175 g): NMR (acetone) δ 8·25 (m, 4H), 8·45 (s, 1H): IR (Nujol) 1604, 1515, 1340 cm^{-1}; mass spectrum *m/e* 190 (P^+), 160, 132, 89.

4,5-*Dicarbomethoxy*-1,2,3-*triazole* (**1m**). To a stirred suspension of sodium azide (1·89 g, 30·5 mmol) in DMF (60 ml) was added dropwise at *ca* 0° over 30 min, a soln of dimethyl acetylenedicarboxylate (4·20 g, 29·6 mmol) in DMF (50 ml). After 30 min the solvent was removed *in vacuo* at 60° to leave a light purple-brown solid. The solid was washed twice with ether and taken up in water. The aqueous soln was neutralized with HCl, extracted with ether and chloroform, and the extract was evaporated to give a light red solid. This was washed with hot hexane and recrystallized from benzene: NMR ($CDCl_3$) δ 4·00 (s, 6H), 11·87 (broad 1H); IR (KBr), 1730 cm^{-1}.

4-*Phenyl-5-formyl*-1,2,3-*triazole* (**1n**). The method was similar to that for **1r**: NMR (dimethylacetamide) δ 7·68 (t, 3·3 Hz, 3H), 8·11 (m, 2H), 11·28 (s, 1H); IR (Nujol) 1693 cm^{-1}.

4-*Phenyl-5-phenylpropiolyl*-1,2,3-*triazole* (**1y**). In a 1l

3-necked flask equipped with inlet and outlet tubes for N_2 and a dropping funnel, sodium azide (6·83 g, 0·105 mol) was suspended in water-free DMF (400 ml). The mixture was stirred magnetically and cooled externally by means of a salt-ice slush to −15° to −20°, while it was flushed with a slow stream of N_2. A cooled soln of diphenylethynylketone (23 g, 0·100 mol) dissolved in dry DMF (200 ml) was added dropwise to the flask in 30 min. The soln turned red-brown and the sodium azide disappeared as the reaction proceeded. After the addition was complete, the mixture was stirred at −10° for another 30 min. Then ice-water (*ca* 500 ml) followed by 10% HCl (40 ml) and *Workup 2* followed. Recrystallization from CCl_4-$CHCl_3$ (4/1) gave the analytical sample: NMR (acetone) δ 7·5 (m, 8H) and 8·0 (m, 2H): IR (KBr) 2180, 1645 cm^{-1}; mass spectrum *m/e* 273 (P^+), 272, 245, 216, 189, 129. (Found: N, 15·23. Calcd. for $C_{17}H_{11}N_3O$: N, 15·40%).

Bis-(5-(4-*phenyl*-1,2,3-*triazolyl*))*ketone* (**1z**). The procedure was similar to that of **1y**. The crude white product was recrystallized from $CHCl_3$-CCl_4 (1/1) and from EtOH to give the *bis*-triazole (12·2 g): NMR (acetone) δ 7·45 (m, 6H), 7·80 (m, 4H), 15·25 to 16·40 (broad 1H), IR (KBr) 3150, 1670, 1480 cm^{-1}; mass spectrum *m/e* 316 (P^+), 288, 287, 232, 231, 204, 172, 117, 104.

4-*Methyl* 5-(2'-*butynoyl*)-1,2,3-*triazole* (**3z**). Sodium azide (3·41 g, 0·0525 mol) was suspended in DMF (80 ml) at −5° and dipropynylketone (5·30 g, 0·050 mol) was added gradually (20 min). The mixture was left at −5° for another 10 min and worked up. Neutralization of the soln with HCl and extraction with chloroform gave a white solid (5·83 g), which was recrystallized from water: NMR (d-acetone) δ 2·57 (s, 3H), 2·14 (s, 3H): IR (KBr) 2240, 1640, 1610, 1578, 1485, 1310, 1260, 895 cm^{-1}.

Bis-(5-(4-*methyl*-1,2,3-*triazolyl*)) *ketone* (**1l**). 4-Methyl-5-(2'-butynoyl) triazole (1·09 g, 0·073 mol) in DMF (10 ml) was added dropwise to sodium azide (0·474 g, 0·073 mol) in DMF (20 ml) at 20° for 10 min. After another 10 min, the solvent was removed under vacuum (1 mm) at 60° for 20 min. Dilution of the residue with water and neutralization with HCl gave a white ppt which was recrystallized from $CHCl_3$-CCl_4 (1/1): NMR (d-acetone) δ 2·61 (s, 6H); IR (Nujol) 1650, 908 cm^{-1}.

Diethyl 5-(4-*phenyltriazolyl*) *phosphonate* (**1cc**). The crude product was a deliquescent material. Two cycles of *Workup 1* followed by chromatography of the product on silica gel with ether and chloroform gave an analytical sample: NMR ($CDCl_3$) δ 13·18 (s, 1H), 7·90 (m, 2H), 7·35 (m, 3H), 4·19 (q, 7·0 Hz, 4H), 1·23 (t, 7·0 Hz, 6H); IR (film) 3075, 1227, 1168, 1102, 1060, 1029, 990 cm^{-1}.

Diethyl 5-(2-*benzyl*-4-*phenyltriazolyl*) *phosphonate*. A soln of diethyl phenylethynylphosphonate[16] (0·483 g, 2·03 mmol) in DMF (5 ml) was gradually added to a suspension of sodium azide (0·138 g, 2·12 mmol) in DMF (5 ml). The mixture was heated at 70° for 4 hr, treated with benzyl chloride (0·270 g, 2·13 mmol) and left at 70° for ~ 12 hr, after which it was filtered. The filtrate was concentrated and chromatographed on silica gel with CCl_4 and ether. A liquid product was separated (0·53 g, 71%): n_D^{25} 1·5563; NMR (acetone) δ 8·02 (m, 2H), 7·46 (m, 3H), 7·42 (s, 5H), 5·79 (s, 2H), 4·15 (q, 7·0 Hz, 4H), 1·23 (t, 7·0 Hz, 6H); IR (film) 1458, 1267, 1027, 977 cm^{-1}. (Found: C, 61·41; H, 6·06. Calcd for $C_{19}H_{22}N_3O_3P$: C, 61·45; 5·97%).

Styryl 4-*phenyl*-1,2,3-*triazoy*-5-*yl ketone* (**1aa**). A suspension of sodium azide (1·0 g, 15·4 mmol) and diphenylethynylcarbinol (3·5 g, 15·0 mmol) in DMF (25 ml) was prepared at 0°, then kept at 30° for 30 min. The mixture was acidified with dil HCl and extracted with ether, which on evaporation, yielded a brown solid. This was cleaned up with activated carbon in refluxing EtOH-water (1/1) to give a yellow compound which was purified by recrystallization from EtOH-water (1/1) (1·57 g): NMR (acetone) δ 8·2–7·4 (m, 12H); IR ($CHCl_3$) 3170, 1670, 1605, 1578, 1468 cm^{-1}. Compound **1aa** was also prepared from 1,5-diphenylpent-1-en-4-yn-3-one by keeping the reagents at 0–5° for 30 min. The separation and purification of the product (65%) were essentially as given above. The rearrangement of the ethynylcarbinol will be discussed elsewhere.[38]

5-(4-*Phenyl*-1,2,3-*triazolyl*) β-(α-*diethylaminostyryl*) *ketone* (**3a**). 4-Phenyl-5-phenylpropiolyl-1,2,3-triazole (2·73 g, 10·0 mmol) and diethylamine (0·75 g, 10·3 mmol) were dissolved in abs MeOH (20 ml) and the soln was left at *ca* 25° overnight. Removal of the volatiles afforded a light yellow solid, which was washed with ether and cyclohexane (1/1), then dissolved in ether and reprecipitated with cyclohexane (3·20 g, 92%); NMR ($CDCl_3$) δ 10·92 (broad 1H), 7·45 (m, 10H), 5·73 (s, 1H), 3·06 (q, 7 Hz, 4H), 0·95 (t, 7 Hz, 6H); IR (Nujol) 1580 cm^{-1}; mass spectrum *m/e* 346 (P^+) 329, 202, 175.

5-(4-*Phenyl*-1,2,3-*triazolyl*) β-(α-N-*anilinostyryl*) *ketone* (**3b**). 4-Phenyl 5-phenylpropiolyl-1,2,3-triazole (1·038 g, 3·81 mmol) and aniline (0·39 g, 4·20 mmol) were heated at reflux for 10 hr in abs EtOH (20 ml). Removal of the EtOH gave a yellow solid which was washed with CCl_4 and recrystallized from ether (1·05 g, 76%): NMR (acetone) δ 12·52 (broad 1H), 8·00 (m, 2H), 7·60–6·50 (m, 10H), 7·39 (s, 5H); IR (Nujol) 1540 cm^{-1}; mass spectrum *m/e* 266 (P^+), 349, 333·1 (metastable), 222, 194.

4-*Phenyl*,5-(5'-(3'-*phenylpyrazolyl*))-1,2,3-*triazole* (**4a**). 4-Phenyl-5-phenylpropiolyl-1,2,3-triazole (1·50 g, 5·5 mmol) and hydrazine hydrate (0·30 g, 6·0 mmol) were mixed in MeOH (20 ml) and the soln was left at −15° for 2 days and at ~ 25° for 4 hr. Workup yielded solid, which was washed with CCl_4 and recrystallized from EtOH: NMR (acetone) δ 7·90–7·70 (m, 5H), 7·70–7·20 (m, 7H), 6·90 (s, 1H); IR (KBr) 1600, 1555, 1495, 1450, 765, 700 cm^{-1}.

4-*Methyl*,5-(5'-(3'-*methylpyrazolyl*))-1,2,3-*triazole* (**4b**). 4-Methyl-5-(2-butynoyl)-1,2,3-triazole (0·240 g, 1·61 mmol) and hydrazine hydrate (0·09 g, 1·90 mmol) in EtOH (10 ml) were left at *ca* 25° for 12 hr and then heated to 80° for 15 min. Evaporation gave a white solid (0·231 g, 88%): NMR (d-acetone) δ 2·56 (s, 3H), 2·32 (s, 3H); IR (Nujol) 1623, 1582, 1293, 1203, 725 cm^{-1}. (Found: N, 42·91. Calcd for $C_7H_9N_5$: N, 43·14%).

4-Phenyl,5-(5'-(3'-phenylisoxazolyl))-1,2,3-triazole (**5a**). Hydroxylamine hydrochloride (0·317 g, 4·6 mmol) and NaOMe (0·229 g, 4·6 mmol) in MeOH (10 ml) were added to 4-phenyl-5-phenylpropiolyl-1,2,3-triazole (1·133 g, 4·2 mmol) in MeOH (20 ml) at ~ 25°. The mixture was heated at reflux for 4 hr; removal of the liquid afforded the product, (0·74 g, 62%), which was purified by reprecipitation from EtOH-water (1/1): NMR ($CDCl_3$) δ 7·85–7·00 (m, 10H), 6·89 (s, 1H); IR (Nujol) 1450, 1223, 1195, 1130, 768, 700 cm^{-1}.

4-*Methyl*,5-(5'-(3'-*methylisoxazolyl*))-1,2,3-*triazole* (**5b**). 4-Methyl-5-n-butynoyl-1,2,3-triazole (0·335 g, 2·25 mmol), hydroxylamine hydrochloride (0·156 g, 2·25 mmol) and triethylamine (0·30 ml) were left at *ca* 25° overnight and then refluxed for 2 hr. Evaporation gave a white solid, which was chromatographed on silica gel with acetone (0·310 g, 84%): NMR (acetone) δ 2·29 (s, 3H), 2·52 (s, 3H); IR (Nujol) 3140, 1650 cm^{-1}.

Treatment of 4-phenyl-5-phenylpropiolyl-1,2,3-triazole with base. 4-Phenyl-5-phenylpropiolyl-1,2,3-triazole (1 g) and triethylamine (0·10 ml) in EtOH (10 ml) were heated at 70° for 2 hr. The soln turned orange, the IR peak at 2200 cm^{-1} disappeared, ν_{CO} (1645 cm^{-1}) shifted upward and split (1675, 1710 cm^{-1}). On evaporation of the soln, a gel was deposited, which was dissolved in benzene and reprecipitated with light petroleum. This was filtered and washed with ether (yield 0·86 g): m.p. 204–210°. Attempted purification of this material, e.g., by reprecipitation, recrystallization, and column chromatography (alumina, $CHCl_3$), failed to yield an identifiable compound: NMR ($CDCl_3$) δ 8·0–7·55 (broad, 15H), 7·6–6·1 (broad, 33H), 3·6 (broad, 4H), 1·07 (t, 6·7 Hz, 5·5H), IR (film) 3055, 2970, 1710, 1675, 1615, 1460, 1083, 994 cm^{-1}. (Found: C, 66·04; H, 3·74. Calcd. for the reactant ($C_{17}H_{11}N_3O$): C, 74·80; H, 3·99%).

Measurement of acidity constants. A Corning Model 10 pH meter, equipped with a Sargent glass combination electrode (s-30072-15), was used for acid-base titration and pK determinations. The meter was calibrated with aqueous buffer solns at pH 7·03 (25°) and pH 10·02 (25°) each day. A "standard" solvent was prepared by mixing 500 ml of deionized and distilled water with 500 ml of EtOH. Standard NaOH (*ca* 0·015 M) was prepared by adding 500 ml of abs EtOH to 500 ml of NaOH aq. Its exact concentration was established by potentiometric titration with standard H_2SO_4.

The pure triazole (0·1 mmol) was weighed and placed in a beaker (100 ml), diluted with 60 ml of EtOH-water (v/v 1/1), and titrated to the potentiometric endpoint with base. The observed molecular weights were calculated from the neutralization point and are given in Tables 1 and 2. When a molecular weight calculated from titration deviated excessively from the expected value, an additional run was made.

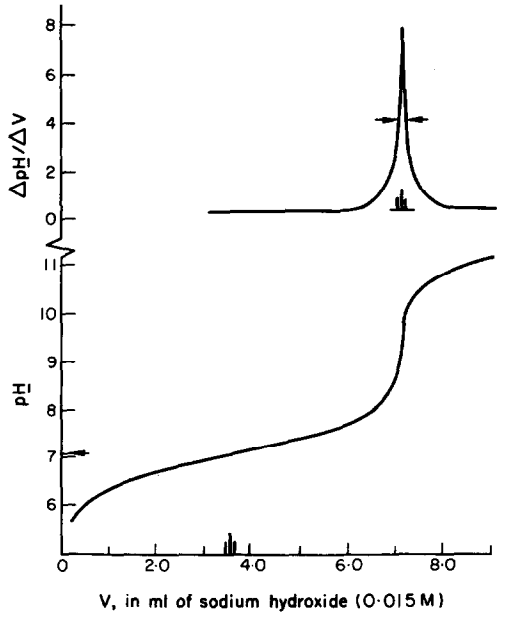


Fig 5. Potentiometric titration of 4-phenyl-5-carbethoxy-1,2,3-triazole with sodium hydroxide in ethanol–water (v/v 1/1) at 25°. The titration curve (lower) and its differential (upper) are shown, together with the equivalence (7·14 ± 0·07) and half-neutralization (3·57 ± 0·04) points and pH = pK, as well as their uncertainties.

A typical titration curve for the neutralization of 4-phenyl-5-carbethoxy-1,2,3-triazole and its derivative are shown in Fig 5. We took the maximum in the derivative curve as defining the equivalence point. In other cases the shape of this curve, either sharper or more rounded, led to less or more uncertainty, respectively, in the equivalence point. This point fixed the value of the titration volume and the pH at half-neutralization, from which we obtained the pK of the triazole through Eq. 14.[22,24]

$$pK = pH + \log f_{HT}/f_{T^-} \simeq pH \qquad (14)$$

The width at half-height of the differential peak was regarded as a measure of the uncertainty in the titration. As indicated in Fig 5, limits on the volume (V) of titrant lead to the estimates in pK. The ranges of pK values given for all triazoles in Tables 1 and 2 were estimated in this manner. Because the slope of titration curve, $\Delta pH/\Delta V$, varies slowly in the range of the half-neutralization point, the uncertainty in pK is relatively small.

The neglect of activity coefficients in Eq. 14 and the uncertainty in the definition of the pH scale in the mixed solvent require, of course, that these pK's be regarded as *apparent* rather than "thermodynamic".[22,24] Adjustments are possible but the uncertainties in determining some of the pK's are often of the same order of magnitude as, and occasionally larger than, the corrections.[24]

REFERENCES

[1] A. N. Nesmeyanov and M. I. Rybinskaya, *Dokl. Akad. Nauk SSSR* **158**, 408 (1964); *Issled. Obl. Org. Khim. Izbr. Tr. Nesmeyanov, A.N.* 291 (1971) or *Chem. Abstr.* **77**, 126517 (1972)

[2] F. P. Woerner and H. Reimlinger, *Chem. Ber.* **103**, 1908 (1970)

[3] Y. Tanaka and S. I. Miller, *J. Org. Chem.* **37**, 3370 (1972)

[4] Y. Tanaka and S. I. Miller, *Tetrahedron.* **29**, 3285 (1973)

[5a] Tanaka and S. I. Miller, *J. Org. Chem.* **38**, 2708 (1973); [b] Unpublished.

[6] M. E. C. Biffin, J. Miller, and D. B. Paul, *The Chemistry of the Azido Group*, (Edited by S. Patai), Chap. 2. Interscience, London (1970)

[7] F. Benson and W. Savell, *Chem. Rev.* **46**, 1 (1950)

[8] J. H. Boyer, *Heterocyclic Compounds* (Edited by R. Elderfield) Vol. 7, Chap. 5. Wiley, N.Y. (1963)

[9] L. W. Hartzel and F. R. Benson, *J. Am. Chem. Soc.* **76**, 667 (1954)

[10] G. Nestler and E. Zbiral, *Monatsh. Chem.* **102**, 1156 (1971)

[11] G. L'Abbé, *Ind. Chim. Belge* **36**, 3 (1971)

[12a] L. Birkofer and P. Wegner, *Org. Syn.* **50**, 107 (1970); [b] L. Birkofer and P. Wegner, *Chem. Ber.* **99**, 2512 (1966)

[13a] R. Huisgen, L. Möbius, and G. Szeimies, *Ibid.* **98**, 1138 (1965); [b] J. G. A. Luijten and G. J. M. Van Der Kerk, *Rec. Trav. Chim. Pays-Bas* **82**, 1181 (1963); **83**, 295 (1964)

[14a] E. Zbiral and J. Stroh, *Monatsh. Chem.* **100**, 1438 (1969); [b] P. Ykman, G. L. Abbé and G. Smets, *Tetradron Letters* 5225 (1970)

[15] J. J. Cooker, *J. Org. Chem.* **30**, 638 (1965)

[16] A. Fujii and S. I. Miller, *J. Am. Chem. Soc.* **93**, 3694 (1971)

[17] J. I. Dickstein and S. I. Miller, *J. Org. Chem.* **37**, 2168 (1972)

[18]T. Metler, A. Uchida and S. I. Miller, *Tetrahedron* **24**, 4285 (1968)
[19]*S. I. Miller and R. Tanaka, Selective Organic Transformations* (Edited by B. S. Thyagarajan) Vol. 1, p. 143. Wiley, N.Y. (1970)
[20]*V. G. Ostroverkhov and E. A. Shilov, Ukr. Khim. Zh.* **23**, 615 (1957); *Chem. Abstr.* **52**, 7828 (1958)
[21][a]R. Huisgen, *Angew. Chem. Int. Ed.* **2**, 565, 633 (1963); *Bull. Soc. Chim. Fr.* 3431 (1965); [b]E. M. Kosower, *An Introduction to Physical Organic Chemistry*, p. 209–218, Wiley, New York (1968)
[22]A. Albert, *Physical Methods in Heterocyclic Chemistry* **I**, 1 (1963)
[23]G. G. Taylor, *Can. J. Research* **20B**, 161 (1942)
[24]R. G. Bates, *Determination of pH*. Wiley, New York (1964)
[25]P. R. Wells, *Chem. Rev.* **63**, 171 (1963); H. H. Jaffé, *Ibid.* **53**, 191 (1953)
[26]I. J. Solomon and R. Filler, *J. Am. Chem. Soc.* **85**, 3492 (1963)
[27]J. Weinstein and G. M. Wyman, *J. Org. Chem.* **23**, 1618 (1958)
[28]E. S. Stern and C. J. Timmons, *Electronic Absorption Spectroscopy in Organic Chemistry*, (3rd Edition) Chaps. 6, 7. St. Martin's Press, New York (1970)
[29]G. Berthier, L. Prand, and J. Serre, *The Jerusalem Symposia on Quantum Chemistry and Biochemistry* (Edited by E. D. Bergmann and B. Pullman) Vol. 1, p. 40. Jerusalem Academic Press, Jerusalem (1970)
[30]*J. E. Oliver and J. B. Stokes, J. Heterocyclic Chem.* **7**, 961 (1970)
[31][a]H. Suzuki, *Electronic Absorption Spectra and Geometry of Organic Molecules* Chaps. *12–14, 18, 21*. Academic Press, New York (1967); [b]H. H. Jaffé and M. Orchin. *Theory and Applications of Ultraviolet Spectroscopy* Chap. 15. Wiley, New York (1962)
[32][a]E. A. Johnson, *J. Chem. Soc.* 4155 (1957); [b]G. F. Woods, A. L. Van Artsdale and F. T. Reed, *J. Am. Chem. Soc.* **72**, 3221 (1950); [c]J. Dale, *Acta. Chem. Scand.* **11**, 650 (1957); [d]H. Dalin and P. Zoller, *Helv. Chim. Acta.* **35**, 1348 (1952); [e]H. Blades, A. T. Blades and E. W. R. Steacie, *Can. J. Chem.* **32**, 298 (1954)
[33]G. Gandiano, A. Quilico and A. Ricea, *Tetrahedron* **7**, 24 (1959)
[34][a]E. Borello, A. Zecchina and E. Guglielminotti, *J. Chem. Soc.* (**B**) 307 (1969); [b]E. Borello and A. Zecchina, *Spectrochim. Acta* **19**, 1703 (1963)
[35]M. K. A. Khan and K. J. Morgan, *J. Chem. Soc.* 2579 (1964)
[36]G. S. Krishnamurthy and S. I. Miller, *J. Am. Chem. Soc.* **83**, 3961 (1961)
[37]R-R. Lii and S. I. Miller, *Ibid.* **95**, 1602 (1973)
[38]K. G. Migliorese, Y. Tanaka and S. I. Miller, unpublished